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Morphometric and Functional Markers as Determinants of Perioperative Risk

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Morphometric and Functional Markers as Determinants of Perioperative Risk

By

Armand N. Mbanya

Doctor of Medicine
University of Yaoundé 1
2014

Thesis Committee Chair: Felipe Lobelo, M.D., Ph.D., FAHA

An abstract of
a thesis submitted to the Faculty of the
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Abstract

Morphometric and Functional Markers as Determinants of Perioperative Risk
By Armand N. Mbanya

Background: The U.S. population is getting older and in need of more high risk surgical procedures. Perioperative risk assessment is a growing field in response to this need and perioperative outcomes such as hospital length of stay are used to evaluate the quality of service in hospitals. Functional and morphometric markers of fitness such as hand grip strength and psoas area are strong predictors of perioperative adverse events. This study assesses the relationship between markers of fitness and perioperative outcomes.

Method: We recruited a cohort of 198 patients scheduled for surgery and measured elements of their physical fitness including hand grip strength, hip strength, and psoas area during their pre-surgical visit. They were followed up to 30 days after surgery. We then performed analyses to evaluate the relationship between different markers of fitness and the postoperative outcomes we observed.

Results: Our population's median age was 60 [51-70], 59.1% were male and 85% classified ASA III. Women in the study had lower lean mass and higher body fat percentages. Men had higher measures for strength markers across the board. Low lean mass and BMI were associated with worse ASA scores. OE ratio was higher in females. Total lean mass (r=0.45), skeletal muscle mass (r= 0.47) and trunk lean mass (0.55) had moderate positive correlations to psoas muscle area while grip strength had a weak correlation (r=0.25) to psoas muscle area, all controlling for age and sex.

Conclusion: Improving hand grip strength, psoas strength and body composition before surgery may help reduce perioperative risk**.** Functional and morphometric markers of fitness are feasible in clinical setting and should be routinely used in pre-surgical workflow.

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CHAPTER 1: INTRODUCTION

The number of surgeries performed in the United States of America (U.S.) is increasing annually, while the population of patients surgeons treat have increasingly complex needs and risks (Chand, Armstrong, Britton, & Nash, 2007). Complications are an inherent risk associated to surgery and can lead to increased health related expenditure. Complications lead to higher length of stay in hospitals which can increase the average hospital cost of surgery by $17,000, and ultimately increase the burden of disease on patients (Krupka, Sandberg, & Weeks, 2012). In addition, this reduces available beds in hospitals, therefore limiting their capacity. As a result, complications and adverse events have become very important measures of health care quality (Meguid, Bronsert, Juarez-Colunga, Hammermeister, & Henderson, 2016).

Perioperative risk assessment is an integral part of improving the quality of health care regarding surgery and surgical outcomes. When assessing a patient’s risk of morbidity and mortality prior to undergoing a surgical procedure, both the type of surgery and the patient’s preoperative physical status must be considered. In the past preoperative risk was based on the surgeon’s experience and intuition (Chand et al., 2007). Currently, there are several validated tools available that are designed to assess surgical and anesthetic risk in an objective manner. The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) risk calculator and the revised Cardiac Risk index are some of such tools and combine historical surgery specific outcomes with a key set of perioperative predictive indicators (Feeney et al., 2018). The ACS-NSQIP risk calculator is one of the more used perioperative risk assessment tools and integrates 21 preoperative risk factors in order to predict 13 perioperative complications (Bilimoria et al., 2013; Yap, Ang, Gonzales-Porciuncula, & Esposo, 2018). However, it is not yet routinely used in the preoperative process.

In the search to improve perioperative risk assessment, tools based on cardio-pulmonary fitness markers have been developed but are not commonly used. Several studies have investigated potential markers of fitness that can be easily administered in clinical settings (Bennett, Parfitt, Davison, & Eston, 2016). Functional markers of fitness such as handgrip strength, quadriceps strength, six-minute walk test and hip flexor strength have been shown to predict surgical outcomes in various types of surgeries (Englesbe et al., 2010; J. N. Myers & Fonda, 2016). Moreover, recent studies have also shown a strong relationship between morphometric markers of fitness obtained from preoperative computer tomography (CT) scans (such as trunk muscle size and density, and adiposity distribution) and postoperative surgical outcomes (J. S. Lee et al., 2011; Luckenbaugh et al., 2016; Sergi, Trevisan, Veronese, Lucato, & Manzato, 2016). However, the predictive validity of combining objective preoperative data on morphometric and functional markers has not been explored in relation to postoperative surgical outcomes.

Identifying the most relevant objective measures of preoperative risk that are also feasible to implement in the anesthesia and surgery workflow may offer an opportunity to improve clinical decision-making and communication with patients and clinical teams. These functional measures which are modifiable factors have led to the concept of pre-habilitation, which is “the process of enhancing a patient’s functional capabilities in order to withstand a stressful event such as surgery and improve patient outcomes” (J. N. Myers & Fonda, 2016). Furthermore, identifying functional measures that are amenable to change should help target patient populations that are likely to benefit from surgical pre-habilitation approaches, thereby significantly reducing rates of complications, adverse events, length of stay and costs.

Specific Aim

To assess morphometric and functional markers of fitness (such as psoas muscle size and density, lower limb strength, hand grip strength, subcutaneous, visceral and total body fat) among patients with a body composition analyzer and available pre-operative CT scan images and test their predictive validity in relation to major surgical outcomes such as general and intensive care unit length of stay (LOS), and observed vs expected LOS (O:E) ratio.

Research Hypothesis

We hypothesize that combining novel morphometric and functional fitness markers will have a higher predictive validity for discriminating perioperative risk.

CHAPTER 2: LITERATURE REVIEW

The purpose of this review is to present the current perioperative risk-determining practices in the United States (U.S). In addition, we will present an overview of surgical outcome measures that are used to evaluate surgical performance. The review will proceed to discuss role of physical fitness as a determinant of surgical outcomes, paying specific attention to markers of physical fitness that can be easily applied in routine perioperative clinical settings. Overall, it will explain the need for inexpensive, easily administered perioperative markers of surgical outcomes.

SURGERY OVERVIEW

Over the last 200 years since its conception, the field of surgery has been constantly evolving. From the use of ether anesthesia and aseptic practice in the 19th century, to the development of modern surgical plastic intravenous catheters in the mid-20th century, innovations have been foundational to practice (Bigelow, 1846; Gawande, 2012; Massa, Lundy, Faulconer, & Ridley, 1950). These innovations have also led to an increase in the number of annual surgeries performed across the world (Gawande, 2012).

In 2014, 17.2 million inpatient and outpatient hospital visits in the U.S included surgical procedures (Steiner, Karaca, Moore, Imshaug, & Pickens, 2006). More than half (57.8%) were ambulatory surgeries, and the remaining (42.2%) were non-ambulatory (Steiner et al., 2006). Notably, hospital costs for surgery are high; for example, the cost of a surgery-related hospital stay was $22,500 in 2013 (Krupka et al., 2012). Surgical complications are a significant cause of morbidity and mortality and further increase length of stay in hospital, and consequently, cost. In 2010, the average cost for a patient who had perioperative complications was $35,465; whereas, for a patient with no complications, it was $18,403 (Krupka et al., 2012). Surgical complications account for up to 40% of all hospital complications (Stensland, 2013). As a result, complications and adverse events are also becoming increasingly important for measuring health care quality (Stokes et al., 2019).

To address complications linked to surgeries, a patient's time from surgical diagnosis to postsurgical recovery and rehabilitation may require many types of services (Akhtar, Macfarlane, & Waseem, 2013). This has brought preoperative risk assessment to the forefront of perioperative morbidity and mortality prevention.

Perioperative Risk Assessment

Historically, surgical risk assessment was based on the intuition and experience of the surgeon, but over time there has been a shift to more objective systems to assess surgical risk. Several objective tools to assess surgical risk have been developed over the last 25 years (Chand et al., 2007). Earlier tools were confined to intensive care settings and required clinicians to collect a lot of data from each patient, making it time-consuming and labor intensive. More modern tools for surgical risk assessment tools are easily accessible and completed in the hospital. More recently, dozens of risk-predicting systems have been developed, many of which include certain aspects of the patient's physical fitness (Chand et al., 2007). While these tools often focus on cardiorespiratory function, they may ignore other relevant factors of physical fitness. Where and when available, a more objective and accurate estimate of a patient's aerobic capacity can be obtained by preoperative cardiopulmonary exercise testing. Cardiopulmonary exercise testing gives a clearer picture of risk from co-morbidity but is neither routinely nor widely used (Meguid et al., 2016).

