



# VCU

Virginia Commonwealth University  
VCU Scholars Compass

---

Theses and Dissertations

Graduate School

---

2021

## Using the Memorial Sloan Kettering Frailty Index to Identify Patients at High Risk for Postoperative Intensive Care Unit Admission, Specialized Advanced Care Unit Admission, and 30-day Readmission

Timothy J. Donoghue  
*Virginia Commonwealth University*

Follow this and additional works at: <https://scholarscompass.vcu.edu/etd>



Part of the [Anesthesiology Commons](#), and the [Geriatrics Commons](#)

© The Author

---

Downloaded from

<https://scholarscompass.vcu.edu/etd/6518>

This Dissertation is brought to you for free and open access by the Graduate School at VCU Scholars Compass. It has been accepted for inclusion in Theses and Dissertations by an authorized administrator of VCU Scholars Compass. For more information, please contact [libcompass@vcu.edu](mailto:libcompass@vcu.edu).

© Timothy Joseph Donoghue 2021  
All Rights Reserved

Using the Memorial Sloan Kettering Frailty Index to Identify Patients at High Risk for  
Postoperative Intensive Care Unit Admission, Specialized Advanced Care Unit Admission, and  
30-day Readmission

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of  
Philosophy at Virginia Commonwealth University.

By Timothy Joseph Donoghue

Bachelor of Arts, Rutgers University, May 1999

Bachelor of Science, Columbia University, May 2001

Master of Science, Columbia University, September 2004

Doctorate in Nurse Anesthesia Practice, Virginia Commonwealth University, December 2015

Dissertation Chair: T. Corey Davis PhD, CRNA

Professor

Department of Nurse Anesthesia

Virginia Commonwealth University

Richmond, Virginia

January 26, 2021

### Acknowledgements

I would like to thank my committee for their expertise, support, patience and advice: Chairman Dr. Corey Davis, Dr. Clarence Biddle, Dr. Armin Shahrokni, Dr. Patricia Slattum, and Dr. Beverly George-Gay.

I am extremely grateful and appreciative of the guidance Dr. Chuck Biddle provided me throughout this journey. Writing this dissertation and navigating the complexities of research would not have been possible without Dr. Biddle's support.

Next, I would like to thank Amy Tin from the Biostatistics Department at Memorial Sloan Kettering Cancer Center (MSKCC). Ms. Tin's help, support, and expertise were instrumental during the writing of the Methods and Results chapters. Without her guidance, this dissertation would not have progressed to completion. Additionally, Dr. Shahrokni provided invaluable advice regarding the research process at MSKCC and frailty assessment. I cannot thank them enough for their kindness and support during this process.

Finally, I would like to thank my everything, Emma, whose endless support, encouragement, and supreme editing skills aided me through this process. Without Emma, this entire dissertation would have been written in the passive voice.

## Table of Contents

<b>Acknowledgements .....</b>	<b>iii</b>
<b>List of Tables .....</b>	<b>vii</b>
<b>List of Figures.....</b>	<b>viii</b>
<b>Abstract.....</b>	<b>ix</b>
<b>Chapter 1: Introduction .....</b>	<b>1</b>
<b>Introduction.....</b>	<b>1</b>
<b>Background .....</b>	<b>2</b>
<b>Frailty: the new ‘old’ kid on the block.....</b>	<b>6</b>
<b>Problem Statement.....</b>	<b>8</b>
<b>Purpose.....</b>	<b>9</b>
<b>Research Questions and Objectives .....</b>	<b>9</b>
<b>Assumptions .....</b>	<b>10</b>
<b>Theoretical Framework.....</b>	<b>11</b>
<b>Delineation and Justification of the Research Problem .....</b>	<b>13</b>
<b>Specific Aims .....</b>	<b>15</b>
<b>Statement of Hypotheses .....</b>	<b>15</b>
<b>Scope of the Investigation.....</b>	<b>15</b>
<b>Overview of Remaining Chapters .....</b>	<b>17</b>
<b>Chapter 2: Review of Literature .....</b>	<b>18</b>
<b>Background .....</b>	<b>18</b>
<b>Phenotype of Frailty .....</b>	<b>18</b>

<b>Accumulated Deficits Model of Frailty</b> .....	<b>21</b>
<b>Frailty Measurement</b> .....	<b>25</b>
The Modified Frailty Index.....	25
The Risk Analysis Index.....	29
The Electronic Rapid Fitness Assessment .....	30
The Memorial Sloan Kettering Frailty Index.....	31
<b>ICU admission</b> .....	<b>32</b>
<b>Covariables</b> .....	<b>34</b>
Demographic Variables .....	34
Type of Surgery .....	35
Surgical Stress Score.....	37
Home and Perioperative Medications.....	37
<b>Application of theory</b> .....	<b>39</b>
Biological components of frailty .....	39
Quantitative component of frailty theory.....	41
<b>Hypotheses</b> .....	<b>45</b>
<b>Chapter 3: Methods</b> .....	<b>46</b>
<b>Methodology</b> .....	<b>46</b>
<b>Research Design</b> .....	<b>47</b>
<b>Selection of Subjects</b> .....	<b>48</b>
<b>Instrumentation</b> .....	<b>49</b>
MSK-FI.....	50
<b>Data Collection and Recording</b> .....	<b>52</b>

<b>Data Processing and Analysis .....</b>	<b>53</b>
<b>Methodological Assumptions .....</b>	<b>53</b>
<b>Limitations.....</b>	<b>54</b>
<b>Summary.....</b>	<b>54</b>
<b>Chapter 4: Results.....</b>	<b>55</b>
<b>Data Preparation and Cleaning.....</b>	<b>57</b>
<b>Data Analysis.....</b>	<b>57</b>
<b>Hypothesis Testing.....</b>	<b>57</b>
Hypothesis one ( $H_1$ ).....	58
Hypothesis two ( $H_2$ ).....	58
Hypothesis three ( $H_3$ ).....	58
<b>Chapter Summary .....</b>	<b>62</b>
<b>Chapter 5: Discussion.....</b>	<b>63</b>
<b>Summary and Overview of the Problem .....</b>	<b>63</b>
<b>Purpose of the Study.....</b>	<b>65</b>
<b>Review of Theory and Research Questions .....</b>	<b>65</b>
<b>Methodology .....</b>	<b>66</b>
<b>Study Findings.....</b>	<b>66</b>
<b>Hypotheses.....</b>	<b>67</b>
Hypothesis one ( $H_1$ ).....	67
Hypothesis two ( $H_2$ ).....	67
Hypothesis three ( $H_3$ ).....	67
<b>Contribution to the Literature.....</b>	<b>68</b>

<b>Theoretical Implications</b> .....	<b>68</b>
<b>Practical Implications</b> .....	<b>68</b>
<b>Limitations</b> .....	<b>69</b>
<b>Threats to Internal Validity</b> .....	<b>69</b>
<b>Threats to External Validity</b> .....	<b>70</b>
<b>Conclusions and Recommendations for Future Research</b> .....	<b>71</b>
<b>References</b> .....	<b>72</b>
<b>Vita</b> .....	<b>90</b>

### List of Tables

Table 1. <i>Optimal preoperative assessment of the geriatric patient</i> (Mohanty et al, 2016). .....	4
Table 2 <i>ASA scoring system</i> (American Society of Anesthesiologists, 2014).....	5
Table 3. <i>Theoretical long-term and short-term benefits of frailty assessment.</i> .....	13
Table 4 <i>Components of the phenotype of frailty</i> (Fried et al, 2001). .....	20
Table 5. <i>Examples of Caloric Expenditure with Activity</i> (Department of Health and Family Services, 2018; Donoghue, 2019). .....	20
Table 6. <i>Sample Items from the Canadian Study of Health and Aging Frailty Index</i> (Mitnitski, Mogilner, & Rockwood, 2001; Rockwood & Mitnitski, 2007).....	23
Table 7. <i>National Surgical Quality Improvement Project variables constituting Saxton's modified frailty index</i> (Saxton & Velanovich, 2011).....	25
Table 8. <i>Examples of studies using modified frailty index based on NSQIP data.</i> .....	27
Table 9. <i>Summary of frailty assessment tools.</i> .....	28
Table 10. <i>Demographic data and covariables</i> .....	47



Table 11. <i>Racial make up of study sample</i> .....	48
Table 12. <i>Inclusion and Exclusion Criteria</i> .....	48
Table 13. <i>Comorbidities Assessed with MSK-FI</i> .....	50
Table 14. <i>Patient characteristics. Results are presented as median (quartiles) and frequency (%)</i> . .....	56
Table 15. <i>Association between variables and postsurgical outcomes on multivariable logistic regression with random intercept models</i> .....	59

### List of Figures

<i>Figure 1. Cycle of Frailty (Image adapted from Hazzard, 1999, pg. 1387-1402)</i> .....	19
<i>Figure 2. Impact of frailty on functional status</i> .....	42
<i>Figure 3. Impact of critical illness on frail compared to non-frail people</i> .....	43
<i>Figure 4. Theoretical applications</i> .....	44
<i>Figure 5. Flow of Data to Electronic Medical Record</i> .....	49
<i>Figure 6. Predicted probability of outcomes based on MSK-FI score</i> .....	61

**Abstract**

Using the Memorial Sloan Kettering Frailty Index to Identify Patients at High Risk for Postoperative Intensive Care Unit Admission, Specialized Advanced Care Unit Admission, and 30-day Readmission

Timothy J Donoghue DNAP, CRNA

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University.

Virginia Commonwealth University, 2021

Dissertation Chair: T. Corey Davis Ph.D., CRNA

Frailty is roughly defined as an accumulation of physiological, emotional, cognitive, and social deficits that impair a person's response to stressful events. A frailty diagnosis has been associated with poor outcomes following surgical procedures. Cancer surgical patients aged 65 or older represent a vulnerable population susceptible to being frail and the potential associated complications that can accompany frailty. Measuring frailty is an objective risk assessment that identifies increased risk better than age or American Society of Anesthesiologists Physical Status (ASA-PS) score such that frailty can independently predict poor surgical outcomes.

Frailty is not specifically a result of having cancer, disability, or advanced age. It represents a separate syndrome that diminishes a person's response to stressful event. The assumption is there are certain domains that encompass a generally accepted definition of frailty that remains applicable to most frailty measures. These domains include comorbidities as well as functional, physiological, nutritional, and psychological statuses. Social activity and social support represent other important areas that the most comprehensive frailty indexes consider in their scoring. Frailty can be assessed using at frailty index where higher scores correlate with

greater susceptibility to poor outcomes. The Memorial Sloan Kettering Frailty Index (MSK-FI) was the frailty measurement used for this dissertation.

Using Rockwood's Frailty Theory of Accumulated Deficits, a non-randomized, non-experimental, retrospective cohort study was conducted.

The independent variable was frailty score. The dependent variables were Intensive Care Unit admission (ICU), Specialized Advanced Care Unit admission (SACU), and 30-day readmission. The sample population consisted of surgical patients, aged 65 or older, who had a surgical procedure at Memorial Sloan Kettering Cancer Center from January 1, 2015 to December 31, 2018.

There were 4,417 subjects in this retrospective analysis. Multivariate logistic regression with fixed effect models were created to assess the relation between frailty and postsurgical admission to the ICU, SACU, and 30-day readmission. The researcher found evidence of an association between greater frailty and increased risk of admission to the ICU (OR 1.44; 95% CI 1.31, 1.59; p-value <0.001), admission to the SACU (OR 1.46; 95% CI 1.33, 1.60; p-value <0.001), and 30-day readmission (OR 1.09, 95% CI 1.02, 1.177; p-value = 0.012).

This study demonstrated that a significant correlation between frailty status and postsurgical ICU admission, SACU admission, and 30-day readmission in geriatric cancer surgical patients exists. Using a frailty assessment in the preoperative assessment has the potential to identify high-risk geriatric patients who may have an elevated risk for poor outcomes following their surgical procedure. Once high-risk patients are identified, a multidisciplinary team can create a patient centered treatment plan and mobilization of appropriate resources to minimize poor outcomes.

*Keywords:* Frailty, frailty assessment, postoperative outcomes, geriatric anesthesia, surgical risk assessment, frailty index, cancer

## Chapter 1: Introduction

### Introduction

Hospital acquired complications (HACs) increase a patient's mortality risk approximately 72% and prolong length of hospital stay by a mean of eight days, adding an average of \$41,000 per patient per admission (Bysshe et al., 2017; IBM Watson Health, 2018). Poor surgical outcomes represent a subset of HACs that contribute an excess of \$40,000 per complication to health care costs along with reduced quality of care (Healy et al, 2016). With the importance of reducing healthcare cost and increasing patient safety, poor surgical outcomes are a prime target for research. Within the domain of HACs, surgical complications represent an area of care in need of great improvement as evidenced by the increased morbidity and mortality that accompanies surgical complications (McIsaac et al., 2018).

Poor outcomes resulting from postoperative complications create a costly burden on the health system. Currently there is no gold standard clinical method for identifying patients who may have a higher chance of poor outcomes following surgery. If these patients could be identified early, perhaps preoperative optimization, medication management, social support, and anticipated rescue resources could be mobilized earlier in an effort to prevent complications.

By 2050, the fastest growing segment of the population in the United States, people 65 years or older, is expected to double to 89 million (Mohanty et al., 2016). Worldwide, the population of geriatric people is predicted to increase from 461 million to 2 billion people over the next four decades (Mohanty et al., 2016). Additionally, the number of people 85 years or older is expected to triple in the next 40 years (Chow, Rosenthal, Merkow, & Ko, 2012). As the geriatric population continues to grow, the number of surgical procedures performed on these patients will likely increase. For instance, the annual growth rate of surgical procedures in the

U.S is projected to be 15-30% over the next decade (Dall et al., 2013). As the number of surgeries performed on geriatric patients increases, focusing on outcomes is an essential part of improving the quality of care. With increasing surgeries on this vulnerable patient population, and as reimbursement payments become more closely tied to patient outcomes, hospitals have tremendous interest in improving care and averting possibly preventable complications (Balentine et al., 2016; Li et al., 2015).

The geriatric patient population is particularly vulnerable to postoperative complications because of diminished physiological reserve and reduced tolerance to stressful events, such as surgery, that accompany aging (Mohanty et al., 2016). According to Balentine (2016), age associated declines in physiological reserve and tolerance of stressful events contribute to greater difficulty in recovery from surgery, regaining independence, and returning home in the geriatric population. Approximately forty-five percent of patients 65 years or older undergoing surgical procedures will require continued medical care in a post acute care facility (PAC) such as a skilled nursing facility, long-term care hospital, or an inpatient rehabilitation center (Balentine et al., 2016). Additionally, post surgery discharge to a PAC facility is associated with a four-fold increase of mortality in geriatric patients (Mechanic, 2014). Growth in surgical procedures in the older population, postoperative complications, and outcomes are important issues that require addressing.

## **Background**

Postoperative complications are a critical part of the discussion of surgical care of geriatric patients because with postoperative complications come increased morbidity, mortality, and cost (Collins, Daley, Henderson, & Khuri, 1999; Mohanty et al., 2015). Surgical site infection (SSI), myocardial infarction (MI), cerebrovascular accident (CVA), pneumonia,

delirium, and falls represent some potential complications affecting geriatric patients undergoing surgery (Bouldin et al., 2013; Ensrud et al., 2007; Futier et al., 2013; Gulliford & Ravindrarajah, 2018; Harris, 2016; Keenan et al., 2014; Ravindrarajah et al., 2013). SSIs lead to an increased length in hospital stay of seven to ten days costing \$10 billion annually (CDC, Oid, Ncezid, & DHQP, 2017).

In addition to postoperative complications, geriatric patients may have increased incidence of intraoperative events such as hypotension, hypertension, dysrhythmia, fluid imbalances and thermoregulatory issues, as well as the need for vasopressor administration. It is not known whether these intraoperative events contribute to postoperative complication risk, intensive care unit admission rates, or mortality in older patients undergoing surgical procedures, although most clinicians would suggest that there is a strong teleological link. A thorough preoperative assessment represents a crucial first step in assessing surgical risk. Preoperative assessment of geriatric surgical patients is critical because it helps identify comorbidities, cardiac, neurologic, pulmonary, cognitive and functional baseline levels for patients prior to surgical interventions. Preoperative evaluations could help prevent postoperative complications and improve patient safety by identifying high-risk patients. Once these patients are identified, a plan of care can be created that is patient-centered and tailored to meet each their individual needs (Chow et al., 2012; Mohanty et al., 2016).

Patients with the same chronological age may differ significantly in functional, cognitive, and physical status (Collard et al, 2012). A thorough preoperative evaluation of geriatric surgical patients is a significant tool that may be used to tailor care with the goal of minimizing poor outcomes. As an initial step towards this goal, Chow et al. (2012) developed general guidelines

for preoperative assessment of geriatric patients. Mohanty et al. (2016) further expanded on the guidelines suggested by Chow et al. (2012).

Preoperative assessment categories include cognitive, behavioral, cardiac, pulmonary, functional performance, nutritional status, medication management, counseling, and frailty (Mohanty et al., 2016). Recommendations for preoperative assessment of the geriatric patient include assessing the patient's cognitive ability, screening for depression, alcohol and illicit substance intake, and identifying risk factors for developing postoperative delirium.

Additionally, cardiac and pulmonary evaluation along with assessing patient's functional status, history of falls, social support, and nutrition status are recommended for the preoperative assessment of the geriatric patient (See Table 1).

Table 1. *Optimal preoperative assessment of the geriatric patient* (Mohanty et al, 2016).

<ul style="list-style-type: none"> <li>▪ Assess the patient's cognitive ability and capacity to understand the anticipated surgery.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Screen the patient for depression.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Identify the patient's risk factors for developing postoperative delirium.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Screen for alcohol and other substance abuse/dependence.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Perform a preoperative cardiac evaluation according to the American College of Cardiology/American Heart Association algorithm for patients undergoing non-cardiac surgery.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Identify the patient's risk factors for postoperative pulmonary complications and implement appropriate strategies for prevention.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Document functional status and history of falls.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Assess patient's nutritional status and consider preoperative interventions if the patient is at severe nutritional risk.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Take an accurate and detailed medication history and consider appropriate perioperative adjustments.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Determine the patient's treatment goals and expectations in the context of the possible treatment outcomes.</li> </ul>
<ul style="list-style-type: none"> <li>▪ Order appropriate preoperative diagnostic tests focused on elderly patients</li> </ul>



The preoperative assessment is the time to initiate postoperative planning, determine patient goals and treatment preferences, analgesic strategies, and allocation of health care resources (Mohanty et al., 2016). Unfortunately, even with these recommendations, there remains a lack of widespread use of thorough preoperative evaluations in geriatric surgical patients (Buta et al., 2016; Chow et al., 2012; McIsaac et al., 2018). By completing these evaluations, there is potential to identify patients with modifiable risk factors. In this lies potential for improved postoperative outcomes by optimizing high-risk patients before surgery.

Currently, there is no standard, widely-embraced, comprehensive tool for identifying patients at highest risk for poor outcomes following surgery (Korc-Grodzicki et al., 2014; Robinson et al., 2015). The American Society of Anesthesiologists Physical Status Score (ASA-PS) represents an attempt at evaluating patients' health statuses (American Society of Anesthesiologists, 2014). The ASA-PS is designed to measure a patient's preoperative health status using a grading scale based on comorbidities (See Table 2). An interviewing anesthesiologist or nurse anesthetist decides upon a patient's physical status, and this subjectivity leads to great variability in scores.

Table 2 *ASA scoring system* (American Society of Anesthesiologists, 2014)

Class I	Normal healthy patient who does not smoke, and drinks alcohol minimally
Class II	Patient with mild systemic disease. Mild diseases only, without substantive functional limitations. Examples include (but not limited to): current smoker, social alcohol drinker, pregnancy, obesity (30 < BMI < 40), well-controlled diabetes or hypertension, mild lung disease.
Class III	Patient with severe systemic disease that is not a constant threat to life, but poses functional limitations. Examples include (but not limited to): uncontrolled DM, HTN, COPD, alcohol dependence, BMI >40, pacemaker implantation, > 3 month history of MI, CVA, or CAD with stents.
Class IV	Patient with severe systemic disease that is a constant threat to life. Examples include (but not limited to): recent (< 3 months) MI, CVA, TIA, or CAD/stents, ongoing cardiac

ischemia or severe valve dysfunction, severe reduction of ejection fraction, sepsis, DIC, ARD or ESRD not undergoing regular dialysis.	
Class V	A moribund patient who is not expected to survive without surgery. Examples include (but not limited to): ruptured abdominal/thoracic aneurysm, massive trauma, intracranial bleed with mass effect, ischemic bowel in the face of significant cardiac pathology or multiple organ/system dysfunction.
Class VI	A patient with declared brain death whose organs are being removed for donation

Health care providers have attempted to use the ASA-PS as a predictor of poor postoperative outcomes, but because of its subjectivity, results have been mixed (Sankar et al., 2014). While a higher ASA-PS grade is associated with postoperative complications, this phenomenon is not consistently replicable because the tool was meant to evaluate preoperative health status and perioperative risk, but not to predict postoperative complications (Robinson et al., 2015; Sankar et al., 2014; Whitlock, Feiner, & Chen, 2015).

If health care providers could identify high-risk patients, they could mobilize hospital resources earlier, establish multidisciplinary care teams, and provide targeted therapy thereby potentially reducing poor outcomes. Geriatricians could more effectively manage patient medications, treat depression, and address social support issues prior to surgery (Partridge et al., 2017; Partridge, Harari, & Dhesi, 2012). Frailty represents a novel concept that may help health care practitioners stratify complication risk amongst surgical patients (Robinson et al., 2013b).

**Frailty: the new ‘old’ kid on the block**

Frailty is broadly defined as an accumulation of physiological, emotional, cognitive, and social deficits that impair a person’s response to stressful events. Numerous studies have found a correlation between frailty status and poor outcomes following surgical procedures (Beggs, et al, 2015; Bellal et al., 2016; Choi et al., 2015; Cooper et al., 2016; Hodari, et al, 2013; McIsaac et al., 2018; Sadiq et al., 2018; Shah et al., 2018; Tsiouris et al., 2013). These studies indicate that



frailty is a better predictor of postoperative morbidity and mortality than the ASA score (Farhat et al., 2012; Joseph et al., 2014; Uppal, et al, 2015). Additionally, measuring frailty is an objective assessment that is a better predictor of poor surgical outcomes than age or ASA score. For instance, Joseph et al. (2016) found frailty to be an independent predictor of poor surgical outcomes [odds ratio (*OR*), 2.13; 95% confidence interval (*CI*), 1.09-4.16;  $p=0.02$ ] and significant complications (*OR*, 3.87; 95% *CI*, 1.69- 8.84;  $p=0.001$ ) in geriatric emergency surgical procedures. Frailty score was a better predictor of surgical outcomes than age ( $R= .64$ ;  $R^2, .53, p=.1$ ) or ASA score ( $R, .51$ ;  $R^2=.44, p=.045$ ), and had 80% sensitivity and 72% specificity with an area under the curve (AUC) of .75 in predicting complications following emergency surgery (Joseph et al., 2016).

With the promise of using frailty to predict postoperative outcomes, there have been a number of studies using an assessment tool to quantify frailty status within a variety of surgical domains. Much of the frailty index data has been obtained from the National Surgical Quality Improvement Program (NSQIP) database. Surgical domains that have been studied thus far include cardiac, colorectal, head and neck, hepatobiliary, orthopedic, thoracic, urology, and vascular surgery (Abt et al, 2016; Augustin et al., 2016; Chappidi et al., 2016; Farhat et al., 2012; Hodari et al., 2013; Karam, et al, 2013; Mogal et al., 2017; Obeid et al., 2012; Shah et al., 2018; Shin et al, 2016). The underlying theme noted in prior frailty literature is that higher frailty scores are associated with longer length in hospital stay, higher rates of morbidity and mortality, and increased utilization of hospital resources following surgery. This phenomenon is not just relegated to inpatient surgery. Seib et al. (2018) used NSQIP data to study ambulatory surgical procedures in approximately 140,000 patients and found increases in frailty index scores were associated with stepwise increases in ambulatory postsurgical complication rates (Seib et al.,

2018). There is a growing body of research detailing the association of higher frailty scores and increased morbidity and mortality. However, the majority of frailty research has focused on non-cancer populations.

This dissertation represents an attempt to explore and assess the value in using a frailty assessment as a potential predictive intervention to identify cancer patients at risk for select postoperative outcomes such as higher rate of Intensive Care Unit (ICU) admission; higher rate of Specialized Advanced Care Unit (SACU) admission; higher rate of 30-day readmission.

Identifying frail patients in the preoperative setting may result in timely resource allocation to mitigate potential complications. A long-term outcome of this research may be finding interventions, such as improving nutritional or functional status, that can change outcomes in geriatric surgical patients. The goal is to find ways to identify high-risk patients, allocate resources to help them cope with stresses of surgery, and have more realistic and effective discussions with patients. It is the hope of the researcher that the feasibility of quantifying frailty status from the electronic medical record (EMR) will be shown, and future prospective studies utilizing the frailty tool can be launched.

### **Problem Statement**

Previous research demonstrates a correlation between frailty and poor surgical outcomes including increased morbidity, mortality, and length of hospital stay in non-cancer patient populations (McIsaac, Bryson, et al., 2016; Shah et al., 2018; Velanovich et al, 2013). Currently, there is a research gap regarding the relationship between frailty and admission to a Specialized Advanced Care Unit (SACU) postoperatively. The SACU functions primarily as a step down nursing unit for patients who need more advanced care than a floor unit can provide, but do not require intensive unit level care. Additionally, there is limited research demonstrating a

correlation between frailty and Intensive Care Unit (ICU) admission, and frailty and 30-day readmission in cancer patients.

