The validation of the mid-upper arm circumference measurement in adults as a weight estimation tool in a high HIV prevalence setting.

by

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Declaration

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Dedication

Sharon, my dearest mum, this dissertation is for you. Thank you for your support, sacrifices and love. I would not be where I am today if it were not for you, I love you lots.

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My amazing husband, thank you for your advice, motivation, and love throughout this journey.

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Abbreviations

ART	Antiretroviral therapy
ARV	Antiretrovirals
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CD4	Cluster of Differentiation 4
CED	Chronically energy deficient
CI	Confidence Interval
Cm	Centimetre
CT	Computed tomography
CVD	Cardiovascular disease
HIV	Human Immunodeficiency Virus
HR	Hazards ratio
ICC	Intraclass correlation coefficient
Kg	Kilogram
MRI	Magnetic Resonance Imaging
MUAC	Mid-upper arm circumference
NCD	Non-communicable disease
NHANES	United States Nation Health and Nutrition Examination Survey
SD	Standard deviation
TB	Tuberculosis
UCT	University of Cape Town
VL	Viral Load
WC	Waist circumference
WHO	World Health Organisation
Wt.	Weight

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PART A. LITERATURE REVIEW

Introduction

The mid-upper arm circumference (MUAC) is an anthropometric tool measured midway between the acromion process of the shoulder and the olecranon of the elbow of the non-dominant arm using a standard measuring tape.[1] The MUAC has largely been researched in paediatrics as a tool to estimate weight and nutritional state, but recently its use for weight estimation has expanded to adults and adolescents.[2,3] South Africa has one of the largest HIV epidemics in the world with a population different to that of high-income countries due to its marked burden of HIV.[4] As a middle-income country where resources are limited, the MUAC's ease of use and cost effectiveness could be beneficial for estimating weight in sick, often bedbound adult patients presenting to the emergency centre. Little is known about MUAC's validity as a tool to estimate weight in the adult South African population, specifically with the extremes of weight seen in the HIV positive population.

The importance of weight estimation

Accurate weight assessment in the emergency centre is important. A patient's weight can be used for risk stratification as weight correlates with metabolic syndrome, which increases the risk of cardiovascular disease.[5] In the emergency centre a patient's weight is needed for diagnostic and therapeutic strategies. In terms of diagnostics, computed tomography (CT) and magnetic resonance imaging (MRI) machines are limited by maximum weight (MRIs are limited to 159kg and standard CT 205kg).[6] In air medical transport, accurate weight estimation determines if a patient can be flown safely as it influences the centre of gravity, fuel usage, aircraft range and whether extra members can be accommodated.[7]

In emergency centres the main reason for accurate weight estimation is in terms of therapeutics. A patient's ideal weight is needed to calculate correct drug dosages (e.g., anticonvulsants, antibiotics with narrow therapeutic ranges, anti-tuberculosis treatment, insulin dosages and sedatives). Fluid regimens used in burn patients are also weight-based[8] and overdose ingestions are risk stratified according amount of drug ingested per kilogram of body weight. Incorrect estimations of drug dosages or fluid regimens can lead to subtherapeutic treatment or adverse outcomes; both of which can be life threatening. Overdosing of thrombolytics or anticoagulants can result in clinically significant bleeding.[9] In Australia, 43.7% of the patients who were not weighed and given therapeutic anticoagulation sustained haemorrhagic complications when compared to those who were weighed,[10] and in those patients with complications, 71.4% were

major haemorrhagic complications requiring some form of intervention.[10] In an United States emergency centre, out of the 958 patients where weights were estimated but not measured, 55.5% were outside the thrombolytic tolerance range, about a third were underdosed and a fifth were dosed too high.[11] Accurate weight estimation by healthcare practitioners is thus important in both the treatment and prevention of adverse outcomes in patients.

Health care practitioners cannot accurately estimate a patient's body weight. Health care practitioners accurately estimate a patient's weight and BMI in 53% and 56% of cases respectively,[12] and estimates are significantly less accurate in underweight and obese patients.[11,13] In critical care patients, only two out of 20 observers correctly estimated all the weights within 25% of their actual values, and weight was underestimated in patient's weighing more than 100kg.[13] Patients are nearly nine times more likely than health care providers to accurately estimate their own weight [14] and it is recommended that if a patient is unable to be weighed, the patient's own weight estimate should be used.[12,15] Thus, health care practitioners are inaccurate when estimating patients' weights and should rather rely on patients' own estimates or validated tools.