The following section will discuss the scoring tools most commonly used in the U.S. for perioperative risk assessment.

American Society of Anesthesiologists (ASA)

The ASA system is widely used and can a patient can be classified simply during clerking. It was originally described by Saklad (Saklad, 1941) and classifies patients into one of six categories of increasing severity (see Table 1). It was initially developed as a pre-surgical risk assessment tool but is rather subjective (Chand et al., 2007). One study showed that when 304 anesthetists graded 10 patients, an average of 5.9 patients were given the same rating by their peers and the author of the study (Owens, Felts, & Spitznagel, 1978). The ASA system is simple to administer and avoids heavy data input making it suitable for clinical use. In addition it is suitable for all patients awaiting surgery. There are many studies that show correlations between the ASA system and postoperative mortality (Chand et al., 2007). The ASA system has also been used to successfully predict the risk of adverse surgical outcomes such as the length of stay in the intensive care unit, intraoperative blood loss and cardiorespiratory complications (Farrow, Fowkes, Lunn, Robertson, & Samuel, 1982; Marx, Mateo, & Orkin, 1973; Wolters, Wolf, Stützer, & Schröder, 1996).

Table 1: ASA Classification System

P1 Normal and healthy
P2 Mild systemic disease
P3 Severe systemic disease
P4 Severe systemic disease that is a constant threat to life
P5 Moribund and not expected to survive without operation
P6 Brain dead, whose organs are being removed for donation

American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) Surgical Risk Calculator

This method is considered a guiding principle in decision-making both in the preoperative and surgical treatment. The ACS-NSQIP Surgical Risk Calculator was created in 2013 and "is a web-based tool that incorporates 21 preoperative risk factors to predict 13 perioperative complications: all-cause mortality, serious complication, any complication, pneumonia, cardiac complication, urinary tract infection, surgical site infection, venous thromboembolism, renal failure, readmission, return to the operating room , discharge to nursing or rehabilitation facility, and length of hospital stay" (Bilimoria et al., 2013; Yap et al., 2018). The preoperative predictor variables used to develop the risk calculator were derived from a data base of about 1.5 million patients in the U.S. and accounts for over 1500 unique surgical procedures spanning different surgical subspecialties (Yap et al., 2018). The ACS NSQIP risk calculator is surgery-specific and goes even further to discriminate open from minimally-invasive procedures.

Regression models were developed to predict the 30-day perioperative outcomes from the ACS-NSQIP database. The ACS-NSQIP Risk Calculator had good predictive capability for mortality, morbidity, pneumonia, cardiac events, renal failure, urinary tract infection, surgical site infections, and venous thromboembolism. The ACS-NSQIP risk calculator is constantly updated and recalibrated to improve its accuracy and performance as more data are added to the database. While the ACS-NSQIP surgical risk calculator is used frequently in perioperative care and has prevented complications, saved lives and reduced cost by millions of dollars, it is difficult to collect all the relevant data in clinical settings.

Cardio-respiratory based risk assessment and Pre-habilitation

Cardiorespiratory fitness is a physiological characteristic that is used to measure an individual's capacity to deliver and use oxygen to perform tasks (J. N. Myers & Fonda, 2016). There has been a lot of interest in cardiorespiratory fitness as its benefits out of the world of athletics are being recognized and accepted. Cardiorespiratory fitness levels have been shown to be a more powerful predictor of mortality risk than the more traditionally used risk factors (Grazzi, Myers, & Chiaranda, 2019; Kodama et al., 2009; J. Myers et al., 2015). Over the years, the number of studies evaluating the relationship between fitness measures and health outcomes have increased exponentially (D.-c. Lee, Artero, Sui, & Blair, 2010). These studies have demonstrated that fitness powerfully predicts outcomes associated with surgical interventions so much so that it is garnering recognition (Colice, Shafazand, Griffin, Keenan, & Bolliger, 2007; Grazzi et al., 2019; Santa Mina et al., 2014). Furthermore, improving preoperative cardiorespiratory fitness has a significant impact on health outcomes (such as mortality and morbidity) post-surgery, both in the short, mid and long term (Colice et al., 2007; Halloway, Buchholz, Wilbur, & Schoeny, 2015; Jack, West, & Grocott, 2011; Santa Mina et al., 2014). This has led to the concept of ‘‘pre-habilitation,’’ a term that has been used to describe the process of enhancing a patient's functional capabilities to withstand a stressful event such as surgery (Jack et al., 2011).

Cardio-pulmonary exercise testing is used to assess preoperative fitness levels but in the ever more complex surgical population (comorbidity-laden), this is not feasible (West et al., 2014). As a result, several tests to evaluate patients' general physical fitness are being developed and validated for use in diverse populations (Ajitsaria, Eissa, & Kerridge, 2018; O'Donnell, 2016). Exploring variables from such tests could provide cost-effective, feasible tools to evaluate perioperative risk in clinical settings.

We will go on to present elements of physical fitness that help measure fitness levels and can be used to evaluate perioperative risk below.

PHYSICAL FITNESS

Physical fitness is "the ability to do physical activity and/or physical exercise using most of the body structures and functions involved in body movements such as the musculoskeletal, cardiorespiratory, circulatory, endocrine-metabolic system, etc." (Castillo-Garzón, Ruiz, Ortega, & Gutiérrez, 2006). It comprises of several elements such as cardiorespiratory fitness, muscular strength and power, body composition, neuromuscular factors, and other factors that include coordination, posture, balance, flexibility, and reaction time (Amaro-Gahete, Alejandrodela, Jurado-Fasoli, Castillo, & Gutiérrez, 2017; Pekka Oja, Bull, Fogelholm, & Martin, 2010).

For the purpose of this review we will focus on cardio-respiratory fitness, muscular strength, body composition and lower extremity muscular structure.

Cardio-Respiratory Fitness

Cardio-respiratory fitness is the hallmark of fitness levels. Maximum oxygen uptake (VO2max) is the physiological variable considered to be a suitable indicator of cardio-respiratory fitness (Fox, 1973; Harber et al., 2017). Additionally, maximum oxygen uptake is a powerful predictor of all-cause mortality in both healthy people of different ages (Blair et al., 1995; Blair et al., 1989). This finding is independent of different lifestyle and clinical factors such as tobacco and alcohol (Kodama et al., 2009; Kokkinos et al., 2008; Jonathan Myers et al., 2002). VO2max is commonly measured by indirect calorimetry, but can also be done with other laboratory and field tests (Bennett et al., 2016; Stickland, Petersen, & Bouffard, 2003). Several submaximal tests exist; laboratory tests include: the Bruce treadmill test (Bruce, Kusumi, & Hosmer, 1973), Astrand and rhyming cycle ergometer test (Åstrand & Ryhming, 1954), and the Madder test (Mader, Heck, &

Hollmann, 1981). Field tests include: the 2-km walk-test (UKK test) (P. Oja, Laukkanen, Pasanen, Tyry, & Vuori, 1991), the Six-minute walk test (L. Cahalin, Pappagianopoulos, Prevost, Wain, & Ginns, 1995), the 20-meter shuttle run test (Leger, Mercier, Gadoury, & Lambert, 1988) and the 3-minute YMCA step test (Golding, 2000). We will delve further into the six-minute walk test which was used in this study.