### **Purpose**

The purpose of this study is to determine whether frail patients undergoing cancer surgery experience higher rates of postoperative ICU admission, SACU admission, and higher 30-day admission rates than non-frail patients.

### **Research Questions and Objectives**

The research questions to be addressed are as follows:

1. What is the relationship between frailty and postoperative ICU admission in cancer surgical patients 65 years or older?
2. What is the relationship between frailty and postoperative SACU admission in cancer surgical patients 65 years or older?
3. What is the relationship between degree of frailty and 30-day readmission in cancer surgical patients 65 years or older at MSKCC?

The primary objectives of this retrospective analysis are to:

- Establish the incidence of frailty in cancer surgical patients 65 years or older between January 1, 2015 and December 31, 2018 at Memorial Sloan Kettering Cancer Center (MSKCC) to learn whether frailty score predicted postoperative admission to the ICU or SACU.
- Examine the relationship between degree of frailty and 30-day readmission in cancer surgical patients 65 years or older at MSKCC.

### Assumptions

There is no standard definition of frailty, and this has led to a variety of frailty measurement tools (Clegg et al., 2016). For instance, a prior study analyzed data from the English Longitudinal Study of Aging (ELSA) in order to compare agreement amongst 35 different frailty measurements. The authors found a wide range of agreement in their study (Cohen's  $\kappa = 0.10-0.83$ ) (Aguayo et al., 2017). Another study examined 32 heterogeneous markers capturing limitations in functional, physical, emotional, and social domains to illustrate the severity of frailty in surgical patients (Sadiq et al, 2018). The purpose of the Sadiq et al. (2018) study was to include a wider range of domains to improve clinical information gained from frailty scoring to determine what precludes a decrease in physiological reserve in the frailest patients. Both Aguayo et al. (2017) and Sadiq et al. (2018) show how many different frailty measurement tools have been used in prior research.

Frailty is not specifically a result of having cancer, disability, or advanced age. It represents a separate syndrome that diminishes a person's response to stressful events (Dasgupta, et al, 2009; Strandberg & Pitkala, 2007). The assumption is there are certain domains that encompass a generally accepted definition of frailty that remains applicable to most frailty measures. These domains include comorbidities as well as functional, physiological, nutritional, and psychological statuses. Social activity and social support represent other important areas that the most comprehensive frailty indexes consider in their scoring. Collard et al. (2012) performed a systematic review to compare the prevalence of frailty across studies. In Collard's analysis, the average frailty rate in community dwelling people aged 65 or older was 10.7% and the prevalence of pre-frailty was 41.6% (Collard, et al, 2012). In their review, Collard et al. found that frailty was common later in life, affected women more than men, and was more prevalent in

the presence of chronic disease. The authors found that the prevalence of frailty noted in each study widely varied (4%-59%), and the variation was likely due to the definition of frailty used in each study (Collard et al., 2012)

At MSKCC, there is a robust geriatric consultation process in place in which frailty assessments are completed, patients are evaluated, and geriatricians make postoperative care recommendations. This consult process is in addition to the anesthesia preoperative evaluation and any other evaluations needed such as cardiac or pulmonary clearance. After initial consultation, geriatricians continue to follow the patient throughout their hospital stay. Frailty can be measured using data from MSKCC. Since 2015, the department of geriatric medicine at MSKCC has incorporated frailty measurement into each consultation and prospectively collected this data (Shahrokni et al., 2017). The ongoing collection and storage of frailty data at MSKCC has created a vast database with potential research opportunities.

### **Theoretical Framework**

Frailty is a valid construct that lacks concise characterization. A broad definition of the term addresses physiological, emotional, cognitive, and social parameters. Strawbridge et al. (1998, pg. S12) defined frailty as the “grouping of problems and losses of capability which make the individual more vulnerable to environmental challenges.” There are four common domains that characterize frailty: the physical, nutritive, cognitive, and sensory domains (Strawbridge et al, 1998).

Frailty is a well-established measure of outcomes in surgical patients (Hall et al., 2017; McIsaac et al., 2018; Sadiq et al, 2018). A primary importance of frailty is that it represents an independent predictor of postoperative complications and length of hospital stay for geriatric patients (McIsaac et al., 2016; Ritt et al., 2015; Rockwood & Mitnitski, 2012). Poor outcomes

can be defined as MI, CVA, hospital acquired pneumonia, SSI, falls, postoperative hemorrhage requiring blood transfusion, delirium, respiratory failure requiring mechanical ventilation, and kidney failure (Abt et al., 2016; Dimick et al., 2004; Warner, Zhang, Liu, & Alterovitz, 2016). ICU and SACU admission rates, length of hospital stay, and 30-day readmission rate may also be associated with frailty (Flaatten et al., 2017; Graham & Brown, 2017; Kim et al., 2014). To date, research concerning frailty and cancer surgical patients is inadequate.

The impact of frailty status can be seen at the patient and the institutional level in both the short term and long-term (Rockwood, Song, & Mitnitski, 2011). For instance, short-term patient level impacts are preoperative medical optimization, maximized nutritional status, and an improved functional status. A multidisciplinary team approach may utilize tailored care plans to optimize frail patients prior to surgery (Korc-Grodzicki et al., 2014). Members of the team could include anesthesia providers, surgeons, cardiologists, pulmonologists, geriatricians, nurses, physical therapists, occupational therapists, social workers, and healthcare administrators. Each team member possesses unique knowledge and experience that could potentially aid the frailty optimization process (Negm et al., 2018).

The short-term impact of utilizing a frailty measurement tool in the preoperative setting at the hospital level includes lower complication rates, decreased patient utilization of health care resources in the pre-, intra-, and postoperative periods, and shorter hospital stays (Puts et al., 2017). All of these factors in conjunction have the potential to reduce health care cost and expenditures.

The potential long-term impacts of identifying frail patients may be seen in improved performance of activities of daily living, mobility, cognitive status, and fewer postoperative complications (McIsaac et al., 2017; Puts et al., 2017; VidÅjn et al., 2005). Optimizing frail



patients prior to surgery may improve their quality of life and lessen the future impact stressful events have on their physiological, cognitive, and social systems. While optimizing frail patients through preoperative exercise programs may not be entirely feasible in the cancer population, measures such as smoking cessation, improved medication management, nutrition, and glucose control may prove beneficial. Lastly, the long-term impact of frailty measurement at the hospital level may include lower readmission rates and improved insurance reimbursement (See Table 3).

Table 3. *Theoretical long-term and short-term benefits of frailty assessment.*

	Patient level	Hospital level
<b>Short term impact</b>	Improved nutritional, functional, and cognitive status. Medical optimization prior to surgery to decrease intra-operative and postoperative complications.	Decreased complication rates, length in hospital stay, and cost in care related to complications.
<b>Long term impact</b>	Improved independence, mobility, performance in activities of daily living, faster return to preoperative baseline level.	Lower readmission rates and improved insurance reimbursement.

**Delineation and Justification of the Research Problem**

The preoperative assessment of frailty identifies patients highly susceptible to stressful events such as surgery in non-cancer patients. The research problem is a gap in the literature detailing the relationship between frailty status, morbidity, and mortality in cancer patients. At MSKCC, which is primarily a hospital that cares for cancer patients, a retrospective analysis of patient data may be possible. This will allow an association between frailty scores and surgical outcomes to be analyzed in the cancer population. Additionally, there is the potential to establish the incidence of frailty in geriatric patients who received care at MSKCC. This is important for three reasons. First, the actual incidence of frailty, independent from the prognosis and treatment of cancer, is not entirely known. Second, substantially more data is needed to understand the relationship between frailty and negative outcomes following surgery in cancer patients. Finally,

using a frailty assessment to stratify patient risk is not performed in mainstream anesthesia practice to date.

This investigation is important for a couple of reasons. Clinical guidelines make up an important part of evidence based practice. However, the current method available to anesthesia staff for determining patient risk, the ASA-PS, is subjective and it represents a construct that was not intended to be predictive of outcomes. There is a need for an objective risk assessment tool in the preoperative evaluation of geriatric surgical patients that is reliable, consistent, and easy to use. The purpose of this investigation is to contribute to the growing body of research that shows frailty assessment can be the objective risk assessment tool that is greatly needed. Specifically, the importance of this study is that it uses frailty measurement in a little studied vulnerable population: cancer patients aged 65 years or older. The results would add to the knowledge base of frailty measurement and possibly provide a stepping-stone for the entrance of routine clinical use of a frailty index at MSKCC. Once a standard part of the geriatric patient pre-anesthesia evaluation, frailty scores may delineate frail from non-frail patients. This delineation of patients could lead to more informed discussions with patients about their anesthesia risk and lead to development of tailored patient-centered care plans.

Studying frailty in cancer patients would provide anesthesia team members with an objective method for risk stratification prior to surgery. In turn, intraoperative and postoperative management plans can be adopted to help mitigate the impact frailty has on a patient's surgical journey. Once frailty measurement has been established as part of the anesthesia pre-operative evaluation, future studies can focus on interventions that reduce frailty scores, change perioperative care plans, and improve surgical outcomes.

### **Specific Aims**

There are four specific aims to this dissertation. The first aim is to show that a relationship exists between degree of frailty status and postoperative ICU admission. The second aim is to demonstrate a relationship is present between degree of frailty status and postoperative SACU admission. The third aim is to demonstrate a relationship is present between degree of frailty status and 30-day readmission.

### **Statement of Hypotheses**

The primary hypotheses are that there is a direct relationship between degree of frailty status, postoperative ICU admission, SACU admission, and 30-day readmission.

### **Scope of the Investigation**

A retrospective, non-experimental, descriptive cohort approach will be utilized (Polit & Tatano-Beck, 2017). From prior research, the range of frailty incidence has been found to be 4-59% in the adult community population (Collard et al., 2012; Denholm, Corrie, Qian, & Hampton, 2018; Hall et al., 2016; McIsaac, Taljaard, et al., 2016; Morley et al., 2013; Shah et al., 2018) However, the incidence of frailty in cancer patients is not entirely known. Recent observational research and a systematic review suggest the frailty rate might be as high as forty-two percent in the cancer population (Atakul & Akyar, 2019; Handforth et al., 2015) A gap in knowledge regarding frailty incidence and the impact frailty has on outcomes in patients diagnosed with cancer remains in the literature. A knowledge gap regarding the relationship between frailty, ICU admission, SACU admission, and 30-day readmission rates also exists.

Electronic medical record data for patients aged 65 years or older who underwent oncologic surgical procedures that required postoperative hospitalization at Memorial Sloan Kettering Cancer Center will be compiled for the period between January 1, 2015 to December

31, 2018. Most patients having surgical resection become inpatients following their procedure, and length of stay varies for each patient (Aquina et al., 2017; Brown et al., 2014; Grant et al., 2013; Korc-Grodzicki et al., 2014). Currently, the majority of patients undergoing surgical procedures are same day hospital admissions. Outpatient surgical procedures will not be analyzed because of limited availability of data.

The proposed study design is non-experimental and descriptive; it will not assess a specific intervention, but rather seek to identify correlations described in the hypotheses. The overall frailty incidence will be calculated and analyzed to see if different degrees of frailty are present. Prior research demonstrated that frailty may occur on a continuum where patients can be robust, pre-frail, and frail in the non-cancer adult population (Rockwood et al., 2005; Shah et al., 2018). The target population of this study is all patients 65 years or older who have undergone surgery for cancer at MSKCC. Type of surgical procedure will be analyzed as a covariable. Additional covariables will be sex, age group, surgical stress score (SSS), and ASA score.

The strength of this target population is the overall number of patients that seek treatment at MSKCC. This makes achieving an appropriate sample size more feasible. A primary weakness of the target population is the patients maybe intrinsically different than people with cancer who do not seek treatment at MSKCC. Patients treated at MSKCC may represent a more homogeneous population than is present in the outside community and this may limit the generalizability of the results. Also, MSKCC may have treatment guidelines and care processes in place that non-cancer hospitals do not. Given MSKCC's focus on cancer research, patients treated at MSKCC may have access to clinical trials that patients treated elsewhere do not. Lastly, surgical expertise developed from the higher than average volume of cancer specific surgeries performed at MSKCC may also affect outcomes in the target population.

**Overview of Remaining Chapters**

This paper is divided into four remaining parts. Chapter two offers a complete review of the literature regarding frailty research. The phenotype of frailty and the accumulated deficits model will be explored. Additionally, various frailty measurement tools will be discussed. Chapter three provides methods and statistical analysis that will be utilized to answer the research questions. Chapter four includes a presentation of the study results. Finally, chapter five will deliver an interpretation and summary of the findings.

## Chapter 2: Review of Literature

### Background

As a concept, frailty is multifactorial involving physiological, cognitive, emotional, and social age related decline. This leads to impaired responses to stressors, and is distinguishable from disability (Rockwood et al., 2011; Strandberg & Pitkala, 2007). It is also not a strictly age related phenomenon. Frailty can further be defined as a biologic syndrome of decreased reserve and resistance to stressors that occurs on a continuum, resulting from cumulative declines across physiologic systems (Fried et al., 2001).

While a gradual age-related decline in physiological reserve occurs, frailty accelerates these declines leading to homeostatic mechanism failure (Mitnitski et al., 2015). Decreased response to stressors makes patients vulnerable to poor outcomes. Fried has defined “ the multidimensional nature of frailty ... [as] age associated declines in physiologic reserve and function across multiple organ systems, resulting in diminished strength and endurance, increased vulnerability to stressors, risk of falls, disability, hospitalization and mortality” (Fried et al., 2001, pg. M146).

### Phenotype of Frailty

According to Fried, frailty can be quantified by evaluating age-related declines in strength, balance, endurance, lean body mass, walking performance, and activity levels (Bieniek et al., 2016; Fried et al., 2001). While many older people have at least one of these declines, multiple elements need to be found clinically to constitute a diagnosis of frailty. Because these components are interrelated, Fried postulates a cycle of frailty that is associated with declining reserve. The foundations of this cycle are the clinical symptoms of frailty, while a decline in physiologic reserve in other systems leads to increased susceptibility and a loss of ability to

withstand stress. Fried hypothesized that a phenotype of frailty is comprised of core clinical presentations such as shrinking, weakness, poor endurance, slowness, and low activity (See Figure 1.)

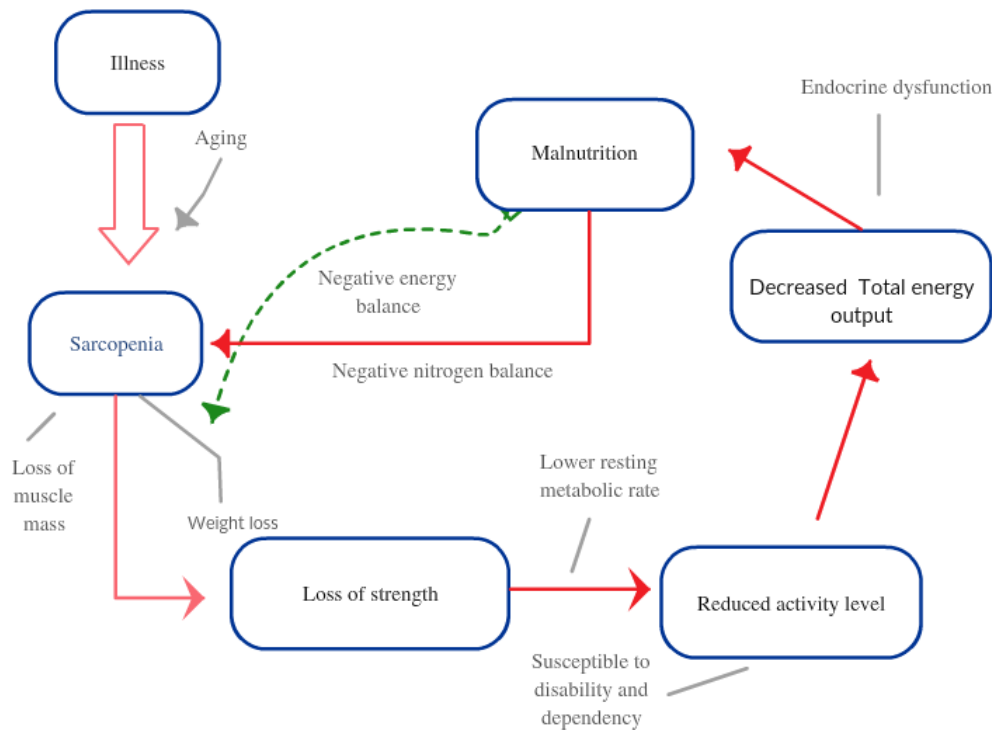


Figure 1. Cycle of Frailty (Image adapted from Hazzard, 1999, pg. 1387-1402)

Note: This figure represents the cycle of frailty. The cycle starts with an illness. Because a patient is frail, they cannot adequately handle the stress from the illness. This leads to sarcopenia, loss of strength, reduced activity, decreased energy output, and malnutrition. The cycle worsens as the patient loses weight and muscle mass. As this occurs, the patient’s metabolic rate lowers, they become more susceptible to disability, endocrine dysfunction, and a negative nitrogen balance. These diminished responses to the illness are separate from the normal aging process. Frailty hinders the response to stress such that the patient may not fully recover.

Common characteristics of frailty in this model include five traits. An unintentional weight loss of greater than or equal to 10 pounds in the previous year, or a greater than 5% loss of body weight at follow up represent one trait. Secondly, strength is measured as an indicator of frailty, specifically grip strength within the lowest 20 percentile at baseline for sex. Poor

endurance and slowness represent the third and fourth elements of frailty, and are measured with a timed fifteen-foot walk, graded exercise testing, and self-reports of exhaustion. The fifth and final element to Fried’s frailty phenotype is low physical activity level as determined by a weighted score of kilocalories expended per week (See Table 4). For instance, males expending less than 383 kilocalories per week and females expending less than 270 kilocalories per week would be considered in the lowest twentieth percentile (Bieniek et al., 2016; Department of Health and Family Services, 2018) (See Table 5). Of these 5 traits, the presence of three or more of these elements is required for a diagnosis of frailty (Fried et al., 2001). Patients with one or two elements present can be classified as pre-frail (Bieniek et al., 2016; Fried et al., 2001).

Table 4 *Components of the phenotype of frailty* (Fried et al, 2001).

1. Unintentional weight loss of greater than or equal to 10 pounds in the previous year, or a greater than 5% loss of body weight at follow up.
2. Strength as measured by grip strength
3. Endurance as measured by self reports of exhaustion
4. Slowness as measured by a timed 15 foot walk
5. Low physical activity level as measured by kilocalorie expenditure per week

Table 5. *Examples of Caloric Expenditure with Activity* (Department of Health and Family Services, 2018; Donoghue, 2019).

Activity	Calories burned per hour for someone with a weight of:		
	130 lbs	165 lbs	190 lbs
Playing basketball	472	563	690
Raking a lawn	236	281	345
Walking 3 mph	207	246	302
Stationary bike	295	352	431

To evaluate the effectiveness of the frailty theory, Fried utilized data from patients who were community dwelling and found the overall prevalence in frailty for this population to be 6.9%. The study indicated frailty was more strongly associated with being African American, lower educational level, poorer income and health, and higher rates of comorbidity. Assessing



the five elements of the frailty cycle allowed Fried to identify patients at most risk of poor health care outcomes (Fried et al., 2001). One study, by Crow et al. (2018), used Fried's frailty criteria to examine the association between frailty and risk of death after adjusting for age, sex, race, smoking history, education, heart disease, diabetes mellitus, and arthritis. The authors found both pre-frailty [hazard ratio (*HR*) = 1.64, 95% confidence interval (*CI*) = 1.45–1.85] and frailty (*HR* = 2.79, 95% *CI* = 2.35–3.30) to be associated with increased risk of death (Crow et al., 2018).

While this five-point assessment method serves as an invaluable tool for assessing frailty, the practicality of using the frailty phenotype to identify inpatients at risk of complications within the hospital setting is limited. The frailty phenotype tests do not discriminate between frailty and disability (Rockwood, Andrew, & Mitnitski, 2007). Often times, hospital patients are bed ridden, and most likely unable to perform the elements of Fried's frailty phenotype tests. A separate theory posited by Rockwood, involves accumulated deficits. This theory represents a more feasible tool for frailty measurement in the clinical arena (Fried et al., 2001; Rockwood et al., 2005).

### **Accumulated Deficits Model of Frailty**

In the Canadian Study of Health and Aging (CSHA), Rockwood studied the theory of accumulated deficits in relation to frailty (Rockwood et al., 2005). The CSHA began in 1991, and subjects were recruited with the aim of describing the epidemiology of cognitive impairment and other significant health issues in older Canadians. During the initial stage of the study, CSHA-1, Rockwood's group enrolled 10,263 people from the general population in Canada aged 65 years or older into a five year prospective cohort study, where they used a rules-based definition of frailty. In the study, a 70-item CSHA Frailty Index (CSHA-FI) was created, and found to have strong predictive value with regards to poor health outcomes in community-

dwelling geriatric patients (See Table 6). In 1996, during the second phase of the study, CSHA-2, the researchers examined 2305 subjects from CSHA-1 and applied the CSHA-FI, the Modified Mini-Mental State exam, and the Cumulative Illness Rating Scale in order to assess the presence of frailty. Subsequently, in 2001, the third phase (CSHA-3) of the study began with the purpose of validating the Clinical Frailty Scale (CFS) as frailty measurement tool. With the CSHA-3 cohort, the authors validated the CFS with the CSHA-FI. The authors found significant correlations between the CFS and CSHA-FI for identifying frailty and a strong association between higher frailty scores and increased risk of mortality and institutionalization (Rockwood et al., 2005)

Subjects for the CSHA were recruited from the general population in Canada. The inclusion criteria for CSHA-1 were Canadian citizens 65 or older on October 1, 1990, who spoke English or French, and lived at home at some point during the recruitment phase. The exclusion criteria for CSHA-1 were subjects who resided in the Yukon Territory, Northwest Territory, Indian reserves, or in the military. As the CSHA-1 transitioned into the CSHA-2 cohort, the sample size was reduced for convenience and cost by the research team. Subjects included in the CSHA-2 and the CSHA-3 were subsets of the CSHA-1 cohort.

As a whole, the CSHA was a prevalence study where subjects were randomly recruited from the community and asked general health questions as well as tested for cognitive impairment. Community sample data was obtained from provincial health plans throughout Canada and the Enumeration Composite Record in Ontario. Subjects were randomly selected in groups aged 65-74, 75-84, and 85 or older by computer. Sampling occurred in 36 cities and their respective rural areas throughout Canada to obtain a representative sample (Mitnitski, Mogilner, & Rockwood, 2001; K. Rockwood et al., 2005).

The deficit accumulation approach was cross-validated by counting deficits in a standardized Comprehensive Geriatric Assessment (CGA) (Kramer et al., 2015; Rockwood, 2016; Rockwood & Mitnitski, 2007). Rockwood established scales for function and overall clinical frailty with the main objective of creating a tool for risk stratification of vulnerability in the geriatric population in the community (McDowell, Hill, & Helliwell, 2001; Rockwood, Wolfson, & McDowell, 2001) The frailty index was created to identify patients in the community at greatest risk for increased morbidity and mortality.

Table 6. *Sample Items from the Canadian Study of Health and Aging Frailty Index* (Mitnitski, Mogilner, & Rockwood, 2001; Rockwood & Mitnitski, 2007).

Functional Status	Changes in everyday activities, problems getting dressed, bathing, toileting, grooming, or eating
Neurological and cognitive status	History of depression, depressed mood, sleep changes, memory changes, clouding, delirium, seizures, tremors, cerebrovascular accident, syncope, headaches, changes in mental functioning, Parkinson’s or Alzheimer’s disease
Cardiac status	Hypertension, myocardial infarction, coronary artery disease, congestive heart failure, arrhythmias, peripheral vascular disease, ability to walk upstairs or complete house work
Pulmonary status	Chronic obstructive pulmonary disease, emphysema, asthma, smoking history
Gastrointestinal status	Bowel habits, any abdominal problems
Other	Diabetes mellitus, thyroid problems, alcohol or substance abuse, kidney problems, current medications, changes in health status, and caloric intake

Frailty scores were found by dividing the number of deficits by the total number of possible deficits. The closer the ratio came to one, the frailer a patient. Specifically, the resulting ratio was used to identify someone as robust (ratio of 0-0.12), pre-frail (ratio of 0.13-0.43), or frail (ratio of 0.44 or greater) (Rockwood et al., 2001). These stratifications were found to be predictive of increased morbidity and mortality (Robinson et al., 2013; Rockwood et al., 2005;

Tsiouris et al., 2013; Wahl et al., 2017). Rockwood compared the frailty index to Fried's phenotype, and found it comparable for predicting adverse health outcomes (Rockwood et al., 2007). Despite its usefulness in predicting adverse outcomes, the 70-item scale is extremely time consuming to perform in a clinical environment.

Rockwood et al. (2005) created the Clinical Frail Scale (CFS) in an effort to create a frailty measurement tool that may be more clinically applicable. The CFS uses clinical judgment to interpret the results of a patient's medical history and physical examination. Patients are scored on a scale of one to seven, and the scores correspond with levels of frailty. For instance, patients can be scored very fit (1), well without active disease (2), well with treated comorbidities (3), apparently vulnerable but not dependent (4), mildly frail with limited dependence (5), moderately frail with increased dependence (6), and severely frail with complete dependence (7) (Rockwood et al., 2005).