Barriers to weight estimation

Even though health care practitioners are not able to reliably estimate weight, patients are not being routinely weighed. Only half of the patients admitted to a hospital in Scotland were weighed.[9] Body weight was only recorded in 13.5 to 55 percent of hospital patients in emergency centres, intensive care units and hospital wards.[16] In the United States, a multi-centre study found that only 65.7% of patients were weighed in the first 36 hours of admission.[17] In those not weighed, about two thirds were asked about their weight and estimations varied from their actual weights by about two kilograms.[17]

A barrier to weight measurement is the lack of availability of equipment. Studies found that the burden of locating equipment was too time consuming and it was easier for staff to ask patients their weights.[9,12] Other barriers include the perceived additional workload with patient handling, inadequate staff, and interruption to the workflow.[16] Nurses in Australia found cognitively impaired and aggressive patients the most difficult patients to weigh regularly.[10] In other surveys, very sick and bed bound patients are barriers to measuring weight.[9] Furthermore, some health care workers perceive weight estimation as unnecessary.[16] Medical ward nurses perceive weighing patients as invasive and unnecessarily distressing for the patient and they do not think it changes the management of the patient.[18] However, in a United Kingdom hospice, there was a difference

in the perceived inconvenience of weighing between health care workers and hospice patients. Where health care practitioners thought weighing a patient was futile and unimportant, 98% of the patients in the study did not think being weighed was upsetting and 89% wanted to know if their weight was changing.[19]

A measure of nutritional status and categorisation

A patient's nutritional state can be assessed by four types of measures: i) a measure of nutritional balance (dietary history, energy expenditure); ii) a measure of body composition by use of anthropometry (e.g. weight, height, BMI, MUAC, triceps skin fold, waist to thigh ratio, and bioelectrical impedance analysis); iii) by measure of inflammatory activity (albumin, C-reactive protein, and cytokine levels); and iv) by measure of function (muscle function such as handgrip strength, immune function or cognitive function).[20] Nutritional balance and diet history relies on recall and is disadvantageous in the elderly or large groups of patients and is not readily available in emergency centres, so where this data cannot be obtained, other measures such as anthropometry are used.[20] Some anthropometrics such as BMI and weight are inexpensive and easy to measure in large populations, whereas others such as bioelectrical impedance analysis (BIA) are more costly and predominantly used in patients that aren't severely ill or malnourished.[20] A disadvantage of BIA is that varying, unvalidated equipment can produce unreliable results.[20] The commonly used inflammatory markers are plasma albumin and C-reactive protein. Plasma albumin is an indicator of inflammatory activity as inflammation leads to catabolism of body cell mass.[20] C-reactive protein rapidly rises and decreases after an insult and is an indicator for mortality and disability.[20] The most easily measurable function is muscle force.[20] Handgrip strength is most often used, but there are other more sophisticated ways to measure muscle strength and endurance.[20] Thus, malnutrition can be determined by a combination of nutritional balance, inflammation, changes in body composition and diminished function.

Weight is the fundamental anthropometric assessment of nutritional status, but other anthropometric measurements such as BMI perform better in terms of body composition. BMI incorporates both height and weight (kg/m^2) and has been widely used as a measure of obesity, energy stores and undernutrition.[21] The rationale for BMI is that weight would be a better indicator of fat mass and energy stores if an allowance were made for height.[22] BMI is easier to measure and inexpensive in epidemiological studies where precise techniques for measuring body composition might be impractical for routine, clinical use.[23] However, BMI cannot differentiate between lean and fat mass,[24] visceral and overall adiposity and its relationship with body composition components differ with age, sex, ethnicity and body shape.[21] Its use is further limited

in individuals who are debilitated or immobile where measurements cannot be taken. Despite these disadvantages, BMI is still currently the standard measure of nutritional status.

BMI is used by the World Health Organization (WHO) Expert Committee on Physical Growth to define malnutrition in adults.[25] Underweight is classified as mild (BMI = 17.00−18.49kg/m^2), moderate (BMI = 16.00−16.99kg/m^2), and severe underweight (BMI < 16.00kg/m^2); where all three of these groups are chronically energy deficient.[25] The WHO Consultation on Obesity classifies overweight as a BMI more than 25kg/m^2. It is further classified as pre-obese (BMI = 25.00−29.99kg/m^2), Grade 1 obesity (BMI = 30.00−34.99kg/m^2), Grade 2 obesity (BMI = 35.00−39.99kg/m^2), and Grade 3 obesity (BMI > 40.00 kg/m^2).[20] Important health effects have been found to occur at BMI values below 18.5kg/m^2 and above 25kg/m^2.[26]

The clinical significance of Body Mass Index

BMI is associated with all-cause mortality. BMI has a non-linear, J-shaped association with all-cause mortality with nadir at BMIs of 20-25kg/m^2.[27] In underweight individuals with a BMI less than 18.5kg/m^2, life expectancy is four years shorter compared to those with healthy weight,[28] and all-cause mortality is increased.[27,29–31] In obese people, life expectancy is also shorter with reductions of eight to ten years in individuals with BMIs above 40kg/m^2.[28,29] A meta-analysis found both overweight and obesity are associated with higher all-cause mortality.[27] This meta-analysis challenged findings found in a collaborative analysis done in 2009 where overweight and grade one obesity were associated with lower all-cause mortality.[32] Both underweight and overweight individuals are associated with an increased risk of all-cause mortality.