Six-Minute Walk Test

The 6-minute walk test (6MWT) is a submaximal exercise test used to evaluate cardiorespiratory fitness and functional exercise capacity in several populations, including adults and even elderly (Amaro-Gahete et al., 2017). During the 6 minute walk test, participants are instructed to walk at the maximum speed (without running) for 6 minutes, in order to complete the maximum distance during that time period (L. Cahalin et al., 1995). The primary measurement is the 6-min walk distance (6MWD), which is the distance covered in six minutes, however additional data can also be collected, such as blood oxygen saturation and perception of dyspnea on exertion (Borg scale) (Enright, 2003). The test is easy to administer, inexpensive, reproducible and better reflects activities of daily living compared to other walk tests e.g. the shuttle walk test (Enright, 2003). In addition, it is considered safe and tolerable because patients are self-limited during exercise (L. P. Cahalin, Mathier, Semigran, Dec, & DiSalvo, 1996; Miyamoto et al., 2000; Roul, Germain, & Bareiss, 1998). In 2002, the American Thoracic Society Pulmonary Function Standards Committee developed standardized protocols for the 6MWT in clinical settings ("ATS Statement," 2002). Despite its safe use in clinical settings, there are absolute contraindications, which include a history of unstable angina or a heart attack during the previous month. Relative contraindications include resting tachycardia or uncontrolled hypertension (Enright, 2003). In critical illness survivors, the 6MWT has established clinometric properties in terms of validity and responsiveness (Parry et al., 2019). It is used measuring the response to therapeutic interventions for pulmonary and cardiac disease (Enright, 2003). Furthermore, it is associated with significant long-term physical, cognitive, and/or mental health morbidity (Parry et al., 2019). It also correlates well with other important outcomes including death (Casanova et al., 2011; Pinto-Plata, Cote, Cabral, Taylor, & Celli, 2004; Pitta et al., 2005).

Muscular Strength

Muscular strength is an indicator of physical fitness that is acquiring great relevance in recent times because of its relation to the aging process. Muscle strength, defined as the maximum force generated at a specific velocity (Pallarés, 2012), is a key contributor to various functions of the human body. The primary function is to produce movement and maintain postural control, providing a possibility for activity, participation and functional independence (Amaro-Gahete et al., 2017; Pallarés, 2012). Muscle strength is essential to the human movement, from when we are born, through adulthood until older age (Tanaka, Monahan, & Seals, 2001), and adequate muscle strength is a major component of the individual's motor system. Muscular strength depends on the lean mass (Atlantis, Martin, Haren, Taylor, & Wittert, 2009) and/or the level of physical activity (Williams et al., 2007). As a result, a significant loss of muscular strength is associated with an accelerated aging and an increase of all-cause mortality risk (Shannon et al., 2004). Loss of muscle strength is also associated with loss of physical functionality and poor recovery of health after surgery (Humphreys et al., 2002; Norman, Stobäus, Gonzalez, Schulzke, & Pirlich, 2011). Interestingly, regardless of factors such as age (Ortega, Silventoinen, Tynelius, & Rasmussen, 2012), body fat percentage, smoking, high blood pressure (Artero et al., 2011), or alcohol consumption (Volaklis, Halle, & Meisinger, 2015), and even without considering cardiorespiratory fitness (Volaklis et al., 2015), an inverse association between muscular strength and mortality risk has been suggested (Shannon et al., 2004). Muscle strength can be measured with free weights, force transducers or dynamometers (Pallarés, 2012). There are also possibilities to measure different types of motor actions, where the muscle is shortening (concentric), lengthening (eccentric) or working statically (isometric). Isometric measurements are the most commonly used (Amaro-Gahete et al., 2017).

Muscular strength has several components but for this review we will focus on maximum muscle strength measures by looking at the gold standards methods, hand grip strength and lower limb strength.

Maximum Muscle Strength

Maximum muscle strength (MMS) can be assessed using several methods both in laboratory and non-laboratory settings. Some methods of evaluating maximum muscle strength are shown below.

Isokinetic dynamometry test**:** It is the gold standard way to measure MMS in laboratory conditions. Its principle is that performing specific movements with a known load at a constant speed can inform MMS. Isokinetic strength in the lower limbs has a direct relationship with lower risk of all-cause mortality (Buckner, Loenneke, & Loprinzi, 2015).

One Repetition Maximum test: It is the gold standard method to measure MMS in non-laboratory settings (Levinger et al., 2009). It is defined as the maximum weight that an individual can lift in a specific exercise on one attempt (Kraemer et al., 1995). The results can be obtained directly or indirectly, depending on the protocol used (Brzycki, 1993; Wiktor et al., 2008)

Hand grip test**:** It is a considered to be a marker of overall strength. It is measured by manual dynamometry and is frequently used as a health marker in elderly population and is considered a general marker of strength (Bohannon, 2008). The starting position is standing and holding a manual dynamometer, which has been regulated and calibrated, with one hand (Ruiz-Ruiz, Mesa, Gutiérrez, & Castillo, 2002). The arm should be separated from the body and the maximum strength must be applied without arm flexion. Several attempts can be performed in each hand, and the average of all attempts is a valid measure depending on the protocol in use. Hand grip strength is affected by factors such as age and sex (Frederiksen, Hjelmborg, Mortensen, McGue, Vaupel & Christensen, 2006; Schlussel, Anjos, Vasconcellos & Kac, 2008). In addition, it predicts all-cause mortality (Rantanen, Volpato, Ferrucci, Heikkinen, Fried & Guralnik, 2003), post-surgical complications (Klidjian, Foster, Kammerling, Cooper & Karran, 1980) and functional recovery limitations (Bohannon, 2008; Rantanen, Guralnik, Foley, Masaki, Leveille, Curb et al., 1999).

A systematic review examining grip strength in relation to a range of health outcomes, described ten studies that showed clear associations between weak grip strength and increased length of hospital stay or complications among those undergoing surgical procedures (Bohannon, 2008). Hand grip strength is the easiest and arguably most inexpensive test when compared to other recommended muscle strength tests such as quadriceps strength and hip strength (Frederiksen et al., 2006; Lauretani et al., 2003; Schlüssel, dos Anjos, de Vasconcellos, & Kac, 2008), thus it is often preferred in research and more feasible in clinical studies (Cruz-Jentoft et al., 2010). Although it can be argued that hand grip is not a marker of general strength because it neglects balance and mobility, it is closely correlated to quadriceps strength (Norman et al., 2011). Furthermore, sarcopenia is thought to be a systemic condition (Lauretani et al., 2003) and hand grip strength correlates closely to sarcopenia, hence, justifying the use of hand grip strength as a measure of overall muscle strength. Grip strength has also been shown to have high repeatability and reliability in community-dwelling older adults (Bohannon & Schaubert, 2005).

Lower Limb Strength

Lower limb strength is associated to mortality therefore is an important measure of muscular strength. It is directly related to the ability to perform daily ambulatory activities, such as rising from a chair, and ascending and descending stairs (Ploutz-Snyder, Manini, Ploutz-Snyder, & Wolf, 2002). Deficit in quadriceps strength is associated with increased pain and disability in knee and hip osteoarthritis (Brandt et al., 2000; O'Reilly, Jones, Muir, & Doherty, 1998; Shakoor, Furmanov, Nelson, Li, & Block, 2008), while good lower extremity muscle strength preserves bone density, quality of life, and reduces the risk for chronic diseases such chronic heart failure and diabetes by improving glycemic control (Seguin & Nelson, 2003).

Isokinetic dynamometry is the gold standard measure for an individual's isometric, concentric, and eccentric strength. However, it is not easily implemented in clinical practice because, it is time-consuming and the necessary equipment is expensive and not portable. In comparison, hand held dynamometers (HHDs) are inexpensive, hence why they are being used with increasing frequency in clinical practice for evaluating muscle strength. HHDs are well known and established as reliable with standardized protocols under controlled conditions (Whiteley et al., 2012). There are more dynamic measures of lower limb strength such as the vertical jump but once more we will focus on the isometric measures using the dynamometer which are more feasible to use in clinical practice.

