Comparison of anthropometric and functional indicators of nutritional status between hospitalized Lao adults with and without malnutrition

By

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Abstract

Introduction: In 2017 in Lao PDR, 33% of children under age 5 suffered from chronic malnutrition (stunting), 9% suffered from acute malnutrition (wasting), 40% of pregnant women were anemic. Obesity and noncommunicable diseases have significantly increased since 2005, evidencing another concerning burden of malnutrition. When energy intake does not meet or exceeds an individual's energy needs, body composition can put an individual at greater risk for health problems. Malnutrition hinders physical and cognitive development, impairs sensory organ function and immune function, and increases susceptibility to infectious disease and its consequences. As a result, malnutrition is the top risk factor for death and disability in Lao PDR. Yet, the risk for and rates of malnutrition in the hospital setting in Lao PDR have not been researched or described in the literature.

Methods: Using a cross-sectional design, 68 patients, 18-70 years of age, were assessed on admission to one of two national hospitals in Vientiane, Lao between August-September 2018. Anthropometric variables were measured including height, weight, body mass index, body composition by bioelectrical impedance analysis, and handgrip strength by dynamometry. A diagnosis of moderate to severe, chronic or acute malnutrition was determined by a registered dietitian using the Academy/ASPEN criteria.

Results: Over half (56%) of adult patients assessed were diagnosed with moderate to severe malnutrition. While 12% of patients had a low body mass index (BMI <18.5 kg/m^2), 36% had a low fat-free mass index (FFMI men <17 kg/m^2, women <15 kg/m^2) and 25% had a low mid-upper arm circumference (MUAC <24 cm), indicating reduced muscle mass. 82% of patients diagnosed with malnutrition had handgrip strength <85% of the age- and sex-based reference value, suggesting diminished functional status. Mean BMI (21.8 ± 3.2 kg/m^2 vs 23.9 ± 4.3 kg/m^2, p=0.03) and MUAC (25.6 ± 3.9 cm vs 27.5 ± 3.9 cm, $p<0.01$) were significantly lower in those with than without malnutrition, respectively. Using linear regression, MUAC predicted BMI and accounted for 68.3% of the explained variability in BMI. Patients with MUAC less than 24 cm were 4 times more likely to be diagnosed with malnutrition ($p = 0.049$, 95% CI: 1.008 to 12.295).

Conclusions: The use of MUAC in adult patients to identify risk for malnutrition may be used effectively, particularly in low-resource settings. Anthropometric measurements can be easily trained to and conducted by healthcare professionals in Lao PDR for nutritional assessment. Quickly identifying patients at risk for malnutrition and initiating appropriate nutrition interventions helps improve patient care and utilization of resources.

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List of Abbreviations

The Academy: Academy of Nutrition and Dietetics

ASPEN: American Society for Parenteral and Enteral Nutrition

BIA: Bioelectrical Impedance Analysis

BMI: Body Mass Index

FAO: Food and Agriculture Organization

FM: Fat Mass

FFM: Fat-Free Mass

FFMI: Fat-Free Mass Index

FMI: Fat Mass Index

HGS: Handgrip Strength

GLIM: Global Leadership Initiative on Malnutrition

GHI: Global Hunger Index

INMUCAL: Institute of Nutrition, Mahidol University Calculation

LANI: Lao-American Nutrition Institute

Lao PDR: Lao People's Democratic Republic

LDC: Least Developed Country

LTPHI: Lao Tropical & Public Health Institute

MUAC: Mid-Upper-Arm-Circumference

NFPE: Nutrition-Focused Physical Exam

UXO: Unexploded Ordinance

WaSH: Water, Sanitation and Hygiene

WHO: World Health Organization

Chapter 1

Introduction and Significance

In 2015, the United Nations implemented the Sustainable Development Goals (SDGs) to collectively promote global development "taking into account different national realities, capacities and levels of development and respecting national policies and priorities".[1] There are 17 SDGs, two of which specifically state a commitment to the role that nutrition and other healthcare professionals share in fulfilling the objectives set out to ensure that all citizens have a chance to achieve their own development. SDG 3 on health and wellness targets "premature mortality from non-communicable diseases through prevention and treatment."[1] SDG 2 addresses the goal of "Zero Hunger". Eradicating hunger is a top goal as hunger leaves already vulnerable individuals more prone to disease and thus less able to work and earn a living to improve their livelihoods.[1] Hunger is indicated by the prevalence of moderate or severe food insecurity in the population, resulting in malnutrition.[2]

Defined by the World Health Organization (WHO) as deficiencies, excesses or imbalances in a person's intake of energy and/or nutrients, malnutrition is a major underlying cause of morbidity and mortality.[3,4] The American Society for Parenteral and Enteral Nutrition (ASPEN) defines malnutrition as "an acute, subacute or chronic state of nutrition, in which a combination of varying degrees of overnutrition or undernutrition, with or without inflammatory activity, have led to a change in body composition and diminished function."[5] The Academy of Nutrition and Dietetics (the Academy) recognizes the detrimental effects of malnutrition, defined as "a physical state of unbalanced nutrition that affects various body systems and functions," as one which must be addressed quickly and comprehensively.[6] Mild to severe malnutrition hinders physical and cognitive development, impairs sensory organ function and immune function, and increases susceptibility to infectious disease and its consequences.[7]

Early detection and treatment of malnutrition among hospitalized patients is associated with improved health and reduced number and intensity of hospital procedures, reduced duration of hospital admissions, and lower number of readmissions following hospital discharge.[8-13]

In the country of Lao People's Democratic Republic (Lao PDR), household poverty, low education levels, poor access to clean water and food, poor sanitation, and lack of health services compromise the nutritional status and increase the risk of malnutrition and chronic disease among Lao citizens.[14,15] Recent data from 2016, indicates one in five Lao citizens routinely consumes less than their minimum estimated daily energy requirement thereby increasing their risk for malnutrition.[16] Addressing factors that contribute to malnutrition is critical for Lao PDR to achieve its SDGs and to graduate from "least developed country" (LDC) status to "developing country" status.

Evidence indicates rates of malnutrition are high in Lao PDR. In 2017, 33% of children under age 5 suffered from chronic malnutrition (stunting), 9% suffered from acute malnutrition (wasting) and 40% of pregnant women were anemic.[17,18] The rates of malnutrition among hospitalized patients in Lao is presumed to be even higher, yet the risk for and rates of malnutrition in the hospital setting in Lao PDR have not been described in the literature. Currently, there are no policies or procedures in place within Lao hospitals to screen patients for malnutrition or to identify patients at-risk for developing malnutrition upon admission.

Administration of a nutrition screening tool is a key first step in the evaluation of nutritional status among hospitalized patients. Over 30 validated nutrition screening tools have been studied in developed countries with high-income and adequate resources. Malnutrition screening tools contain questions that assess weight change, body mass index (BMI), food and fluid intake, current disease or recent surgery, gastrointestinal symptoms, functional capacity, physical examination characteristics, lab parameters, nutritional and past medical history, indication for a special diet, medication and supplement use, socioeconomic situation, and anthropometry.[19] To better detect malnutrition in patients admitted to Lao hospitals, studies comparing the independent predictive value of a nutritional screening tool are needed.[19]

Body composition is an important indicator of nutrition status which considers an individual's weight, height, BMI, amount of fat mass (FM) and fat-free mass (FFM). When energy intake does not meet or exceeds an individual's energy needs, resulting changes in body composition can put an individual at greater risk for health problems.[20] Methods used to assess body composition including weight, height, BMI, mid-upper arm circumference (MUAC) and nutrition-focused physical exam (NFPE) can be conducted in low-resource hospital settings. In addition, FM and FFM can be measured by bioelectrical impedance analysis (BIA), which is quick, relatively inexpensive and non-invasive.[21] Fat mass index (FMI) and fat-free mass index (FFMI) can be calculated by dividing FM and FFM by height to further classify body composition into underweight, normal weight and overweight categories. Furthermore, handgrip strength (HGS), measured by dynamometry, is a measure of functional nutritional status, specifically FFM. Serial measurements of HGS have been validated as a nutrition assessment tool and is one criterion in the Global Leadership Initiative on Malnutrition (GLIM) and the Academy/ASPEN guidelines to diagnose malnutrition.[22-24] Among a variety of biochemical and anthropometric measurements, impaired muscle function assessed by HGS has demonstrated greater sensitivity in detecting malnutrition.[25,26] Although bioelectrical impedance and hand dynamometry methods are relatively inexpensive and easy to implement, they have not been used in the diagnosis of malnutrition, or its severity, in hospitalized adults in Lao PDR.