To validate the CFS, 2305 geriatric participants enrolled in the second phase of the CSHA study were followed longitudinally for five years (Rockwood et al., 2005). The authors found the CFS to correlate highly with the CSHA-FI ( $r=0.80$ ) with regards to predicting mortality and institutionalization. Rockwood et al. (2005) found that each one-category increment of the CFS scale considerably increased the risk of death (21% within 70 months, 95% confidence interval (CI) 12.5%-30.6%) and institutionalization (23.9%, 95% CI 8.8-41%).

The authors further found a dose response effect in mortality and hospitalization in the study to validate the CFS as a frailty measure (Rockwood et al., 2005). The CFS is more applicable to the clinical environment because it is a smaller and faster assessment of frailty status than the CSHA-FI. The geriatrician administering the CFS can use clinical judgment, and does not have to account for the 70 metrics noted in the CSHA-FI thereby reducing frailty

assessment time. The CFS was created to be a tool that clinicians could easily administer and interpret using their medical knowledge and judgment based upon the patient's history.

Additional retrospective research projects using smaller frailty indexes have shown variations of the CSHA frailty index may be useful in identifying vulnerable patients (Clegg et al., 2013; Cohen et al., 2012; Cooper et al., 2016; McIsaac et al., 2016; Partridge, Harari, & Dhesi, 2012; Rockwood et al., 2005; Tsiouris et al., 2013; Velanovich et al., 2013).

## Frailty Measurement

### The Modified Frailty Index

Prior research demonstrates the modified frailty index (mFI) identifies geriatric patients at high risk of poor health outcomes following surgery. The mFI is a smaller version of the CSHA-FI. This reduction in size likely makes the mFI more appealing to use in a busy clinical environment. Various modified frailty indexes have used five to forty-two variables from the CSHA-FI with similar predictability of poor outcomes (Cooper et al., 2016; Hodari et al., 2013; Karam et al., 2013; Partridge et al., 2012; Tsiouris et al., 2013; Velanovich et al., 2013).

Versions of the mFI have been validated using data from the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database. For example, Velanovich et al. (2013) matched 11 items from the National Surgical Quality Improvement Program (NSQIP) to the 70-item CSHA frailty index and found a stepwise increase in mortality and morbidity for each unit increase in frailty index across surgical specialties (Velanovich et al., 2013) (See Table 7). Additional research from Saxton created a mFI by matching 15 variables from the NSQIP to 11 variables from the CSHA-FI (Saxton & Velanovich, 2011).

Table 7. *National Surgical Quality Improvement Project variables constituting Saxton's modified frailty index* (Saxton & Velanovich, 2011).

- History of Diabetes mellitus
- Functional status score of least 2
- History of chronic obstructive pulmonary disease
- History of pneumonia within 30 days of surgery
- History of congestive heart failure
- History of myocardial infarction
- History of ischemic chest pain
- High blood pressure requiring medication
- History of peripheral vascular disease
- History of impaired sensorium or clouding
- History of transient ischemic attack
- History of cerebrovascular accident with neurological deficit
- History of percutaneous coronary intervention, stenting, or angina.

Development of a modified frailty index based on variables from the NSQIP database was promising. Eleven NSQIP variables commonly used were matched from the CSHA-FI. These variables are similar to the ones presented in Table 7. One study found frailer patients are more likely to experience severe complications after an endovascular abdominal aortic aneurysm repair [odds ratio (*OR*), 1.7; 95% *CI*, 1.3-2.1] or an open aortic aneurysm repair (*OR*, 1.8; 95% *CI*, 1.5-2.1) and a higher rate of failure to thrive (*OR*, 1.7; 95% *CI*, 1.2-2.5) (Arya et al., 2015). Other studies have found a dose response relationship between frailty, complications, and failure to thrive across surgical specialties (Shah et al., 2018).

Recently, some issues have arisen with the NSQIP database. Changes to the NSQIP database have created some limitations concerning the use of NSQIP data to diagnose frailty. For instance, after 2012, the NSQIP removed some variables from its data collection and no longer required the reporting of other variables. This has led to the problem of missing data within the NSQIP database that pertains to modified frailty indexes. From 2011 to 2015, mFI variables with missing data increased from 44% to almost 100% in the NSQIP database (Gani, Canner, &

Pawlik, 2017). The missing data problem limits the usefulness of the NSQIP database and the modified frailty index. Therefore, other frailty measurement tools that are not dependent on the NSQIP database are needed.

Table 8. *Examples of studies using modified frailty index based on NSQIP data.*

Year	Surgery Type	Authors
2012	Trauma	(Farhat et al., 2012)
2012	Colorectal	(Obeid et al., 2012)
2013	Thoracic	(Hodari et al., 2013)
2013	Vascular	(Karam et al., 2013)
2015	Vascular	(Arya et al., 2015)
2016	Head/Neck	(Abt et al., 2016)
2016	Hepatobiliary	(Augustin et al., 2016)
2016	Urology	(Chappidi et al., 2016)
2016	Vascular	(Ehlert et al., 2016)
2016	Hepatobiliary	(Louwers, Schnickel, & Rubinfeld, 2016)

Table 8 (continued)

Year	Surgery Type	Authors
2016	Urology	(Suskind et al., 2016)
2016	Orthopedic	(Shin et al., 2016, 2017)
2017	Orthopedic	(Runner et al., 2017)
2017	Hepatobiliary	(Mogal et al., 2017)
2017	Head and neck	(Wachal et al., 2017)
2018	Ambulatory	(Seib et al., 2018)

Table 9. Summary of frailty assessment tools.

Author	Year	Frailty instrument	Outcome	Roots in the literature
<b>Fried</b>	2001	Frailty Phenotype (FP)	Patients diagnosed with 3 or more frailty criteria are diagnosed as frail. Fried et al. found frailty not synonymous with comorbidity or disability, but rather comorbidity is a risk factor for, and disability an outcome of, frailty	Gerontology
<b>Rockwood</b>	2005	Canadian Health and Aging Study Frailty Index (CHSA-FI).	Used 70 metric frailty measurement to diagnose frailty in community dwelling population	Gerontology
<b>Saxton</b>	2011	CSHA-FI	Found that measurement of preoperative functional status using a modified frailty index (mFI) identified patients at high risk for postoperative complications	Surgery
<b>Tsiouris</b>	2013	Modified Frailty Index (mFI)	mFI of 11 variables from mapping of the CHSA-FI to NSQIP comorbidities in patients undergoing thoracic lobectomies. Found mFI may help identify patients at higher risk for postoperative complications following lobectomy	Surgery
<b>Velanovich</b>	2013	mFI	mFI of 11 variables created by mapping CHSA-FI to NSQIP database for cardiac, general, gynecological, neurosurgical, orthopedic, plastic, thoracic, urological, and vascular surgical procedures. Found a simplified frailty index correlated with morbidity and mortality for all surgical specialties in the study	Surgery
<b>Cooper</b>	2016	Compared FP to FI	Used a 42 variable frailty index to prospectively compare the frailty phenotype to the CHSA-FI and found similar predictability for poor postoperative outcomes in orthopedic patients	Surgery
<b>McIsaac</b>	2016, 2017	John's Hopkins Adjusted Clinical Groups Frailty defining diagnoses indicator.	Found frailty was associated with increased risk of 1 year mortality following surgery	Surgery
<b>Wahl</b>	2017	mFI	Frailty was associated with increased risk of 1 year mortality following surgery	Surgery

Table 9. (continued)



Author	Year	Frailty instrument	Outcome	Roots in the literature
<b>Partridge</b>	2017	Comprehensive Geriatric Assessment (CGA) combined with preoperative patient optimization	Studied use of the Comprehensive Geriatric Assessment (CGA) combined with preoperative patient optimization in patients undergoing abdominal aortic aneurysm repair or lower limb arterial surgery. Found patients who received CGA and optimization had decreased length of stay, delirium, and complications	Surgery
<b>Bellal</b>	2017	Trauma Specific Frailty Index (TS-FI)	Created and validated a 50 variable frailty index called the Trauma Specific Frailty Index (TS-FI) Found geriatric frail patients to be 3 times more likely to be diagnosed with failure to thrive	Surgery
<b>Hall</b>	2016, 2017	Risk Analysis Index (RAI)	Created and validated the Risk Analysis Index (RAI) to screen for frailty in surgical patients. RAI-C is a questionnaire that can be used prospectively to identify frailty while the RAI-A is a retrospective measurement tool comparing patient data and NSQIP data. Found implementing a frailty screening initiative was associated with decreased mortality	Surgery

### The Risk Analysis Index

Hall et al. developed a similar mFI, the Risk Analysis Index (RAI). The RAI represents a 14-item tool for measuring frailty in surgical patients. It can be used prospectively to identify frail patients by utilizing a clinical questionnaire (RAI-C) or retrospectively using variables from the NSQIP (RAI-A) (Hall et al., 2016). The RAI is based on adaptations from the Minimum Data Set Mortality Risk Index-Revised in which 12 variables that consistently predicted mortality were selected. From these variables, a 14-point survey was created for measurement purposes (Hall et al., 2016). The easily administered survey relies on patient reports. In his research, Hall validated the RAI-C and the RAI-A as effective tools for measuring frailty when compared to other measures (Hall et al., 2017). The RAI has similar predictive ability regarding frailty as the CSHA-FI and the mFI created by Saxton and Velanovich, and moderate correlation between

these measures has been noted (Hall et al., 2016). Hall's research demonstrated that a large frailty screening initiative is feasible and is associated with reduced mortality (Hall et al., 2017).

### **The Electronic Rapid Fitness Assessment**

The geriatric medicine department at MSKCC created the electronic Rapid Fitness Assessment (eRFA) in order to make the geriatric assessment process more clinically feasible. In conjunction with a National Cancer Institute funded entity for secure online questionnaires, Web Survey Core Facility (Webcore), the final version of the eRFA addresses physiological, emotional, psychological, functional, nutritional, and cognitive domains. The final eRFA survey also accrues data regarding demographics, polypharmacy, comorbidities, and history of falls (Shahrokni et al., 2017).

During a consultation visit, patients complete a comprehensive geriatric assessment (CGA) electronically using a tablet. Within the eRFA, the CGA domains include functional status, emotional state, cognition, social support, level of social activity, nutritional status, sensory deficits, and medication history. Clinicians administer a Timed Up and Go and Mini Cog test during the examination to further assess functional status and cognition (Shahrokni et al., 2017).

The Timed Up and Go test assesses patient mobility by asking them to rise from a chair and walk 10 feet. Walk times > 12 seconds have been associated with higher fall risk (Borson, Scanlan, Chen, & Ganguli, 2003). The Mini Cog test is administered to assess patient cognition. The Mini Cog consists of asking a patient to remember three unrelated words, drawing the numbers on a blank clock face, drawing clock hand placement for either 11:10 or 8:20, and then repeating the three unrelated words. Research has demonstrated the Mini Cog and the Timed Up and Go test to be objective, consistent, and valid measures of cognition and mobility when administered by trained healthcare professionals (Borson et al, 2000; Yeung et al, 2008). These

two tests are part of the functional domain score in the eRFA and are used to identify cognitive deficits and mobility issues respectively. Information collected by the eRFA is stored in an electronic database.

The median time to complete the eRFA was 11 minutes (*CI* 95%, 11-12 minutes) with 90% of patients completing the eRFA in less than 25 minutes (Shahrokni et al., 2017). During the expansion phase of the initial eRFA study, 636 patients completed the assessment. In this sample, the eRFA was able to identify that 16% of patients had a previously unknown cognitive deficit and 26% ((95% *CI*, 23%–30%) had experienced a fall within the previous year (Shahrokni et al., 2017). During their study, Shahrokni et al (2017) established the feasibility, reliability, and validity of using the eRFA in a busy clinical environment in order to prospectively identify geriatric syndromes. The data collected by the eRFA is stored electronically in a MSKCC secure database.

### **The Memorial Sloan Kettering Frailty Index**

Researchers at MSKCC developed the Memorial Sloan Kettering Frailty Index (MSK-FI) to address the missing data problem noted with the NSQIP modified frailty indexes. The MSK-FI has been cross-validated with components from the Comprehensive Geriatric Assessment (CGA) (Shahrokni et al., 2018). It uses *International Classification of Diseases (ICD)* versions 9 and 10 to identify comorbidities and postoperative complications from the electronic medical record. CGA impairments are assessed during a clinical interview and from patient reports.

Shahrokni et al. (2019) analyzed data from 1137 patients 75 or older who received a geriatric consultation prior to having surgery at Memorial Sloan Kettering Cancer Center. 51.2% of the subjects were female; the median age of the sample was 80 years with an age range of 77-84. The timeframe for the study was February 2015 to September 2017. The researchers looked

at the correlation of MSK-FI score with CGA impairments. Additionally, they assessed the association between MSK-FI score and short-term surgical outcomes including frequency of complications, length of hospital stay, 30-day surgical complications, 30-day ICU admissions, and 30-day readmissions. In the study, the research team found that each one-point increase in frailty score was associated with increased length of hospital stay (0.58 days; 95% *CI*, 0.22-0.95;  $p = .002$ ) and increased intensive care unit admission rate [odds ratio (*OR*), 1.28; 95% *CI*, 1.04-1.58;  $p = .02$ ] (Shahrokni et al., 2019).

### **ICU admission**

Frailty as a clinical assessment is extensively documented in the literature, but until recently, frailty was not a part of ICU outcomes studies (Muscedere et al., 2017). Prior studies have demonstrated that in addition to poor survival rates, frail patients who suffer a critical illness have a diminished quality of life if they survive to hospital discharge. Recently, a significant association between frailty status and ICU admission rate has been shown (Le Maguet et al., 2014; Muscedere et al., 2017). Additionally, frail patients are more likely than their non-frail counterparts to exhibit disabilities following a critical illness (Flaatten et al., 2017; Le Maguet et al., 2014). Specifically, in one study, frailty [adjusted risk ratio, 1.41; 95% (*CI*), 1.12-1.78] was associated with a 41% greater chance of disability following a critical illness (Ferrante et al., 2018). In the same study, pre-frailty was also associated with a 28% chance of disability following an ICU admission [adjusted risk ratio, 1.28; 95% (*CI*), 1.01-1.63] (Ferrante et al., 2018). Furthermore, frailty tended to be associated with higher nursing home admission rates following discharge from an ICU (*OR*, 2.01; 95% *CI*, 0.77-5.24) (Ferrante et al., 2018). For each one point increase in frailty score, a patient's risk of death after ICU admission doubled (*HR*, 2.00; 95% *CI*, 1.33-5.00) to a follow up of six months post-ICU stay (Ferrante et al., 2018).

Finally, Ferrante et al. (2018) and Le Maguet et al. (2014) demonstrated that an increased frailty score is associated with increased post-ICU discharge disability, new nursing home admission amongst survivors, and higher rates of mortality.

In a study of ICU patients 80 years or older, Flaaten et al. (2017) found a 43% incidence of frailty in their patient population, and frailty to be independently associated with diminished 30 day survival rate following ICU admission (*HR*, 1.54, 95% *CI*, 1.38-1.73) when compared to non-frail ICU patients (Flaatten et al., 2017). In their study, Flaaten et al. found no perfect combination of predictive factors associated with who would benefit most from ICU care in their older ICU population. They did find that separate from age, comorbidities and the presence of acute organ failure, coupled with a higher frailty score, increased a critically ill older person's chances of a poor outcome. Flaaten et al. posited that a geriatric syndrome comprised of frailty, sarcopenia, delirium, and dementia may diminish an older person's ability to withstand a stressful event such as a critical illness (Flaatten et al., 2017).

As a predictor of unsatisfactory outcomes, frailty is independently associated with 30 day mortality in ICU patients (Flaatten et al., 2017). The fastest growing portion of ICU patients, people aged 80 or older, need appropriate triage, resource allocation, patient centered treatment plans, and improved models predicting survivability (Flaatten et al., 2017). Increased intensity of ICU interventions in older patients is associated with a reduction in mortality rate (Flaatten et al., 2017). While it would be interesting to look at these effects in the cancer patients, currently, frailty research in this patient population is limited. Research analyzing the relationship between frailty status, ICU admission, SACU admission, 30-day readmission rate and cancer diagnosis is also lacking. It is not known whether frailty has a similar or more significant impact on outcomes in frail cancer patients when compared to non-frail cancer patients. There is minimal existing

research in cancer populations that includes frailty status, ICU admission rate, SACU admission rate, length of hospital stay and 30-day readmission rate.

## **Covariables**

### **Demographic Variables**

Disparities in health care outcomes exist in the United States, and often these disparities are linked to variables that researchers can study (Chin, Walters, Cook, & Huang, 2007). For instance, age, sex, and race represent covariables that likely play some role in the frailty- surgical outcomes relationship (Gilbert et al., 2018; Strandberg & Pitkala, 2007). The impact age has on surgical outcomes has been well documented in the literature, showing that the normal aging process affects how people react to physiological stressors (Makary et al., 2010; McIsaac et al., 2017; Wick et al., 2011). It is understood that older patients have increased risk for postoperative complications, prolonged length of stay, and readmission (Clegg et al., 2013; Gilbert et al., 2018; Rockwood et al., 2011; Sadiq et al., 2018).

Additionally, the impact sex has on surgical outcomes has also been demonstrated with previous research (Guth, Hiotis, & Rockman, 2005). Gender bias in clinical research is a potential pitfall that merits attention. Finally, racial differences, although not independent from health disparities and social determinants, have been shown to influence health care outcomes (Aladdin et al., 2019; Kim, et al., 2018; Rana et al., 2020). For instance, Aladdin et al. (2019) found that African Americans average a longer length of hospital stay and have higher odds of 30-day and 90-day readmission following spinal surgery. Considering age, sex, and race is an important part of accurately assessing the relationship between frailty and postoperative outcomes. Although racial differences have been noted in past research, these studies often do

not account for societal, systemic, or institutional inequities in healthcare (Azar et al., 2020; Boyd et al., 2020; Hardeman, et al. 2018; C. P. Jones, 2000; Phelan, Link, & Tehranifar, 2010).

### **Type of Surgery**

The relationship between frailty, surgical stress, and post operative outcomes is not completely understood (Shinall et al., 2019). The amount of stress patients encounter during an operation varies across types of the surgical procedures, and this variation in stress likely has some effect on postoperative outcomes. It is plausible that negative postoperative outcomes have a strong association with high stress surgical procedures especially in the frail geriatric population (Shinall et al., 2019).

To date, much of the frailty research focuses on high risk surgical procedures. However, the definition of a high-risk surgical procedure is not clear as it varies considerably from one reported study to another (Schwarze et al., 2015). Most accepted definitions of high-risk surgeries include procedures that have a one percent in-hospital or 30-day mortality rate associated with them (Schwarze et al., 2015; Shinall et al., 2019). These procedures likely represent operations with the highest level of operative stress associated with them, and include open intra-abdominal, intra-thoracic, or neurosurgical procedures (Bertges et al., 2010; Glance et al., 2012; Gupta et al., 2013; Lee et al., 2010; Liu et al., 2016; Sahara et al., 2019; Shinall et al., 2019). Prior research demonstrates a strong association between frailty and postoperative outcomes such as prolonged length of hospital stay, failure to thrive, increased rate of morbidity, and higher rate of mortality across surgical specialties (Dasgupta et al., 2009; Gajdos et al., 2013; Hall et al., 2017; Kristjansson et al., 2010; Makary et al., 2010; Robinson et al., 2013; Saxton & Velanovich, 2011; Shah et al., 2018; Velanovich et al., 2013). Recent research by Shinall et al. (2019) analyzed the relationship between frailty, operative stress, and outcomes.

In their study, Shinall et al. (2019) used the Delphi technique to develop an operative stress score (OSS) metric (J. Jones & Hunter, 1995; McMillan, King, & Tully, 2016; Powell, 2003). The different categories of OSS included: very low stress (OSS 1); low stress (OSS 2); moderate stress (OSS 3); high stress (OSS 4); and very high stress (OSS 5) (Shinall et al., 2019). Shinall et al. (2019) found that frail patients have higher rates of mortality across all levels of operative stress, not just high stress operations. The authors concluded a significant association exists between frailty, the level of stress encountered by each surgical procedure, and mortality (Shinall et al., 2019). Additionally, Shinall et al. (2019) found frail patients undergoing low and intermediate stress procedures had greater than one percent mortality risk which is greater than the standard for surgeries to be considered high-risk.

Important to note with the Shinall study, the researchers obtained their data from the Veteran's Affairs Surgical Quality Improvement program database where the sample population was 92.8% male and 69.3% Caucasian. While the demographics may limit generalizability of the author's conclusions, the Shinall et al. (2019) study demonstrates that operative stress plays some role in the relationship between frailty and postoperative outcomes. Further research is needed to analyze the relationship between OSS, frailty, and surgical outcomes in other patient populations.

The results from Shinall et al. (2019) demonstrate a need to have improved multidisciplinary, patient-centered care plans and more informed discussions with patients undergoing low and intermediate stress operations. The type of surgical procedure represents an important covariable when analyzing the relationship between frailty and surgical outcomes. By including type of surgical procedure in data analysis, modifiable risk factors may be identified to optimize care in low and intermediate stress surgical procedures, ultimately improving outcomes.



### **Surgical Stress Score**

The surgical stress score (SSS) estimates the stress of surgery in order to predict postoperative morbidity (Haga, Ikei, & Ogawa, 1999). The SSS is comprised of intraoperative blood loss in relation to patient's weight in kilograms, type of surgical incision, and duration of surgery to determine surgical stress encountered during a procedure. For surgical incision, laparoscopic incisions receive a score of zero, laparotomy or thoracotomy incisions receive a score of 1, and both laparotomy and thoracotomy incisions in the same procedure receive a score of two. The SSS was previously validated by Haga (1999), and has been used subsequently to assess the relationship between surgical stress and surgical outcomes.

Surgical domains using the SSS in the past include: digestive surgery (Haga et al., 2004), thoracic surgery (Yamashita, et al., 2004), cardiovascular surgery (Kotera, et al., 2016), and abdominal cardiovascular surgery (Tang et al., 2007). Prior research demonstrates that increasing SSS score correlates significantly with postoperative complications (Coelen et al., 2016; Hirose et al., 2015; Nagata et al., 2015; Tang et al., 2007; Tominaga et al., 2016). To date, the SSS has rarely been included as a confounding variable when analyzing the relationship between frailty and postoperative outcomes.

### **Home and Perioperative Medications**

With a high prevalence of polypharmacy, geriatric patients represent a significant number of medication consumers in the United States (Ineke Neutel et al., 2012; Kouladjian et al., 2014). The Beers criteria list of medications, developed in 1991 by Dr. Mark Beers, was created to educate healthcare providers about medications that maybe harmful to geriatric patients (Marcum & Hanlon, 2012). Dr. Beers updated the list several times, and the American Geriatrics Society (AGS) continued to update the list after Dr. Beers passed away. In 2011, the

AGS updated this list of potentially inappropriate medications in older adults. The AGS expert panel evaluated current research at the time in order to provide criteria, recommendations, rationale, and strength of recommendations for clinicians (American Geriatrics Society Beers Criteria Update Expert Panel, 2019). Since 2011, the AGS interdisciplinary expert panel has met every three years to update the list. The latest update occurred in 2019.

According to the Beers criteria list, certain classes of medications affect geriatric physical and cognitive function (Fick et al., 2019). For instance, prior research suggests that drugs such as anticholinergic and sedative medications may result in poorer function and cognitive status in geriatric patients (Cao et al., 2008; Gray et al., 2003; Hilmer et al., 2007; Landi et al., 2007; Mulsant et al., 2003). Furthermore, research shows that there is a significant relationship between use of anticholinergic and sedative medications, cognitive impairment, and poor functional status (Cancelli et al., 2009; Cardwell et al., 2020; Fick et al., 2019; Fox et al., 2011; Glass et al., 2005; Jamieson et al., 2019; Koyama et al., 2014; Nishtala et al., 2014).

There is mounting evidence to support an association between anticholinergic and sedation drugs and poor outcomes in community dwelling adults aged 65 or older (Billioti et al., 2012; Campbell et al., 2009; Cao et al., 2008; Gray et al., 2006; Hilmer et al., 2009; Nishtala et al., 2014). This association is likely present in frail geriatric patients because of diminished response to stress and increased sensitivity to certain medications (Fox et al., 2011; Koyama et al., 2014; McIsaac, Bryson, et al., 2016; Shah et al., 2018; Shinall et al., 2019). The relationship between frailty and polypharmacy is likely a bidirectional relationship influenced by environmental and social factors (Matteo Cesari, 2020). Home and perioperative medications represent important covariables because they may potentially alter the relationship between frailty and postoperative outcomes. When data collected includes the medications patients take at

home and receive during their operation, researchers have a greater opportunity to identify modifiable risk factors for anesthesia providers to consider when assessing frail surgical patients.

### **Application of theory**

The incidence of frailty is approximately 4-59% in community dwelling adults. This variation in incidence is likely due to the numerous frailty measurements present in the literature. Frailty is more common later in life and in the presence of chronic disease (Collard et al., 2012). Frailty appears when physiologic reserve has decreased below a critical threshold such that even an inconsequential stressor can trigger a cascade of untoward events. Molecular and physiological markers of frailty are documented in prior research. For instance, research shows the presence of increased inflammatory markers (Soysal et al., 2016) and epigenetic changes resulting from deoxyribonucleic acid (DNA) methylation (Breitling et al., 2016) in frail patients. Despite various definitions and multiple measurement tools, frailty theory has two core components: biological and quantitative.