Knee Extension Strength

Knee extension strength is an important marker of lower limb strength. The main muscle group responsible for extending the knee is the quadriceps. Several studies have shown that quadriceps strength (knee extension) is a key aspect for activities of daily living (ADL) in different populations (Buckinx et al., 2019; Ushiyama, Kurobe, & Momose, 2017; Wearing, Stokes, & de Bruin, 2019). The reliability of hand-held dynamometers for testing knee extension strength has been studied in many populations including healthy young and elderly adults (A. W. Andrews, Thomas, & Bohannon, 1996; Scott, Bond, Sisto, & Nadler, 2004), community-dwelling elderly fallers (C. Y. Wang, Olson, & Protas, 2002), people with acquired brain injury (Riddle, Finucane, Rothstein, & Walker, 1989), older adults after hip fracture (Roy & Doherty, 2004), and adolescents with cerebral palsy (O'Shea, Taylor, & Paratz, 2007; Taylor, Dodd, & Graham, 2004). Studies found a significant relation between quadriceps strength and functional recovery with total knee replacement and total hip replacement surgeries (Holm, Thorborg, Husted, Kehlet, & Bandholm, 2013). Furthermore, knee extension strength has been shown to determine gait and postural stability in older populations (Nakayama, Suzuki, & Hamaguchi, 2019). Evaluating quadriceps strength is a feasible clinical way to predict functional recovery from surgery (Nocera, Buckley, Waddell, Okun, & Hass, 2010).

Hip Flexion Strength

The iliopsoas is the major muscle responsible for hip flexion in the human body. Hip flexion strength is an important indicator of lower limb strength and is often used to infer the degree of recovery after hip injury or surgery (Fukumoto et al., 2013; Holm et al., 2013). Like knee extension strength it can be reliable measured using handheld dynamometry in clinical settings (O'Shea et al., 2007). Hip flexion strength is also important for routine daily activities (Hyodo, Masuda, Aizawa, Jinno, & Morita, 2017). It is a major predictor of both short term and long term recovery from hip replacement surgeries (Holm et al., 2013).

Body Composition

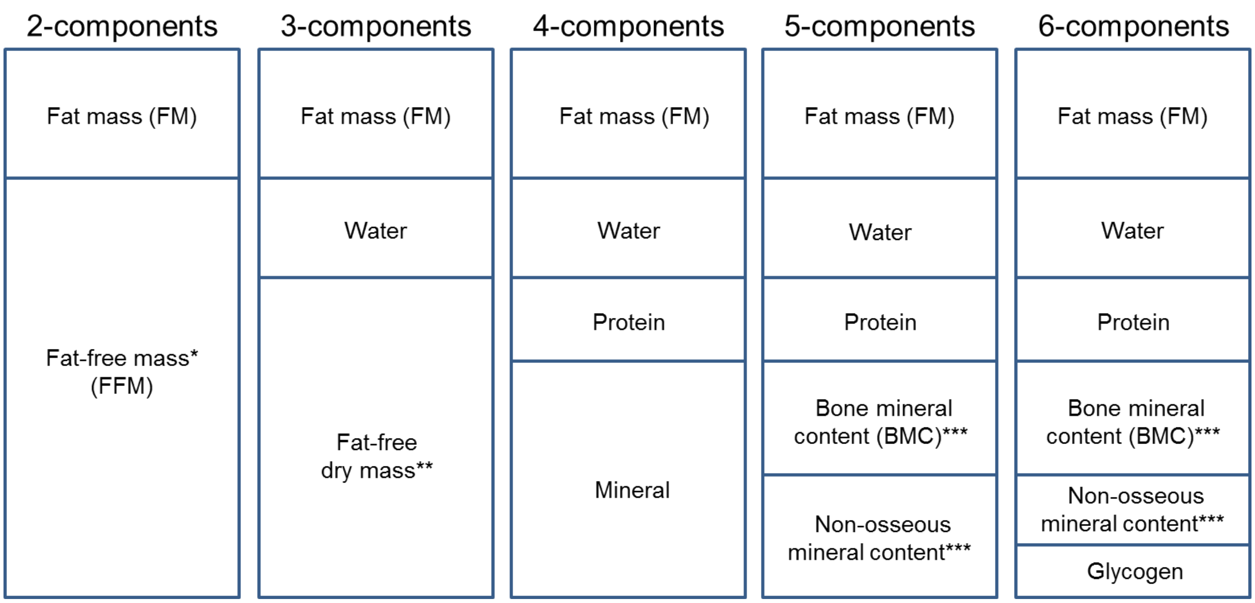
Body composition is one of the most important health-related components of physical fitness. It is a major health biomarker associated with the prevention and/or pathogenesis of several diseases such as diabetes (Amaro-Gahete et al., 2017). The proper measurement of body composition plays a key role in grading health and nutritional status, the impact of disease, and changes due to preventive/therapeutic interventions (Toomey, Cremona, Hughes, Norton, & Jakeman, 2015). Body Mass Index Index (BMI) has been routinely used to evaluate health as it correlates well to key indicators of cardiovascular health and is easily calculated. The pitfall is that it cannot differentiate between adiposity and fat-free mass (which can be healthy and metabolically active) or reflect the distribution of these components in the body (Toomey et al., 2015). By analyzing body composition, we gain a more complete representation of the anthropometric phenotype, that is, measurement of adiposity, lean mass, and bone (Wells & Fewtrell, 2006). There have been several models proposed over time which we will discuss below:

Two-Compartment Models (2-C): In the 2-C model, the body is divided into two parts: the first is body fat, and every other tissue is considered fat-free mass (FFM) (Ellis, 2000). The total amount of body fat consists of essential fat and storage fat. These two types of fat each play a physiological role with essential fat being necessary for normal body function. Storage fat on the other hand, is located around organs and subcutaneously serving to conserve body heat (Elia, 1992). Measuring body fat directly has always been a challenge. However, in the 2-C model, if you can measure total FFM then you can indirectly derive body fat from the body weight (Forsum, Henriksson, & Löf, 2014). The measurement of total body density is the most frequent application of the 2-C model. This model worked under the assumption that the relative concentration of water or potassium in FFM is constant for all ages, for body water and for body potassium (Forbes, Gallup, & Hursh, 1991; Pace & Rathbun, 1945). Likewise, the density of the FFM for the 2-C model was assumed constant. Studies showed that this was not the case, so another model was developed.

Three-Compartment Models (3-C): From the limitations of the 2-C model presented above, it was necessary to further understand expand the model to the (3-C) configuration. In the 3-C model, body fat remains the same as the 2-C model but the FFM is divided into two parts: water and the remaining solids (Ellis, 2000). Therefore, the three components considered are water, fat, and body solids. This model improved on the 2-C model in both healthy adults and older children (Toomey et al., 2015). However, for patients low body protein and/or osteoporosis, density estimates for the solid components will be inaccurate, leading to an incorrect derivation of fat mass (Ellis, 2000).

Four-Compartment Models (4-C): This is considered the reference in vivo assessment of total body composition. In this model, the body's FFM is divided into three basic compartments, namely; body cell mass (BCM), extracellular solids (ECS), and extracellular water (ECW) (Ellis, 2000; Fields & Goran, 2000). BCM measurement is based on quantifying whole-body potassium or by tracing the dilution of a potassium isotope in plasma (Moore et al., 1968). In the determination of the ECW compartment, the dilution of sulfate or bromide tracer compounds are used (Edelman, Olney, James, Brooks, & Moore, 1952; Gamble, Robertson, Hannigan, Foster, & Farr, 1953). The ECS compartment is described based on bone mineral content or total body calcium (G. A. Andrews, Gibbs, Morris, & Ross, 1973). Fat-free mass is then defined as the sum of BMC, ECW and ECS. Total body fat mass is the body weight minus FFM. In summary, this model subdivides FFM into water, protein and minerals. A simpler way to look at the 4-C model is FM + Water + Protein + Minerals.

Multicompartment Models: The multicompartment model includes the 5 and 6-component models. As each model builds upon the previous it adds another element to be measured usually requiring an additional test, thus evolving towards the cellular model (Heymsfield et al., 2015). Multicompartment models tend to be more generalizable because the relationship between naturally occurring elements in the human body (e.g. nitrogen, carbon, oxygen, etc.) and the molecular structure of tissues (protein, water, etc.) remain relatively fixed in both healthy and diseased states (Ellis, 2000; Heymsfield et al., 2015). The five-component model consists of FM, protein, water, bone mineral content and non-osseous mineral content, whereas the six-compartment model adds glycogen as a measured component (Heymsfield et al., 2015). It is important to note that as the number of components increase, more variables need to be measured and therefore require better measurement tools and techniques.