Specific Aims and Hypotheses

This cross-sectional study was designed to characterize and evaluate various markers of body composition and functional muscle strength in relation to a malnutrition diagnosis in hospitalized adults in Lao PDR. To accomplish this goal, we carried out the following specific aims:

1) Characterize body composition measured by BMI, FMI, FFMI, and MUAC, and HGS measured by hand dynamometry, of hospitalized Lao adults admitted to one of two national hospitals in Vientiane, Lao PDR.
2) Compare body composition variables and HGS between patients who met and who did not meet criteria for malnutrition as defined by Academy/ASPEN diagnostic characteristics.[7]
3) Compare HGS measured by hand dynamometry of hospitalized Lao adults who met and who did not meet Academy/ASPEN criteria for malnutrition to normative values of presumably healthy South East Asian adults established by the PURE study.[27]
4) Determine the relationships between 1) FFM and MUAC, 2) FFM and HGS, and 3) MUAC and HGS, among hospitalized Lao adults who met and who did not meet the Academy/ASPEN criteria for malnutrition.
5) Determine the criterion or set of criteria (BMI <18.5 kg/m^2, FFMI <17 kg/m^2 for men and <15 kg/m^2 for women, MUAC <24 cm, and HGS <85% of the reference value) that best predicted the diagnosis of malnutrition among hospitalized Lao adults as established by the Academy/ASPEN guidelines.[7]

The hypotheses that were tested include:

1) Mean markers of body composition and functional muscle strength would be significantly lower among hospitalized Lao adults with than without a diagnosis of malnutrition (Aim 2).
2) Mean HGS of hospitalized Lao adults would be significantly lower than normative values of presumably healthy South East Asian adults between 35-70 years of age (Aim 3).
3) FFM, MUAC and HGS would be positively associated among hospitalized Lao adults who met the criteria for malnutrition and those who did not meet the criteria for malnutrition (Aim 4).
4) HGS <85% of the reference value would have the greatest predictive value defined by the highest true positive rate (sensitivity) and true negative rate (specificity) to correctly identify hospitalized Lao adults who are malnourished (Aim 5).

Chapter 2

Background

Lao PDR is a landlocked country in Southeast Asia, bordered by China, Myanmar (Burma), Thailand, Cambodia and Vietnam (Figure 1). The country's eighteen provinces are characterized by mountainous regions and plains along the Mekong River. The people who live in Lao represent 49 different ethnic groups with a high diversity of languages spoken, culture and traditions.[28] The total population of the country is approximately 7.2 million and the capital city, Vientiane, is the largest city with about 665,000 people.[29] Approximately 80% of the population works in agriculture and practices subsistence farming primarily growing rice, the country's staple crop.[30] One of the major problems constraining agricultural development in 15 of 18 provinces in Lao PDR is the presence of undetected, unexploded ordnances (UXOs) dropped during the Vietnam War. Forty years after the Vietnam war, UXOs continue to impact rural lives by limiting the amount of arable land, thus affecting the livelihoods and food security of a large number of households in Lao PDR.[28]

The 2018 Global Hunger Index (GHI) established by the United Nations and other multilateral agencies, and determined by insufficient caloric intake, child undernutrition, and child mortality rates, indicates that the level of hunger and undernutrition in Lao PDR falls within the "serious" category.[31] A reduction in GHI score of 23 points from 48 points (alarming hunger levels) for Lao PDR since 2000 provides evidence for the efforts put forth to achieve SDG #2 which aims to end hunger, ensure food security and improved nutrition, and promote sustainable agriculture, by 2030.[31]

Figure 1. Map showing the geographical location of Laos and its provinces

Foreign and Commonwealth Office, United Kingdom

Prevalence of Malnutrition in Children

Stunting, when height is significantly lower than expected for chronological age (height-for-age z-score between -2 and -3 based on WHO Child Growth Charts), reflects chronic malnutrition, and affects approximately 33% of children under five years of age in Laos. Wasting, when weight is significantly lower than expected for height (weight-for-height z-score between -2 and -3 based on WHO Child Growth Charts), reflects acute malnutrition, and affects approximately 9% of children under five years of age in Laos as of 2017.[17] Severe acute malnutrition (weight-for-height z-score below -3) may be characterized by visible severe muscle wasting (marasmus) or nutritional edema (kwashiorkor). The wasting of muscle mass and the depletion of body fat stores that result from malnutrition can be due to inadequate intake of all nutrients, but especially dietary energy sources (e.g. protein, fat and carbohydrate). Factors associated with protein-energy malnutrition include: socioeconomic status, access to clean water and sanitation, unsanitary food handling practices, subsistence farming, climate change and natural disasters such as flooding and crop failure, and low educational level and limited nutrition knowledge of mothers.[32] Cultural practices and traditional ethnic beliefs, as well as medicinal and infant and young child feeding practices, vary according to the different ethnic groups in Laos and can contribute to micronutrient deficiencies.[33] For example, thiamin deficiency, a deficiency of vitamin B1, among ethnic groups in northern Laos is commonly found in mothers with poor dietary diversity who practice food avoidance traditions during the postpartum period.[34]

Double Burden of Malnutrition in Lao Adults

Recent trends in Laos show a decrease in communicable diseases (e.g. infectious diseases) and an increase in noncommunicable diseases (e.g. obesity and diabetes).[3] WaSH (water, sanitation and hygiene) has improved and pre-term births have decreased by 20%, but BMI has significantly increased and heart disease prevalence is up by 10% since 2005.[3] At the same time, malnutrition has remained the top risk factor for death and disability.[3] As these health trends show, the country is now experiencing another concerning burden of malnutrition with the increasing prevalence of overweight or obesity in adults; this trend parallels an increase in food energy supply which does not support a healthy diet.[35] National food consumption survey data shows the average macronutrient distribution among Lao adults appears sufficient according to intake goals set by the joint Food and Agriculture Organization (FAO)/WHO expert consultation of 55-75% carbohydrate, 10-15% protein and 15-30% fat. Yet, the average total energy intake of 1,296 kcal/day is inadequate.[4,36] In contrast, an abundance of data shows that micronutrient intakes typically fall below recommendations as a result of lack of food variety primarily due to economic instability, specifically calcium, iron and vitamin A.[14,36,37] Micronutrient deficiencies are associated with adverse health outcomes.[37] In an effort to prevent the negative effects of prolonged malnutrition on growth and development, body composition markers are being used to help define nutrient needs for optimal function in infants.[38,39] In the adult population, malnutrition presents with signs and symptoms of micronutrient deficiencies as well as changes in muscle, fat and fluid status. Studies of hospitalized adults in China, Singapore and Vietnam report prevalence of nutritional risk between 20-45%.[8,40-44] A retrospective study of patients admitted to a government teaching hospital in Vientiane capital revealed that the most common underlying causes of death among adults aged 20-59 years were injury (37.9%), cerebrovascular diseases (23.7%), renal disease (12.3%), infectious diseases (10.2%), and malignant neoplasm including brain tumor (5.0%).[45] All of these medical conditions are associated with high nutritional risk. In response to a full analysis of the nutrition situation in Lao PDR, the National Nutrition Strategy was established by the government of Lao PDR in 2015. A Priority 1 Intervention was aimed to "promote capacity building in organizations in order to ensure nutrition and food security efficiently and effectively", achieved by training nutrition service providers in the treatment of malnutrition at central, provincial and district hospitals.[14]

Anthropometric Indicators of Nutritional Status

Body Mass Index. BMI is a simple reliable measurement of weight indexed to height and is used to monitor health-related changes. Many regions of the world currently use a BMI <18.5 kg/m^2 as a criterion for the recognition of malnutrition, and low BMI is included the GLIM consensus. However, the GLIM also stated the need for further research to “secure consensus reference BMI data for Asian populations in clinical settings.”[22] International BMI reference ranges were established by the expert WHO consultation, and have been widely applied in public health for detecting differences in disease risks between population groups.[46] A common observation from epidemiological data is that body composition, specifically percent body fat, varies within designated BMI ranges across populations. Factors that may contribute to this difference in body composition include nutritional status, amount and type of physical activity, race, genetics and intrauterine undernutrition.[47] While it has long been understood that higher BMI indicates higher body fat percent, multiethnic studies have shown that among Asians, body composition, specifically FM, tends to be higher at lower BMI values..[48,49] Referred to as the “thin-fat syndrome”, those with a healthy BMI may accumulate visceral fat which increases risk for heart disease and other related metabolic disorders.[47,50] A study including white participants in the United Kingdom (UK; n=196) and the United States (US; n=221), African American participants in the US only (n=254), and Asians in Japan (n=955) revealed that BMI in Asians is lower overall compared to non-Asian populations. Yet, within similar BMI ranges, body fat percentages appear to be higher in Asians.[51] As a result of these and similar observations, the 2004 WHO Expert Consultation on appropriate BMI in Asian populations identified increasing risk for chronic disease along the range of BMI categories and proposed new cut-off points to be used in both public health efforts and the development of clinical protocols (Table 1).[46]

Table 1. Population-specific body mass index cut-off points compared to international standards

International BMI ranges (kg/m^2)	**<18.5**	**18.5–24.9**	**25.0-29.9**	**≥30.0**
Weight classification	Underweight	Normal weight	Overweight	Obese
Corresponding Asian BMI ranges[46] (kg/m^2)	<18.5	18.5–23.0	23.0–27.5	>27.5
Weight and chronic disease classification	Underweight	Increasing but acceptable risk for chronic disease	Increased risk for chronic disease	High risk for chronic disease