BMI is also associated with cause specific mortality. A BMI higher than 25 kg/m^2 is positively related to coronary heart disease, stroke, diabetes, renal, hepatic and respiratory disease, and cancer.[27–29] A systematic review and a separate dose response meta-analysis found that there was no increased risk of stroke at BMIs less than 24 kg/m^2, but there was an increased risk at BMIs more than 25 kg/m^2.[33] Thus, BMI in the overweight and obese range is associated with an increased risk of cause specific mortality.

Mid-upper arm circumference as a weight estimation tool

MUAC is measured by palpating the acromion process and the olecranon with the arm relaxed and flexed at 90 degrees.[1] The midpoint between the acromion process and olecranon is marked and the circumference measured at this point with the arm relaxed at the patient's side.[1] The tape measure should be flexible, not be made of expandable material such as cloth and be measured to the closest 0.1 centimetre (cm) rather than in inches for better precision.[1]

MUAC was studied as a weight estimation tool in the late 1980's. In 1985, Larson noted a correlation between MUAC and weight and found MUAC increased by one to three centimetres with roughly every ten kilogram (kg) increase in weight.[34] In 1990, Utley found for every three centimetre increase in MUAC, there was an increase in eight to twelve kilograms of weight.[1] These findings were not validated in immobile, elderly or severely underweight or obese patients.

The use of the MUAC in adults as a weight estimation tool has continuously been researched, but there has never been one formula applicable to all adults. In India, MUAC is used to predict muscle mass using the equation $[kg = (1.641 * MUAC) - 15.58]$.[3] Cattermole et al. used data from the 2011-2012 United States Nation Health and Nutrition Examination Survey (NHANES) and derived a MUAC based weight estimation equation using linear regression: $[kg = (3.8484 * MUAC) - 46.8585]$.[2] To simplify this equation, the coefficients were rounded to one significant figure: $[kg = (4 * MUAC) - 50]$. Cattermole et al. tested four alternative MUAC-based weight estimation methods using 9022 subjects from the 2009 -2010 NHANES dataset. The four alternative MUAC-based weight estimation methods were: i) a gender-neutral model; ii) a gender specific model; iii) the exact linear regression equation; and iv) the simplified equation. The gender specific model performed the best in terms of proportions of estimates within 10%, 20% and 30% of actual weight and the simplified equation performed the worst, but the differences were insignificant. Differences between the exact linear regression equation and the simplified equation were only significant at estimates within 20%. In all the models, at least 60%, 90% and 98% of estimates fell, respectively, within 10%, 20% and 30% of actual weights in adults and adolescents.[2] Proportions of estimates within 20% of actual weight were worse for children and all methods performed poorly in patients with MUACs less than 20cm or weights less than 30kg.

Opdam et al. externally validated Cattermole's formula in the European and American elderly population.[35] In American elderly, Cattermole's formula ($[kg = (4 * MUAC) - 50]$ accurately and precisely estimated actual body weights and the performance of the formula was comparable to the data initially published.[35] In the American cohort, 56.5%, 87.1%, and 97.1% of the estimates fell within 10%, 20%, and 30%, respectively, of the actual body weight.[35] However, Cattermole's formula was not accurate in the Dutch elderly, MUAC was poorly associated with actual body weight, and thus the formula was not recommended to be used in Dutch emergency centres. For the elderly Dutch data set, 41.6%, 78.0%, and 96.3% of the estimates fell, respectively, within 10%, 20%, and 30% of the actual body weight. The actual body weight of Dutch elderly was better estimated with the formula $[kg = (3.33 * MUAC) - 46.67]$.[35] A limitation of this study was that it was performed on pre-existing datasets and the formula was not tested in the clinical setting.[35] In

emergency centres, diseases causing oedema could likely influence MUAC's accuracy. This study was the first validation of Cattermole's formula, and little is known whether the formula can be applied to other populations such as the underweight or obese.