#### **Biological components of frailty**

Frailty is comprised of a phenotype that includes chronic systemic inflammation, sarcopenia, and neuroendocrine dysfunction. Sarcopenia is the condition of having low lean muscle mass combined with weak muscle strength (Studenski et al., 2014). According to López-Otín et al. (2013), there are molecular and cellular hallmarks of aging associated with frailty. These hallmarks are affected by environmental, genetic, and epigenetic factors such as immune senescence, mitochondrial dysfunction, and possible telomere reduction (López-Otín et al, 2013). The interaction between outside factors and frailty can diminish a person's physiological response to a stressful event because of the resulting chronic inflammation, endocrine dysfunction, and sarcopenia (López-Otín et al., 2013; Singer, Lederer, & Baldwin, 2016).

Once frailty develops, disability, morbidity, or mortality may occur in the presence of a new stressor that exceeds a person's remaining physiologic reserve (Singer et al., 2016). One of the main drivers of frailty, chronic systemic inflammation, results in deficiencies in protein and micronutrients and also may cause decreased endocrine function (Cohen et al., 2003; Schalk et al., 2004). For instance, frail patients have increased blood levels of pro-inflammatory cytokine IL-6, tumor necrosis factor (TNF), and C-reactive protein (Barzilay, 2007; Cesari et al., 2004; Hubbard et al, 2008; Hubbard et al, 2009; Leng et al, 2002; Puts et al, 2005). Frail adults also have increased levels of insulin-like growth factor-1 (IGF-1) which is an anabolic activator of muscle and needed for the signaling of growth hormone (Cappola et al., 2003; Leng et al., 2002; Puts et al., 2005). Prior research has noted frail patients also have lower amounts of estrogen, testosterone, and 25-hydroxyvitamin D levels than non-frail people (Cawthon et al., 2009; C. Joseph et al., 2005; Shardell et al., 2009; Swiecicka et al., 2018; Tiidus, Lowe, & Brown, 2013).

In the biological component of frailty theory, a heterogeneous combination of disability, chronic disease, cognitive impairment, and social susceptibility comprise the frailty state. Unintentional weight loss, exhaustion, weakness, slow walking speed, and low levels of physical activity comprise this phenotype. The traits are biologically linked to create a cycle of dysfunction that affects various physiological systems (Montgomery, Rolfson, & Bagshaw, 2018). The catalysts of this cycle are the activation of inflammatory responses, immune senescence, and endocrine malfunction. These catalysts can be manifested in the renin-angiotensin-aldosterone system, hypothalamic-pituitary-adrenal system, and the sympathetic nervous system (Singer et al., 2016). The increased susceptibility seen in frailty remains silent until the person faces a stressful event such as surgery or a critical illness (Singer et al., 2016). Frailty is a complex, non-linear state and a syndrome at the same time. Frailty results in

diminished homeostatic reserve in physiological, cognitive, immune, and social systems. With diminished reserve, frail patients present with a much higher risk of experiencing a profound adverse event from a minor stressor (Montgomery et al., 2018; Singer et al., 2016).

### **Quantitative component of frailty theory**

The multidimensional model of frailty represents the quantitative component of frailty theory. The accumulation of deficits over time and across domains leads to increased susceptibility to adverse events because of a diminished physiological response. This model of frailty was first characterized in the Canadian Study of Health and Aging (Mitnitski et al., 2001; Rockwood & Mitnitski, 2007; Song et al., 2007). Frailty status includes impairments from chronic diseases, lab abnormalities, cognitive decline, and decreased social activity. The physiological, cognitive, emotional, social, nutritional, and functional domains are assessed within the quantitative model such that as deficits increase, so does a person's frailty score. The higher the frailty score, the less likely a person is to handle a stressful event adequately. As deficits accumulate, a person's ability to withstand physiological or environmental insults decreases, and the cycle of frailty begins. The frailty cycle most likely prevents full recovery from the stressor. As the cycle continues, a frail person continues to decompensate to the point of significant disability or even death (Chao, Wu, Wu, & Chen, 2018; Dent, Kowal, & Hoogendijk, 2016; Mitnitski et al., 2015; Rockwood & Mitnitski, 2010).

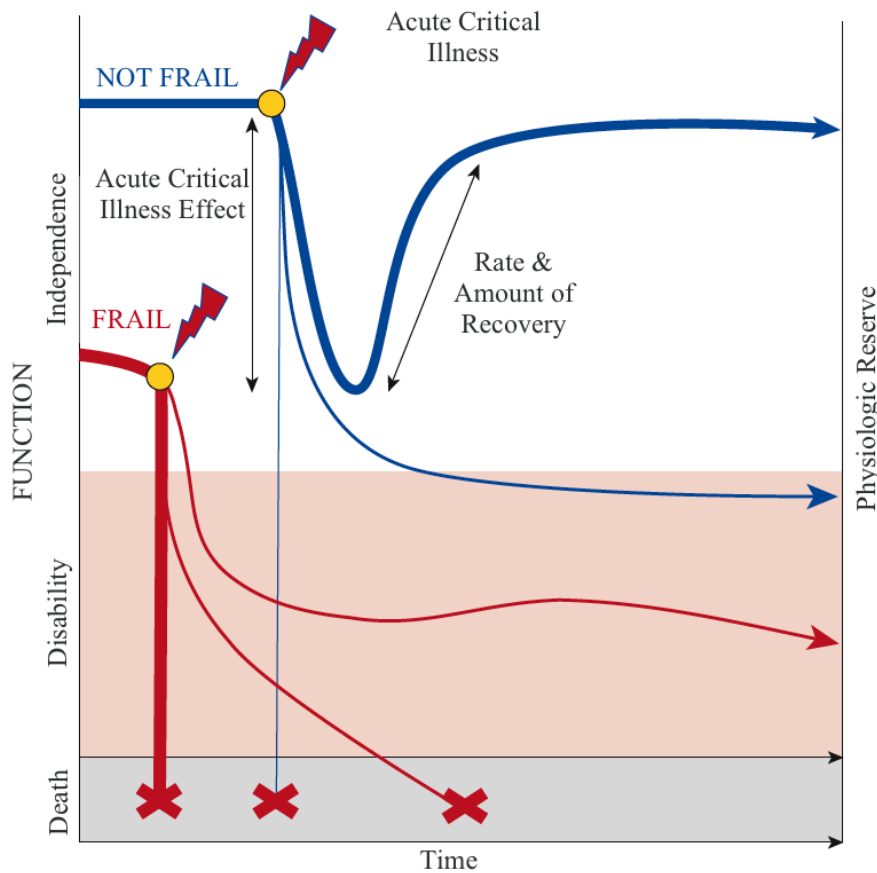


Figure 2. Impact of frailty on functional status.

Hypothetical trajectories for patients who are frail (red line) and not frail (blue line) prior to becoming critically ill. The thickness of the trajectory lines represents the proportion of patients in each trajectory. For a given insult, frail patients are susceptible to becoming critically ill sooner. Patients who are frail prior to critical illness are more likely to die in the hospital and more likely to develop chronic critical illness or severe disability leading to an early death. If they survive their critical illness, they are prone to recover functional status more slowly or develop permanent disability and a shorter lifespan than those who are not frail.

Reprinted with permission of the American Thoracic Society. Copyright © 2019 American Thoracic Society. Cite: Singer, J., Lederer, D., Baldwin, M./2016/AnnalsATS/Volume 13/Number 8/Pages 1394-1404. Annals of the American Thoracic Society is an official journal of the American Thoracic Society.

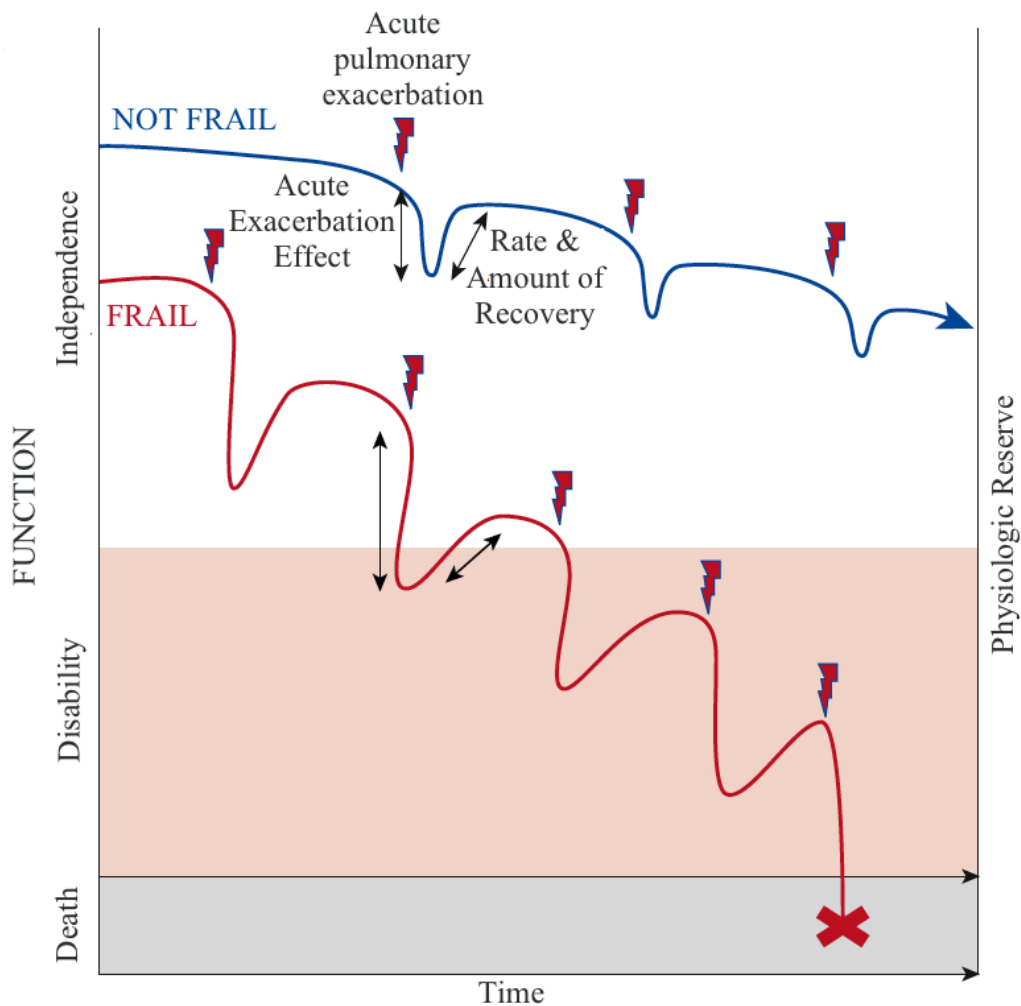


Figure 3. Impact of critical illness on frail compared to non-frail people.

Theoretical trajectories of functional status for patients experiencing a critical illness who are frail (red line) and non-frail (blue line). Frail patients are susceptible to more frequent exacerbations with less recovery in between, resulting in faster loss of functional status, earlier onset of disability, and a shorter lifespan.

Reprinted with permission of the American Thoracic Society. Copyright © 2019 American Thoracic Society. Cite: Singer, J., Lederer, D., Baldwin, M./2016/AnnalsATS/Volume 13/Number 8/Pages 1394-1404. Annals of the American Thoracic Society is an official journal of the American Thoracic Society.

An important objective of a theory is to enable researchers to comprehend phenomena in multiple contexts (Simon & Goes, 2013). In accordance with this objective, the constructs of

frailty and surgical outcomes can be studied using the accumulated deficits of frailty theory. According to this theory, deficits come from a variety of domains including physiological, cognitive, emotional, functional, and nutritive (Mitnitski, Mogilner, MacKnight, & Rockwood, 2002). Over time, deficits can accumulate to a point where a person can no longer adequately respond to and rebound from stressful events such as surgery (See Figures 2 and 3).

The process of deficit accumulation is independent of the aging process and separate from disability (Fried et al, 1994; Rockwood & Mitnitski, 2007). The construct of frailty can be measured using a frailty index similar to the one created in the Canadian Study of Health and Aging (Rockwood et al., 2001) and the construct of surgical outcomes can be measured with morbidity and mortality rates, length of hospital stay, and readmission rates (Sadiq et al, 2018) (See Figure 4). This has been accomplished with prior research in non-cancer surgical patients (Hall et al., 2016; McIsaac et al., 2016; Velanovich et al., 2013).

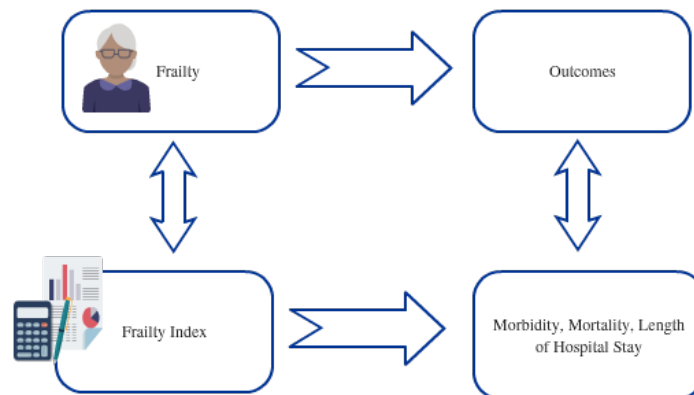


Figure 4. Theoretical applications

Note: This figure represents the constructs of frailty and health outcomes. A frail person is likely more susceptible to poor health outcomes (i.e. morbidity, mortality, and disability) because they have a weakened response to stressful events such as surgery. Frailty occurs on a continuum and can be measured using a frailty index. Frailty scores and their relationship to poor health outcomes can be directly measured by analyzing outcomes such as morbidity, mortality, and length of hospital stay.



**Hypotheses**

The hypotheses are as follows:

H<sub>1</sub>: There is a direct relationship between degree of frailty status and subsequent postoperative ICU admission in patients 65 years or older following cancer surgery.

H<sub>2</sub>: There is a direct relationship between degree of frailty status and postoperative SACU admission in patients 65 years or older following cancer surgery.

H<sub>3</sub>: There is a direct relationship between degree of frailty status and 30-day readmission in patients 65 years or older following cancer surgery.

### Chapter 3: Methods

This chapter represented the methodology to address the hypotheses and research questions concerning the relationship between frailty, postoperative ICU admission, SACU admission, and 30-day readmission in cancer surgical patients at a specialty cancer care hospital.

The stated objectives of this dissertation were to:

1. Establish the incidence of frailty in cancer surgical patients 65 years or older between January 1, 2015 and December 31, 2018 at MKSCC.
2. Determine whether frailty score predicted postoperative admission to the ICU, and separately, SACU during the specified time period.
3. Examine the relationship frailty and 30-day readmission in cancer surgical patients 65 years or older at MSKCC.

#### Methodology

This research was a non-experimental, non-randomized retrospective study design. Because the purpose of the study was to analyze previously collected data to learn about the relationship between frailty status and ICU admission, SACU admission, and 30-day readmission following cancer surgical resection, a retrospective design was used for this dissertation (Hulley, Cummings, & Browner, 2013). Specifically, the researcher attempted to determine if frailty status had a relationship with the postoperative admission rates to ICU or SACU and 30-day readmission. The research questions for this study were:

1. Was there a relationship between frailty and postoperative ICU admission in cancer surgical patients 65 years or older at MSKCC?
2. Was there a relationship between frailty and postoperative SACU admission in cancer surgical patients 65 years or older at MSKCC?

3. Was there a relationship between degree of frailty and 30-day readmission in cancer surgical patients 65 years or older at MSKCC?

### Research Design

The independent variable was frailty status, as determined by the MSK-FI. The dependent variables were postoperative ICU admission, SACU admission, and 30-day readmission. Postoperative ICU admission, SACU admission, and 30-day readmission were categorical variables. Demographic variables assessed included age and sex (See Table 10). Race was not included because the majority of the sample was Caucasian (See Table 11). Primary surgical department, surgical stress score, sex, age, MSK-FI score, Beers criteria medications, and preoperative albumin level were collected as covariables. All patients in this study underwent general anesthesia and were subsequently admitted as inpatients for at least one day following their surgical procedure.

Table 10. *Demographic data and covariables*

Variable	Measurement
Age	Years
Sex	Male or Female
Surgical stress score	Continuous numerical variable
Primary Surgical Department	Surgical category
Beers Criteria Medications	Categorical, Yes or no patient takes a medication on the list
Preoperative Albumin level	Continuous numerical variable

Table 11. *Racial make up of study sample*

Race	Number in sample
Caucasian	3690 (84%)
African American	192 (4.3%)
Asian	268 (6.1%)
Other	72 (1.6%)
Unknown	195 ( 4.4%)

### Selection of Subjects

The study occurred at MSKCC. The population of interest was all patients aged 65 or older who were seen by surgeons as a new visit, underwent surgery for cancer treatment within 2 months of the surgical visit, and stayed in the hospital for at least one day following surgery. The number of surgeries performed at MSKCC on an annual basis limited the number of cases in the sample. Additionally, the number of cases was limited by the number of surgeries performed on patients 65 or older at MSKCC.

Using G\*Power 3.1 software, a power analysis for logistic regression calculated sample size to be 721 subjects when two-tailed significance ( $\alpha$ ) equals 0.05, power was set at 0.8, and effect size was 0.2 (Tabachnick & Fidell, 2013). The average number of surgeries at MSKCC performed on subjects likely meeting inclusion criteria was approximately 1,000 annually. The annual surgical volume, during the selected timeframe, increased the likelihood of meeting sample size requirements for the dissertation. All records during the study timeframe were accessed, and every subject meeting entry criteria was included. Inclusion and exclusion criteria are presented in Table 11.

Table 12. *Inclusion and Exclusion Criteria*

Inclusion Criteria	Exclusion Criteria
Patients 65 years or older undergoing cancer surgery at MSKCC; were seen by a surgeon as	Patients less than 65 years old and any patient who does not meet all inclusion criteria.

<p>a new visit; had surgery within 2 months of the new surgery visit; and stayed in the hospital at least one day following surgery.</p>	
--	--

**Instrumentation**

The variables described previously were metrics found in the patient’s electronic chart from OpTime and EPIC (See Figure 5).

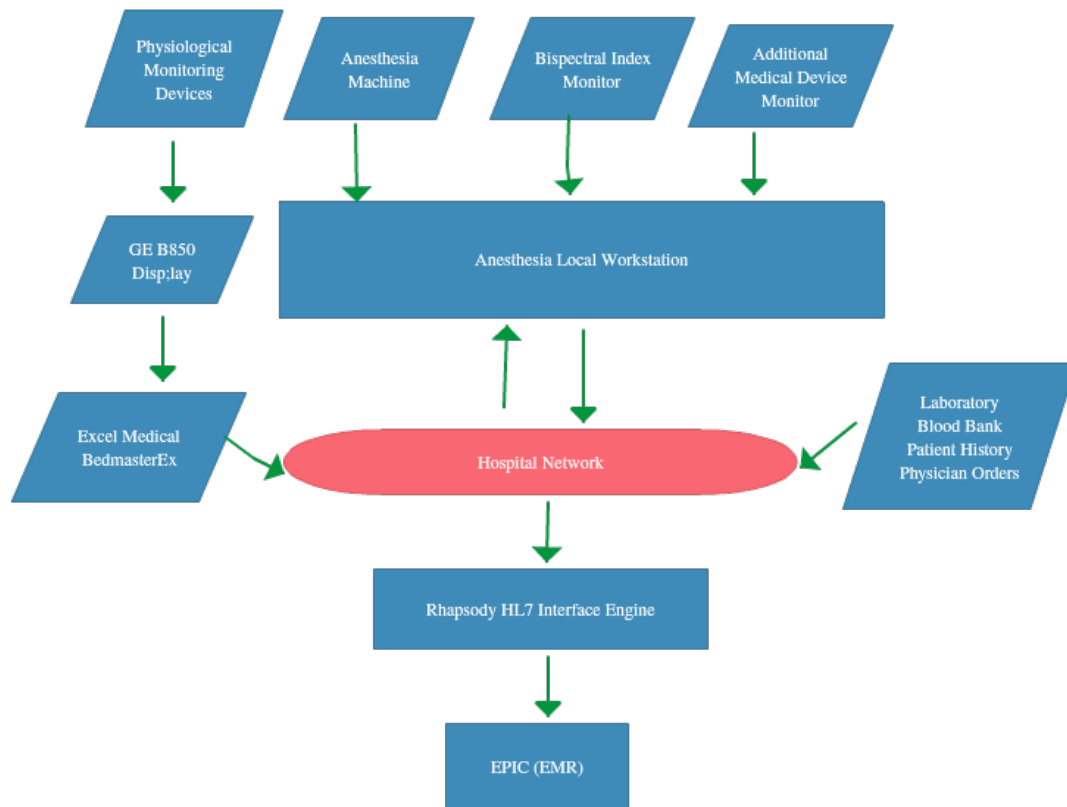


Figure 5. Flow of Data to Electronic Medical Record

Note: This figure shows the flow of data from the patient to the electronic medical record (EMR). Data flowed from the patient to various computer interfaces (anesthesia record, operating room record, laboratory record, and the EMR) via APIs, and JSONs. Additionally, various health care providers entered data into the EMR with flow sheets and notes. The different applications communicated with each other using REST architecture and HL7 programming specifications on the hospital network. Abbreviations: API=Application Interface, JSON= JavaScript Object Notation, REST: computer architecture allowing APIs to deliver data in multiple formats, HL7= Health Level 7 interface and integration engine.

**MSK-FI**

The Memorial Sloan Kettering Frailty Index (MSK-FI) was the frailty measurement instrument that used for this study. The primary investigator chose this frailty index because of its successful implementation in prior research at the study site. The MSK-FI was developed using parameters from the NSQIP mFI. Previous research from Saxon (2011) and Velanovich (2013) used the same variables measured with the MSK-FI. The studies retrospectively abstracted information from the NSQIP database, and found mFI scores correlated significantly with frailty and postoperative complications (Saxton & Velanovich, 2011; Velanovich et al., 2013). Instead of taking data from the NSQIP database, the MSK-FI collected information directly from the physical exam, patient history, and *International Classification of Diseases, Ninth Revision* (ICD-9) and ICD-10 codes contained in the electronic medical record. Using these sources to collect patient data minimized the risk of missing data, a problem that has plagued the NSQIP database (Shahrokni et al., 2018).

Both the mFI and the MSK-FI included functional status and comorbidities’ assessments. The MSK-FI measured functional status with four simple patient reported activities of daily living (bathing, dressing, grooming, and walking outside of the residence) and one instrumental activity of daily living (meal preparation). A limitation in any of these activities was scored as a one (impaired functional status). Independent patients who completed all activities receive a score of zero. This information was routinely collected in the geriatric consultation process in place at MSKCC for people 65 years or older (Shahrokni et al., 2019).

The MSK-FI included assessment of 10 comorbidities that highly correlate with poor health outcomes (Afilalo et al., 2017;Rockwood, 2016) (See Table 12).

Table 13. *Comorbidities Assessed with MSK-FI*

Comorbidity	Scoring
-------------	---------



Chronic obstructive pulmonary disease or pneumonia 30 days prior to surgery.	1= present 0= not present
Diabetes	1= present 0= not present
Congestive heart failure	1= present 0= not present
Myocardial infarction	1= present 0= not present
Coronary artery disease	1= present 0= not present
Hypertension	1= present 0= not present
Peripheral vascular disease	1= present 0= not present
Impaired sensorium (includes Alzheimer’s disease, delirium, dementia, Lewy body disease, memory loss, and mild cognitive impairment)	1= present 0= not present
Cerebrovascular accident	1= present 0= not present
Transient ischemic attack	1= present 0= not present

The comorbidities were abstracted from the *International Classification of Diseases, Ninth Revision* (ICD-9) and ICD-10 codes recorded in the electronic medical record from the pre-surgical visit through two days after surgery. Scores for the comorbidity assessment range from 0-10 where one point was given for the presence of each health condition. Combining the patient reported functional assessment score with the presence of the ten comorbidities gave a MSK-FI score ranging from 0-11. Because frailty occurs on a continuum, the higher the score, the more frail the patient was considered.

In a previous study, Shahrokni et al. (2018) validated the MSK-FI with the purpose of examining the relationship between frailty and surgical complications in cancer patients 75 years or older. Comparing the MSK-FI to the Comprehensive Geriatric Assessment (CGA) tested construct and instrument validity of the MSK-FI. In the study, the MSK-FI was found to correlate moderately with the CGA ( $\rho = 0.52$ ; bootstrapped 95% *CI*, 0.47-0.56) in diagnosing

impairments connoting frailty status (Shahrokni et al., 2018). The CGA is considered one of the most comprehensive tools for assessing the health of older patients and for diagnosing frailty (Andreou et al., 2018; Korc-Grodzicki et al., 2014; Shahrokni, Vickers, Mahmoudzadeh, & Korc-Grodzicki, 2016). Prior research using the CGA to validate frailty assessment tools demonstrates the process to be a feasible, replicable, and reliable manner to establish construct and instrument validity of new frailty tools (Ghignone et al., 2016; Jones, Song, & Rockwood, 2004; Jones, Song, Mitnitski, & Rockwood, 2005; Kramer et al., 2015; Kristjansson et al., 2010; McCarthy et al., 2018). Despite its usefulness, it must be noted that the geriatric assessment is time consuming to perform and can only be administered by geriatricians or gerontologists. On the other hand, the MSK-FI is a more rapid assessment measure and can be administered by any health care practitioner.