Amount and Distribution of Body Composition Assessed by BIA. Body composition analysis is the clinical assessment of the FFM (metabolic tissue, intracellular and extracellular water, bone tissue) and FM in the human body. A bioelectrical impedance analyzer produces small electrical currents of opposite charges and measures the amount of charge that moves through the body. Depending on the composition of the material through which the electrical current moves, specifically the amount of FM or FFM, resistance to the current can be higher or lower, respectively. Body fat acts as an insulator, which has high electrical resistance. Fat-free mass, including muscles tissue and other organs, acts as a conductor due to high water content. Water, the primary component of FFM, is charged by ions which conduct electricity, while lipids, the primary component of FM, are made up of uncharged groups. Ohm's law describes the relationship among voltage "V", resistance "R" and current "I" with the equation $I = V / R$, so that when resistance increases, current decreases. While BIA measures resistance (ohms), proprietary regression equations that include resistance are used to calculate variables such as FM, FFM, and body water. Factors like altered body geometry, fluid status and increased fat fraction can result in measurement errors.[21] Factors affecting hydration status include the use of diuretics, anabolic medications, diet, hydration habits, and exercise habits. Currently, there are numerous validated prediction equations to estimate FFM and FM from resistance in different populations, and accuracy is dependent on the criterion used to determine the dependent variable in the equation.[52] For the study conducted here, the BIA machine (Biodynamics Model 310e, Seattle, Washington, USA) used nine proprietary equations to predict body fat, four for men, three for woman, one for children, and one for elite athletes, each in the following form: FFM = A * height^2 + B * weight + C * Age + D * resistance + E, where A, B, C, D, and E are coefficient constants that produce the lowest standard error of estimate and the highest correlation for the given morphological classification. Using body composition characteristics based on height, weight, and measured bioresistance for a specific individual, an equation is automatically selected based on the individual's morphological classification. The morphological classifications are as follows: 1) mesomorph – stocky, predominantly muscular build, high BMI, low bioresistance 2) ectomorph – lean, thin features with low degree of muscle and fat, low BMI, low bioresistance 3) endomorph – thick, rounded limbs, predominance of fat, high BMI, high bioresistance 4) normal – a combination of the characteristics, normal BMI, moderate bioresistance. Morphological classifications do not factor in differences in limb length between ethnic groups such as relatively short limbs among Asians which may result in an underestimation of bioelectrical impedance and thus FM.[53] However, the validity of BIA equations between Asians, Hispanics, Caucasians and African Americans has been tested and found to not have significant differences between ethnic groups ($P>0.05$).[54]

Fat Mass Index and Fat-Free Mass Index. FMI and FFMI reflect the concept of BMI as a measure of body composition indexed to height. Mathematically, BMI = FFMI + FMI where FFMI = FFM / height^2 (kg/m^2) and FMI = FM / height^2 (kg/m^2). BMI can be viewed as a constant relative to total body mass, so iff FFMI is lower at a given BMI then it follows that FMI is higher, which allows for a more discriminant interpretation of body composition. Men and women with FFMI of <17 and <15 kg/m^2, respectively, are considered to have reduced muscle mass according to GLIM criteria for diagnosis of malnutrition.[22] As shown in Table 2, the cutoff values for low FFMI are established from a large cross-sectional study of apparently healthy Caucasians between 18-98 years of age (n = 5635), which used BIA to measure FMI and FFMI and then generated regression equations to calculate these variables based on BMI.[55] Similar calculations have been done to highlight racial differences in body composition, such as in a 2011 multi-ethnic study in the US (n = 1339) which reported that mean BMI and thus mean FFMI and FMI was highest in African Americans (FFMI 21.1 ± 2.3 kg/m^2 in men, 17.4 ± 1.9 kg/m^2 in women) and lowest in Asians (FFMI 18.8 ± 1.8 kg/m^2 in men, 15.0 ± 1.2 kg/m^2 in women; $P \leq 0.001$).[56] Researchers also found a significant difference between ethnic groups in the percent decrease in FFMI between 20 to 90 years of age, with the greatest decline in FFMI in Asians (-13.3% in men and -11.0% in women) and the least decline in African Americans (-11.8% in men and -9.5% in women, $p<0.001$).[56] Based on studies that reveal that body fat among Asians tends to be higher than other ethnic groups at a specific BMI, it follows that FMI would be higher and FFMI would be lower among Asians compared to age- and sex-matched Caucasians with the same BMI.

Table 2. Estimated fat-free mass index (FFMI) and fat mass index (FMI) at various BMIs among apparently healthy Caucasian adults aged 18-98 years[55]

	BMI (kg/m^2)		
Men	18.5 (underweight)	20.0 (normal weight)	25.0 (overweight)
FFMI (kg/m^2)	16.7	17.5	19.8
FMI (kg/m^2)	1.8	2.5	5.2
Women			
FFMI (kg/m^2)	14.6	15.1	16.7
FMI (kg/m^2)	3.9	4.9	8.3

FFMI and FMI predicted from the following regression equations: for FFMI prediction, Men $y=4.809+0.773*x-0.007*x^2$; $r^2=0.619$, $P<0.001$; women $y=7.127+0.459*x-0.003*x^2$; $r^2=0.606$, $P<0.001$; where y is FFMI (kg/m^2) and x is BMI (kg/m^2). For FMI prediction: Men $y=-4.74+0.222*x+0.007*x^2$; $r^2=0.772$, $P<0.001$; women $y=-7.12+0.54*x+0.003*x^2$; $r^2=0.885$, $P<0.001$; where y is FMI (kg/m^2) and x is BMI (kg/m^2).

Mid-Upper Arm Circumference. MUAC correlates well with BMI and is an indicator of muscle mass, serving as a simple to measure and reliable alternative to other anthropometric measures.[57-60] While used as a malnutrition diagnostic criteria among pediatric populations, MUAC is not considered to have adequate evidence for use among adults. A cross-sectional study among rural adult males between 18-70 years of age from India's Oraon tribe (n = 205) showed strong positive association between MUAC and BMI (r = 0.45, p<0.001), as well as an inverse relationship between the prevalence of chronic energy deficiency defined as BMI <18.5 (kg/m^2) with MUAC values (X^2 = 49.10, p<0.001).[58] In a systematic review that determined the association between low MUAC and poor health outcomes in adolescents and adults, 43 of the 47 studies were conducted in low-resource settings.[60] Low MUAC in adults defined as ≤23 cm was significantly associated with underweight status (BMI <18.5 kg/m^2), self-reported sick days, patients who have tuberculosis without anti-tuberculosis drug-induced hepatotoxicity, and pregnant women with low birthweight infants, anemia and postpartum endometritis-myometritis[60] Following this systematic review, a meta-analysis of 17 studies of men and non-pregnant women was performed. Two of the included studies were conducted in Vietnam and participants had mean MUAC values of 24.5 ± 2.3 cm and 25.6 ± 2.6 cm compared to the combined mean MUAC of 26.0 ± 4.4 cm from all other study participants combined. The authors concluded that a MUAC of ≤24.0 cm was the most appropriate cutoff value to identify underweight status in adults when BMI was < 18.5 kg/m^2 because of its high sensitivity (true positive rate 81.9%) and specificity (true negative rate of 85.6%). In other words, among adults with BMI <18.5 kg/m^2, using MUAC of ≤24 cm resulted in the lowest percent of misclassification of underweight status.[61]

Functional Indicators of Nutritional Status

Handgrip Strength. Handgrip dynamometry, which is used to measure HGS, is an assessment tool used to estimate functional muscle stores in humans.[62] HGS is correlated with cellular muscle mass as indicated by muscle contractility, relaxation rate, and endurance.[25,63] Loss of muscle function associated with loss of strength may predict changes in body composition, specifically loss of muscle mass, and may help detect functional impairment at sub-clinical levels.[26,63] GLIM criteria recommends HGS as a supportive measure for reduced muscle mass. In a study of 127 patients with cancer that excluded those with coexisting conditions that could lead to nutritional depletion, HGS correlated well with mid-arm muscle circumference and with creatinine height index in both men and women ($r=0.6$, $p<0.01$), confirming its reliability as an indicator of nutritional status.[13] Brazilian men of all ages with underweight status (BMI <18.5 kg/m^2) had significantly lower HGS (min 4.4, max 12.6 kg, mean 8.1 kg, $p=0.001$) than those with overweight status (BMI ≥25 kg/m^2), while Brazilian women of all ages had less of a difference in HGS between underweight and overweight BMI status (min 1.5, max 5.2 kg, mean 3.2 kg, $p=0.40$).[64] HGS is also strongly positively correlated with height in various ethnic adult populations including Mexican ($r=0.757$, $p<0.001$), British ($r=0.67$, $p<0.01$), and Greek ($r=0.553$, $p<0.001$), suggesting that populations will have differing HGS values based on differences in anthropometric values.[65-67] Mean HGS has been shown to vary by ethnic origin with average handgrip strength of South Asians among the lowest, as evidenced by 40% of men and 33% of women having a handgrip strength in the lowest tertile.[68] Handgrip strength in the adult Malaysian population has measured to be 1.5 times lesser than in western populations, demonstrating the need for HGS data specific to South East Asians.[69]