MUAC as a weight estimation tool has been studied in obese patients. Crandall et al. found that the MUAC was better than thigh circumference in predicting obese patient's weight and the addition of height to the formula substantially improved the predictive capacity.[7] In obese women, the formula was $[kg = -64.6 + (2.15 * MUAC\ in\ cm) + (0.54 * height\ in\ cm)]$, and for males $[kg = -93.2 + (3.29 * MUAC\ in\ cm) + (0.43 * height\ in\ cm)]$. However, at the lowest tolerance error of 5%, only 43% of men's and 44% of women's actual weights fell in the range, which fares poorly, but performs better than visual estimates of obese patients' weights.[7]

In South Africa, MUAC as a weight estimation tool has only been studied in pregnant women. Fakier et al. found MUAC correlated strongly with BMI in pregnancy up to a gestation of 30 weeks and MUAC could reliably substitute BMI to assess nutritional status.[36] No studies have been done on the use of MUAC as a weight estimation tool in emergency centres in South Africa, especially in a high HIV prevalence setting.

The relationship between MUAC and Body Mass Index

MUAC and BMI are highly correlated in adults and MUAC can thus be used as an additional measure of nutritional state.[37] James et al. noted a linear relationship between the BMI and the MUAC and attempted to determine MUAC cut-off points that would categorise the nutritional state of adults in a similar fashion to BMI. A BMI of 17kg/m^2 approximated to the mean BMI minus one standard deviation (SD), the -1 SD BMI value. Similarly, BMI values of 18.5kg/m^2 and 16kg/m^2 approximated to the -0.5 SD BMI and the -1.5 SD BMI values. Since a linear relationship between BMI and MUAC was noted, James et al then used the same SD cut-off points for MUAC (e.g. the -1 SD MUAC value) to categorise adult nutritional status in an attempt to determine whether the MUAC could replace the BMI.[37] However, the -1 SD MUAC cut-off point (24.0 cm in men, 23.0 cm in women) could only differentiate patients with a BMI <16 kg/m^2 from those with a BMI >18 kg/m^2.[37] Regrettably, the MUAC cut-off values cannot be applied universally as they differ between populations.[38–41] In South Africa, a MUAC less than 24 cm corresponds to a BMI of less than 18.5kg/m^2 and in obese patients, a MUAC greater than 29 cm corresponds to a BMI greater than 29.9kg/m^2.[42]

MUAC as a predictor of mortality

MUAC is predictive of all-cause and cause specific mortality in both Western and Asian populations.[24] A low MUAC is associated with an increased mortality.[43] In non-obese individuals in the United States, MUAC is inversely associated with all-cause mortality.[44] A small prospective study in Bangladesh showed MUAC is an independent risk factor for any cause mortality and cardiovascular disease in individuals with low BMIs.[45] In patients being admitted to a tuberculosis ward, undernutrition assessed using MUAC, is strongly associated with mortality within the first month of admission.[46]

In the elderly, MUAC has a stronger association with mortality than BMI.[47,48] When compared to BMI, the MUAC's stronger and consistent association with mortality risk and ease of use in immobile elderly makes it the preferred anthropometric tool to assess undernutrition.[48,49] MUAC is better than BMI in predicting 12 month follow-up mortality in institutionalized elderly.[43,50] In one study, both MUAC and BMI predict long term mortality in elderly but the strength of their associations vary and is age dependent.[43] Low MUACs (less than 23.5cm in men and less than 22cm in women) are more strongly associated with mortality risk than BMI in 53 to 74 year olds, but not in those older than 74 years old. Conversely, an increase in MUAC is associated with improved physical performance and function and a lower risk of death.[51] In the elderly, MUAC is a better measure for mortality risk and undernutrition than BMI.

The relationship between HIV, weight and BMI

South Africa has one of the largest HIV epidemics in the world. In 2019, an estimated 7.9 million South Africans were living with HIV,[46] of which only 62% were on antiretroviral therapy (ART).[53] The burden of HIV in South Africa is high and it is estimated that 12 to 23% of patients presenting to emergency centres in South Africa are HIV positive.[48]

HIV positive patients have different body composition compared to HIV negative patients. In Sub Saharan Africa, the most common presentation is the HIV wasting syndrome.[23] HIV wasting syndrome is characterized by more than 10% involuntary weight loss (both fat and lean body mass) and is often accompanied by muscle fatigue and weakness.[55,56] Malnutrition during the course of HIV infection is due to a combination of dietary reduction, nutrient malabsorption, metabolic disturbances and endocrine dysfunction.[57,58] Additionally, HIV itself or opportunistic infections can result in an increased energy expenditure[58] which contribute to wasting. The role of weight loss is predictive of HIV disease progression independent of powerful indicators such as low CD4 cell counts.[57] In rural South Africa, HIV positive people both on and not on ART have

lower weights, lower BMIs, lower fat and lean mass, and lower body percentage fat than the HIV negative population.[59,60]

Since the availability of ARTs, the incidence of wasting has decreased dramatically.[61] However, the initial lean body mass loss may not be fully restored with effective viral suppression and a high incidence of wasting is still evident in some populations during the ART era.[62–66] In HIV positive patients, being underweight prior to ART is associated with more than double the rate of Acquired Immunodeficiency Syndrome (AIDS) deaths.[45] This extreme underweight body habitus of HIV positive patients is one that is commonly seen in South African emergency centres and estimation of weight in these patients can prove to be difficult.