Source: MRC Epidemiology Unit.
*Includes water, protein, glycogen, bone mineral content, and non- osseous mineral content.
**Includes protein, glycogen, bone mineral content, and non-osseous mineral content.
***There is a difference between mineral content and mineral mass. Measures of mineral content are typically converted to mineral mass to reflect the ashing process.

Figure 1: Components of the different multi-component models.

Measuring Body Composition

There are several methods to measure body composition but, in this section, we will review dual-energy x-ray absorptiometry, magnetic resonance imaging (MRI), computed tomography (CT) and (DXA), bioelectrical impedance analysis (BIA).

***Dual-energy x-ray absorptiometry*: ** This is considered the gold standard method of measurement of body composition (Shepherd, Ng, Sommer, & Heymsfield, 2017). DXA was developed to measure bone mineral mass. It does this by emitting two different x-ray energies and then measures the difference in absorption of said energies (Lorente Ramos et al., 2012).It is necessary not to forget that bone is covered by soft tissue, so this has to be factored into calculations, as a result, fat mass and FFM are also calculated based on algorithm specific to the DXA (Wells & Fewtrell, 2006). As expected, because of this overlying soft tissue, trunk composition is less accurate than the limbs since it is based on prediction rather than accrual measurements (Shepherd et al., 2017). DXA is therefore useful to assess relative fat and lean masses in an individual when comparing it to limb lean mass (Lorente Ramos et al., 2012).

Magnetic Resonance Imaging: MRIs create images by analyzing the emission and absorption of energy within the electromagnetic spectrum and recreating the spatial variations in the frequency and phase of the energy emitted and absorbed. Consequently, it estimates adipose tissue volume rather than mass (Grover et al., 2015; Wells & Fewtrell, 2006). It achieves this by analyzing hydrogen nuclei located in either water or fat. It uses this information to differentiate between tissue and based on "image slice" diameters sum them up to calculate regional tissue volume (Wells & Fewtrell, 2006).

The main limitation of MRI in body composition analyses is that fat mass is derived from both fat content of adipose tissue and fat density. Because fat density is relatively constant, it does not pose an issue, but, fat content of adipose tissue does vary and the MRI is not equipped to evaluate this accurately (Ross, Goodpaster, Kelley, & Boada, 2000). Secondly, MRI can only locate fat mass in adipose tissue (no fat mass in water where other hydrogen nuclei are) compounding its limited availability and relative high cost (Ross et al., 2000).

Nonetheless, MRI has an advantage in that it measures regional body composition better than other techniques, and it is currently the only accurate approach for measuring intra-abdominal adipose tissue (Wells & Fewtrell, 2006).

Computer Tomography: Computer tomography (CT) is the gold standard for the evaluation of qualitative and quantitative changes in muscle and fat, especially for the trunk area where other techniques are limited (e.g. DXA) (K. Lee et al., 2019). This reliable estimation of both qualitative and quantitative changes in fat and muscle mass has been demonstrated in several studies (Bazzocchi et al., 2014; Sergi et al., 2016). This makes CT key to measuring fatty infiltration of muscle tissue (K. Lee et al., 2019). Nonetheless, it is limited, as it does not distinguish between intramuscular and intramyocellular fat or the fat content (Miljkovic & Zmuda, 2010). Furthermore, the use of CT is associated to high-dose radiation exposure and it is also expensive.

Bioelectrical impedance analysis: Bioelectrical impedance analysis (BIA) is based on the principle that the human body is composed of intracellular and extracellular fluids which conduct electricity at different speeds (Kyle et al., 2004). A low current is sent through the body via electrodes and because fat-free body weight is made of 72% water, it is a better conductor of electricity than fat which has a very low water content (Böhm & Heitmann, 2013). Therefore, this method measures total body water from which FFM is derived (Kyle et al., 2004). The BIA method is used because it is painless, quick, and can be easily administered.

MORPHOMETRIC MARKERS FROM PREOPERATIVE IMAGING

As discussed above MRI and CT scans can be used to evaluate body composition preoperatively. Because CT scans can accurately measure muscle and fat, CT is the gold standard for evaluating qualitative and quantitative changes in fat and muscle particularly the trunk (K. Lee et al., 2019). As a result, imaging techniques can be used to evaluate trunk muscle size and density, adiposity distribution and vascular calcification for predicting postoperative outcomes (Luckenbaugh et al., 2016; Sabel et al., 2013). For this review we will focus on trunk muscle size and density, and adiposity distribution.

Trunk muscle size and density

The psoas is a core muscle of the trunk and it is susceptible to changes during chronic illness, but not acute illness. This makes it a good marker for underlying conditions and co-morbidities in patients because it gives a broader picture of the patient's health status (Englesbe et al., 2010).

Total psoas surface area is a measure of sarcopenia and frailty across several surgical specialties. Psoas muscle size is predictive of several adverse perioperative outcomes such as mortality, major complications in emergency, pancreatic and colorectal surgery (Hawkins et al., 2018). In addition, low psoas surface area is a strong marker of physical frailty associated with increased hospital length of stay in adults over 65 years old undergoing cardiac surgery (Balsam, 2018).

Psoas density is a marker of physiological reserve and psoas muscle fat infiltration (Yoo, Lo, & Evans, 2017). CT psoas muscle measurement at the L3 vertebral body level has been shown to predict poor outcomes in major surgeries (Buettner et al., 2016; Joglekar et al., 2015; Jones, Doleman, Scott, Lund, & Williams, 2015; Lo, Evans, & Yoo, 2018). Recently, several studies have validated the CT psoas density captures information regarding the degree of fatty muscular infiltration, quality, and strength, which can be used to predict outcomes after elective gastrointestinal oncologic surgery (Buettner et al., 2016; Goodpaster et al., 2001; Joglekar et al., 2015). Moreover, combined with psoas area, they are markers of poor prognosis in blunt trauma injuries (Yoo et al., 2017). Psoas area and density are easily measured markers from CT scans that predict surgical outcomes in several types of surgeries.

Adiposity distribution

BMI is the most used variable to evaluate obesity, but it fails to account for the location of fat which has been shown to play a key physiological role. This has led to more attention to fat location in the body. CT scans can show adiposity distribution and measure visceral fat area and subcutaneous fat area (Wells & Fewtrell, 2006). CT determined abdominal subcutaneous fat is a predictor of surgical site infection even after adjusting for other common factors (J. S. Lee et al., 2011). Furthermore, when defining obesity based on CT derived visceral fat area, obese patients spent significantly longer time in surgery compared with non-obese patients during laparotomies (Tsujinaka, Kawamura, Konishi, Maeda, & Mizokami, 2008). In addition, postoperative hospital LOS was significantly longer in obese patients based on visceral fat area (Tsujinaka et al., 2008). CT derived fat area can be used as a predictive marker for abdominal surgeries. More studies need to be done on its prognostic value in other types of surgeries.

CHAPTER 3: METHODS

Study Design: This study was a prospective cohort study with 198 enrolled participants**.**

Inclusion and Exclusion Criteria:

Inclusion criteria: 1) age 18 and older, 2) American Society of Anesthesiologists physical classification system (ASA) level 2, 3 & 4) undergoing a non-ambulatory abdominal/pelvis surgical procedure requiring anesthesia 4) able to ambulate freely, 5) provide informed consent to participate in the study. For participants enrolling in the wearable activity monitor portion of the study, inclusion criteria included criteria 1-5 as above, plus 6) own a smartphone, and 7) preoperative visit at least 7 days prior to surgery.

Exclusion criteria: 1) patients undergoing ambulatory surgical procedures, 2) cardiac bypass procedures, and 3) cystoscopy and transurethral resection of the prostate procedures.

Data Collection:

Patients who came to the Emory University Hospital (EUH) anesthesiology perioperative clinic (APC) for preoperative visits were screened and assessed by members of the study team. During the APC visit, grip strength, hip flexor strength, knee extensor strength, and a 6-minute walk test were assessed on patients who provided informed consent for the study (description of assessments below). The measurements of perioperative risk used in the ACS-NSQIP risk calculator were also recorded and entered into REDCap. Study data were recorded and managed using the REDCap electronic data capture tools hosted by Emory University (Harris et al., 2009).