Normative values are established using comparable tools and large populations, and consolidated HGS values obtained from multinational data offers a strong standard for comparison (see Table 3, 4).[27,70] In the clinical setting, early detection of functional muscle impairment can be determined by comparison of serial HGS measurements to established normative values. In hospitalized patient populations, decreased HGS is associated with increased postoperative complications, increased duration of hospitalization, higher rehospitalization rates and decreased physical status.[71] Changes in HGS during illness can be due to electrolyte and metabolite abnormalities, medications, decreased physical activity, and lack of motivation in addition to negative energy and protein balance.[63] In a study of 287 hospitalized adults in a community hospital in Berlin, Germany, patients with normal weight and overweight BMI classified as malnourished by a Subjective Global Assessment had a significantly lower mean absolute HGS than patients classified as well-nourished (mean difference of 28.9% and 22.7% in men and women, respectively; $p<0.001$).[25] Patients with HGS values below 85% of the standard value for age and sex had lower BMI ($P<0.05$), body cell mass determined by BIA ($P<0.001$), arm mass area calculated using mid arm circumference and triceps skinfold ($P<0.001$), and longer hospital stays (median 10 days (min 2–max 26) versus median 7 days (min 2–max 27), $P<0.05$).[25]

Table 3. Median (interquartile range) handgrip strength of South East Asian men and women[27]

	Handgrip strength of men in kg (n=4097)			Handgrip strength of women in kg (n=6002)		
Age (years)	Both hands (average)	Right hand (dominant)	Left hand (non-dominant)	Both hands (average)	Right hand (dominant)	Left hand (non-dominant)
35-40	40 (34–44) n=562	40 (34–46) n=561	38 (32–42) n=560	23 (19–27) n=1091	24 (20–28) n=1091	22 (18–26) n=1089
41-50	37 (32–42) n=1320	38 (33–44) n=1320	36 (30–40) n=1316	22 (19–26) n=2234	24 (20–28) n=2232	22 (18–25) n=2226
51-60	33 (29–38) n=1331	34 (30–40) n=1330	32 (28–37) n=1321	20 (17–23) n=1739	21 (18–24) n=1735	19 (16–22) n=1716
61-70	29 (24–33) n=884	30 (24–34) n=883	28 (22–32) n=877	18 (14–21) n=938	18 (15–22) n=937	18 (14–20) n=902

Average handgrip strength calculated from the maximum of three measurements obtained from each hand. Where values were missing for one hand but present for the other hand, values for the missing hand were imputed using the coefficient and constant from the linear regression of right and left handgrip strength.

Table 4. Mean handgrip strength reference values consolidated from 12 studies in USA, Australia, Canada and Sweden[70]

	Men (n=1586)		Women (n=1731)	
Age range (years)	Left hand (95% CI)	Right hand (95% CI)	Left hand (95% CI)	Right hand (95% CI)
20-24	47.4 (38.8-56.1)*	53.3 (45.2-61.5)	27.9 (23.1-32.6)	30.6 (26.7-34.4)
25-29	50.0 (41.1-58.9)	53.9 (44.3-63.6)	30.8 (27.2-34.5)	33.8 (29.5-38.1)
30-34	49.2 (40.4-57.9)	52.8 (44.1-61.5)	31.8 (29.0-34.4)	33.8 (28.9-38.6)
35-39	51.6 (44.0-59.3)	53.3 (44.0-62.6)	30.2 (25.8-34.5)	33.2 (28.6-37.8)
40-44	49.8 (42.5-57.1)	54.1 (47.1-61.2)	29.3 (24.5-34.0)	32.8 (28.0-37.6)
45-49	48.7 (40.3-57.2)	50.4 (42.5-58.3)	30.8 (25.8-35.7)	33.9 (28.9-39.0)
50-54	45.2 (39.4-51.1)	50.6 (44.2-56.9)	28.8 (24.0-33.5)	30.9 (26.7-35.2)
55-59	41.0 (33.7-48.8)	44.1 (36.7-51.4)	27.2 (24.6-29.5)	29.9 (26.4-33.6)
60-64	38.7 (33.4-44.0)	41.7 (36.8-46.7)	23.0 (18.6-27.3)	25.9 (22.2-29.6)
65-69	38.2 (32.0-44.4)	41.7 (35.4-47.9)	22.9 (19.6-26.2)	25.6 (22.5-28.8)

*Mean (95% CI)

Use of anthropometric indicators to support the diagnosis and severity of malnutrition in hospitalized adult patients including BMI, FM, FFM, MUAC, and HGS has not been established in Lao PDR. To gain a better understanding of the anthropometric and muscle strength indicators of malnutrition in hospitalized Lao adults, we measured body composition and HGS and compared these variables between patients who met and who did not meet criteria for malnutrition, assessed the relationships between these variables, and determined the criterion or set of criteria that best predicted the diagnosis of malnutrition.

Chapter 3

Methods

Subjects and Setting

The sample for this cross-sectional study included hospitalized Lao men and women, 18-70 years of age, admitted to one of two government hospitals, Mahosot or Setthathirath, in Vientiane, Lao PDR. Patients are referred to these two hospitals from village health clinics, district hospitals, and provincial hospitals if they require higher levels of care.

Recruitment

Patients at Mahosot and Setthathirath hospitals who were admitted to the Surgery, Internal Medicine, Diabetes, Pulmonary, Human Immunodeficiency Virus (HIV), Tuberculosis, and Infectious Disease wards were recruited within 24 hours of admission to participate in this study during a nutrition screening procedure conducted as part of a larger study.

Exclusion Criteria

Exclusion criteria included: age less than 18 or greater than 70 years and/or currently pregnant by self-report. For BIA measurements, participants with significant amputations of an extremity, intravenous (IV) placement at the right wrist, or edema were excluded. HGS measurements were not conducted in individuals with upper limb deformities or conditions that led to an inability to carry out the HGS measurements including osteoarticular diseases, pain, sedation, placement of an IV on the wrist, burns, cognitive impairment and surgery on an upper limb.

IRB Approval

The study protocol was approved by the Lao Health Research Board for Ethical Review and by the Oregon Health & Science University Institutional Review Board.

Informed Consent

All study documents were provided for participants/caregivers to review in the Lao language. The study process and procedures were described in the Lao language before written consent was obtained, any medical information was retrieved, or measurements were performed. Written informed consent (Appendix A) was obtained from patients or their caregivers by trained Lao-speaking research assistants.

Confidentiality/Data Management/Human Subjects Research Training

All study participant data was de-identified and hard copies of all study-related documents were stored under lock and key in the Lao American Nutrition Institute (LANI) office at the Lao Tropical and Public Health Institute (LTPHI) in Vientiane, Lao. Study forms were scanned using a device protected with encryption and dual-password technology and were uploaded to a secure OHSU Box file. All research staff received training regarding their respective tasks.

Assessment of Body Composition – Anthropometric Measurements

Height. Height was measured without shoes using a stadiometer with participants standing straight against a fixed vertical backboard with an adjustable head piece. On the rare occasion when a stadiometer was not available or if the participant was unable to stand, the measurement recorded in the medical record was used. Height was recorded to the nearest 0.01 centimeter.

Weight. Weight was measured using a digital scale and recorded to the nearest 0.1 kg. On the rare occasion when a digital scale was not available, a beam scale was used. Measurements were done with patients wearing light clothing and shoes removed. If the patient was unable to stand to be weighed, the measurement recorded in the medical record was used.

Body Mass Index (BMI). BMI was calculated as weight in kilograms divided by height in meters-squared. BMI will be used to classify participants into one of four categories based on the 2004 WHO expert consultation Asian BMI cut-off points: <18.5 kg/m^2 = underweight; 18.5–23.0 kg/m^2 = acceptable risk for chronic disease; 23.0–27.5 kg/m^2 = increased risk for chronic disease, >27.5 kg/m^2 = high risk for chronic disease.

Mid Upper Arm Circumference (MUAC). MUAC was measured with patients in a seated position, while the right arm was extended but relaxed at the side, at the midpoint between the shoulder and elbow. A non-stretch tape measure was used and MUAC was recorded to the nearest millimeter (mm).

Fat Mass (FM) and Fat-Free Mass (FFM). A bioelectrical impedance analyzer (Biodynamics Model 310e, Seattle, Washington, USA) was used to measure resistance (ohms) and estimate FM and FFM in kg using proprietary regression equations. These measurements were obtained by attaching two sets of electrode pads and leads to cleaned sites at the wrists and ankles on the right side of the body. Participant weight, height, sex and age were entered into the analyzer for use in the programmed equations. In addition to recording the raw data (ohms, FM (kg), FFM (kg), FM (%), FFM (%)), FMI (kg/m^2) and FFMI (kg/m^2) were calculated as the ratio of FM or FFM in kilograms divided by height in meters-squared.