On the other end of the spectrum, a higher prevalence of obesity has been noticed in HIV positive patients. This new phenomenon is a result of HIV positive patients living longer and gaining weight due to ARTs.[67,68] In the United States, obesity was more prevalent than wasting in HIV positive patients.[69] Almost half of the patients were overweight or obese at ART initiation and one in five patients moved to a BMI in the overweight category within two years of ART initiation.[67] The prevalence of obesity in one South African sample of both HIV positive and HIV negative patients was approximately 59%.[59] In KwaZulu-Natal, the prevalence of obesity and hypertension were both very high despite the high prevalence of HIV.[70] One study in South Africa showed that more than half of the female HIV positive patients were overweight or obese.[71] In Johannesburg, Hamill et al. found that one in four premenopausal women not on ARTs were overweight and 37% were obese,[71] which is similar to the 36.4% who were overweight in the Limpopo province.[72]

ART use is associated with weight gain. A recent systematic review and meta-analysis showed that ART use is associated with an increased BMI, waist circumference, overweight and abdominal obesity.[73] These increases were seen in patients with lower CD4 cell counts (<350 cells/mm^3), but not among patients with higher CD4 cell counts. In Sub-Saharan African HIV positive persons initiating ARTs with a high CD4 cell count at baseline, there was a high prevalence of overweight and obesity and after a year on ARTs, their weights increased further.[74] In Durban, after a year on ARTs, HIV positive women had significant increases in waist circumferences that increased their risk of cardiovascular disease and increases in the incidence of lipodystrophy and obesity were noted.[75] Thus, ART use is associated with weight gain.

Obesity is difficult to define in HIV positive patients with low muscle mass. Patients may have excess adiposity but still remain in the “normal” BMI range of 18.5-24.9kg/m^2.[76] HIV positive people may have an increased BMI-to-visceral adipose tissue ratio and thus BMI may underestimate adiposity in this population.[76] In the setting of a high prevalence of obesity in HIV

positive patients, immunosuppression may change body composition, however, these differences may only become evident at very advanced stages of the disease.[59] Thus, defining obesity in HIV positive patients with standard anthropometry may be inaccurate. The extremes of weights seen in HIV positive patients make weight estimation difficult and can place HIV positive patients at an increased risk for early mortality.

HIV and the risk of mortality and cardiovascular disease

HIV positive patients are at risk for early mortality. Risk factors for early mortality include delayed ART initiation (low CD4 cell count, advanced WHO disease stage) and opportunistic infections.[77] A low or increased BMI in HIV positive patients is associated with an increased risk of cancers, cardiovascular disease (CVD) and all-cause mortality.[76,78] A high BMI in HIV positive patients is associated with the risk of diabetes.[76,78] The introduction of ARTs in South Africa has extended the survival of HIV positive patients and CVD has emerged as a comorbidity and mortality risk.[79] HIV infection with chronic viremia and persistent immune activation impacts atherogenesis risk including increased systemic inflammation, hypercoagulation and decreased vascular reactivity.[79] Specific ARV drugs such as protease inhibitors change serum lipid profiles and are associated with central obesity and myocardial infarctions whilst other ARVS have been linked to insulin resistance.[79] Even though the use of ARTs can adversely impact CVD risk, the long-term benefits of chronic HIV suppression and immune constitution outweigh the CVD risks they might have.[79]

The association between HIV, MUAC and mortality

There is a correlation between HIV, MUAC and mortality. In HIV positive patients in Malawi, both BMI and MUAC increased linearly with increased time on ARTs and were closely correlated with each other. Furthermore, a BMI increase of less than 0.5kg/m^2 or a MUAC increase of less than 0.5cm were strong predictors of mortality independent of the participant's baseline characteristics.[80] The increase in BMI and MUAC after ART initiation is due to effective treatment and recovery, and the lack of weight gain could be a sign of inadequate treatment (e.g. adherence problem, presence of an opportunistic infection) resulting in ineffective immune reconstitution.[80] In Tanzanian and Zambian HIV positive patients, MUAC showed a strong, independent association with mortality with a 13% decrease rate of death with every 1cm gain in MUAC.[77] Thus, MUAC is correlated to mortality in HIV positive patients.