Data Safety and Confidentiality: Data obtained was stored in accordance with HIPAA regulations. REDCap and Emory Box.net were used to store soft copies as they are secure Emory networks. Signed informed consent forms and hard copies of the APC data were kept in de-identified files in a locked office within the Department of Anesthesiology at EUH. The data collected was not and will not be disseminated to any other individuals not involved in the study.

Grip Strength Testing: Grip strength was measured using a portal grip strength dynamometer (Takei Model T.K.K. 540) by following the National Health and Nutrition Examination Survey Protocol (Y. C. Wang et al., 2019) during the initial perioperative APC visit. The handgrip strength dynamometer was calibrated once prior to the beginning of the study. Prior to testing, patient handedness was recorded via asking patient and the dynamometer grip size was adjusted according to the participant's hand size. A member of the study team verbally explained and demonstrated proper form prior to data collection, and participants were also given the opportunity to complete warm up exercises to loosen up the hands and fingers. Grip strength testing was administered on each hand separately, completing three trials on each hand. Metrics included peak force. All grip strength testing was administered by study team members trained on the proper protocol described above. Data was recorded and entered REDCap.

Hip Flexor and Knee Extensor Strength Testing: Hip flexor and knee extension strength will be assessed using published protocols for a portable hand-held dynamometer (Lafayette system 01165) (Mentiplay et al., 2015) during the initial perioperative APC visit. The portable hand-held strength dynamometer was calibrated once prior to the beginning of the study. Prior to data collection, patient's dominant leg was recorded. A member of the study team verbally explained the testing procedures and proper positioning prior to data collection. Participants were given a trial run prior to official testing to ensure proper form. Leg strength testing, including both hip flexor and knee extensor strength, were administered on each leg separately, completing 2 trials of each test on each leg. Metrics recorded included peak force, average force, and time to peak. Muscle strength was evaluated by averaging the 2 peak force measures. All leg muscle strength testing was administered by study team members trained on the proper protocol described above. Data was recorded and entered into REDCap.

6 Minute Walk Test: Aerobic capacity was measured using the 6-minute walk test (6MWT), a widely used, reliable, and safe assessment of sub-maximal aerobic capacity. The test was administered via the guidelines and procedures described in the “MyHeart Counts” study for gathering 6MWT data from patients (McConnell et al., 2017). Distance covered in the 6MWT was assessed using the Garmin Vivofit® 3 device. Once the Garmin Vivofit® 3 device was placed on the wrist of the participant, distance covered during the 6MWT was obtained using a timed workout feature on the device. The 6MWT was administered indoors in a low-traffic area of the clinic. The study team member administering the 6MWT used a separate stop watch to monitor progress of the 6MWT. Metrics recorded included the distance covered via the Garmin Vivofit® 3 device and the start and stop time. Data was recorded and entered REDCap.

Bio-impedance Analysis: Using the body composition analyzer (InBody 270), participants body composition was analyzed via the use of electrodes (see Fig 1 below). The results were automatically measured and recorded within the analyzer device itself. Therefore, no measurements were manually recorded by the research study member team other than indications if the test was performed. Output included total lean mass, total fat mass, body fat percentage, segmental lean mass, skeletal muscle mass.

The body composition analyzer was used during the initial APC visit for study participants and required input on the device screen of the participants name and MRN number.

Figure 1: Posture for Bio-impedance Analysis

Preoperative CT scan –derived Morphometrics: Co-Investigators within the Radiology department assisted in measuring a number of variables as evaluated through a body composition analyzer and patient abdominal/pelvis CT scans. Such variables included psoas muscle size and density, subject scan quality, noise, obesity, scoliosis, artifact, and contrast phase. These measures were then recorded in a REDCap form.

Primary Outcomes: The primary outcome was ratio of observed to expected length of stay (O:E ratio), general and ICU LOS. The O:E ratio was calculated by dividing the observed LOS by the expected LOS. The expected lengths of stays were part of metrics obtained by Emory Healthcare that are used for research purposes, operations, and quality. General LOS was calculated as number of days spent in the hospital after surgery based on admission and discharge dates. ICU LOS was defined as the number of days spent in the ICU following surgery based on admission date into the ICU and discharge date into the ward.

Data Analysis

Statistical analysis was performed in STATA 16 (STATA corp, College Station, TX, USA). Normality was assessed with visual assessment of normalized quantile-quantile plots and Shapiro-Wilk test where in visual assessment was not conclusive. Chi square test was used to perform univariate analysis to examine for associations between the primary outcomes and morphometric and functional markers; t-test was used to examine for differences in age, ASA class, gender and potential predictor variables. Partial correlations were used to better understand the relationship between predictor variables and outcome variables.

CHAPTER 4: RESULTS

Demographics: The median [IQR] age of the study population was 60 [51-70] years. Majority of the study participants (52%) were aged 40-64 years. There were more males (59.1%) than females in the study. Based on ASA classification, most of the participants were classified as stage 3 (85.9%) [Table 2].

Table 2: Demographics of study participants

Demographics	All Patients, No. (%) (N=198)
Age, median [IQR], y	60 [51-70]
Age, y	
<40	19 (9.6)
40-64	103 (52)
65+	76 (38.4)
Gender	
Male	117 (59.1)
Female	81 (40.9)
ASA Classification	
II	18 (9)
III	170 (85.9)
IV	10 (5.1)

Markers of Fitness and outcome measures:

Functional markers: Female participants in the study had lower total lean mass, skeletal muscle mass, trunk lean mass, arm lean mass than male counterparts. Females also had a higher body fat percentage than males in this study. Males had higher peak knee extension force, peak hip flexion force and grip strength (Table 3).

Participants aged 20-39, had the lowest skeletal muscle mass, arm lean mass and hand grip strength whereas the 40-64 age group had the highest mean values for the same functional markers (Table 4).

Participants with an ASA classification of IV had the lowest mean values for BMI and total lean mass, while those classified as ASA II had the highest BMI and total lean mass (Table 5).

Morphometric Markers:

Male participants had a higher psoas area on CT scans than female participants. (Table 3).

Outcomes: Our female population had a higher OE ratio than our male population (Table 3).

Partial Correlations:

There were no significant correlations between the markers of fitness and our primary outcome measures, however there were significant correlations between psoas area and some of the functional markers.

When we control age and sex on the relationship between psoas area and total lean mass, we find the following partial correlation $r= 0.45$, $p=0.0009$ (Figure 2a).

When we control age and sex on the relationship between psoas area and skeletal muscle mass, we find the following partial correlation $r= 0.47$, $p=0.0004$ (Figure 2b).

When we control age and sex on the relationship between psoas area and trunk lean mass, we find the following partial correlation $r= 0.55$, $p= <0.0001$ (Figure 2c).

When we control age and sex on the relationship between psoas area and hand grip strength, we find the following partial correlation $r= 0.25$, $p=0.022$ (Figure 2d).

Table 3: Functional, Morphometric Markers, and Outcomes categorized by Gender

Variable	All N=198	Gender Mean (SD) Male n=117	Female (81) n=81	p-value
Functional Marker				
B.M.I.	29.6 (7)	28.8 (6.1)	30.8 (8.3)	0.194
Total Lean Mass	34 (6.8)	37.1 (6)	28.8 (4.6)	<0.001
Total Fat Mass	65.6 (32.2)	61.1 (28.8)	72.9 (36.4)	0.076
Skeletal Muscle Mass	71.2 (15.5)	78.5 (13.5)	59.3 (10.4)	<0.001
Body Fat Percentage, %	32.5 (10.2)	29 (8.3)	38 (10.6)	<0.001
Trunk Lean Mass	57.1 (12.3)	62.9 (10.5)	47.7 (8.7)	<0.001
Leg Lean Mass	8.8 (1.9)	9.7 (1.6)	7.4 (1.5)	<0.001
Arm Lean Mass	3.3 (0.9)	3.7 (0.8)	2.5 (0.6)	<0.001
Six-minute walk test distance, m	442.62 (156.5)	436.6 (162.2)	455.1 (148)	0.685
Grip Strength	28.8 (9.9)	33.6 (9.4)	21.5 (4.7)	<0.001
Peak Knee Extension Strength	41.6 (14)	45.7 (13.7)	35.3 (12.2)	<0.001
Peak Hip Flexion Strength	36.49 (15.15)	41.90 (15.15)	27.63 (10.24)	<0.001
Morphometric Marker				
Psoas Density, HU	51.24 (9.07)	50.61 (9.88)	52.35 (7.43)	0.37
Psoas Area, cm^2	1139.34 (345.5)	1294.51 (294.62)	864.46 (244.2)	<0.001
Outcomes				
General LOS, days	5.68 (6.27)	5.46 (7.1)	6 (4.89)	0.553
Intensive-care LOS, days	0.55 (2.59)	0.76 (3.29)	0.25 (0.91)	0.192
OE	1.20 (1.66)	0.97 (1.08)	1.52 (2.22)	0.024

*All body composition measures (except body fat percentage and BMI) and forces are in lbs.