Assessment of Functional Indicators of Nutritional Status

Handgrip strength. HGS was measured using a Jamar dynamometer (Patterson Medical, Warrenville, IL). To obtain this measurement participants were seated with their back and arms unsupported, with their arms positioned at the sides of the body and elbows flexed to 90 degrees. Participants were asked to grip the handle of the dynamometer and squeeze the dynamometer for 4-5 seconds with the readout dial pointing away from their body. This procedure was repeated three times on each hand, alternating between hands for each measurement. HGS was recorded in kilograms and measurements were compared to reference values as determined by Leong et. al. (Table 3).[70]

Assessment of Severity of Malnutrition

Patients were diagnosed with malnutrition by a Registered Dietitian. A malnutrition diagnosis was based on the Academy and ASPEN Consensus on the Diagnosis of Malnutrition.[23] The severity of malnutrition was characterized as one of the following: moderate acute, moderate chronic, severe acute, or severe chronic based on the presence of two or more of the following characteristics: reduced energy intake, weight loss, decreased body fat, decreased muscle mass, or fluid accumulation, as described in Table 5. Body fat, muscle mass and fluid accumulation were assessed objectively by NFPE. Energy needs were estimated individually for each patient using calories per kilogram ranges. Actual nutrient intake was then calculated by entering 24-hour dietary recall forms into Institute of Nutrition, Mahidol University Calculation (INMUCAL) and compared to estimated needs. Patients were asked about their percentage of usual intake consumed, usual body weight and any noticeable weight loss over time. Reduced HGS was left out of the diagnostic characteristics to prevent this variable from directly influencing the outcome assessment.

Table 5. Academy/ASPEN clinical characteristics used to support a diagnosis of malnutrition

Clinical Characteristics A minimum of 2 of the 6 characteristics is recommended for diagnosis of either severe or non-severe malnutrition	**Malnutrition in the Context of Acute Illness or Injury**		**Malnutrition in the context of Chronic Illness**		**Malnutrition in the Context of Social or Environmental Circumstances**	
	Non-Severe (Moderate) Malnutrition	**Severe Malnutrition**	**Non-Severe (Moderate) Malnutrition**	**Severe Malnutrition**	**Non-Severe (Moderate) Malnutrition**	**Severe Malnutrition**
(1) Energy Intake	<75% of estimated energy requirement for >7 days	≤50% of estimated energy requirement for ≥5 days	<75% of estimated energy requirement for ≥1 month	≤75% of estimated energy requirement for ≥1 month	<75% of estimated energy requirement for ≥3 months	≤50% of estimated energy requirement for ≥1 month
(2) Interpretation of Weight Loss (% of unintentional weight loss from UBW)	1%-2% in 1 week 5% in 1 month 7.5% in 3 months	>2% in 1 week >5% in 1 month >7.5% in 3 months	5% in 1 month 7.5% in 3 months 10% in 6 months 20% in 1 year	>5% in 1 month >7.5% in 3 months >10% in 6 months >20% in 1 year	5% in 1 month 7.5% in 3 months 10% in 6 months 20% in 1 year	>5% in 1 month >7.5% in 3 months >10% in 6 months >20% in 1 year
Physical Findings:						
(3) ↓ Body Fat **Loss of subcutaneous fat (e.g., orbital, triceps, ribs)**	Mild	Moderate	Mild	Severe	Mild	Severe
(4) ↓ Muscle Mass **Muscle Loss (e.g. wasting of the temporalis muscle, clavicles, shoulders, interosseous, scapula, thigh, calf)**	Mild	Moderate	Mild	Severe	Mild	Severe
(5) ↑Fluid Accumulation **Evaluate generalized or localized fluid accumulation evident on exam. Weight loss is often masked by general fluid retention and weight gain may be observed.**	Mild	Moderate to Severe	Mild	Severe	Mild	Severe
(6) ↓ Grip Strength **Using normative standards supplied by the manufacturer of the measurement device.**	N/A	Measurably ↓	N/A	Measurably ↓	N/A	Measurably ↓

Statistical Analysis

To achieve the primary aim of characterizing body composition measured by BIA and MUAC, and HGS measured by hand dynamometry of hospitalized Lao adults, means and standard deviations, minimum and maximum values, medians and interquartile ranges, frequency and percentages were summarized. To determine if mean body composition and HGS variables were significantly different between participants who met and did not meet the criteria for malnutrition, 2-sample unpaired t-tests were used with a Bonferroni adjustment setting the level of significance at $p<0.04$. To compare average maximum HGS of hospitalized Lao adults to age and sex-matched reference values, two-sample t-tests with unequal variances were used. To determine the relationships between FFM, MUAC and HGS, Pearson's correlations were used. To determine the criterion or set of criteria that best predicts the diagnosis of malnutrition among hospitalized Lao adults, odds ratios, sensitivity tests, logistic regression, linear regression and one-way ANOVA with a Tukey post-hoc test were used.

Chapter 4

Results

This study aimed to evaluate various anthropometric and functional measurements as characteristics of the nutritional status of hospitalized Lao adults. It was hypothesized that among hospitalized Lao adults, mean markers of body composition would be significantly lower among those diagnosed with malnutrition, HGS would be significantly lower than population-specific normative values, FFM would positively correlate with handgrip strength and MUAC, and handgrip strength would have the best predictive value of malnutrition diagnosis.

Sixty-eight participants 18-70 years of age were included in this analysis. BMI was calculated for 67 participants, body composition by BIA was estimated for 56 participants, and MUAC was measured on 67 participants. Handgrip strength measurements were the most limited in this study sample, with a total of 47 participants able to perform this measurement with both hands (Figure 2).

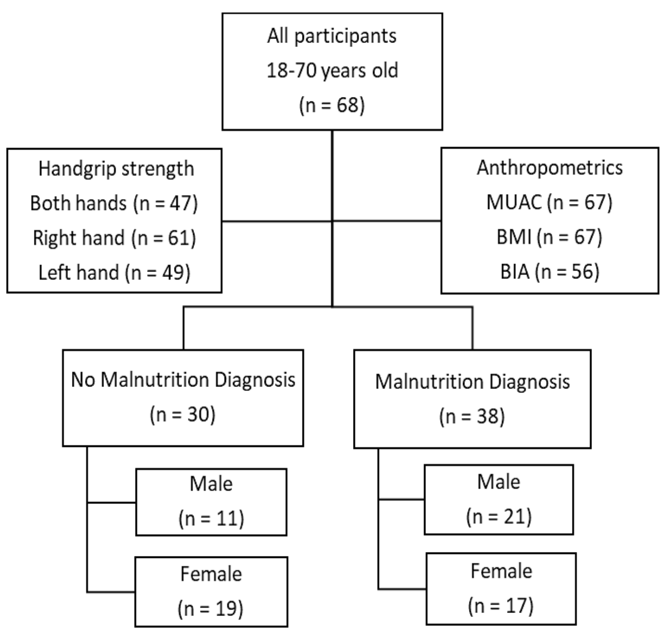

Figure 2. Flow diagram of the number of study participants for which data was collected

Characterization of Nutritional Status among Hospitalized Lao Adults

Characteristics of patients admitted and screened for nutritional risk within 24 hours are illustrated in Table 6. Diabetes, Pulmonary and Infectious Disease wards had the highest prevalence of screened patients diagnosed with acute or chronic, moderate to severe malnutrition upon admission. Acute malnutrition was diagnosed most among patients with infectious disease (56%), while chronic malnutrition was diagnosed most among patients with pulmonary disease (36%). In total, malnutrition was prevalent in hospitalized adults in Lao PDR, evidenced by 56% of all patients diagnosed with malnutrition. While 12% of patients had a low BMI (<18.5 kg/m$^{2)}$, 36% had a low FFMI (men <17 kg/m^2, women <15 kg/m^2) and 25% had a low MUAC (<24 cm), indicating reduced muscle mass among hospitalized Lao adults.

Anthropometrics are further described in Table 7. Mean BMI and MUAC were significantly lower among patients with a diagnosis of malnutrition (Figure 3). Following one-way ANOVAs comparing acute, chronic and no malnutrition diagnoses, Tukey post-hoc tests revealed that mean difference in MUAC and BMI were significant between those with acute malnutrition compared to those not malnourished (-2.49 ± 0.97 cm, $p = 0.03$ and -2.54 ± 1.02 kg/m^2, $p = 0.04$, respectively). Mean HGS, FM and FFM in kg and when indexed to height (FMI and FFMI) for men and women were not significantly different based on malnutrition diagnosis.