HIV and lipodystrophy

BMI alone is not an adequate parameter to predict nutritional status in patients with lipodystrophy.[81] Lipodystrophy, also known as fat redistribution syndrome, is found in some HIV

positive patients on ARTs and is characterised by peripheral subcutaneous lipoatrophy and central, abdominal lipohypertrophy.[82] Patients present with thinning of the face, an increased dorso-cervical fat pad, truncal obesity and thinning of the extremities.[82] This syndrome is difficult to define as body weight may not change, nor is the lean body mass out of normal range.[82] One study suggested to include BMI with waist/hip ratio, MUAC, mid-thigh circumference and triceps skin fold in the definition[76] since it found that, despite normal BMIs, MUACs were well below normal for this population.[82] With the increase in obesity prevalence and some lipodystrophy occurring in treated HIV positive patients, some patients may experience an overlap syndrome with components of lipodystrophy and obesity.[76] Measuring just the BMI or MUAC in HIV positive patients may incorrectly categorise nutritional statuses in HIV positive patients with lipodystrophy.

Identification of gaps or needs for further research

In South Africa, MUAC is known to strongly correlate with BMI, however, little is known on its use as a weight estimation tool, especially in HIV positive patients. More research will be required to validate the existing MUAC based weight estimation formulae in the South African population.

Conclusion

Health care professionals are poor estimators of patients' weights even though correct weight estimation is important for treatment and prevention of adverse outcomes in the emergency centre. Despite its disadvantages, BMI is the current standard measure used to assess nutritional status in adults and quickly identifies patients at an increased risk for mortality. The MUAC is strongly correlated to BMI and can be used as a substitute. Formulae using MUAC to estimate weight in adults exist, but no research has been done to validate its use in the South African acute care population. HIV positive patients can present with extremes of weights and the use of ART can result in changes in body composition which make BMI and MUAC ineffective anthropometric tools to predict nutritional status. It is possible that MUAC based weight estimation formulae are population dependent and a standardised formula might be invalid in different countries.

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PART B. MANUSCRIPT IN ARTICLE FORMAT

(prepared for submission to the International Journal of Emergency Medicine)

A cross-sectional study validating the mid-upper arm circumference measurement in adults as a weight estimation tool in a high HIV prevalence setting.

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Abstract

Background

Accurate weight estimation in emergency centres is important to ensure accurate treatment and limit adverse outcomes. The mid-upper arm circumference (MUAC) as a weight estimation tool has recently expanded to adults. The MUAC's ease of use and cost effectiveness could be beneficial to estimate the weight of sick, adult patients presenting to emergency centres. The objectives were to assess correlation between MUAC and both weight and body mass index (BMI) in adults, externally validate an existing MUAC-based weight estimation formula in a high HIV prevalent emergency centre, and if inaccurate, to derive a MUAC-based weight estimation formula more suitable to the adult study population.

Methods

A cross-sectional diagnostic study was done in the emergency centre of Khayelitsha hospital, South Africa. Anthropometric data (MUAC, weight and height) and HIV status were obtained from consecutive adult (≥18 year) participants. Correlation of MUAC with weight and BMI were determined using Spearman's correlation coefficient with 95% confidence intervals in all participants and in HIV positive participants. Predicted weights were calculated from previously developed formulae (regression formula: kg=(3.8484×MUAC)−46.8585; simplified formula: kg=(4×MUAC)−50). The agreement between the predicted and observed weights were graphically assessed with a calibration plot. Linear regression was used to derive a MUAC-based formula in the study population.

Results

A total of 244 participants (median age = 37 years; 111 male) were included, of whom 121 (49.6%) were HIV positive. The correlation between MUAC and weight was 0.93 (HIV positive 0.92), and between MUAC and BMI 0.93 (HIV positive 0.94). The regression formula predicted weight within 10%, 20% and 30% of actual weight in 43.9%, 77.5% and 90.2% of all participants and 33.1%, 69.5% and 85.1% in HIV positive participants. The simplified formula predicted weights within 10%, 20% and 30% of actual weight in 46.7%, 77.5% and 89.8% of all participants and in 35.5%, 70.2% and 85.1% in HIV positive participants. The locally derived formula (kg=(3x MUAC) -16) better estimated weight in the local population.

Conclusion

MUAC is highly correlated with weight and BMI. The existing MUAC based formulae performed poorly and the derived formula (kg=(3xMUAC)-16) should rather be used in the study setting.