### **Data Collection and Recording**

Data was retrieved from patient electronic medical records (EMR). The EMR contained information from admission forms, intraoperative records, the electronic anesthesia record, and laboratory values. The information was entered into OpTime and EPIC by a number of health care professionals involved in each patient's care throughout their hospital stay. The data collection period was from January 1, 2015 to December 31, 2018. The data was obtained once the Institutional Review Board (IRB) review process had been completed at both MSKCC and Virginia Commonwealth University (VCU), and IRB permission granted to access patient records. Data was queried at MSKCC because it was MSKCC data used for the analysis. The data being queried was part of routine care information collected at MSKCC.

This research project only used de-identified data. This patient information was de-identified prior to entrance into the database in order to maintain compliance with the Health



Insurance Portability and Accountability Act. For additional protection procured data was stored on a password protected, encrypted computer at MSKCC that only the primary investigator was able to access.

### **Data Processing and Analysis**

Summary statistics were reported as means and interquartile range (IQR) for continuous variables. Missing data was handled with imputation. Categorical variables were reported as percentages. Separate multivariable logistic regression with random intercept models for each outcome were created, with continuous MSK-FI as the primary predictor, and adjusted for age, gender, primary surgical department, preoperative albumin, surgical stress score, and whether patients took any medication on the American Geriatrics Society Beers Criteria. The researchers used the fixed-effects model with random intercept to allow for the intercept to vary for each primary surgical department, while assuming the effects of the predictors to be the same. This dissertation was a multivariable multivariate analysis. Reported  $p$  values were 2-tailed with  $p$  values  $< 0.05$  thought to be significant. All statistical analyses were conducted using STATA 15.0 (StataCorp, College Station, TX) and R 4.0.1.

### **Methodological Assumptions**

The researcher assumed healthcare professionals were equally competent in providing patient care to the study population. Additionally, the researcher assumed frailty status, as defined by the theory of accumulated deficits, was captured accurately in the data collection. Furthermore, the researcher assumed the MSK-FI was a reliable and valid measurement of frailty as it has been used in prior research studies in the population of interest, and has been shown to correlate with the CGA to diagnose frailty (Shahrokni et al., 2019). This method of using the CGA to assess the validity and reliability of a new frailty measurement tool has been used in past

research (Ghignone et al., 2016; Jones et al., 2005; Kristjansson et al., 2012; McCarthy et al., 2018; Rockwood et al., 2005).

### **Limitations**

The most significant limitation of this study was that causality could not be inferred from the results. A correlation between frailty and postoperative outcomes such as ICU admission, SACU admission, and 30-day readmission may be found, but it cannot be concluded that frailty caused the outcomes. Lack of randomization also limited the generalizability of the results. Unfortunately, randomizing patients to frail or non-frail groups was not possible. The study site, a world renowned cancer center, may have limited the generalizability of study results because of differences in care provided at hospitals that perform the same surgical procedures, but did not specialize in cancer care. Patients treated at MSKCC may have been more homogeneous than the population as a whole. Individuals who collected the data were assumed to be equal, but personal bias presented a possible problem warranting attention. Given the retrospective nature of the study, data collection might have been incomplete or inaccurate.

### **Summary**

Chapter 3 described the methodology for this non-experimental, retrospective research design. This chapter discussed a plan for assessing the relationship between frailty and postoperative ICU admission, SACU admission, and 30-day readmission in surgical cancer patients 65 years or older. Additionally, the chapter provided information about variables, data collection and management, sampling methods, statistical analysis. Finally, study assumptions and limitations were discussed.

### Chapter 4: Results

Frailty is broadly defined as an accumulation of physiological, emotional, cognitive, and social deficits that impair a person's response to stressful events. While previous studies have found a correlation between frailty status and poor outcomes following surgical procedures, routine preoperative frailty assessment does not occur. The purpose of this research was to examine the utility of using a frailty assessment with the electronic medical record to identify high-risk geriatric cancer surgical patients. In this study, the relationships between frailty, postoperative admission to ICU, postoperative admission to the SACU, and 30-day readmission in cancer patients 65 or older were analyzed.

A non-randomized, non-experimental, retrospective cohort design was used to meet study objectives: to assess whether there is a relationship between a) frailty status and postoperative admission to the ICU in cancer patients 65 or older, b) frailty status and postoperative admission to the SACU in cancer patients 65 or older, and c) frailty status and 30-day readmission in cancer surgical patients.

Data collection, preparation, and statistical analysis examining the relationship between the variables are described in chapter 4. The chapter begins with a description of the variables. A summary of statistical results concerning the objectives is then presented.

Following IRB approval from MSKCC and VCU, data was obtained from January 1, 2015 to December 31, 2018. After an initial review by the VCU IRB, the study was deemed exempt because of its retrospective nature and lack of an intervention. A total of 4,417 patients were identified and included in the analysis. Among patients who underwent multiple surgeries during this time frame, only the first surgery was included for analysis. Patient characteristics are shown in Table 13. Over half of patients (51%) had an MSK-FI score of 0 or 1, and less than 5%

of patients had a score of 5 or more. Among the patients in the cohort, 3.8% (95% confidence interval (CI) 3.2%, 4.4%), 5.4% (95% CI 4.8%, 6.1%) and 10% (95% CI 9.1%, 10.9%) were admitted to ICU, admitted to the SACU, or readmitted to the hospital within 30-days of surgery. The results for the logistic regression models are presented in Table 14. Figure 6 illustrates the predicted probability of the outcomes based on the different values of the MSK-FI, when all continuous covariates are set to the mean and the categorical covariates are set to the mode.

Table 14. *Patient characteristics. Results are presented as median (quartiles) and frequency (%).*

Characteristic	N = 4,417
Age at surgery, years	73 (68, 78)
Male, sex	2,143 (49%)
MSK-FI score, numerical score 0 to 11	
0	810 (18%)
1	1,440 (33%)
2	1,059 (24%)
3	596 (13%)
4	305 (6.9%)
5+	207 (4.7%)
ASA-PS Score, numerical score 1-6	
1	4 (<0.1%)
2	597 (14%)
3	3517 (80%)
4	298 (6.7%)
5	1 (<0.1%)
Preoperative albumin, g/dl	4.10 (3.90, 4.30)
Beers criteria medication use, yes	2,475 (56%)
Surgical stress score, numerical score	0.13 (-0.16, 0.21)
Primary surgical category, number of patients	
Colorectal	555 (13%)
Gastric Mixed Tumor	532 (12%)
Gynecology	410 (9.3%)
Head and Neck	563 (13%)

Characteristic	N = 4,417
Hepato-pancreato-biliary	669 (15%)
Thoracic	947 (21%)
Urology	466 (11%)
Other	275 (6.2%)
Length of stay, days	4 (2, 7)
ICU admission within 30-days, yes	166 (3.8%)
SACU admission within 30-days, yes	239 (5.4%)
Readmission within 30-days, yes	440 (10.0%)

Note. ASA-PS is American Society of Anesthesiologists Physical Status Score

### Data Preparation and Cleaning

The primary investigator combined the data using an Excel spreadsheet. For the purposes of analysis, data was inspected for accuracy of input and assigned as either binary or continuous. All variables were assessed for normality of skewness and kurtosis, and distribution. Additionally, outliers were identified, and assumptions assessed.

### Data Analysis

The following section describes variables in the final analysis. The data of 4417 cases provided evidence regarding the research hypotheses being tested ( $H_1$ - $H_3$ ). The hypotheses address the relationship between frailty status and the outcome variables of ICU admission, SACU admission, and 30-day readmission in postsurgical cancer patients aged 65 or older. Multivariate logistic regression with random intercept modeling was used to assess the relationship between frailty and the outcome variables.

### Hypothesis Testing

Data was confirmed to not be in violation of assumptions of normality, linearity, homoscedasticity. Following this, the three hypotheses were tested.

**Hypothesis one (H<sub>1</sub>)**

Hypothesis one (H<sub>1</sub>) assessed for a relationship between frailty status and postoperative ICU admission in cancer surgical patients 65 or older. Results for H<sub>1</sub> are shown in Table 14.

- H<sub>1</sub>: There is a direct relationship between degree of frailty status and subsequent postoperative ICU admission in patients 65 years or older following cancer surgery.

Hypothesis one was tested with multivariable logistic regression. Thirty day ICU admission was the outcome variable, and continuous MSK-FI was the predictor. Covariables included age, sex, surgical stress score, preoperative albumin, and whether patients took any medication on the American Geriatrics Society Beers Criteria. A significant association between greater frailty score and increased risk of admission to the ICU (OR 1.44; 95% CI 1.31, 1.59; p-value <0.001) was found.

**Hypothesis two (H<sub>2</sub>)**

H<sub>2</sub> assessed the relationship between frailty status and postoperative SACU admission in cancer surgical patients 65 years or older. Results for H<sub>2</sub> are shown in Table 14.

- H<sub>2</sub>: There is a direct relationship between degree of frailty status and postoperative SACU admission in patients 65 years or older following cancer surgery.

Hypothesis two was tested using a multivariable logistic regression with postoperative SACU admission as the outcome, continuous MSK-FI as the predictor, and adjustment for the same covariates as in the first model. A significant association between frailty and admission to the SACU (OR 1.46; 95% CI 1.33, 1.60; p-value <0.001) was found.

**Hypothesis three (H<sub>3</sub>)**

H<sub>3</sub> analyzed the relationship between frailty and 30-day readmission rate in cancer surgical patients 65 years or older. Results for H<sub>3</sub> are shown in Table 14.

- H<sub>3</sub>: There is a direct relationship between degree of frailty status and 30-day readmission in patients 65 years or older following cancer surgery.

Hypothesis three was tested with a multivariable logistic regression model with 30-day readmission as the outcome, continuous MSK-FI as the predictor, and adjusted for the same covariates as in the first model. According to the results, the correlation between frailty status and 30-day readmission (OR 1.09, 95% CI 1.02, 1.177; p-value = 0.012) was significant.

Table 15. Association between variables and postsurgical outcomes on multivariable logistic regression with random intercept models.

Outcome	Characteristic	OR	95% CI	p-value
ICU admission	MSK-FI score, numerical score 0-11	1.44	1.31, 1.59	<0.001*
	Age at surgery, years	1.02	0.99, 1.04	0.13
	Male, sex			
	No	—	—	
	Yes	1.38	0.99, 1.93	0.058
	Preoperative albumin, g/dl	0.41	0.29, 0.58	<0.001*
	Surgical stress score (per tenth of a unit), numerical score	1.32	1.24, 1.40	<0.001*
Beers criteria medication use, yes	0.69	0.50, 0.95	0.025*	
SACU admission	MSK-FI score, numerical score 0-11	1.46	1.33, 1.60	<0.001*
	Age at surgery, years	1.06	1.03, 1.08	<0.001*
	Male, sex			
	No	—	—	
	Yes	1.14	0.83, 1.56	0.4
	Preoperative albumin, g/dl	0.45	0.32, 0.64	<0.001*
	Surgical stress score (per tenth of a unit), numerical score	1.50	1.40, 1.60	<0.001*
Beers criteria medication use, yes	0.76	0.56, 1.03	0.073	
Readmission	MSK-FI score, numerical score 0-11	1.09	1.02, 1.17	0.012*
	Age at surgery, years	1.00	0.98, 1.02	>0.9

Outcome	Characteristic	OR	95% CI	p-value
	Male, sex			
	No	—	—	
	Yes	1.22	0.99, 1.51	0.067
	Preoperative albumin, g/dl	0.58	0.46, 0.74	<0.001*
	Surgical stress score (per tenth of a unit), numerical score	0.99	0.94, 1.03	0.5
	Beers criteria medication use, yes	1.79	1.43, 2.23	<0.001*

\*Significance  $p \leq .05$



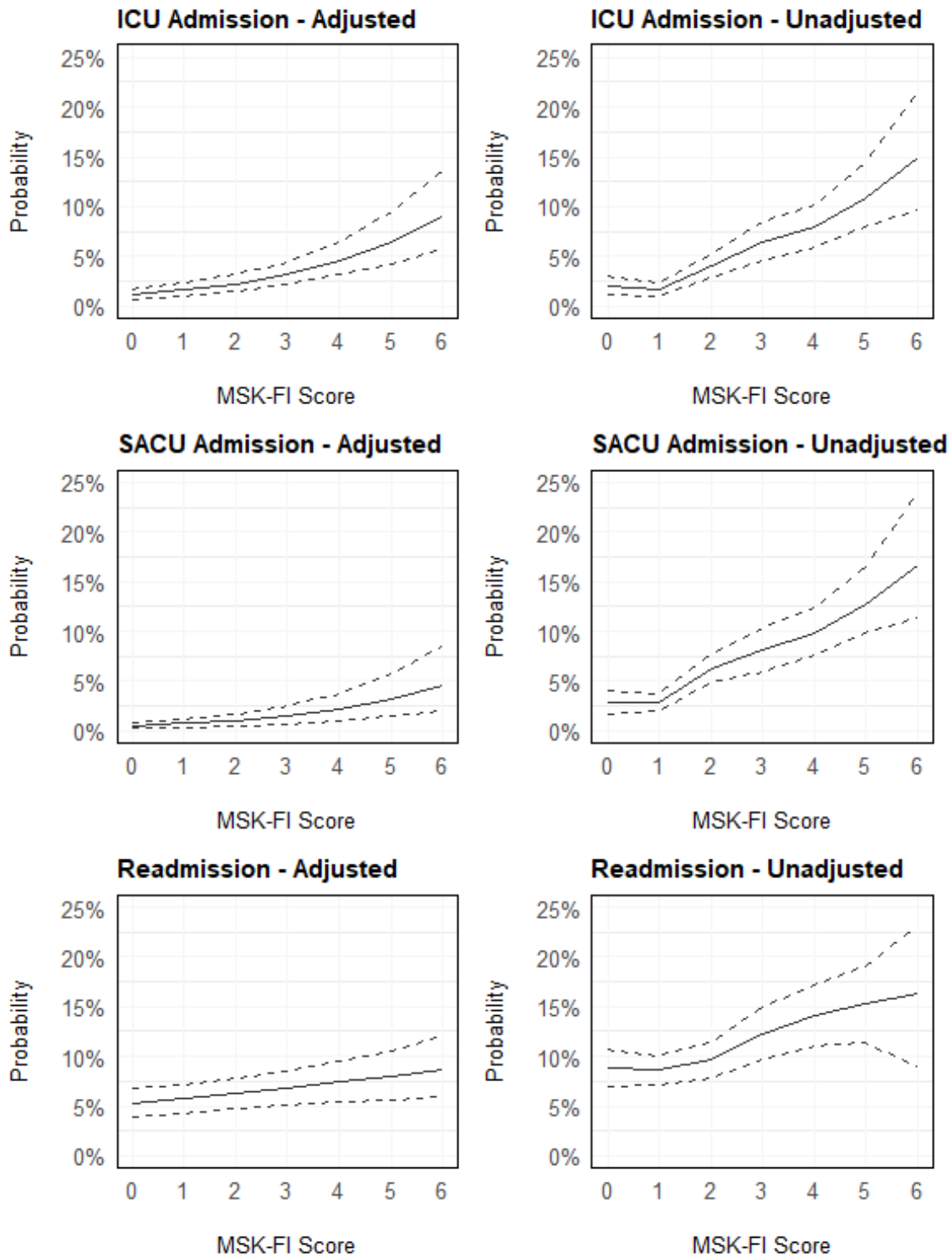


Figure 6. Predicted probability of outcomes based on MSK-FI score.

Note. This table depicts predicted probability of outcomes based on MSK-FI. The left panels represent the adjusted analysis while the right panels show the unadjusted analysis. For adjusted

analysis, predictions are for all covariates set to the mean (continuous) and mode (categorical). Dashed lines correspond to 95% confidence intervals.

### Chapter Summary

Chapter 4 presented the results from the statistical analysis of this dissertation with the purpose of examining the relationship between frailty, ICU admission, SACU admission, and 30-day readmission in post surgical cancer patients 65 years or older. Multivariable logistic regression with random intercept models were created for each outcome, with continuous MSK-FI as the primary predictor, and adjusted for age, gender, primary surgical department, preoperative albumin, surgical stress score, and whether patients are taking any medication on the American Geriatrics Society Beers criteria list. Fixed-effects model with random intercepts were specifically used to allow for the intercept to vary for each primary surgical department, while assuming the effects of the predictors to be the same.

A significant association was found between frailty status and ICU admission, SACU admission, and 30-day readmission. Additionally, as the MSK-FI score increased, so did the likelihood of an ICU, SACU, and 30-day readmission.

Chapter five will discuss the research findings as they pertain to the study objectives. Additionally, the advantages and limitations of the study will be presented as well as any recommendations for future research.

## Chapter 5: Discussion

Chapter 5 provides a summary of the study and an interpretation of the results presented in chapter 4.

### Summary and Overview of the Problem

Poor outcomes resulting from postoperative complications create a burden on patients, their families, and the health system. Currently there is no widely accepted, clinically relevant gold standard for identifying patients who may have a higher chance of poor outcomes following surgery. Measurement of frailty using a valid, reliable and easily applied tool has the potential to aid health care providers in identifying high-risk surgical patients. Once these patients are identified, care plans and resources can be tailored to meet patient-specific needs. Earlier mobilization of resources towards high-risk patients has the potential to reduce the impact of postoperative complications (McIsaac, MacDonald, & Aucoin, 2020; Nidadavolu, Ehrlich, Sieber, & Oh, 2020).

Frailty is a well-established predictor of surgical outcomes (Hall et al., 2017; McIsaac et al., 2018; Sadiq et al., 2018). A primary importance of frailty is that it represents an independent predictor of postoperative complications and length of hospital stay for geriatric patients (McIsaac et al., 2016; Ritt et al., 2015; Rockwood & Mitnitski, 2012). Prior research has demonstrated a correlation between frailty and poor surgical outcomes including increased morbidity, mortality, and length of hospital stay in non-cancer patient populations. (Mahanna-Gabrielli et al., 2020; McIsaac et al., 2020; Paul, Whittington, & Baldwin, 2020; Shah et al., 2018). To date, most of the research has focused on non-cancer surgical patients. There is a research gap regarding the relationship between frailty and admission to a Specialized Advanced

Care Unit (SACU) postoperatively. Additionally, there is limited research demonstrating a correlation between frailty and Intensive Care Unit (ICU) admission, and frailty and 30-day readmission in cancer patients.

Although the value of frailty assessment is acknowledged by prior research, routine use of a preoperative frailty assessment has not occurred (Nidadavolu et al., 2020). The current method available and routinely used by anesthesia staff for determining patient risk, the ASA-PS, is subjective and it represents a construct that was not intended to be predictive of outcomes. The ASA-PS also does not identify or assess domains that may benefit from prehabilitation. There is a need for an objective risk assessment tool in the preoperative evaluation of geriatric surgical patients that is reliable, consistent, and easy to use. This tool may offer insight where targeted preoperative intervention (prehabilitation) has the potential to benefit the patient's perioperative experience.

Studying frailty in cancer patients may provide anesthesia team members with an objective method for risk stratification prior to surgery. In turn, intraoperative and postoperative management plans can be adopted to help mitigate the impact frailty has on a patient's surgical journey. Frailty assessment can be performed in the pre-surgical clinic by a healthcare provider in order to learn more about the patient's health and functional status. Performing the assessment during the initial pre-surgical visit may provide enough time for the creation and implementation of a multidisciplinary treatment plan. Once frailty measurement has been established as part of the anesthesia pre-operative evaluation, future studies can focus on interventions that reduce frailty scores, change perioperative care plans, and improve surgical outcomes. Components of the frailty score that may be amenable to intervention include cardiovascular function, pulmonary function, and nutrition. Because frailty occurs on a continuum and is dynamic, it may

be beneficial to perform a frailty assessment at each patient encounter. Multiple frailty assessments will allow providers to follow a frailty trend in order to detect deteriorations in patient status.

### **Purpose of the Study**

The purpose of this study was to examine the relationship between frailty status and postoperative outcomes in cancer surgical patients 65 years or older. The postoperative outcomes of interest were ICU admission, SACU admission, and 30-day readmission.

### **Review of Theory and Research Questions**

Frailty is a syndrome of physiological, cognitive, emotional, and social age related decline leading to impaired responses to stressors. Frailty can further be defined as a biologic syndrome of decreased reserve and resistance to stressors that occurs on a continuum, resulting from cumulative declines across physiologic systems (Fried et al., 2001). While a gradual age-related decline in physiological reserve occurs, frailty accelerates these declines leading to homeostatic mechanism failure (Paul et al., 2020). Decreased response to stressors possibly increases vulnerability to poor surgical outcomes. Frailty is distinguishable from disability, and is not a strictly age related phenomenon (Rockwood et al., 2011; Strandberg & Pitkala, 2007). The role cancer plays in the frailty continuum is complex and challenging given the physiological impacts cancer treatments have on the patient. It is possible the relationship between frailty and cancer is cyclic and bidirectional because frail patients can develop cancer and cancer patients can become frail from treatment (Matteo Cesari, 2020; Morley et al., 2013; Singer et al., 2016).

The theory of Accumulated Deficits, posited by Rockwood et al., was used as the theoretical basis for this study. Over time, patients accumulate deficits in various domains

including physiological, mental, nutritional, and social (Rockwood et al., 2005). These deficits can be quantified using a frailty index. For the purposes of this study, the MSK-FI was used to retrospectively determine frailty status from the electronic medical record. In order to address the research questions, frailty scores were calculated and the relationships between frailty and postoperative ICU admission, SACU admission, and 30-day readmission were assessed.

### **Methodology**

A non-experimental, non-randomized retrospective study design was used for this dissertation. Data obtained from the anesthesia, surgical, and geriatric databases were analyzed from January 1, 2015 and December 31, 2018 at MKSCC. Descriptive statistics were used to analyze the variables and assess for relationships. Multivariable logistic regression with random intercept models were used to address the research questions. Adjustment for covariables, including age, sex, surgical stress score, preoperative albumin, and whether patients took any medication on the American Geriatrics Society Beers Criteria was completed.

### **Study Findings**

The researcher found evidence of a significant association between greater frailty and increased risk of admission to the ICU (OR 1.44; 95% CI 1.31, 1.59; p-value <0.001), admission to the SACU (OR 1.46; 95% CI 1.33, 1.60; p-value <0.001), and 30-day readmission (OR 1.09, 95% CI 1.02, 1.177; p-value = 0.012) (See Table 14). Figure 6 illustrates the predicted probability of the outcomes based on the different values of the MSK-FI, when all continuous covariates are set to the mean and the categorical covariates are set to the mode. For example, for a patient with an MSK-FI score of 2, the predicted probability of ICU admission, SACU admission, and readmission are 2.2%, 1.1%, and 6.3%, respectively, compared to 4.5%, 2.2%, and 7.4%, respectively, for a patient with an MSK-FI score of 4.

## Hypotheses

All three hypotheses were supported by the findings.

### Hypothesis one ( $H_1$ )

Hypothesis one ( $H_1$ ) assessed for a relationship between frailty status and postoperative ICU admission in cancer surgical patients 65 or older.

- $H_1$ : There is a direct relationship between degree of frailty status and subsequent postoperative ICU admission in patients 65 years or older following cancer surgery.

A significant association was found between frailty status and postoperative admission to the ICU in cancer surgical patients 65 years and older. Therefore,  $H_1$  is upheld.

### Hypothesis two ( $H_2$ )

$H_2$  assessed the relationship between frailty status and postoperative SACU admission in cancer surgical patients 65 years or older.

- $H_2$ : There is a direct relationship between degree of frailty status and postoperative SACU admission in patients 65 years or older following cancer surgery.

A significant association was found between frailty status and postoperative admission to the SACU in cancer surgical patients 65 years and older. Therefore,  $H_2$  is upheld

### Hypothesis three ( $H_3$ )

$H_3$  analyzed the relationship between frailty and 30-day readmission rate in cancer surgical patients 65 years or older.

- $H_3$ : There is a direct relationship between degree of frailty status and 30-day readmission in patients 65 years or older following cancer surgery.

A significant association was found between frailty status and 30-day readmission in cancer surgical patients 65 years and older. Therefore,  $H_3$  is upheld

### **Contribution to the Literature**

The intention of this investigation was to add to the growing body of research that shows frailty assessment can be the objective risk assessment tool that is greatly needed in anesthesia care. Specifically, the importance of this study is that it uses frailty measurement in a little studied vulnerable population: cancer patients aged 65 years or older. The results add to the knowledge base of frailty measurement and possibly provide a stepping-stone for the entrance of routine clinical use of a frailty index at MSKCC. Once a standard part of the geriatric patient pre-anesthesia evaluation, frailty scores may delineate frail from non-frail patients. This delineation of patients could lead to more informed discussions with patients about their anesthesia risk and lead to development of tailored patient-centered care plans. There is potential for future prospective research in which preoperative frailty assessments are used, and the relationship between frailty status and factors such as medication burden, medication administration, and patient outcomes can be examined.

### **Theoretical Implications**

The theoretical implication of this study is that the study may contribute to improving patient care guidelines. Using evidence based practice to improve patient outcomes in the geriatric cancer patient population would likely lead to better outcomes and reduced postoperative complications. Identifying high-risk surgical patients in the preoperative period, could potentially improve the care provider-patient dialogue and informed consent process where operative and anesthetic risk are discussed more thoroughly with patients.

### **Practical Implications**

Studying frailty assessment in cancer patients provides anesthesia team members with an objective method for risk stratification prior to surgery. In turn, intraoperative and postoperative



management plans can be adopted to help mitigate the impact frailty has on a patient's surgical journey. Frailty may mitigate certain patient deficits that have the potential to be addressable preoperatively, such as strength, nutrition, weight loss, and psychosocial factors. Once frailty measurement has been established as part of the anesthesia preoperative evaluation, future studies can focus on interventions that reduce frailty scores, change perioperative care plans, and improve surgical outcomes.