Table 6. Hospital admission characteristics classified by sex and malnutrition diagnosis

Characteristic	All Participants	No Malnutrition	Acute Malnutrition	Chronic Malnutrition
National Hospital Admission				
Setthathirath	23 (34%)	11 (48%)	7 (30%)	5 (22%)
Mahosot	45 (66%)	19 (42%)	19 (42%)	7 (16%)
Hospital Ward Admission				
Infectious Disease	18 (26%)	6 (33%)	10 (56%)	2 (11%)
Surgery	16 (24%)	10 (63%)	5 (31%)	1 (6%)
Pulmonary	14 (21%)	4 (28%)	5 (36%)	5 (36%)
Internal Medicine	12 (18%)	6 (50%)	3 (25%)	3 (25%)
Diabetes	4 (6%)	1 (25%)	2 (50%)	1 (25%)
Gynecology	4 (6%)	3 (75%)	1 (25%)	0 (0%)

Table 7. Anthropometric characteristics classified by malnutrition diagnoses			
Characteristic	All Participants (n = 68)	Not Malnourished (n = 30)	Malnourished (n = 38)
Sex			
Male	32 (47%)	11 (34%)	21 (66%)
Female	36 (53%)	19 (53%)	17 (47%)
Age (years)			
Male	41 ± 17 (18, 66)	38 ± 15 (21, 62)	43 ± 18 (18, 66)
Female	43 ± 14 (19, 66)	41 ± 14 (20, 65)	44 ± 15 (19, 66)
Weight (kg)			
Male	60.3 ± 10.3 (40.0, 82.0)	64.2 ± 10.9 (46.0, 82.0)	58.3 ± 9.3 (40.0, 77.0)
Female	52.7 ± 9.0 (37.3, 77.0)	55.4 ± 9.7 (42.0, 77.0)	49.0 ± 6.4 (37.3, 61.3) *
Height (m)			
Male	1.63 ± 0.0 (1.49, 1.69)	1.64 ± 0.1 (1.49, 1.68)	1.63 ± 0.0 (1.55, 1.69)
Female	1.53 ± 0.1 (1.38, 1.65)	1.54 ± 0.1 (1.38, 1.65)	1.51 ± 0.0 (1.45, 1.60)
BMI (kg/m^2)			
Male	22.8 ± 3.5 (16.0, 29.3)	24.3 ± 3.3 (19.5, 29.1)	22.0 ± 3.3 (16.0, 29.3)
Female	22.7 ± 4.2 (16.5, 34.9)	23.7 ± 4.8 (16.5, 34.9)	21.5 ± 3.0 (17.2, 27.2)
FMI (kg/m^2)			
Male	4.6 ± 2.2 (0.9, 8.7)	5.2 ± 2.3 (1.8, 8.7)	4.2 ± 2.1 (0.9, 7.5)
Female	6.8 ± 2.0 (2.8, 13.4)	6.7 ± 1.7 (2.8, 9.0)	6.9 ± 2.3 (3.8, 13.4)
FFMI (kg/m^2)			
Male	18.4 ± 2.6 (11.4, 23.5)	18.9 ± 2.7 (13.9, 23.5)	18.1 ± 2.6 (11.4, 22.6)
Female	15.6 ± 2.9 (10.8, 26.4)	16.4 ± 3.4 (12.2, 26.4)	14.8 ± 2.1 (10.8, 18.6)
MUAC (cm)			
Male	26.6 ± 3.8 (20, 34)	28.1 ± 3.6 (23, 34)	25.3 ± 3.2 (20, 33) *
Female	26.7 ± 4.2 (19, 38)	27.2 ± 4.1 (21, 36)	24.6 ± 2.7 (19, 29) *
% Fat mass			
Male	19.5 ± 8.3 (4.4, 33.3)	21.1 ± 8.3 (9.1, 33.3)	18.6 ± 8.2 (4.4, 33.3)
Female	30.1 ± 6.4 (16.7, 49.2)	28.8 ± 4.8 (16.7, 38.1)	31.5 ± 7.4 (20.7, 49.2)
% Fat free mass			
Male	80.5 ± 8.3 (66.7, 95.6)	78.9 ± 8.3 (66.7, 90.9)	81.4 ± 8.2 (66.7, 95.6)
Female	69.9 ± 6.4 (50.8, 83.3)	71.2 ± 4.8 (61.9, 83.3)	68.5 ± 7.4 (50.8, 79.3)

All values are displayed as mean ± standard deviation (min, max). * denotes statistically significant difference in means between malnourished and not malnourished groups with a Bonferroni adjustment applied, p<0.04.

p = 0.03 p < 0.01

BMI (kg/m^2) MUAC (cm)

No Malnutrition Diagnosis Malnutrition Diagnosis

Figure 3. Body Mass Index **(**BMI) in and Mid-Upper Arm Circumference (MUAC) of all patients with and without a diagnosis of malnutrition. The middle lines represent the medians, "x" represents the means, shaded boxes represent the interquartile ranges, and whiskers are minimum and maximum values. P values indicate statistically significant differences in means.

Evaluation of Functional Status Using Handgrip Strength Reference Values

Mean HGS of hospitalized Lao adults was significantly lower than age- and sex-matched normative values of presumably healthy South East Asian adults established by the PURE study[27] (Table 8). Mean maximum HGS of both hands among hospitalized adults was 21.7 ± 8.8 kg compared to 26.2 ± 6.8 kg among reference values, $p = 0.04$. Eighty two percent of patients (n=22) diagnosed with malnutrition had HGS <85% of the age-and sex-based reference value, suggesting diminished functional status. Men with underweight status BMI had significantly lower average right HGS (15.7 ± 6.6 kg) than those with normal weight status (29.8 ± 8.1 kg, $p=0.01$) and overweight status (27.1 ± 7.8 kg, $p=0.02$) (Figure 4A). Among all study participants, there was a significant positive relationship between height and average right HGS ($r(58) = 0.48$, $p<0.001$).

Table 8. Average maximum handgrip strength measurements of hospitalized Lao adults compared to age- and sex-matched reference values			
Handgrip strength (kg)	Study Participants	Reference Values	Study Participants < 85% of Reference Value
Left hand (n = 28)	20.3 ± 8.8 [16.8-23.7] *	25.9 ± 6.7 [23.3-28.5]	
Male	25.5 ± 9.7	32.5 ± 2.5	79%
Female	15.8 ± 3.9	19.8 ± 1.6	
Right hand (n = 35)	22.5 ± 8.1 [19.7-25.3] *	26.7 ± 6.0 [24.6-28.8]	
Male	27.3 ± 9.1	33.3 ± 2.8	71%
Female	19.2 ± 5.1	22.3 ± 5.1	
Average both (n = 26)	21.7 ± 8.8 [18.2-25.3] *	26.2 ± 6.8 [23.5-29.0]	
Male	27.1 ± 9.3	32.9 ± 3.5	77%
Female	17.1 ± 4.2	20.5 ± 1.5	

Values are displayed as mean ± standard deviation [95 % confidence interval] and * denotes statistically significant difference in means, $p<0.05$. Reference values for South East Asian adults between 35-70 years of age were taken from multinational data and established by Leong, et al.

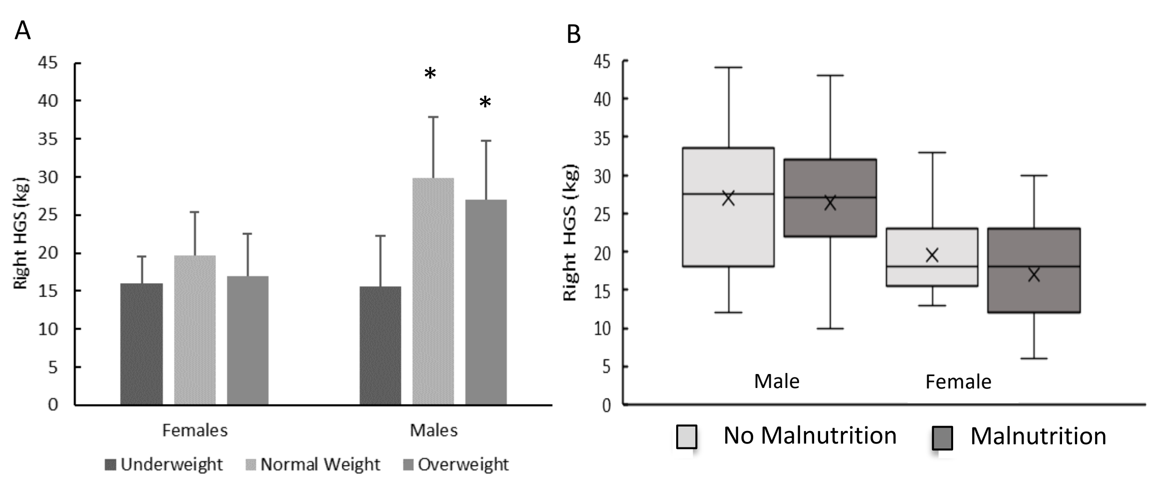

Figure 4. A) Mean right handgrip strength (HGS) of female and male hospitalized Lao adults by BMI category. Underweight BMI = <18.5 kg/m^2, Normal weight BMI = 18.5-23.0 kg/m^2, Overweight BMI = >23.0 kg/m^2. Asterisks denote a statistically significant difference in means from those who are underweight, $p<0.05$. B) Average of right HGS measurements of all patients with and without a diagnosis of malnutrition. The middle lines represent the medians, "x" represents the means, shaded boxes represent the interquartile ranges, and whiskers are minimum and maximum values.