Table 4: Functional, Morphometric Markers, and Outcomes categorized by Age Groups

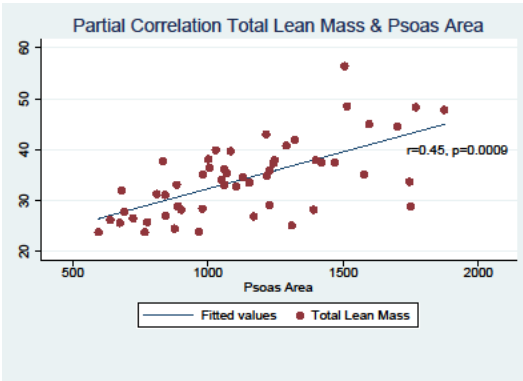
	Age Group, Mean (SD)				
Variable	**All N=198**	**20-39y n=19**	**40-64y n=103**	**65-85y n=76**	**P value**
Functional Marker					
B.M.I.	29.6 (7)	30.8 (9.6)	30.4 (7.2)	28.3 (6.1)	0.325
Total Lean Mass	34 (6.8)	29.7 (5.3)	35.2 (7)	33.5 (6.5)	0.078
Total Fat Mass	65.6 (32.2)	72.6 (40.6)	69.2 (33.9)	59.7 (27.9)	0.314
Skeletal Muscle Mass	71.2 (15.5)	61.4 (12.3)	74 (15.8)	69.9 (15)	0.067
Body Fat Percentage, %	32.5 (10.2)	36.8 (12.7)	32.8 (10.1)	31.1 (9.6)	0.364
Trunk Lean Mass	57.1 (12.3)	49.5 (10.4)	60.2 (12.3)	55.1 (11.8)	0.021
Leg Lean Mass	8.8 (1.9)	7.5 (1.5)	9.1 (1.9)	8.8(2)	0.082
Arm Lean Mass	3.3 (0.9)	2.7 (0.8)	3.5 (0.9)	3.1 (0.9)	0.028
Six-minute walk test distance, m	442.6 (156.5)	507.8 (81.5)	438.2 (165.5)	429.3 (162.5)	0.556
Grip Strength	28.8 (9.9)	25.8 (5.9)	31.2 (11.4)	26.4 (7.5)	0.007
Peak Knee Extension Strength	41.6 (14)	38.4 (9)	41.8 (15)	42.1 (14)	0.653
Peak Hip Flexion Strength	36.5 (15.2)	31.2 (7.5)	37.3 (14.3)	36.8 (17.3)	0.382
Morphometric Marker					
Psoas Density, HU	51.24 (9.07)	54.3 (6.5)	51.4 (8.9)	50.3(9.7)	0.485
Psoas Area, cm^2	1139.3 (345.5)	1131 (309.4)	1127.8(354.3)	1156.3 (349.7)	0.938
Outcomes					
General LOS, days	5.68 (6.27)	4.6 (3.3)	6 (6.5)	5.5 (6.5)	0.625
ICU LOS, days	0.55 (2.59)	0 (0)	0.6 (3.1)	0.6 (2.2)	0.623
OE	1.20 (1.66)	1.4 (1.9)	1.3 (2)	1 (1)	0.335

*All body composition measures (except body fat percentage and BMI) and forces are in lbs.

Table 5: Functional, Morphometric Markers, and Outcomes categorized by ASA Classification

		ASA Classification, Mean (SD)			
Variable	**All N=198**	**Class II n=18**	**Class III n=170**	**Class IV n=10**	**P value**
Functional Marker					
B.M.I.	29.6 (7)	28.6 (6.9)	30.1 (6.9)	20.4 (3.9)	0.022
Total Lean Mass	34 (6.8)	34.5 (5.7)	34.2 (6.8)	26.9 (3.6)	0.049
Total Fat Mass	65.6 (32.2)	66 (35.6)	67.2 (32)	30.2 (14.7)	0.08
Skeletal Muscle Mass	71.2 (15.5)	71.7 (13)	71.9 (15.6)	55.1 (8.1)	0.105
Body Fat Percentage, %	32.5 (10.2)	32.4 (10.3)	33 (10.1)	22 (8.4)	0.107
Trunk Lean Mass	57.1 (12.3)	58.6 (10.4)	57.6 (12.3)	43.5(9)	0.076
Leg Lean Mass	8.8 (1.9)	8.8 (1.6)	8.9 (2)	7.4 (0.8)	0.298
Arm Lean Mass	3.3 (0.9)	3.3 (0.8)	3.3 (0.9)	2.2 (0.7)	0.074
Six-minute walk test distance, m	442.6 (156.5)	431.6 (0)	441 (162)	471.5 (73.4)	0.947
Grip Strength	28.8 (9.9)	29.8 (8.4)	28.7 (9.8)	29.3 (13.1)	0.914
Peak Knee Extension Strength	41.6 (14)	45 (14.6)	41.8 (13.8)	32.3 (14.6)	0.117
Peak Hip Flexion Strength	36.5 (15.2)	37.6 (14.5)	37.2 (15.2)	24.4 (11.5)	0.067
Morphometric Marker					
Psoas Density, HU	51.24 (9.07)	50.1 (10.2)	51.4 (8.9)	49.7 (13.9)	0.888
Psoas Area, cm^2	1139.3 (345.5)	1141.5(338.9)	1141.5 (339)	809.7 (208.7)	0.074
Outcomes					
General LOS, days	5.68 (6.27)	4.1 (4.1)	6 (6.5)	2.9 (2.7)	0.176
ICU LOS, days	0.55 (2.59)	0.1 (0.5)	0.6 (2.8)	0.6 (1.9)	0.774
OE	1.20 (1.66)	1.6 (2.1)	1.2 (1.7)	0.4 (0.2)	0.182

*All body composition measures (except body fat percentage and BMI) and forces are in lbs.



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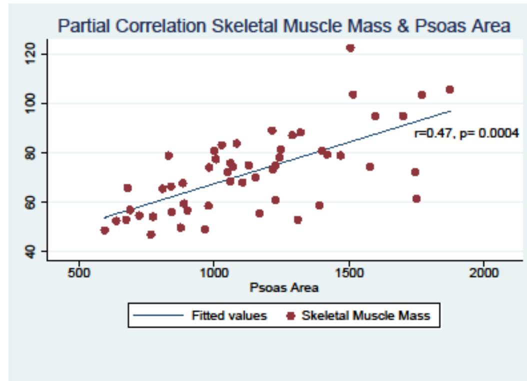

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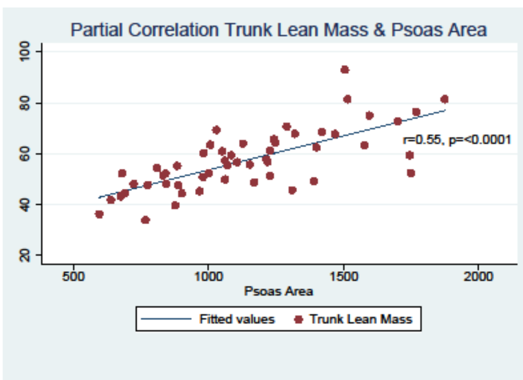

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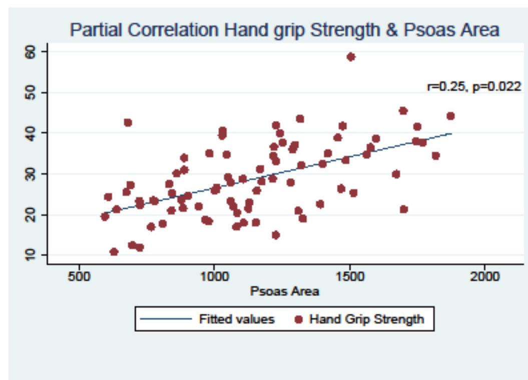

2.d

Figure 2: Partial Correlations between Functional & Morphometrics Markers.