### **Limitations**

The investigator's limited control over the method of data gathering and the quality of the baseline measurements, represent disadvantages of a retrospective study design. Furthermore, it is difficult to account for data input failures, different forms of bias, maturation, and practice changes. The most significant limitation of this investigation is that it is not possible to infer causality from the results. Lack of randomization limits the attributing causality of the results. Patients treated at MSKCC may be more homogeneous than the population as a whole, and this limits the generalizability of the results. Patients treated at MSKCC may be more homogeneous than the population as a whole. Individuals who collected the data were assumed to be equal, but personal bias presents a possible limitation. Given the retrospective nature of the study, data collection may be incomplete or inaccurate (Hulley S. B, Cummings S. R, Browner W. S, 2013).

### **Threats to Internal Validity**

The lack of randomization represents a threat to internal validity (Cuncic, 2020). However, it is not possible to randomize frailty. Selection bias is a threat to internal validity in retrospective study designs. One could argue that frail patients undergoing cancer surgery are predisposed to unique categorical complications. If a population is intrinsically likely to demonstrate certain characteristics, variables that influence outcomes may be difficult to account

for. Additionally, frail patients may not be offered the same treatment options as non-frail patients.

Historical threats are occurrence of events concurrent with variables under investigation that can affect the outcome (Polit & Tatano-Beck, 2017). In this case, an example of a historical threat is a change in patient care practices over time that may have had an influence on the outcomes being measured. If anesthesia providers improved their anesthetic technique or eliminated certain medications from their anesthetic plan because of increased risk of poor outcomes, this would have an effect on validity of the findings.

Retrospective study design compels investigators to include alternative explanations for their findings. Rival variables that were not included in the analysis cannot be excluded as potential confounders leading to the findings (Polit & Tatano-Beck, 2017). Some possible rival variables include the time of day the surgery started, time of day the surgery finished, and whether a patient received chemotherapy, immunotherapy, or radiation treatment.

### **Threats to External Validity**

The population under investigation, which is patients 65 or older under going cancer surgical procedures, is narrow. The practices at one medical center may not be applicable to those at other institutions. For example, surgeons at MSKCC may perform more cancer surgeries than surgeons at non-cancer medical centers. The experience gained by greater surgical volume of cancer surgeries at MSKCC may lead to better surgical techniques and improved patient outcomes not translatable to other hospitals. Additionally, anesthesia providers at MSKCC may have more experience providing anesthesia care to cancer patients than their colleagues at non-cancer medical centers. Therefore, it may only be safe to say the findings reported in this

investigation are applicable to the population investigated at the institution where the study was conducted.

### **Conclusions and Recommendations for Future Research**

This study demonstrated that a correlation between frailty and higher rates of ICU, SACU, and 30-day readmission exists in geriatric cancer surgical patients. While a causal effect cannot be determined, the study shows the correlation between frailty and postoperative outcomes seen in non-cancer surgical populations also exists in cancer surgical populations. Potential areas for future study include prospective inclusion of preoperative frailty assessments, biological markers of frailty, and the role that Beers criteria medications play in the frailty-postoperative outcomes relationship. It will be essential for additional studies to analyze the relationship between preoperative frailty diagnosis and whether treatment plan changes improve outcomes in frail patients. What interventions are appropriate for frail surgical cancer patients, and when is the best time to implement them? Future studies and implementations should continue to assess the potential for improving patient outcomes, allocating healthcare resources more efficiently, and lowering health care costs.

## References

- Abt, N. B., Richmon, J. D., Koch, W. M., Eisele, D. W., & Agrawal, N. (2016). Assessment of the Predictive Value of the Modified Frailty Index for Clavien-Dindo Grade IV Critical Care Complications in Major Head and Neck Cancer Operations. *JAMA Otolaryngology--Head & Neck Surgery*, *142*(7), 658–664. <https://doi.org/10.1001/jamaoto.2016.0707>
- Afilalo, J., Lauck, S., Kim, D. H., Lefèvre, T., Piazza, N., Lachapelle, K., ... Perrault, L. P. (2017). Frailty in Older Adults Undergoing Aortic Valve Replacement: The FRAILITY-AVR Study. *Journal of the American College of Cardiology*, *70*(6), 689–700. <https://doi.org/10.1016/j.jacc.2017.06.024>
- Aguayo, G. A., Donneau, A.-F., Vaillant, M. T., Schritz, A., Franco, O. H., Stranges, S., ... Witte, D. R. (2017). Agreement Between 35 Published Frailty Scores in the General Population. *American Journal of Epidemiology*, *186*(4), 420–434. <https://doi.org/10.1093/aje/kwx061>
- Aladdin, D. E. H., Tangel, V., Lui, B., Pryor, K. O., Witkin, L. R., & White, R. S. (2019). Black Race As A Social Determinant of Health and Outcomes After Lumbar Spinal Fusion Surgery. *SPINE*, *1*. <https://doi.org/10.1097/BRS.0000000000003367>
- American Geriatrics Society Beers Criteria Update Expert Panel. (2019). American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *Journal of the American Geriatrics Society*, *00*(00), 1–21. <https://doi.org/10.1111/jgs.15767>
- American Society of Anesthesiologists. (2014). American Society of Anesthesiologists - ASA Physical Status Classification System. Retrieved September 14, 2017, from <https://www.asahq.org/resources/clinical-information/asa-physical-status-classification-system>
- Andreou, A., Lasithiotakis, K., Venianaki, M., Xenaki, S., Chlouverakis, G., Petrakis, I., & Chalkiadakis, G. (2018). A Comparison of Two Preoperative Frailty Models in Predicting Postoperative Outcomes in Geriatric General Surgical Patients. *World Journal of Surgery*. <https://doi.org/10.1007/s00268-018-4734-3>
- Aquina, C. T., Mohile, S. G., Tejani, M. A., Becerra, A. Z., Xu, Z., Hensley, B. J., ... Fleming, F. J. (2017). The impact of age on complications, survival, and cause of death following colon cancer surgery. *British Journal of Cancer*, *116*(3), 389–397. <https://doi.org/10.1038/bjc.2016.421>
- Arya, S., Kim, S. I., Duwayri, Y., Brewster, L. P., Veeraswamy, R., Salam, A., & Dodson, T. F. (2015). Frailty increases the risk of 30-day mortality, morbidity, and failure to rescue after elective abdominal aortic aneurysm repair independent of age and comorbidities. *Journal of Vascular Surgery*, *61*(2), 324–331. <https://doi.org/10.1016/j.jvs.2014.08.115>
- Atakul, E., & Akyar, İ. (2019). Frailty Prevalence and Characteristics in Older Adults with Hematologic Cancer: a Descriptive Study. *Asia-Pacific Journal of Oncology Nursing*, *6*(1), 43. [https://doi.org/10.4103/apjon.apjon\\_35\\_18](https://doi.org/10.4103/apjon.apjon_35_18)
- Augustin, T., Burstein, M. D., Schneider, E. B., Morris-Stiff, G., Wey, J., Chalikonda, S., & Walsh, R. M. (2016). Frailty predicts risk of life-threatening complications and mortality after pancreatic resections. *Surgery*, *160*(4), 987–996. <https://doi.org/10.1016/j.surg.2016.07.010>
- Azar, K. M. J., Shen, Z., Romanelli, R. J., Lockhart, S. H., Smits, K., Robinson, S., ... Pressman, A. R. (2020). Disparities in outcomes among COVID-19 patients in a large health care

- system in California. *Health Affairs*, 39(7), 1253–1262.  
<https://doi.org/10.1377/hlthaff.2020.00598>
- Balentine, C. J., Naik, A. D., Berger, D. H., Chen, H., Anaya, D. A., & Kennedy, G. D. (2016). Postacute Care After Major Abdominal Surgery in Elderly Patients. *JAMA Surgery*, 151(8), 759. <https://doi.org/10.1001/jamasurg.2016.0717>
- Barzilay, J. I. (2007). Insulin Resistance and Inflammation as Precursors of Frailty. *Archives of Internal Medicine*, 167(7), 635. <https://doi.org/10.1001/archinte.167.7.635>
- Beggs, T., Sepehri, A., Szwajcer, A., Tangri, N., & Arora, R. C. (2015). Frailty and perioperative outcomes: a narrative review. *Canadian Journal of Anesthesia/Journal Canadien d'anesthésie*, 62(2), 143–157. <https://doi.org/10.1007/s12630-014-0273-z>
- Bellal, J., Phelan, H., Hassan, A., Orouji Jokar, T., O'Keefe, T., Azim, A., ... Rhee, P. (2016). The impact of frailty on failure-to-rescue in geriatric trauma patients. *Journal of Trauma and Acute Care Surgery*, 81(6), 1150–1155. <https://doi.org/10.1097/TA.0000000000001250>
- Bertges, D. J., Goodney, P. P., Zhao, Y., Schanzer, A., Nolan, B. W., Likosky, D. S., ... Cronenwett, J. L. (2010). The Vascular Study Group of New England Cardiac Risk Index (VSG-CRI) predicts cardiac complications more accurately than the Revised Cardiac Risk Index in vascular surgery patients. *Journal of Vascular Surgery*, 52(3). <https://doi.org/10.1016/j.jvs.2010.03.031>
- Bieniek, J., Wilczyński, K., & Szewieczek, J. (2016). Fried frailty phenotype assessment components as applied to geriatric inpatients. *Clinical Interventions in Aging*, 11, 453–459. <https://doi.org/10.2147/CIA.S101369>
- Billioti, S., Bégaud, B., Bazin, F., Verdoux, H., Dartigues, J. F., Pérès, K., ... Pariente, A. (2012). Benzodiazepine use and risk of Dementia: Prospective population based study. *BMJ (Online)*, 345(7880). <https://doi.org/10.1136/bmj.e6231>
- Borson, S., Scanlan, J., Brush, M., Vitaliano, P., & Dokmak, A. (2000). The mini-cog: a cognitive “vital signs” measure for dementia screening in multi-lingual elderly. *International Journal of Geriatric Psychiatry*, 15(11), 1021–1027. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11113982>
- Borson, Soo, Scanlan, J. M., Chen, P., & Ganguli, M. (2003). The Mini-Cog as a Screen for Dementia: Validation in a Population-Based Sample. *Journal of the American Geriatrics Society*, 51(10), 1451–1454. <https://doi.org/10.1046/j.1532-5415.2003.51465.x>
- Bouldin, E. L. D., Andresen, E. M., Dunton, N. E., Simon, M., Waters, T. M., Liu, M., ... Shorr, R. I. (2013). Falls among adult patients hospitalized in the United States: prevalence and trends. *Journal of Patient Safety*, 9(1), 13–17. <https://doi.org/10.1097/PTS.0b013e3182699b64>
- Boyd, R. W., Lindo, E. G., Weeks, L. D., & McLemore, M. R. (2020). On Racism: A New Standard For Publishing On Racial Health Inequities | Health Affairs. <https://doi.org/10.1377/hblog20200630.939347>
- Breitling, L. P., Saum, K.-U., Perna, L., Schöttker, B., Holleczeck, B., & Brenner, H. (2016). Frailty is associated with the epigenetic clock but not with telomere length in a German cohort. *Clinical Epigenetics*, 8(1), 21. <https://doi.org/10.1186/s13148-016-0186-5>
- Brown, S. R., Mathew, R., Keding, A., Marshall, H. C., Brown, J. M., & Jayne, D. G. (2014). The Impact of Postoperative Complications on Long-term Quality of Life After Curative Colorectal Cancer Surgery. *Annals of Surgery*, 259(5), 916–923. <https://doi.org/10.1097/SLA.0000000000000407>
- Buta, B. J., Walston, J. D., Godino, J. G., Park, M., Kalyani, R. R., Xue, Q.-L., ... Varadhan, R.

- (2016). Frailty assessment instruments: Systematic characterization of the uses and contexts of highly-cited instruments. *Ageing Research Reviews*, 26, 53–61. <https://doi.org/10.1016/j.arr.2015.12.003>
- Bysse, T., Yue Gao, M., Krysta Heaney-Huls, M., Jason Hockenberry, M., Hovey, L., Alison Laffan, M. M., ... Watts, E. (2017). *Draft Final Report Estimating the Additional Hospital Inpatient Cost and Mortality Associated with Selected Hospital Acquired Conditions*. Retrieved from [www.ahrq.gov](http://www.ahrq.gov)
- Campbell, N., Boustani, M., Limbil, T., Ott, C., Fox, C., Maidment, I., ... Gulati, R. (2009). The cognitive impact of anticholinergics: a clinical review. *Clinical Interventions in Aging*. <https://doi.org/10.2147/cia.s5358>
- Cancelli, I., Beltrame, M., Gigli, G. L., & Valente, M. (2009). Drugs with anticholinergic properties: Cognitive and neuropsychiatric side-effects in elderly patients. *Neurological Sciences*. <https://doi.org/10.1007/s10072-009-0033-y>
- Cao, Y. J., Mager, D. E., Simonsick, E. M., Hilmer, S. N., Ling, S. M., Windham, B. G., ... Abernethy, D. R. (2008). Physical and cognitive performance and burden of anticholinergics, sedatives, and ACE inhibitors in older women. *Clinical Pharmacology and Therapeutics*, 83(3), 422–429. <https://doi.org/10.1038/sj.clpt.6100303>
- Cappola, A. R., Xue, Q. L., Ferrucci, L., Guralnik, J. M., Volpato, S., & Fried, L. P. (2003). Insulin-like growth factor I and interleukin-6 contribute synergistically to disability and mortality in older women. *Journal of Clinical Endocrinology and Metabolism*, 88(5), 2019–2025. <https://doi.org/10.1210/jc.2002-021694>
- Cardwell, K., Kerse, N., Ryan, C., Teh, R., Moyes, S. A., Menzies, O., ... Hughes, C. M. (2020). The Association Between Drug Burden Index (DBI) and Health-Related Outcomes: A Longitudinal Study of the ‘Oldest Old’ (LiLACS NZ). *Drugs and Aging*. <https://doi.org/10.1007/s40266-019-00735-z>
- Cawthon, P. M., Ensrud, K. E., Laughlin, G. A., Cauley, J. A., Dam, T. T. L., Barrett-Connor, E., ... Orwoll, E. S. (2009). Sex hormones and frailty in older men: The osteoporotic fractures in men (MrOS) study. *Journal of Clinical Endocrinology and Metabolism*, 94(10), 3806–3815. <https://doi.org/10.1210/jc.2009-0417>
- CDC, Oid, Ncezd, & DHQP. (2017). 9 Surgical Site Infection (SSI) Event. Retrieved from <https://www.cdc.gov/nhsn/pdfs/pscmanual/9pscscssicurrent.pdf>
- Cesari, M., Penninx, B. W. J. H., Pahor, M., Lauretani, F., Corsi, A. M., Williams, G. R., ... Ferrucci, L. (2004). Inflammatory Markers and Physical Performance in Older Persons: The InCHIANTI Study. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 59(3), M242–M248. <https://doi.org/10.1093/gerona/59.3.m242>
- Cesari, Matteo. (2020, November 1). How polypharmacy affects frailty. *Expert Review of Clinical Pharmacology*. Taylor and Francis Ltd. <https://doi.org/10.1080/17512433.2020.1829467>
- Chao, Y.-S., Wu, H.-C., Wu, C.-J., & Chen, W.-C. (2018). Index or illusion: The case of frailty indices in the Health and Retirement Study. *PLOS ONE*, 13(7), e0197859. <https://doi.org/10.1371/journal.pone.0197859>
- Chappidi, M. R., Kates, M., Patel, H. D., Tosoian, J. J., Kaye, D. R., Sopko, N. A., ... Bivalacqua, T. J. (2016). Frailty as a marker of adverse outcomes in patients with bladder cancer undergoing radical cystectomy. *Urologic Oncology: Seminars and Original Investigations*, 34(6), 256.e1-256.e6. <https://doi.org/10.1016/J.UROLONC.2015.12.010>
- Chin, M. H., Walters, A. E., Cook, S. C., & Huang, E. S. (2007, October). Interventions to

- reduce racial and ethnic disparities in health care. *Medical Care Research and Review*.  
<https://doi.org/10.1177/1077558707305413>
- Choi, J.-Y., Yoon, S.-J., Kim, S.-W., Jung, H.-W., Kim, K., Kang, E., ... Kim, C.-H. (2015). Prediction of Postoperative Complications Using Multidimensional Frailty Score in Older Female Cancer Patients with American Society of Anesthesiologists Physical Status Class 1 or 2. *Journal of the American College of Surgeons*, 221(3), 652-660.e2.  
<https://doi.org/10.1016/j.jamcollsurg.2015.06.011>
- Chow, W. B., Rosenthal, R. A., Merkow, R. P., & Ko, C. Y. (2012). Optimal Preoperative Assessment of the Geriatric Surgical Patient: A Best Practices Guideline from the American College of Surgeons National Surgical Quality Improvement Program and the American Geriatrics Society. *ACS*, 215, 453-466. <https://doi.org/10.1016/j.jamcollsurg.2012.06.017>
- Clegg, A., Bates, C., Young, J., Ryan, R., Nichols, L., Ann Teale, E., ... Marshall, T. (2016). Development and validation of an electronic frailty index using routine primary care electronic health record data. *Age and Ageing*, 45(3), 353-360.  
<https://doi.org/10.1093/ageing/afw039>
- Clegg, A., Young, J., Iliffe, S., Rikkert, M. O., & Rockwood, K. (2013). Frailty in elderly people. *The Lancet*, 381(9868), 752-762. [https://doi.org/10.1016/S0140-6736\(12\)62167-9](https://doi.org/10.1016/S0140-6736(12)62167-9)
- Coelen, R. J. S., Olthof, P. B., Van Dieren, S., Besselink, M. G. H., Busch, O. R. C., & Van Gulik, T. M. (2016). External validation of the estimation of physiologic ability and surgical stress (E-PASS) risk model to predict operative risk in perihilar cholangiocarcinoma. *JAMA Surgery*, 151(12), 1132-1138. <https://doi.org/10.1001/jamasurg.2016.2305>
- Cohen, H. J., Harris, T., & Pieper, C. F. (2003). Coagulation and activation of inflammatory pathways in the development of functional decline and mortality in the elderly. *American Journal of Medicine*, 114(3), 180-187. [https://doi.org/10.1016/S0002-9343\(02\)01484-5](https://doi.org/10.1016/S0002-9343(02)01484-5)
- Cohen, R. R., Lagoo-Deenadayalan, S. A., Heflin, M. T., Sloane, R., Eisen, I., Thacker, J. M., & Whitson, H. E. (2012). Exploring predictors of complication in older surgical patients: A deficit accumulation index and the Braden Scale. *Journal of the American Geriatrics Society*, 60(9), 1609-1615. <https://doi.org/10.1111/j.1532-5415.2012.04109.x>
- Collard, R. M., Boter, H., Schoevers, R. A., & Oude Voshaar, R. C. (2012). Prevalence of frailty in community-dwelling older persons: a systematic review. *Journal of the American Geriatrics Society*, 60(8), 1487-1492. <https://doi.org/10.1111/j.1532-5415.2012.04054.x>
- Collins, T. C., Daley, J., Henderson, W. H., & Khuri, S. F. (1999). Risk factors for prolonged length of stay after major elective surgery. *Annals of Surgery*, 230(2), 251-259. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/10450740>
- Cooper, Z., Rogers, S. O., Ngo, L., Guess, J., Schmitt, E., Jones, R. N., ... Marcantonio, E. R. (2016). Comparison of Frailty Measures as Predictors of Outcomes After Orthopedic Surgery. *Journal of the American Geriatrics Society*, 64(12), 2464-2471.  
<https://doi.org/10.1111/jgs.14387>
- Crow, R. S., Lohman, M. C., Titus, A. J., Bruce, M. L., Mackenzie, T. A., Bartels, S. J., & Batsis, J. A. (2018). Mortality Risk Along the Frailty Spectrum: Data from the National Health and Nutrition Examination Survey 1999 to 2004. *Journal of the American Geriatrics Society*, 66(3), 496-502. <https://doi.org/10.1111/jgs.15220>
- Cuncic, A. (2020). Understanding Internal and External Validity. Retrieved December 22, 2020, from <https://www.verywellmind.com/internal-and-external-validity-4584479>
- Dall, T. M., Gallo, P. D., Chakrabarti, R., West, T., Semilla, A. P., & Storm, M. V. (2013). An aging population and growing disease burden will require a large and specialized health

- care workforce by 2025. *Health Affairs (Project Hope)*, 32(11), 2013–2020.  
<https://doi.org/10.1377/hlthaff.2013.0714>
- Dasgupta, M., Rolfsen, D. B., Stolee, P., Borrie, M. J., & Speechley, M. (2009). Frailty is associated with postoperative complications in older adults with medical problems. *Archives of Gerontology and Geriatrics*, 48(1), 78–83.  
<https://doi.org/10.1016/j.archger.2007.10.007>
- Denholm, M., Corrie, P., Qian, W., & Hampton, J. (2018). The Rockwood geriatric clinical frailty scale is a more discriminatory tool for assessing older cancer patients compared with standard oncology performance status scales. *European Journal of Surgical Oncology*, 44, S39. <https://doi.org/10.1016/j.ejso.2018.01.575>
- Dent, E., Kowal, P., & Hoogendijk, E. O. (2016). Frailty measurement in research and clinical practice: A review. *European Journal of Internal Medicine*.  
<https://doi.org/10.1016/j.ejim.2016.03.007>
- Department of Health and Family Services. CALORIES BURNED PER HOUR (2018). Retrieved from <https://www.dhs.wisconsin.gov/publications/p4/p40109.pdf>
- Dimick, J. B., Chen, S. L., Taheri, P. A., Henderson, W. G., Khuri, S. F., & Campbell, D. A. (2004). Hospital costs associated with surgical complications: A report from the private-sector National Surgical Quality Improvement Program. *Journal of the American College of Surgeons*, 199(4), 531–537. <https://doi.org/10.1016/J.JAMCOLLSURG.2004.05.276>
- Donoghue, T. J. (2019). AANA Journal Course Assessing Frailty and Its Implications on Anesthesia Care and Postoperative Outcomes in Surgical Patients. *AANA Journal*, 87(2), 1–8. Retrieved from [www.aana.com/aanajournalonline](http://www.aana.com/aanajournalonline)
- Ehlert, B. A., Najafian, A., Orion, K. C., Malas, M. B., Black, J. H., & Abularrage, C. J. (2016). Validation of a modified Frailty Index to predict mortality in vascular surgery patients. *Journal of Vascular Surgery*, 63(6), 1595-1601.e2.  
<https://doi.org/10.1016/J.JVS.2015.12.023>
- Ensrud, K. E., Ewing, S. K., Taylor, B. C., Fink, H. A., Stone, K. L., Cauley, J. A., ... Study of Osteoporotic Fractures Research Group. (2007). Frailty and risk of falls, fracture, and mortality in older women: the study of osteoporotic fractures. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 62(7), 744–751. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17634322>
- Fahimnia, S., Mirhedayati Roudsari, H., Doucette, J., & Shahrokni, A. (2018). Falls in Older Patients with Cancer Undergoing Surgery: Prevalence and Association with Geriatric Syndromes and Levels of Disability Assessed in Preoperative Evaluation. *Current Gerontology and Geriatrics Research*, 2018, 1–7. <https://doi.org/10.1155/2018/5713285>
- Farhat, J. S., Velanovich, V., Falvo, A. J., Horst, H. M., Swartz, A., Patton, J. H., & Rubinfeld, I. S. (2012). Are the frail destined to fail? Frailty index as predictor of surgical morbidity and mortality in the elderly. *Journal of Trauma and Acute Care Surgery*, 72(6), 1526–1531.  
<https://doi.org/10.1097/TA.0b013e3182542fab>
- Ferrante, L. E., Pisani, M. A., Murphy, T. E., Gahbauer, E. A., Leo-Summers, L. S., & Gill, T. M. (2018). The Association of Frailty With Post-ICU Disability, Nursing Home Admission, and Mortality. *Chest*, 153(6), 1378–1386. <https://doi.org/10.1016/j.chest.2018.03.007>
- Fick, D., Semla, T., Beizer, J., Brandt, N., Dombrowski, R., DuBeau, C., ... Linnebur, S. (2019). American Geriatrics Society 2019 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *JAGS*, 67, 674–694. <https://doi.org/10.1111/jgs.15667>
- Flaatten, H., de Lange, D. W., Artigas, A., Bin, D., Moreno, R., Christensen, S., ... Guidet, B.