Relationships between Fat-Free Mass and Nutritional Assessment Variables

FFM was directly related to MUAC (r=0.59, p<0.001, Figure 5A) and HGS (r=0.46, p=0.003, Figure 5B) for all patients. FFM explained 21% of the variation in HGS and 35% of the variation in MUAC. There was evidence of a strong link between MUAC and BMI (r=0.83, p<0.001). Using linear regression, MUAC predicted BMI and accounted for 68.3% of the explained variability in BMI (regression equation: BMI = 1.686 + 0.796 x (MUAC); p<0.01).

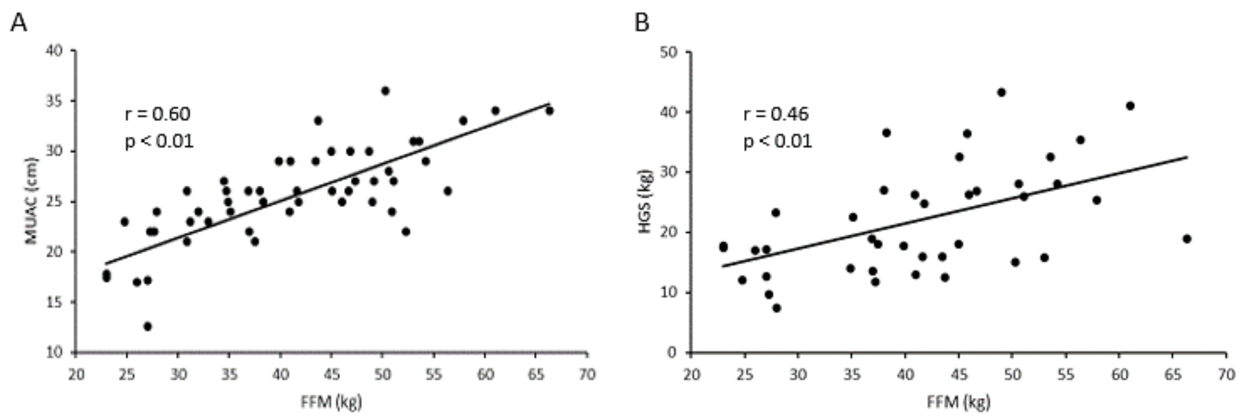

Figure 5. Correlation between A) fat-free mass (FFM) and mid-upper arm circumference (MUAC) (n = 52, y = 0.3666x + 10.347), and B) FFM and handgrip strength (HGS) (n = 41, y = 0.4176x + 4.8386) in hospitalized Lao adults. r = Pearson correlation coefficient; p = p-value of the correlation.

Validity of Nutritional Indicators

In addition to over half of patients diagnosed with malnutrition according to the Academy/ASPEN consensus, 67% of patients met one or more phenotypic criteria included in the GLIM consensus (MUAC <24 cm, HGS <85% of the reference value, FFMI <17 kg/m^2 for men and <15 kg/m^2 for women, BMI <18.5 kg/m^2). These results suggest both the high prevalence of malnutrition and reduced muscle mass among hospitalized Lao adults. Of note, GLIM recommends two or more of both phenotypic (non-volitional weight loss, low BMI, reduced muscle mass) and etiologic criteria (reduced food intake or assimilation, disease burden/inflammatory condition) for the diagnosis of malnutrition. For the purpose of this study, only anthropometric phenotypic criteria were analyzed independently and in combination.

Patients with a MUAC less than 24 cm were four times more likely to be diagnosed with malnutrition (p = 0.049, 95% CI: 1.008 to 12.295). A binomial logistic regression was run to determine which nutritional assessment variables (BMI, FFMI, MUAC, and HGS) predict malnutrition diagnosis, however none were statistically significant (n=38, df=5, p=0.68). Sensitivity and specificity analyses revealed which variables were more accurate identifiers of malnutrition. MUAC values below reference criteria correctly identified 76% of patients diagnosed with malnutrition, FFMI 65%, HGS 64%, and BMI 63% (sensitivity). Conversely, HGS measurements above reference criteria correctly identified 56% of patients without a malnutrition diagnosis, MUAC 52%, FFMI 50%, and BMI 44% (specificity). FFMI was only slightly more of a sensitive indicator of malnutrition than BMI. Using BMI cutoff values specific to Asian adults, participant body fat percentages reflected standard body fat ranges and thus risk for chronic disease. Interestingly, 29 to 30 year-old participants with underweight status had higher than predicted body fat, illustrating what is known as the “thin-fat syndrome” (Table 9). Additionally, the body composition of Lao adults evidences that the relationship between BMI and body fat is ethnic-specific, as comparable to the body composition of Asian adults in the US (Table 10).

Table 9. Mean percentage body fat of hospitalized Lao adults by sex, age and BMI ranges compared to standard ranges for adults					
Age and BMI[a]	Body Fat % of Lao Adults		Standard Body Fat % Ranges for Adults[b]		
	Men	Women		Men	Women
20-39 years			20-39 years		
BMI <18.5	22.2	27.1	Underfat	1-7	1-20
BMI 18.5-23.0	13.1	28.2	Healthy	8-19	21-32
BMI >23.0	20.9	30.8	Overfat	20-24	33-38
BMI >27.5	21.0	29.7	Obese	25-50	39-50
40-59 years			40-59 years		
BMI <18.5	-	-	Underfat	1-10	1-22
BMI 18.5-23.0	22.9	30.7	Healthy	11-21	23-33
BMI >23.0	24.2	29.7	Overfat	23-27	34-39
BMI >27.5	19.7	-	Obese	28-50	40-50
60-70 years			60-70 years		
BMI <18.5	-	-	Underfat	1-12	1-23
BMI 18.5-23.0	15.3	27.4	Healthy	13-24	24-35
BMI >23.0	28.9	35.6	Overfat	25-29	36-40
BMI >27.5	-	23.7	Obese	30-50	42-50

Body fat percentages for all study participants are displayed as mean values. a) Body Mass Index (BMI) ranges for Asian adults are based on the 2004 World Health Organization Expert Consultation. Cells missing values indicate that there were no participants within that BMI range. b) Gallagher, et. al measured body fat in apparently healthy subjects from 3 ethnic groups (Caucasian, African American and Asian, n = 1626) using a 4-compartment model, and body fat % ranges were adapted by Tanita Corporation of America, Inc.

Table 10. Mean body composition characteristics among Asian adults in the United States compared to hospitalized Lao adults				
Variable	Asian Males		Asian Females	
	n=58 (US)	n=32 (Laos)	n=58 (US)	n=36 (Laos)
Body weight (kg)	67.3 ± 8.2	60.3 ± 10.3	53.3 ± 6.8	52.7 ± 9.0
Age (years)	44.5 ± 20.1	41 ± 17	48.5 ± 23.2	44 ± 15
Body fat (%)	18.4 ± 6.4	19.5 ± 8.3	29.3 ± 7.1	30.1 ± 6.4
Height (m)	1.70 ± 6.9	1.63 ± 0.0	1.57 ± 7.1	1.53 ± 0.1
BMI (kg/m^2)	23.2 ± 2.6	22.8 ± 3.5	21.7 ± 2.5	22.7 ± 4.2
FMI (kg/m^2)	4.4 ± 1.8	4.6 ± 2.2	6.4 ± 2.1	6.8 ± 2.0
FFMI (kg/m^2)	18.8 ± 1.8	18.4 ± 2.6	15.0 ± 1.2	15.6 ± 2.9

Values are displayed as mean ± standard deviation. Measurements by dual x-ray absorptiometry were used to calculate fat mass index (FMI) and fat free mass index (FFMI) in the US study.

Chapter 5

Discussion

Evaluation of various measures of nutritional status among hospitalized Lao adults revealed that there are differences between those with and without malnutrition, yet not all variables were significantly different. MUAC, HGS, BMI and BIA are all underutilized in the screening for those at risk of malnutrition among Lao adults. GLIM consensus criteria for the diagnosis of malnutrition acknowledges that body compositions methods such as BIA are often not available or preferred, so standard anthropometric measurements like MUAC or functional assessments like HGS may be used.

Kamarul and Ahmad found that HGS of Malaysian adults (n=412) correlated with anthropometrics as well as age, occupation and gender ($p<0.01$), just as HGS correlated with height in our study population. Similar to HGS comparisons based on age, sex and BMI conducted by Schlussel, et. al. among Brazilian adults, Lao males with low BMI (<18.5 kg/m^2) had significantly lower handgrip strength values than those with higher BMI.

BMI was significantly lower in malnourished patients, as well as MUAC which had a strong association with BMI. This connection between BMI and MUAC is consistent with findings from Chackraborty, et. al. who concluded the use of 24 cm as a cutoff for MUAC to be a simple measure as reliable as BMI, with implications for both primary care and public health policy.