Keywords

Emergency centre, Mid-upper arm circumference, Weight estimation tool, BMI, HIV

Introduction

Weight is the fundamental anthropometric assessment of nutritional status. Body mass index (BMI) incorporates both height and weight (kg/m^2) and has been widely used as a measure of obesity, energy stores and undernutrition.[1] The rationale for BMI use is that weight would be a better indicator of fat mass and energy stores if an allowance were made for height.[2] BMI is easier to measure and inexpensive in epidemiological studies where precise techniques for measuring body composition might be impractical for routine, clinical use.[3] However, BMI cannot differentiate between lean and fat mass,[4] visceral and overall adiposity and its relationship with body composition components differ with age, sex, ethnicity and body shape.[1] Furthermore, the extremes of weights seen in HIV positive patients make weight estimation difficult and defining obesity in HIV positive patients with standard anthropometry such as BMI may be inaccurate.[5]

Accurate estimation of adult body weight is often required in acute care settings. A patient's ideal body weight is required to prescribe appropriate drug dosages (e.g. anti-tuberculosis treatment, anticoagulants and sedatives), and to calculate fluid requirement in patients with burn wounds.[6] A patient's weight is also taken into account to determine whether the patient can be transported by air.[7] Physicians further use patients' weight for risk stratification and most radiology equipment has a maximum weight limit for patients.[8] Health care providers are poor estimators of a patient's weight[9–11] and an accurate weight estimation tool would be useful, particularly in immobile patients. Hospital beds with built in scales are ideal but seldom available in resource-limited settings.

The mid-upper arm circumference (MUAC) is a well-known anthropometric tool for weight estimation in paediatrics and its use has recently expanded to adults.[12,13] The MUAC is measured midway between the acromion process of the shoulder and the olecranon of the elbow on the non-dominant arm using a standard measuring tape.[14] There are several MUAC based formulae that have been developed to estimate weight in adults, but in contrast to paediatrics, there is no universally accepted and validated tool. In India, MUAC is used to predict muscle mass using the equation $[kg = (1.641 * MUAC) - 15.58]$.[13] Cattermole et al.[12] used data from the 2011-2012 United States Nation Health and Nutrition Examination Survey (NHANES) and derived a MUAC-based weight estimation equation using linear regression: $[kg = (3.8484 * MUAC) - 46.8585]$. To simplify this equation, the coefficients were rounded to one significant number: $[kg = (4 * MUAC) - 50]$. Differences between the exact linear regression equation and the simplified equation were only significant for estimates within 20% of actual weight. In both the models, at least 60%, 90% and 98% of estimates fell, respectively, within 10%, 20% and 30% of actual

weights in adults and adolescents.[12] Both methods performed poorly in patients with a MUAC less than 20cm or a weight less than 30kg.

Opdam et al. was the first to externally validate Cattermole's formula ($[kg = (4 * MUAC) - 50]$) in an elderly population.[15] In American elderly, Cattermole's formula accurately estimated actual body weights and the performance of the formula was comparable to the data initially published.[15] However, Cattermole's formula was not accurate in Dutch elderly and only 41.6%, 78.0%, and 96.3% of the estimates fell, respectively, within 10%, 20%, and 30% of the actual body weight.[15] MUAC was poorly associated with actual body weight, and thus the formula was not recommended for use in Dutch emergency centres.

In South Africa, MUAC as a weight estimation tool has only been studied in pregnant women. MUAC correlated strongly with BMI in pregnancies up to 30 week gestation and could reliably substitute BMI to assess nutritional status.[16] No studies have been done on the use of MUAC as a weight estimation tool in emergency centres in South Africa, especially in a high Human Immunodeficiency Virus (HIV) setting.

The objectives of the current study were, therefore: i) to assess the correlation between MUAC and both weight and BMI in all adult patients and in adult HIV positive patients, ii) to externally validate an existing MUAC-based weight estimation formula in all adult patients and in adult HIV positive patients and if inaccurate, iii) to derive a MUAC-based weight estimation formula more suitable to the adult study population.

Methods

Study design

A cross-sectional diagnostic study was conducted at Khayelitsha Hospital, a district-level hospital situated in the informal settlement of Khayelitsha, Cape Town. The study was approved by the Human Research Ethics Committee of the University of Cape Town (HREC REF: 640/2019).

Study setting and participants

Khayelitsha is an informal settlement situated in Cape Town, South Africa. It has a predominantly black African population of approximately 391,000 people,[17] with a high unemployment rate (38%) and over half of the households living in informal dwellings.[13] Khayelitsha district hospital is a 300

bed hospital which sees a high burden of HIV, tuberculosis (TB) and interpersonal violence,[18] and provides emergency, surgical, medical, paediatric and obstetric care services to this district.[19]

All patients older than 18 years of age that presented to the emergency centre of Khayelitsha Hospital were eligible to participate. Patients were excluded from the study if they were pregnant, had previous trauma or illness to the non-dominant arm that would influence the MUAC measurement (e.g., circumferential burns, polio etc), had lower limb fractures or were unable to stand independently unassisted. Patients whose HIV status was not known and who declined informed consent were also excluded. Data collection was completed between 08h00 and 16h00 on 11 randomly selected weekdays during the months of February and March 2020. All consecutive patients that were admitted to the emergency centre were screened for eligibility. The trained investigator and translator recruited patients from the entire emergency centre, including patients that were on trolleys. The potential participants were stable and did not require emergent, resuscitative care. Patients who received emergent care and had stabilised were later offered the opportunity to participate in the study. All sick, frail patients on a trolley were all given a trial to stand independently unassisted for a few minutes; they were enrolled if this was possible. Patients who were unable to stand independently unassisted were excluded.