- (2017). The status of intensive care medicine research and a future agenda for very old patients in the ICU. *Intensive Care Medicine*, 43(9), 1319–1328. <https://doi.org/10.1007/s00134-017-4718-z>
- Flaatten, Hans, De Lange, D. W., Morandi, A., Andersen, F. H., Artigas, A., Bertolini, G., ... VIP1 study group. (2017). The impact of frailty on ICU and 30-day mortality and the level of care in very elderly patients ( $\geq 80$  years). *Intensive Care Medicine*, 43(12), 1820–1828. <https://doi.org/10.1007/s00134-017-4940-8>
- Fox, C., Richardson, K., Maidment, I. D., Savva, G. M., Matthews, F. E., Smithard, D., ... Brayne, C. (2011). Anticholinergic medication use and cognitive impairment in the older population: The medical research council cognitive function and ageing study. *Journal of the American Geriatrics Society*, 59(8), 1477–1483. <https://doi.org/10.1111/j.1532-5415.2011.03491.x>
- Fried, L. P., Ettinger, W. H., Lind, B., Newman, A. B., & Gardin, J. (1994). Physical disability in older adults: a physiological approach. Cardiovascular Health Study Research Group. *Journal of Clinical Epidemiology*, 47(7), 747–760. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/7722588>
- Fried, L. P., Tangen, C. M., Walston, J., Newman, A. B., Hirsch, C., Gottdiener, J., ... Cardiovascular Health Study Collaborative Research Group. (2001). Frailty in older adults: evidence for a phenotype. *The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences*, 56(3), M146-56. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/11253156>
- Futier, E., Constantin, J.-M., Paugam-Burtz, C., Pascal, J., Eurin, M., Neuschwander, A., ... IMPROVE Study Group. (2013). A trial of intraoperative low-tidal-volume ventilation in abdominal surgery. *The New England Journal of Medicine*, 369(5), 428–437. <https://doi.org/10.1056/NEJMoa1301082>
- Gajdos, C., Kile, D., Hawn, M. T., Finlayson, E., Henderson, W. G., & Robinson, T. N. (2013). Advancing age and 30-day adverse outcomes after nonemergent general surgeries. *Journal of the American Geriatrics Society*, 61(9), 1608–1614. <https://doi.org/10.1111/jgs.12401>
- Gani, F., Canner, J. K., & Pawlik, T. M. (2017). Use of the Modified Frailty Index in the American College of Surgeons National Surgical Improvement Program Database: Highlighting the Problem of Missing Data. *JAMA Surgery*, 152(2), 205–207. <https://doi.org/10.1001/jamasurg.2016.3479>
- Ghignone, F., van Leeuwen, B. L., Montroni, I., Huisman, M. G., Somasundar, P., Cheung, K. L., ... Ugolini, G. (2016). The assessment and management of older cancer patients: A SIOG surgical task force survey on surgeons' attitudes. *European Journal of Surgical Oncology (EJSO)*, 42(2), 297–302. <https://doi.org/10.1016/j.ejso.2015.12.004>
- Gilbert, T., Neuburger, J., Kraindler, J., Keeble, E., Smith, P., Ariti, C., ... Conroy, S. (2018). Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. *Lancet (London, England)*, 391(10132), 1775–1782. [https://doi.org/10.1016/S0140-6736\(18\)30668-8](https://doi.org/10.1016/S0140-6736(18)30668-8)
- Glance, L. G., Lustik, S. J., Hannan, E. L., Osler, T. M., Mukamel, D. B., Qian, F., & Dick, A. W. (2012). The surgical mortality probability model: Derivation and validation of a simple risk prediction rule for noncardiac surgery. *Annals of Surgery*, 255(4), 696–702. <https://doi.org/10.1097/SLA.0b013e31824b45af>
- Glass, J., Lanctôt, K. L., Herrmann, N., Sproule, B. A., & Busto, U. E. (2005). Sedative

- hypnotics in older people with insomnia: Meta-analysis of risks and benefits. *British Medical Journal*, 331(7526), 1169–1173. <https://doi.org/10.1136/bmj.38623.768588.47>
- Graham, A., & Brown, C. H. (2017). Frailty, aging, and cardiovascular surgery. *Anesthesia and Analgesia*, 124(4), 1053–1060. <https://doi.org/10.1213/ANE.0000000000001560>
- Grant, F. M., Protic, M., Gonen, M., Allen, P., & Brennan, M. F. (2013). Intraoperative fluid management and complications following pancreatectomy. *Journal of Surgical Oncology*, 107(5), 529–535. <https://doi.org/10.1002/jso.23287>
- Gray, S. L., LaCroix, A. Z., Hanlon, J. T., Penninx, B. W., Blough, D. K., Leveille, S. G., ... Buchner, D. M. (2006). Benzodiazepine use and physical disability in community-dwelling older adults. *Journal of the American Geriatrics Society*, 54(2), 224–230. <https://doi.org/10.1111/j.1532-5415.2005.00571.x>
- Gray, S. L., Penninx, B. W. J. H., Blough, D. K., Artz, M. B., Guralnik, J. M., Wallace, R. B., ... LaCroix, A. Z. (2003). Benzodiazepine use and physical performance in community-dwelling older women. *Journal of the American Geriatrics Society*, 51(11), 1563–1570. <https://doi.org/10.1046/j.1532-5415.2003.51502.x>
- Gulliford, M., & Ravindrarajah, R. (2018). Frailty: from clinical syndrome to epidemiological construct? *The Lancet Public Health*, 3(7), e305–e306. [https://doi.org/10.1016/S2468-2667\(18\)30112-9](https://doi.org/10.1016/S2468-2667(18)30112-9)
- Gupta, H., Gupta, P. K., Schuller, D., Fang, X., Miller, W. J., Modrykamien, A., ... Morrow, L. E. (2013). Development and validation of a risk calculator for predicting postoperative pneumonia. *Mayo Clinic Proceedings*, 88(11), 1241–1249. <https://doi.org/10.1016/j.mayocp.2013.06.027>
- Guth, A. A., Hiotis, K., & Rockman, C. (2005). Influence of Gender on Surgical Outcomes: Does Gender Really Matter? <https://doi.org/10.1016/j.jamcollsurg.2004.09.049>
- Haga, Y., Ikei, S., & Ogawa, M. (1999). Estimation of physiologic ability and surgical stress (E-PASS) as a new prediction scoring system for postoperative morbidity and mortality following elective gastrointestinal surgery. *Surgery Today*, 29(3), 219–225. <https://doi.org/10.1007/BF02483010>
- Haga, Y., Wada, Y., Takeuchi, H., Kimura, O., Furuya, T., Sameshima, H., & Ishikawa, M. (2004). Clinical research Estimation of physiologic ability and surgical stress (E-PASS) for a surgical audit in elective digestive surgery. *Surgery*, 135(6), 586–594. <https://doi.org/10.1016/j.surg.2003.11.012>
- Hall, D. E., Arya, S., Schmid, K. K., Blaser, C., Carlson, M. A., Bailey, T. L., ... Johanning, J. (2016). Development and Initial Validation of the Risk Analysis Index for Measuring Frailty in Surgical Populations. *JAMA Surgery*, 152(2), 1–8. <https://doi.org/10.1001/jamasurg.2016.4202>
- Hall, D. E., Arya, S., Schmid, K. K., Carlson, M. A., Lavedan, P., Bailey, T. L., ... Johanning, J. M. (2017). Association of a Frailty Screening Initiative With Postoperative Survival at 30, 180, and 365 Days. *JAMA Surgery*, 152(3), 233. <https://doi.org/10.1001/jamasurg.2016.4219>
- Handforth, C., Clegg, A., Young, C., Simpkins, S., Seymour, M. T., Selby, P. J., & Young, J. (2015). The prevalence and outcomes of frailty in older cancer patients: a systematic review. *Annals of Oncology : Official Journal of the European Society for Medical Oncology*, 26(6), 1091–1101. <https://doi.org/10.1093/annonc/mdu540>
- Hardeman, R. R., Murphy, K. A., Karbeah, J., & Kozhimannil, K. B. (2018). Naming Institutionalized Racism in the Public Health Literature: A Systematic Literature Review.

- Public Health Reports*. <https://doi.org/10.1177/0033354918760574>
- Harris, J. (2016). Frailty, Sarcopenia Increased Risk for Hospitalization, Functional Decline in Diabetics. *Caring for the Ages*, 17(10), 15. <https://doi.org/10.1016/j.carage.2016.09.012>
- Hazzard, W. R. (1999). *Principles of geriatric medicine and gerontology*. McGraw-Hill, Health Professions Division.
- Healy, M. A., Mullard, A. J., Campbell, D. A., & Dimick, J. B. (2016). Hospital and Payer Costs Associated With Surgical Complications. *JAMA Surgery*, 151(9), 823. <https://doi.org/10.1001/jamasurg.2016.0773>
- Hilmer, S. N., Mager, D. E., Simonsick, E. M., Cao, Y., Ling, S. M., Windham, B. G., ... Abernethy, D. R. (2007). A drug burden index to define the functional burden of medications in older people. *Archives of Internal Medicine*, 167(8), 781–787. <https://doi.org/10.1001/archinte.167.8.781>
- Hilmer, S. N., Mager, D. E., Simonsick, E. M., Ling, S. M., Windham, B. G., Harris, T. B., ... Abernethy, D. R. (2009). Drug Burden Index Score and Functional Decline in Older People. *American Journal of Medicine*, 122(12). <https://doi.org/10.1016/j.amjmed.2009.02.021>
- Hirose, J., Taniwaki, T., Fujimoto, T., Okada, T., Nakamura, T., Usuku, K., & Mizuta, H. (2015). Validity of E-PASS system for postoperative morbidity of spinal surgery. *Journal of Spinal Disorders and Techniques*, 28(10), E595–E600. <https://doi.org/10.1097/BSD.0000000000000056>
- Hodari, A., Hammoud, Z. T., Borgi, J. F., Tsiouris, A., & Rubinfeld, I. S. (2013). Assessment of morbidity and mortality after esophagectomy using a modified frailty index. *Annals of Thoracic Surgery*, 96(4), 1240–1244. <https://doi.org/10.1016/j.athoracsur.2013.05.051>
- Hubbard, R. E., O'Mahony, M. S., Calver, B. L., & Woodhouse, K. W. (2008). Nutrition, inflammation, and leptin levels in aging and frailty. *Journal of the American Geriatrics Society*, 56(2), 279–284. <https://doi.org/10.1111/j.1532-5415.2007.01548.x>
- Hubbard, R. E., O'Mahony, M. S., Savva, G. M., Calver, B. L., & Woodhouse, K. W. (2009). Inflammation and frailty measures in older people. *Journal of Cellular and Molecular Medicine*, 13(9 B), 3103–3109. <https://doi.org/10.1111/j.1582-4934.2009.00733.x>
- Hulley S. B, Cummings S. R, Browner W. S, G. D. G. and N. T. B. (2013). *Designing clinical research*. (4th ed.). Philadelphia: Lippincott, Williams, and Wilkins.
- IBM Watson Health. (2018). *Hospital-Acquired Conditions lead to avoidable cost and excess deaths*. New York. Retrieved from [https://public.dhe.ibm.com/common/ssi/ecm/51/en/51020151usen/prov\\_19427\\_1018\\_hac\\_a\\_dverseoutcomes\\_rb\\_51020151USEN.pdf](https://public.dhe.ibm.com/common/ssi/ecm/51/en/51020151usen/prov_19427_1018_hac_a_dverseoutcomes_rb_51020151USEN.pdf)
- Ineke Neutel, C., Skurtveit, S., & Berg, C. (2012). Polypharmacy of potentially addictive medication in the older persons--quantifying usage. *Pharmacoepidemiology and Drug Safety*, 21(2), 199–206. <https://doi.org/10.1002/pds.2214>
- Jamieson, H. A., Nishtala, P. S., Scrase, R., Deely, J. M., Abey-Nesbit, R., Hilmer, S. N., ... Schluter, P. J. (2019). Drug Burden Index and Its Association with Hip Fracture among Older Adults: A National Population-Based Study. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 74(7), 1127–1133. <https://doi.org/10.1093/gerona/gly176>
- Jones, C. P. (2000). Levels of racism: A theoretic framework and a gardener's tale. *American Journal of Public Health*. American Public Health Association Inc. <https://doi.org/10.2105/AJPH.90.8.1212>
- Jones, D. M., Song, X., & Rockwood, K. (2004). Operationalizing a Frailty Index from a

- Standardized Comprehensive Geriatric Assessment. *Journal of the American Geriatrics Society*, 52(11), 1929–1933. <https://doi.org/10.1111/j.1532-5415.2004.52521.x>
- Jones, D., Song, X., Mitnitski, A., & Rockwood, K. (2005). Evaluation of a frailty index based on a comprehensive geriatric assessment in a population based study of elderly Canadians. *Aging Clinical and Experimental Research*, 17(6), 465–471. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/16485864>
- Jones, J., & Hunter, D. (1995). Qualitative Research: Consensus methods for medical and health services research. *BMJ*, 311(7001), 376. <https://doi.org/10.1136/bmj.311.7001.376>
- Joseph, B., Pandit, V., Zangbar, B., Kulvatunyou, N., Hashmi, A., Green, D. J., ... Rhee, P. (2014). Superiority of Frailty Over Age in Predicting Outcomes Among Geriatric Trauma Patients: A Prospective Analysis. *JAMA Surgery*, 85724(8), 766–772. <https://doi.org/10.1001/jamasurg.2014.296>
- Joseph, B., Zangbar, B., Pandit, V., Fain, M., Mohler, M. J., Kulvatunyou, N., ... Rhee, P. (2016). Emergency General Surgery in the Elderly: Too Old or Too Frail? Presented orally at the Surgical Forum of the American College of Surgeons 100th Annual Clinical Congress, San Francisco, CA, October 2014. *Journal of the American College of Surgeons*, 222(5), 805–813. <https://doi.org/10.1016/j.jamcollsurg.2016.01.063>
- Joseph, C., Kenny, A. M., Taxel, P., Lorenzo, J. A., Duque, G., & Kuchel, G. A. (2005). Role of endocrine-immune dysregulation in osteoporosis, sarcopenia, frailty and fracture risk. *Molecular Aspects of Medicine*, 26(3), 181–201. <https://doi.org/10.1016/j.mam.2005.01.004>
- Karam, J., Tsiouris, A., Shepard, A., Velanovich, V., & Rubinfeld, I. (2013). Simplified frailty index to predict adverse outcomes and mortality in vascular surgery patients. *Annals of Vascular Surgery*, 27(7), 904–908. <https://doi.org/10.1016/j.avsg.2012.09.015>
- Ke, L. S. (2013). Frailty in the elderly: A concept analysis. *Journal of Nursing*, 60(1), 105–110. <https://doi.org/10.1503/cmaj.050051>
- Keenan, J. E., Speicher, P. J., Thacker, J. K. M., Walter, M., Kuchibhatla, M., & Mantyh, C. R. (2014). The Preventive Surgical Site Infection Bundle in Colorectal Surgery. *JAMA Surgery*, 149(10), 1045. <https://doi.org/10.1001/jamasurg.2014.346>
- Kim, D., Lockett, M., Zhang, J., Mauldin, P., & Baliga, P. (2018). South Carolina Surgical Quality Collaborative Colon Surgery Outcomes Vary by Age and Race. *The American Surgeon*, 84(8), 1312–1313. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/30185307>
- Kim, S. W., Han, H. S., Jung, H. W., Kim, K. Il, Hwang, D. W., Kang, S. B., & Kim, C. H. (2014). Multidimensional frailty score for the prediction of postoperative mortality risk. *JAMA Surgery*, 149(7), 633–640. <https://doi.org/10.1001/jamasurg.2014.241>
- Korc-Grodzicki, B., Downey, R. J., Shahrokni, A., Kingham, T. P., Patel, S. G., & Audisio, R. A. (2014). Surgical Considerations in Older Adults With Cancer. *Journal of Clinical Oncology*, 32(24), 2647–2653. <https://doi.org/10.1200/JCO.2014.55.0962>
- Kotera, A., Haga, Y., Kei, J., Okamoto, M., & Seo, K. (n.d.). Evaluation of Estimation of Physiologic Ability and Surgical Stress to predict in-hospital mortality in cardiac surgery. <https://doi.org/10.1007/s00540-011-1162-z>
- Kouladjian, L., Gnjdjic, D., Chen, T. F., Mangoni, A. A., & Hilmer, S. N. (2014). Drug Burden Index in older adults: theoretical and practical issues. *Clinical Interventions in Aging*, 9, 1503–1515. <https://doi.org/10.2147/CIA.S66660>
- Koyama, A., Steinman, M., Ensrud, K., Hillier, T. A., & Yaffe, K. (2014). Long-term cognitive and functional effects of potentially inappropriate medications in older women. *Journals of*

- Gerontology - Series A Biological Sciences and Medical Sciences*, 69(4), 423–429.  
<https://doi.org/10.1093/gerona/glt192>
- Kramer, M. W., Hennig, M. J., von Klot, C. A. J., Wegener, G., Heinisch, A., Peters, I., ... Merseburger, A. S. (2015). Correlation of the clinical frailty scale with long-term survival after radical cystectomy. *Journal of Clinical Oncology*, 33(7\_suppl), 314–314.  
[https://doi.org/10.1200/jco.2015.33.7\\_suppl.314](https://doi.org/10.1200/jco.2015.33.7_suppl.314)
- Kristjansson, S. R., Nesbakken, A., Jordhøy, M. S., Skovlund, E., Audisio, R. A., Johannessen, H.-O., ... Wyller, T. B. (2010). Comprehensive geriatric assessment can predict complications in elderly patients after elective surgery for colorectal cancer: A prospective observational cohort study. *Critical Reviews in Oncology/Hematology*, 76(3), 208–217.  
<https://doi.org/10.1016/J.CRITREVONC.2009.11.002>
- Kristjansson, S. R., Rønning, B., Hurria, A., Skovlund, E., Jordhøy, M. S., Nesbakken, A., & Wyller, T. B. (2012). A comparison of two pre-operative frailty measures in older surgical cancer patients. *Journal of Geriatric Oncology*, 3(1), 1–7.  
<https://doi.org/10.1016/j.jgo.2011.09.002>
- Landi, F., Russo, A., Liperoti, R., Cesari, M., Barillaro, C., Pahor, M., ... Onder, G. (2007). Anticholinergic drugs and physical function among frail elderly population. *Clinical Pharmacology and Therapeutics*, 81(2), 235–241. <https://doi.org/10.1038/sj.clpt.6100035>
- Le Maguet, P., Roquilly, A., Lasocki, S., Asehnoune, K., Carise, E., Saint Martin, M., ... Seguin, P. (2014). Prevalence and impact of frailty on mortality in elderly ICU patients: a prospective, multicenter, observational study. *Intensive Care Medicine*, 40(5), 674–682.  
<https://doi.org/10.1007/s00134-014-3253-4>
- Lee, D. H., Buth, K. J., Martin, B.-J., Yip, A. M., & Hirsch, G. M. (2010). Cardiovascular Surgery Frail Patients Are at Increased Risk for Mortality and Prolonged Institutional Care After Cardiac Surgery. <https://doi.org/10.1161/CIRCULATIONAHA.108.841437>
- Leng, S., Chaves, P., Koenig, K., & Walston, J. (2002). Serum levels of insulin-like growth factor-I and dehydroepiandrosterone sulfate and their relationship with serum interleukin-6 in the geriatric syndrome of frailty. *Journal of American Geriatrics Society*, 50(2), 1268–1271.
- Li, L. T., Barden, G. M., Balentine, C. J., Orcutt, S. T., Naik, A. D., Artinyan, A., ... Anaya, D. A. (2015). Postoperative Transitional Care Needs in the Elderly. *Annals of Surgery*, 261(4), 695–701. <https://doi.org/10.1097/SLA.0000000000000673>
- Liu, Y., Cohen, M. E., Hall, B. L., Ko, C. Y., & Bilimoria, K. Y. (2016). Evaluation and Enhancement of Calibration in the American College of Surgeons NSQIP Surgical Risk Calculator. *Journal of the American College of Surgeons*, 223(2), 231–239.  
<https://doi.org/10.1016/j.jamcollsurg.2016.03.040>
- López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M., & Kroemer, G. (2013). The Hallmarks of Aging Europe PMC Funders Group. *Cell*, 153(6), 1194–1217.  
<https://doi.org/10.1016/j.cell.2013.05.039>
- Louwers, L., Schnickel, G., & Rubinfeld, I. (2016). Clinical Science Use of a simplified frailty index to predict Clavien 4 complications and mortality after hepatectomy: analysis of the National Surgical Quality Improvement Project database. *The American Journal of Surgery*, 211, 1071–1076. <https://doi.org/10.1016/j.amjsurg.2015.09.015>
- Mahanna-Gabrielli, E., Zhang, K., Sieber, F. E., Lin, H. M., Liu, X., Sewell, M., ... Boockvar, K. S. (2020). Frailty Is Associated With Postoperative Delirium But Not With Postoperative Cognitive Decline in Older Noncardiac Surgery Patients. *Anesthesia and Analgesia*, 130(6),

- 1516–1523. <https://doi.org/10.1213/ANE.0000000000004773>
- Makary, M. A., Segev, D. L., Pronovost, P. J., Syin, D., Bandeen-Roche, K., Patel, P., ... Fried, L. P. (2010). Frailty as a Predictor of Surgical Outcomes in Older Patients. *J AM Coll Surg*, *210*(6), 901–908. <https://doi.org/10.1016/j.jamcollsurg.2010.01.028>
- Marcum, Z. A., & Hanlon, J. T. (2012). Commentary on the new American geriatric society beers criteria for potentially inappropriate medication use in older adults. *American Journal Geriatric Pharmacotherapy*, *10*(2), 151–159. <https://doi.org/10.1016/j.amjopharm.2012.03.002>
- McCarthy, A. L., Peel, N. M., Gillespie, K. M., Berry, R., Walpole, E., Yates, P., & Hubbard, R. E. (2018). Validation of a frailty index in older cancer patients with solid tumours. *BMC Cancer*, *18*(1), 892. <https://doi.org/10.1186/s12885-018-4807-6>
- Mcdowell, I., Hill, G., & Helliwell, B. (2001). Disability and Frailty Among Elderly Canadians: A Comparison of Six Surveys. *International Psychogeriatrics*, *13*(S1), 159–167. <https://doi.org/10.1017/S1041610202008104>
- McIsaac, D. I., Bryson, G. L., van Walraven, C., RS, J., L, C., T, T., ... P, M. (2016). Association of Frailty and 1-Year Postoperative Mortality Following Major Elective Noncardiac Surgery. *JAMA Surgery*, *151*(6), 538. <https://doi.org/10.1001/jamasurg.2015.5085>
- McIsaac, D. I., Jen, T., Mookerji, N., Patel, A., & Lalu, M. M. (2017). Interventions to improve the outcomes of frail people having surgery: A systematic review. *PLoS ONE*, *12*(12), 1–18. <https://doi.org/10.1371/journal.pone.0190071>
- McIsaac, D. I., MacDonald, D. B., & Aucoin, S. D. (2020). Frailty for Perioperative Clinicians: A Narrative Review. *Anesthesia and Analgesia*, *130*(6), 1450–1460. <https://doi.org/10.1213/ANE.0000000000004602>
- McIsaac, D. I., Taljaard, M., Bryson, G. L., Beaulé, P. E., Gagné, S., Hamilton, G., ... Forster, A. J. (2016). Comparative assessment of two frailty instruments for risk-stratification in elderly surgical patients: Study protocol for a prospective cohort study. *BMC Anesthesiology*, *16*(1). <https://doi.org/10.1186/s12871-016-0276-0>
- McIsaac, D. I., Taljaard, M., Bryson, G. L., Beaulé, P. E., Gagné, S., Hamilton, G., ... Forster, A. J. (2018). Frailty as a Predictor of Death or New Disability After Surgery. *Annals of Surgery*, *1*. <https://doi.org/10.1097/SLA.0000000000002967>
- McIsaac, D. I., Wijeyesundera, D. N., Huang, A., Bryson, G. L., & van Walraven, C. (2017). Association of the Hospital Volume of Frail Surgical Patients Cared for with Outcomes after Elective, Major Noncardiac Surgery. *Anesthesiology*, *126*(4), 602–613. <https://doi.org/10.1097/ALN.0000000000001536>
- McMillan, S. S., King, M., & Tully, M. P. (2016, June 1). How to use the nominal group and Delphi techniques. *International Journal of Clinical Pharmacy*. Springer Netherlands. <https://doi.org/10.1007/s11096-016-0257-x>
- Mechanic, R. (2014). Post-Acute Care — The Next Frontier for Controlling Medicare Spending. *New England Journal of Medicine*, *370*(8), 692–694. <https://doi.org/10.1056/NEJMp1315607>
- Mitnitski, A., Collerton, J., Martin-Ruiz, C., Jagger, C., von Zglinicki, T., Rockwood, K., & Kirkwood, T. B. L. (2015). Age-related frailty and its association with biological markers of ageing. *BMC Medicine*, *13*(1), 161. <https://doi.org/10.1186/s12916-015-0400-x>
- Mitnitski, A B, Mogilner, A. J., & Rockwood, K. (2001). Accumulation of deficits as a proxy measure of aging. *TheScientificWorldJournal*, *1*, 323–336.