2a: Scatterplot of Total Lean Mass (lbs) on the y-axis and Psoas Area (cm^2) on the x-axis.
2b. Scatterplot of Skeletal Muscle Mass (lbs) on the y-axis and Psoas Area (cm^2) on the x-axis.
2c. Scatterplot of Trunk Lean Mass (lbs) on the y-axis and Psoas Area (cm^2) on the x-axis.
2d. Scatterplot of Hand Grip Strength (lbs) on the y-axis and Psoas Area (cm^2) on the x-axis.
***All partial correlations are adjusted for age and sex.**

CHAPTER 5: DISCUSSION

The main aim of this study was to assess morphometric (psoas area and density) and functional (lower limb strength, hand grip strength, and body composition) markers and test their relationship with major surgical outcomes such as general and intensive-care unit length of stay and observed vs expected length of stay (OE) ratio.

Our study showed the following:

- Gender differences: Women had lower skeletal muscle mass, total lean mass, trunk lean mass and arm lean mass but higher percentage body fat and OE ratio than men.
- Age differences: Participants aged 20-39 years had the lowest skeletal muscle mass, arm lean mass and hand grip strength while participants aged 40-64 years had the highest.
- ASA classification differences: Participants classified as ASA IV had the lowest BMI and total lean mass whereas ASA class II participants had the highest.
- Correlation between markers: total lean body mass, skeletal muscle mass, trunk lean mass and hand grip strength had significant positive correlations with psoas area.

Variations in Body composition and BMI

Most of the markers that showed significance in our study were associated to leanness. Men had significantly higher lean mass and particularly skeletal muscle mass than women as measured by bio-impedance. Gender differences in body composition have been studied extensively and men have a more fat free mass (FFM) and less fat mass (FM) than women when matched for age (Bredella, 2017; Iqbal et al., 2014; Lafortuna, Maffiuletti, Agosti, & Sartorio, 2005). A study that looked at the effect of gender and obesity on body composition found that men had significantly higher FFM than women in both obese and non-obese participants. In addition, females had higher body fat percentage and fat mass than men even when controlling for obesity (Lafortuna et al., 2005). These findings are consistent in children, early adulthood and elderly populations as shown by Lindle *et al.* in a study population ranging from 20 to 93 (Lindle et al., 1997).

The study population aged 20-39 years had the lowest skeletal muscle mass and arm lean mass whereas the 40-64 age range had the highest. This is different from other findings which have shown that skeletal muscle mass decreases with age with reports of up to 8% lost per decade after the age of 30 and even more after the age of 60 (Volpi, Nazemi, & Fujita, 2004). Furthermore, sarcopenia is known to affect individuals from their 40s (McCormick & Vasilaki, 2018). A possible explanation for this finding in our study is that we did not account for comorbidities which can lead to premature loss of skeletal muscle mass (Chen, Nelson, Zhao, Cui, & Johnston, 2013). Also, the 20-39 year old age group had the smallest number of participants in our study, and thus may not reflect findings from larger populations.

Total body lean mass and BMI decreased with ASA classification, so, participants classified as ASA IV had the lowest values. ASA is based on physical status, so it is expected that participants with a worse physical status should have less lean mass as physical inactivity is associated to loss of lean mass when controlling for age (Ajitsaria et al., 2018; Chen et al., 2013; Volpi et al., 2004). Also, at ASA IV, patients are in a constantly life-threatened state that places them under sustained stress which in itself can lead to increased sarcopenia via increased oxidative stress (Farrow et al., 1982; Gomes et al., 2017; Wolters et al., 1996).

Variations in Markers of Strength

Skeletal muscle mass and strength are positively correlated independent of the associations of age and gender with muscle mass and muscle strength (Chen et al., 2013). These findings are similar to our study where markers of strength such as knee extension strength, hip flexion strength, grip strength and psoas area followed the same trend as leanness based on gender and age. Several studies have corroborated our findings but some have shown that muscle mass is not determinative of muscle strength. Heyward *et al.* found that men had higher muscle strength than women but there was no significant difference when they controlled for arm and thigh girth, body weight, triceps and thigh skin fold (Heyward, Johannes-Ellis, & Romer, 1986). These differences may be because of the way muscle strength was evaluated. In a study which measured concentric, eccentric and isometric strength in knee extension found men to have significantly higher muscle strength than women (Lindle et al., 1997).

A study determined that trained female athletes had grip strength values corresponding to the 25^{th} percentile of male counterparts. Furthermore, grip strength linearly correlated with lean body mass in both younger and older populations (Leyk et al., 2007; Sevene et al., 2017). Psoas muscle area has been shown to be a good measure of whole body lean mass and cardiorespiratory fitness; our study showed similar findings with respect to gender (Fitzpatrick et al., 2017; Morrell et al., 2016).

Muscle strength peaks at an individual's twenties and thirties, then plateaus till around their 50s and then declines (Lindle et al., 1997). This is different from the results of our study with peak grip strength in the 40-60 age group. These findings align with the lean body mass trends in our study population; however, other factors such as comorbidities discussed above may influence the observed differences.

Variation in Outcomes

Female participants had a higher OE ratio signifying that they spent longer time in hospital than expected. This observation ties in with the gender differences in muscle strength and body composition. High body fat especially at the incision site has been linked to increased risk of surgical site infection and such post-surgical complications may increase length of stay in hospital and as a result cost. Moreover, Aldea *et al.* found that women have higher post-surgical morbidity and mortality than men following major surgeries (Aldea et al., 1999). This was believed for a long time and prompted several other studies which both supporting and refuted this claim (Butterworth et al., 2000; Hammar, Sandberg, Larsen, & Ivert, 1997). One in particular studied gender influence on length of stay of patients following coronary bypass and found that there was no difference between men and women after adjusting for comorbidities and risk factors (Butterworth et al., 2000). However, another study on coronary artery surgery found that women had a higher risk of mortality in a population of similar age (Aldea et al., 1999). Such contrasting findings for the same surgical procedure highlights the need for better, more consistent predictors of perioperative risk such as those suggested in this study. Utilizing these newer markers of strength and cardiorespiratory fitness may provide the tools to improve perioperative risk assessment and more easily identify high risk groups irrespective of gender or age.

Relationship between Functional and Morphometric Markers of Fitness

Measures of leanness (total lean mass, skeletal muscle mass and trunk lean mass) had a moderate positive correlation with psoas muscle area. Hand grip strength had a weak positive correlation with psoas muscle area, all when controlling for age and gender. This suggests that leanness as measured by bio-impendence, may give similar information about trunk leanness as the more expensive and less accessible CT scan (Bazzocchi et al., 2014; K. Lee et al., 2019). Bio-impedance may therefore be a cost effective and less time-consuming way to assess pre-operative leanness in the pre-surgical workflow.

In summary, body composition analysis by bio-impedance featured markedly in most differences observed in this study making it a potential item to include routinely into pre-surgical work flow. Secondly, improving body composition as measured by bio-impedance prior to surgery may improve post-surgical outcomes. Hip strengthening exercises that help develop the psoas so as to increase its area and in consequence the psoas index should be used in the pre-operative workflow to reduce adverse events.

The main limitation of this study is the sample size which makes it primarily good for generating hypotheses rather than drawing conclusions.

CONCLUSION

Despite its limitations, this study highlights some potential markers of perioperative risk that are feasible and can be easily administered in the pre-operative visits. It also shows potential targets for prehabilitation prior to surgeries in high risk populations. More studies with larger sample sizes need to be conducted to fully explore these markers, their relationship with each other and with adverse postoperative outcomes.

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