A low FFMI (<17 kg/m^2 for men and <15 kg/m^2 for women) was three times more prevalent than low BMI and may be a more sensitive indicator of malnutrition in this study population. The cutoff criteria for FFMI are based on healthy Caucasian adults,[55] yet studies have revealed that Asians have a lower BMI and thus lower FMI and FFMI than other ethnic groups, warranting population-based criteria. In 2000, Gallagher et. al. developed predicted percentage body fat according to BMI by sex, age and ethnic group, and Asians had the highest body fat estimates. Two years later, Deurenberg et. al. conducted a literature review concluding that BMI cut-off points for obesity in Asians should be lower, as well as potential revision of BMI <18.5 kg/m^2 as the global cut-off point for under-nutrition. In our study sample, BMI was significantly lower among those diagnosed with malnutrition, yet a BMI <18.5 kg/m^2 was the weakest criteria for identifying malnutrition. As Deurenberg, et. al. acknowledged, other risk factors are important along with BMI and body fat such as diet and physical activity.

Patients with diabetes had the highest percentage of malnutrition diagnoses. Lao adults living with diabetes may have difficulty maintaining adequate nutrition due to limited resources, lack of training in nutrition interventions, and availability and cost of fruits and vegetables. The Prospective Urban Rural Epidemiology study conducted in 18 countries determined that in low-income countries, the cost of two servings of fruits and three servings of vegetables per day per individual accounted for 51.97% of household income. The next highest percentages of malnutrition diagnoses were among patients with pulmonary or infectious disease, which cause critical energy loss and perpetuate the cycle of malnutrition, disease and poverty.

Strengths of this study include the wide range of anthropometric measurements taken following established procedures, using population-specific HGS and BMI reference values, and full nutrition assessments for nutrition diagnoses using validated criteria. Clearly stated study aims were supported by comparable results found in similar populations. The results from our study are applicable to policies in clinical settings as well as public health measures in Lao PDR. Limitations include characteristics of the study sample that may not reflect the overall adult population in Lao PDR which may decrease generalizability, procedural variability in research assistants collecting measurements which may introduce measurement error, and smaller sample sizes which limits statistical power.

As a feasibility study, the implications, strengths and weaknesses of various anthropometric and functional markers of nutritional status were summarized. Not all mean markers of body composition and functional muscle strength were significantly lower among hospitalized Lao adults with a diagnosis of malnutrition than those without a diagnosis of malnutrition as hypothesized. Mean HGS of hospitalized Lao adults was significantly lower than normative values of presumably healthy South Asian adults between 35-70 years of age. FFM positively correlated with MUAC and HGS, however MUAC and HGS were not significantly correlated. While HGS had the highest true negative rate, MUAC had the greatest predictive value defined by the highest true positive rate correctly identifying hospitalized patients who are malnourished.

Conclusion

While screening identifies potential risk for a problem, assessment determines presence of a problem. Malnutrition screening tools are preventive in that they identify patients who require nutrition intervention based on early signs and symptoms that malnutrition may be present. Within the Lao population, where malnutrition in known to be prevalent, early identification of malnutrition requires simple validated screening tools to correctly identify patients who need a full nutrition assessment. The Academy defines nutrition assessment as the process “to obtain, verify, and interpret data needed to identify nutrition-related problems, their causes, and significance.” Further, nutrition assessment data is used collectively to target nutrition interventions and monitor outcomes. Assessment of body composition and functional status can be done in low-resource hospital settings to evaluate nutritional status and identify patients at high risk for malnutrition so that comprehensive nutrition therapy can be initiated early in the hospital course. In this study, anthropometric measurements were quickly trained to and conducted by Lao healthcare workers. It is recommended that MUAC and BMI be used as a routine part of malnutrition screening upon admission, to identify those at risk for malnutrition. Just as nutrition screening is critical in Lao hospitals, so is establishing training and resources for nutrition intervention. HGS assessed by dynamometry and muscle mass assessed by BIA are valid, reliable supportive measures to use during a full nutrition assessment. Ultimately, providing appropriate nutrition intervention should improve patient outcomes, quality of care and utilization of resources.

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Appendix A. Informed Consent

OREGON HEALTH & SCIENCE UNIVERSITY

IRB#: __________

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

Clinical Research Consent Summary

Research Study Informed Consent Document

Study Title for Participants: Nutrition-Risk Screening for Lao PDR

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: Nutrition Risk Screening Tool for Hospitalized Patients in Lao PDR: A Pilot Study

Overview and Key Information

What am I being asked to do?

We are asking you to take part in a research study. We do research studies to try to answer questions about risk for malnutrition upon admission to the hospital.

We are asking you to take part in this research study because an effective nutrition risk screening tool is needed to identify patients at risk for or admitted with malnutrition. Timely and appropriate nutrition intervention and continued management can occur if patients are screened. This screening questionnaire will ask you 4 questions and then follow-up nutritional assessment will be conducted by a trained professional. This is a non-invasive study. No blood or urine will be taken during the study.

Do I have to take part in this study?

Taking part in this study is your choice. You can choose to take part or you can choose not to take part in this study. You also can change your mind at any time. Whatever choice you make, you will not lose access to your medical care or give up any legal rights or benefits.

This document has important information to help you make your choice. Take time to read it. Talk to your doctor, family, or friends about the risks and benefits of taking part in the study. It's important that you have as much information as you need and that all your questions are answered.

CO1450

Why is this study being done?

This study is being done to answer the following question[s]:

What is the usual approach to screening for malnutrition?

Currently, there is no nutrition-risk screening tool used within Lao PDR.

What are my choices if I decide not to take part in this study?

- You may choose to have the standard of care
- You may choose to take part in a different research study, if one is available.

What will happen if I decide to take part in this study?

If you decide to take part in this study, upon admission you will be asked 4 questions about your health. Within 24 hours of admission you will be given a full nutrition assessment and nutrition diagnosis by a trained clinician.

After the full nutrition assessment is completed, you will continue to be cared for by a clinical nutrition specialist and provided appropriate nutrition intervention until discharge.

What are the risks and benefits of taking part in this study?

There are both risks and benefits to taking part in this study. It is important for you to think carefully about these as you make your decision.

Risks

We want to make sure you know about a few key risks right now. We give you more information in the "WHAT RISKS CAN I EXPECT FROM TAKING PART IN THIS STUDY?" section.

If you choose to take part in this study there is very little risk involved. Some risks aware to the investigators are:

- Personal data will be documented and every effort taken to protect your privacy

There may be some risks that the investigators do not yet know about.

Benefits

This nutrition risk screen may be helpful if you screen positively for malnutrition. This study may help the investigators learn things that may help other people in the future.

If I decide to take part in this study, can I stop later?

Yes, you can decide to stop taking part in the study at any time.

If you decide to stop, let the investigator know as soon as possible.

The investigator will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

Are there other reasons why I might stop being in the study?

Yes. The investigator may take you off the study if:

- Your health changes and the study is no longer in your best interest.
- New information becomes available and the study is no longer in your best interest.
- You do not follow the study rules.
- The study is stopped by the Institutional Review Board (IRB), Food and Drug Administration (FDA), Lao Health Research Portal Review Board, or study funder (Lao-American Nutrition Institute).

It is important that you understand the information in the informed consent before making your decision. Please read, or have someone read to you, the rest of this document. If there is anything you don't understand, be sure to ask the investigator or nurse.

OREGON HEALTH & SCIENCE UNIVERSITY

IRB#: __________

MED. REC. NO. _____
NAME _____
BIRTHDATE _____

Clinical Research Consent and Authorization Form

TITLE: *Nutrition-risk screening Tool for Lao PDR.*

PRINCIPAL INVESTIGATOR: Dr. Diane Stadler (503) 494-0168

CO-INVESTIGATORS: Joanna Cummings, MS RD CNSC (303) 204-6444
Slackchay (Nina) Rasprasith, BsN
+856-020-2882-7625

The Principal Investigator (PI) must be listed on the consent form. Listing co-investigators on the consent form is optional. It is recommended that you limit the number of co-investigators listed here by only listing those most likely to conduct the consent discussion.

WHO IS PAYING FOR THE STUDY?: *This study is unfunded and will be conducted with volunteer support from the Lao-American Nutrition Institute and the Lao Ministry of Health.*

WHO IS PROVIDING SUPPORT FOR THE STUDY?: *Lao-American Nutrition Institute*

DO ANY OF THE RESEARCHERS HAVE A CONFLICT OF INTEREST WITH THIS STUDY?:
No conflicts of interest exist between researchers and this study.

WHY IS THIS STUDY BEING DONE?:

You have been invited to be in this research study because you are being admitted to the hospital. The purpose of this study is to conduct a nutrition-risk screen to identify malnutrition or risk for malnutrition in hospitalized patients.

This study aims to identify patients at risk or currently malnourished upon admission to the hospital. The study aims to validate an easy to use screening tool to quickly identify patients in need of nutrition support in the hospital.

This study begins upon your admission to the hospital and ends upon your discharge. No bodily specimens or genetic material will be collected during this study.

CO1450

This study will be conducted at both Mahosot Hospital and Setthathirath Hospital in Vientiane Capital, Lao PDR. The study has also been approved through the Lao Health Research Portal Review Board.

This study will require a minimum of 2 visits from trained clinicians but you may receive on-going follow-up care if determined you are at risk for malnutrition.