- <https://doi.org/10.1100/tsw.2001.58>
- Mitnitski, Arnold B, Mogilner, A. J., MacKnight, C., & Rockwood, K. (2002). The mortality rate as a function of accumulated deficits in a frailty index. *Mechanisms of Ageing and Development*, 123(11), 1457–1460. [https://doi.org/10.1016/S0047-6374\(02\)00082-9](https://doi.org/10.1016/S0047-6374(02)00082-9)
- Mogal, H., Vermilion, S. A., Dodson, R., Hsu, F.-C. C., Howerton, R., Shen, P., & Clark, C. J. (2017a). Modified Frailty Index Predicts Morbidity and Mortality After Pancreaticoduodenectomy. *Annals of Surgical Oncology*, 24(6), 1714–1721. <https://doi.org/10.1245/s10434-016-5715-0>
- Mogal, H., Vermilion, S. A., Dodson, R., Hsu, F.-C., Howerton, R., Shen, P., & Clark, C. J. (2017b). Modified Frailty Index Predicts Morbidity and Mortality After Pancreaticoduodenectomy. *Annals of Surgical Oncology*, 24(6), 1714–1721. <https://doi.org/10.1245/s10434-016-5715-0>
- Mohanty, S., Liu, Y., Paruch, J. L., Kmiecik, T. E., Cohen, M. E., Ko, C. Y., & Bilimoria, K. Y. (2015). Risk of Discharge to Postacute Care. *JAMA Surgery*, 150(5), 480. <https://doi.org/10.1001/jamasurg.2014.3176>
- Mohanty, S., Rosenthal, R. A., Russell, M. M., Neuman, M. D., Ko, C. Y., & Esnaola, N. F. (2016). Optimal Perioperative Management of the Geriatric Patient: A Best Practices Guideline from the American College of Surgeons NSQIP and the American Geriatrics Society. *Journal of the American College of Surgeons*, 222(5), 930–947. <https://doi.org/10.1016/j.jamcollsurg.2015.12.026>
- Montgomery, C. L., Rolfson, D. B., & Bagshaw, S. M. (2018). Frailty and the Association Between Long-Term Recovery After Intensive Care Unit Admission. *Critical Care Clinics*, 34(4), 527–547. <https://doi.org/10.1016/j.ccc.2018.06.007>
- Morley, J. E., Vellas, B., Abellan van Kan, G., Anker, S. D., Bauer, J. M., Bernabei, R., ... Walston, J. (2013). Frailty consensus: A call to action. *Journal of the American Medical Directors Association*, 14(6), 392–397. <https://doi.org/10.1016/j.jamda.2013.03.022>
- Mulsant, B. H., Pollock, B. G., Kirshner, M., Shen, C., Dodge, H., & Ganguli, M. (2003). Serum anticholinergic activity in a community-based sample of older adults: Relationship with cognitive performance. *Archives of General Psychiatry*, 60(2), 198–203. <https://doi.org/10.1001/archpsyc.60.2.198>
- Muscudere, J., Waters, B., Varambally, A., Bagshaw, S. M., Boyd, J. G., Maslove, D., ... Rockwood, K. (2017). The impact of frailty on intensive care unit outcomes: a systematic review and meta-analysis. *Intensive Care Medicine*, 43(8), 1105–1122. <https://doi.org/10.1007/s00134-017-4867-0>
- Nagata, T., Hirose, J., Nakamura, T., Tokunaga, T., Uehara, Y., & Mizuta, H. (2015). Evaluation of the utility of the Estimation of Physiologic Ability and Surgical Stress score for predicting post-operative morbidity after orthopaedic surgery. *International Orthopaedics*, 39, 2167–2172. <https://doi.org/10.1007/s00264-015-2993-2>
- Negm, A. M., Kennedy, C. C., Ioannidis, G., Gajic-Veljanoski, O., Lee, J., Thabane, L., ... Papaioannou, A. (2018). Getting fit for hip and knee replacement: a protocol for the Fit-Joints pilot randomized controlled trial of a multi-modal intervention in frail patients with osteoarthritis. *Pilot and Feasibility Studies*, 4(1), 127. <https://doi.org/10.1186/s40814-018-0316-2>
- Nidadavolu, L. S., Ehrlich, A. L., Sieber, F. E., & Oh, E. S. (2020). Preoperative Evaluation of the Frail Patient. *Anesthesia and Analgesia*, 130(6), 1493–1503. <https://doi.org/10.1213/ANE.0000000000004735>

- Nishtala, P. S., Narayan, S. W., Wang, T., & Hilmer, S. N. (2014). Associations of drug burden index with falls, general practitioner visits, and mortality in older people. *Pharmacoepidemiology and Drug Safety*, 23(7), 753–758. <https://doi.org/10.1002/pds.3624>
- Obeid, N. M., Azuh, O., Reddy, S., Webb, S., Reickert, C., Velanovich, V., ... Rubinfeld, I. (2012). Predictors of critical care-related complications in colectomy patients using the National Surgical Quality Improvement Program: Exploring frailty and aggressive laparoscopic approaches. *Journal of Trauma and Acute Care Surgery*, 72(4), 878–883. <https://doi.org/10.1097/TA.0b013e31824d0f70>
- Partridge, J. S. L., Harari, D., Martin, F. C., Peacock, J. L., Bell, R., Mohammed, A., & Dhesi, J. K. (2017). Randomized clinical trial of comprehensive geriatric assessment and optimization in vascular surgery. *British Journal of Surgery*, 104(6), 679–687. <https://doi.org/10.1002/bjs.10459>
- Partridge, Judith S L, Harari, D., & Dhesi, J. K. (2012). Frailty in the older surgical patient: A review. *Age and Ageing*, 41(2), 142–147. <https://doi.org/10.1093/ageing/afr182>
- Paul, J. A., Whittington, R. A., & Baldwin, M. R. (2020). Critical Illness and the Frailty Syndrome: Mechanisms and Potential Therapeutic Targets. *Anesthesia and Analgesia*, 130(6), 1545–1555. <https://doi.org/10.1213/ANE.0000000000004792>
- Phelan, J. C., Link, B. G., & Tehranifar, P. (2010). Social Conditions as Fundamental Causes of Health Inequalities: Theory, Evidence, and Policy Implications. *Journal of Health and Social Behavior*, 51(1\_suppl), S28–S40. <https://doi.org/10.1177/0022146510383498>
- Polit, D., & Tatano-Beck, C. (2017). *Nursing Research generating and assessing evidence for nursing practice* (10th ed.). New York: Wolters-Kluwer.
- Powell, C. (2003, February 15). The Delphi technique: Myths and realities. *Journal of Advanced Nursing*. <https://doi.org/10.1046/j.1365-2648.2003.02537.x>
- Puts, M. T. E., Toubasi, S., Andrew, M. K., Ashe, M. C., Ploeg, J., Atkinson, E., ... Mcgilton, K. (2017). Interventions to prevent or reduce the level of frailty in community-dwelling older adults: A scoping review of the literature and international policies. *Age and Ageing*, 46(3), 383–392. <https://doi.org/10.1093/ageing/afw247>
- Puts, M. T. E., Visser, M., Twisk, J. W. R., Deeg, D. J. H., & Lips, P. (2005). Endocrine and inflammatory markers as predictors of frailty. *Clinical Endocrinology*, 63(4), 403–411. <https://doi.org/10.1111/j.1365-2265.2005.02355.x>
- Rana, N., Gosain, R., Lemini, R., Wang, C., Gabriel, E., Mohammed, T., ... Mukherjee, S. (2020). Socio-Demographic Disparities in Gastric Adenocarcinoma: A Population-Based Study. *Cancers*, 12(1), 157. <https://doi.org/10.3390/cancers12010157>
- Ravindrarajah, R., Lee, D. M., Pye, S. R., Gielen, E., Boonen, S., Vanderschueren, D., ... European Male Aging Study Group. (2013). The ability of three different models of frailty to predict all-cause mortality: results from the European Male Aging Study (EMAS). *Archives of Gerontology and Geriatrics*, 57(3), 360–368. <https://doi.org/10.1016/j.archger.2013.06.010>
- Ritt, M., Schwarz, C., Kronawitter, V., Delinic, A., Bollheimer, L. C., Gassmann, K.-G., & Sieber, C. C. (2015). Analysis of Rockwood et al's Clinical Frailty Scale and Fried et al's frailty phenotype as predictors of mortality and other clinical outcomes in older patients who were admitted to a geriatric ward. *The Journal of Nutrition, Health & Aging*, 19(10), 1043–1048. <https://doi.org/10.1007/s12603-015-0667-9>
- Robinson, T. N., Walston, J. D., Brummel, N. E., Deiner, S., Brown Iv, C. H., Kennedy, M., & Hurria, A. (2015). Frailty for Surgeons: Review of a National Institute on Aging Conference



- on Frailty for Specialists. *Journal of the American College of Surgeons*, 221(6), 1083–1092. <https://doi.org/10.1016/j.jamcollsurg.2015.08.428>
- Robinson, T. N., Wu, D. S., Pointer, L., Dunn, C. L., Cleveland, J. C., & Moss, M. (2013a). Simple Frailty Score Predicts Post-Operative Complications Across Surgical Specialties. *American Journal of Surgery*, 206(4), 544–550. <https://doi.org/10.1016/j.amjsurg.2013.03.012>
- Robinson, T. N., Wu, D. S., Pointer, L., Dunn, C. L., Cleveland, J. C., & Moss, M. (2013b). Simple frailty score predicts postoperative complications across surgical specialties. *The American Journal of Surgery*, 206(4), 544–550. <https://doi.org/10.1016/j.amjsurg.2013.03.012>
- Rockwood, K., Andrew, M., & Mitnitski, A. (2007). A Comparison of Two Approaches to Measuring Frailty in Elderly People. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 62(7), 738–743. <https://doi.org/10.1093/gerona/62.7.738>
- Rockwood, K., & Mitnitski, A. (2012). How might deficit accumulation give rise to frailty? *The Journal of Frailty & Aging*, 1(1), 8–12. <https://doi.org/10.14283/jfa.2012.2>
- Rockwood, K., Song, X., MacKnight, C., Bergman, H., Hogan, D. B., McDowell, I., & Mitnitski, A. (2005). A global clinical measure of fitness and frailty in elderly people. *Canadian Medical Association Journal*, 173(5), 489–495. <https://doi.org/10.1503/cmaj.050051>
- Rockwood, K., Song, X., & Mitnitski, A. (2011). Changes in relative fitness and frailty across the adult lifespan: evidence from the Canadian National Population Health Survey. *Canadian Medical Association Journal*, 183(8), E487–E494. <https://doi.org/10.1503/cmaj.101271>
- Rockwood, K., Wolfson, C., & McDowell, I. (2001). The Canadian Study of Health and Aging: organizational lessons from a national, multicenter, epidemiologic study. *Int Psychogeriatr*, 13 Supp 1(S1), 233–237. <https://doi.org/10.1017/S1041610202008177>
- Rockwood, Kenneth. (2016). Conceptual Models of Frailty: Accumulation of Deficits. *Canadian Journal of Cardiology*, 32(9), 1046–1050. <https://doi.org/10.1016/j.cjca.2016.03.020>
- Rockwood, Kenneth, & Mitnitski, A. (2007). Frailty in relation to the accumulation of deficits. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 62(7), 722–727. <https://doi.org/10.1093/gerona/62.7.722>
- Rockwood, Kenneth, Rockwood, M. R. H., & Mitnitski, A. (2010). Physiological redundancy in older adults in relation to the change with age in the slope of a frailty index. *Journal of the American Geriatrics Society*, 58(2), 318–323. <https://doi.org/10.1111/j.1532-5415.2009.02667.x>
- Runner, R. P., Bellamy, J. L., Vu, C. C. L., Erens, G. A., Schenker, M. L., & Guild, G. N. (2017). Modified Frailty Index Is an Effective Risk Assessment Tool in Primary Total Knee Arthroplasty. *The Journal of Arthroplasty*, 32(10), 2963–2968. <https://doi.org/https://doi.org/10.1016/j.arth.2017.04.056>
- Sadiq, F., Kronzer, V. L., Wildes, T. S., McKinnon, S. L., Sharma, A., Helsten, D. L., ... Abdallah, A. Ben. (2018). Frailty phenotypes and relations with surgical outcomes: A latent class analysis. *Anesthesia and Analgesia*, 127(4), 1017–1027. <https://doi.org/10.1213/ANE.0000000000003695>
- Sadiq, F., Kronzer, V. L., Wildes, T. S., McKinnon, S. L., Sharma, A., Helsten, D. L., ... Ben Abdallah, A. (2018). Frailty Phenotypes and Relations With Surgical Outcomes. *Anesthesia & Analgesia*, 1. <https://doi.org/10.1213/ANE.0000000000003695>

- Sahara, K., Paredes, A. Z., Merath, K., Tsilimigras, D. I., Bagante, F., Ratti, F., ... Pawlik, T. M. (2019). Evaluation of the ACS NSQIP Surgical Risk Calculator in Elderly Patients Undergoing Hepatectomy for Hepatocellular Carcinoma. *Journal of Gastrointestinal Surgery*. <https://doi.org/10.1007/s11605-019-04174-4>
- Sankar, A., Johnson, S. R., Beattie, W. S., Tait, G., Wijesundera, D. N., & Myles, P. S. (2014). Reliability of the American Society of Anesthesiologists physical status scale in clinical practice. *BJA: British Journal of Anaesthesia*, *113*(3), 424–432. <https://doi.org/10.1093/bja/aeu100>
- Saxton, A., & Velanovich, V. (2011). Preoperative Frailty and Quality of Life as Predictors of Postoperative Complications. *Annals of Surgery*, *253*(6), 1223–1229. <https://doi.org/10.1097/SLA.0b013e318214bce7>
- Schalk, B. W. M., Visser, M., Deeg, D. J. H., & Bouter, L. M. (2004). Lower levels of serum albumin and total cholesterol and future decline in functional performance in older persons: The Longitudinal Aging Study Amsterdam. *Age and Ageing*, *33*(3), 266–272. <https://doi.org/10.1093/ageing/afh073>
- Schwarze, M. L., Barnato, A. E., Rathouz, P. J., Zhao, Q., Neuman, H. B., Winslow, E. R., ... Greenberg, C. C. (2015). Development of a list of high-risk operations for patients 65 years and older. *JAMA Surgery*, *150*(4), 325–331. <https://doi.org/10.1001/jamasurg.2014.1819>
- Seib, C. D., Rochefort, H., Chomsky-Higgins, K., Gosnell, J. E., Suh, I., Shen, W. T., ... Finlayson, E. (2018). Association of Patient Frailty With Increased Morbidity After Common Ambulatory General Surgery Operations. *JAMA Surgery*, *153*(2), 160. <https://doi.org/10.1001/jamasurg.2017.4007>
- Shah, R., Attwood, K., Arya, S., Hall, D. E., Johanning, J. M., Gabriel, E., ... Massarweh, N. N. (2018). Association of Frailty With Failure to Rescue After Low-Risk and High-Risk Inpatient Surgery. *JAMA Surgery*, e180214. <https://doi.org/10.1001/jamasurg.2018.0214>
- Shahrokni, A., Tin, A., Alexander, K., Sarraf, S., Afonso, A., Filipova, O., ... Korc-Grodzicki, B. (2018). Memorial Sloan Kettering-Frailty Index (MSK-FI): Validation and its relationship with postoperative outcomes of older survivors of cancer. *Journal of Clinical Oncology*, *36*(34\_suppl), 172–172. [https://doi.org/10.1200/JCO.2018.36.34\\_suppl.172](https://doi.org/10.1200/JCO.2018.36.34_suppl.172)
- Shahrokni, A., Tin, A., Alexander, K., Sarraf, S., Afonso, A., Filippova, O., ... Korc-Grodzicki, B. (2019). Development and Evaluation of a New Frailty Index for Older Surgical Patients With Cancer. *JAMA Network Open*, *2*(5), e193545. <https://doi.org/10.1001/jamanetworkopen.2019.3545>
- Shahrokni, A., Tin, A., Downey, R. J., Strong, V., Mahmoudzadeh, S., Boparai, M. K., ... Korc-Grodzicki, B. (2017). Electronic Rapid Fitness Assessment: A Novel Tool for Preoperative Evaluation of the Geriatric Oncology Patient. *Journal of the National Comprehensive Cancer Network : JNCCN*, *15*(2), 172–179. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/28188187>
- Shahrokni, A., Vickers, A. J., Mahmoudzadeh, S., & Korc-Grodzicki, B. (2016). Assessing the clinical feasibility of electronic Rapid Fitness Assessment (eRFA): A novel geriatric assessment tool for the oncology setting. *Journal of Clinical Oncology*, *34*(15\_suppl), 10011–10011. [https://doi.org/10.1200/JCO.2016.34.15\\_suppl.10011](https://doi.org/10.1200/JCO.2016.34.15_suppl.10011)
- Shardell, M., Hicks, G. E., Miller, R. R., Kritchevsky, S., Andersen, D., Bandinelli, S., ... Ferrucci, L. (2009). Association of low vitamin D levels with the frailty syndrome in men and women. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, *64*(1), 69–75. <https://doi.org/10.1093/gerona/gln007>

- Shin, J. I., Keswani, A., Lovy, A. J., & Moucha, C. S. (2016). Simplified Frailty Index as a Predictor of Adverse Outcomes in Total Hip and Knee Arthroplasty. *The Journal of Arthroplasty*, 31(11), 2389–2394. <https://doi.org/10.1016/J.ARTH.2016.04.020>
- Shin, J. I., Kothari, P., Phan, K., Kim, J. S., Leven, D., Lee, N. J., & Cho, S. K. (2017). Frailty Index as a Predictor of Adverse Postoperative Outcomes in Patients Undergoing Cervical Spinal Fusion. *SPINE*, 42(5), 304–310. <https://doi.org/10.1097/BRS.0000000000001755>
- Shinall, M. C., Arya, S., Youk, A., Varley, P., Shah, R., Massarweh, N. N., ... Hall, D. E. (2019). Association of Preoperative Patient Frailty and Operative Stress With Postoperative Mortality. *JAMA Surgery*, 15213, e194620. <https://doi.org/10.1001/jamasurg.2019.4620>
- Simon, M. K., & Goes, J. (2013). *Dissertation and scholarly research : recipes for success : a practical guide to start and complete your dissertation, thesis or formal research project* (13th ed.). Dissertation Success LLC.
- Singer, J. P., Lederer, D. J., & Baldwin, M. R. (2016). Frailty in pulmonary and critical care medicine. *Annals of the American Thoracic Society*, 13(8), 1394–1404. <https://doi.org/10.1513/AnnalsATS.201512-833FR>
- Song, X., MacKnight, C., Latta, R., Mitnitski, A. B., & Rockwood, K. (2007). Frailty and survival of rural and urban seniors: results from the Canadian Study of Health and Aging. *Aging Clinical and Experimental Research*, 19(2), 145–153. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/17446726>
- Soysal, P., Stubbs, B., Lucato, P., Luchini, C., Solmi, M., Peluso, R., ... Veronese, N. (2016). Inflammation and frailty in the elderly: A systematic review and meta-analysis. *Ageing Research Reviews*, 31, 1–8. <https://doi.org/10.1016/j.arr.2016.08.006>
- Strandberg, T. E., & Pitkala, K. H. (2007). Frailty in elderly people. *Lancet*, 369, 1328–1329. [https://doi.org/10.1016/S0140-6736\(12\)62167-9](https://doi.org/10.1016/S0140-6736(12)62167-9)
- Strawbridge, W. J., Shema, S. J., Balfour, J. L., Higby, H. R., & Kaplan, G. A. (1998). Antecedents of frailty over three decades in an older cohort. *The Journals of Gerontology. Series B, Psychological Sciences and Social Sciences*, 53(1), S9-16. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed/9469175>
- Studenski, S. A., Peters, K. W., Alley, D. E., Cawthon, P. M., McLean, R. R., Harris, T. B., ... Vassileva, M. T. (2014). The FNIH sarcopenia project: Rationale, study description, conference recommendations, and final estimates. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences*, 69 A(5), 547–558. <https://doi.org/10.1093/gerona/glu010>
- Suskind, A. M., Jin, C., Cooperberg, M. R., Finlayson, E., Boscardin, W. J., Sen, S., & Walter, L. C. (2016). Preoperative Frailty Is Associated With Discharge to Skilled or Assisted Living Facilities After Urologic Procedures of Varying Complexity. *Urology*, 97. <https://doi.org/10.1016/j.urology.2016.03.073>
- Swiecicka, A., Eendebak, R. J. A. H., Lunt, M., O'Neill, T. W., Bartfai, G., Casanueva, F. F., ... Rutter, M. K. (2018). Reproductive hormone levels predict changes in frailty status in community-dwelling older men: European male ageing study prospective data. *Journal of Clinical Endocrinology and Metabolism*, 103(2), 701–709. <https://doi.org/10.1210/jc.2017-01172>
- Tabachnick, B. G., & Fidell, L. S. (2013). *Using multivariate statistics* (6th ed.). Pearson Education.
- Tang, T., Walsh, S. R., Fanshawe, T. R., Gillard, J. H., Sadat, U., Varty, K., ... Boyle, J. R. (2007). Clinical surgery-International Estimation of physiologic ability and surgical stress

- (E-PASS) as a predictor of immediate outcome after elective abdominal aortic aneurysm surgery. <https://doi.org/10.1016/j.amjsurg.2006.10.032>
- Tang, T. Y., Walsh, S. R., Fanshawe, T. R., Seppi, V., Sadat, U., Hayes, P. D., ... Boyle, J. R. (2007). Comparison of Risk-scoring Methods in Predicting the Immediate Outcome after Elective Open Abdominal Aortic Aneurysm Surgery. *Eur J Vasc Endovasc Surg*, *34*, 505–513. <https://doi.org/10.1016/j.ejvs.2007.07.019>
- Tiidus, P. M., Lowe, D. A., & Brown, M. (2013). Estrogen replacement and skeletal muscle: mechanisms and population health. *Journal of Applied Physiology*, *115*(5), 569. <https://doi.org/10.1152/JAPPLPHYSIOL.00629.2013>
- Tominaga, T., Takeshita, H., Takagi, K., Kunizaki, M., To, K., Abo, T., ... Sawai, T. (2016). E-PASS score as a useful predictor of postoperative complications and mortality after colorectal surgery in elderly patients. *Int J Colorectal Dis*, *31*, 217–225. <https://doi.org/10.1007/s00384-015-2456-7>
- Tsiouris, A., Hammoud, Z. T., Velanovich, V., Hodari, A., Borgi, J., & Rubinfeld, I. (2013). A modified frailty index to assess morbidity and mortality after lobectomy. *Journal of Surgical Research*, *183*(1), 40–46. <https://doi.org/10.1016/j.jss.2012.11.059>
- Uppal, S., Igwe, E., Rice, L. W., Spencer, R. J., & Rose, S. L. (2015). Frailty index predicts severe complications in gynecologic oncology patients. *Gynecologic Oncology*, *137*(1), 98–101. <https://doi.org/10.1016/j.ygyno.2015.01.532>
- Velanovich, V., Antoine, H., Swartz, A., Peters, D., & Rubinfeld, I. (2013). Accumulating deficits model of frailty and postoperative mortality and morbidity: Its application to a national database. *Journal of Surgical Research*, *183*(1), 104–110. <https://doi.org/10.1016/j.jss.2013.01.021>
- Vidán, M., Serra, J. A., Moreno, C., Riquelme, G., & Ortiz, J. (2005). Efficacy of a Comprehensive Geriatric Intervention in Older Patients Hospitalized for Hip Fracture: A Randomized, Controlled Trial. *Journal of the American Geriatrics Society*, *53*(9), 1476–1482. <https://doi.org/10.1111/j.1532-5415.2005.53466.x>
- Wachal, B., Johnson, M., Burchell, A., Sayles, H., Rieke, K., Lindau, R., ... Panwar, A. (2017). Association of Modified Frailty Index Score With Perioperative Risk for Patients Undergoing Total Laryngectomy. *JAMA Otolaryngology?Head & Neck Surgery*, *68*(14), 1–7. <https://doi.org/10.1001/jamaoto.2017.0412>
- Wahl, T. S., Graham, L. A., Hawn, M. T., Richman, J., Hollis, R. H., Jones, C. E., ... Morris, M. S. (2017). Association of the Modified Frailty Index With 30-Day Surgical Readmission. *JAMA Surgery*, *352*(8), 1–9. <https://doi.org/10.1001/jamasurg.2017.1025>
- Warner, J. L., Zhang, P., Liu, J., & Alterovitz, G. (2016). Classification of hospital acquired complications using temporal clinical information from a large electronic health record. *Journal of Biomedical Informatics*, *59*, 209–217. <https://doi.org/10.1016/J.JBI.2015.12.008>
- Whitlock, E. L., Feiner, J. R., & Chen, L.-L. (2015). Perioperative Mortality, 2010 to 2014: A Retrospective Cohort Study Using the National Anesthesia Clinical Outcomes Registry. *Anesthesiology*, *123*(6), 1312–1321. <https://doi.org/10.1097/ALN.0000000000000882>
- Wick, E. C., Shore, A. D., Hirose, K., Ibrahim, A. M., Gearhart, S. L., Efron, J., ... Makary, M. A. (2011). Readmission Rates and Cost Following Colorectal Surgery. *Diseases of the Colon & Rectum*, *54*(12), 1475–1479. <https://doi.org/10.1097/DCR.0b013e31822ff8f0>
- Yamashita, S., Haga, Y., Nemoto, E., Nagai, S., & Ohta, M. (2004). E-PASS (The Estimation of Physiologic Ability and Surgical Stress) Scoring System Helps the Prediction of Postoperative Morbidity and Mortality in Thoracic Surgery. *European Surgical Research*,

36(4), 249–255. <https://doi.org/10.1159/000078860>

Yeung, T. S. M., Wessel, J., Stratford, P., & Macdermid, J. (2008). The Timed Up and Go Test for Use on an Inpatient Orthopaedic Rehabilitation Ward. *Journal of Orthopaedic & Sports Physical Therapy*, 38(7), 410–417. <https://doi.org/10.2519/jospt.2008.2657>

### Vita

Timothy Joseph Donoghue received a Bachelor's Degree in Psychology from the Rutgers University in 1999, a Bachelor's Degree in Nursing from Columbia University in 2001, a Master's of Science Degree in Nurse Anesthesia from Columbia University in 2004, and a Doctorate Degree in Nurse Anesthesia Practice from Virginia Commonwealth University in 2015. Tim is currently the Coordinator of Nurse Anesthesia Services at the David Koch Center for Cancer Care within Memorial Sloan Kettering Cancer Center (MSKCC) in New York, NY. Tim has been a Certified Registered Nurse Anesthetist for the past sixteen years at MSKCC, providing anesthesia care to patients of all ages having cancer related surgery.