The required sample size was estimated to be 240 participants, of which 50% (n=120) would have to be HIV positive. The minimum sample size was determined on the assumption that 10 candidate variables will be tested. Assuming 8-10 participants with HIV for each candidate variable tested, based on Peduzzi et al.[20] rules, about 100 HIV-positive participants would be required. Therefore, 100 HIV-negative participants were also needed. A further 20% was added to ensure adequate power was obtained. This was more than the minimum effective sample size (n=100) required for external validation.[21] It was also more than Green's rule-of-thumb for multiple correlation ($n \geq 50 + 8 \times$ number of variables) and partial correlation ($n \geq 104 +$ number of variables),[22] since the original model only included one predictor variable.[12]

Data collection and management

Eligible patients were taken to a single room within the emergency centre one at a time. A translator assisted with translation into isiXhosa if the patient could not understand English. Consent was obtained from the patient to disclose their HIV status to the research team and their HIV status was confirmed from clinical notes (opt-out HIV testing and counselling are routinely offered in the emergency centre at the hospital) or from the web portal of the National Health Laboratory Services. HIV testing was not conducted during the study.

Variables collected included patient demographics (age, gender); hand dominance; HIV status, adherence to antiretroviral therapy (ART), viral load and CD4 cell count; current Tuberculosis (TB) status (known with TB or being investigated for TB) and adherence to TB treatment, recent hospital admissions (for longer than a week in the last year); current cancer diagnoses and food or drink intake in the last six hours. Patients were asked to undress to a single layer of clothes, similar in thickness to a material theatre gown, before their weight, height and MUAC were measured. Weight (Wt.) was measured to the closest 0.1kg on a calibrated Micro scale (Model A12E) that was provided by a company specialising in weighing equipment (Scales Incorporated®, https://scalesinc.co.za). The MUAC was measured midway between the acromion process of the shoulder and the olecranon of the elbow of the non-dominant arm relaxed at the patient's side using a standard, flexible measuring tape and measured in centimetres (cm). Participants' heights were measured to the closest 0.1cm with a standard measuring tape mounted to the wall. Each participant was requested to stand barefoot with the back and legs straight and the back of the head placed against the wall. A flat board was placed at right angles to the wall to ensure correct reading and the participant's head was positioned so that the line of site was parallel with the floor.

The measurements were performed by a single trained investigator and all the assessments were done on the same day. A different physician blinded to the initial measurements, measured the MUAC of 28 (11%) participants. The measurements were done on two randomly selected days and the sample was selected using a computer-generated random number list on the allocated days.

Statistical analysis

Summary statistics were used to describe all variables. Intraclass correlation coefficient (ICC) with 95% confidence intervals (CI) was used to determine interrater reliability for MUAC measurements. Underweight was defined by a BMI of less than 18.5 kg/m^2, normal weight 18.5-24.99 kg/m^2, pre-obese 25.00−29.99 kg/m^2, Grade 1 obesity 30.00−34.99 kg/m^2, Grade 2 obesity 35.00−39.99 kg/m^2, and Grade 3 obesity more than 40.00 kg/m^2. Correlation of MUAC with weight and BMI were determined using Spearman's correlation coefficients with 95% CIs. Predicted weights were calculated from Cattermole's previously developed formulae (regression formula: kg=(3.8484xMUAC)−46.8585; simplified formula: kg=(4×MUAC)−50).[12] The agreement between the predicted and observed weights was graphically assessed with a calibration plot and goodness of fit regression lines were used to calculate the coefficient of determination (R squared) to determine the best fit formula. A MUAC based weight estimation formula was derived with

linear regression using locally collected data. Analyses were performed using Microsoft Excel 365 ProPlus and SPSS Statistics for Windows, Version 26.0 (IBM Corp. Released 2017. Armonk, NY: IBM Corp.).

Results

Demographics

A total of 280 participants were screened, of which 36 were excluded (unknown HIV status: n=18; unknown if pregnant: n=16; declined participation: n=1; unable to stand: n=1). A total of 244 participants were included of whom 121 (49.6%) were HIV positive. More females (n=129, 52.9%) were enrolled and the ethnicity reflected that of Khayelitsha's population.[17] The average height of the patients was 163cm and BMI was 23.61kg/m^2. The demographics and characteristics of all participants as well as subgroups according to HIV status are presented in Table 1.

In the 121 HIV positive participants, 22 (18%) had a viral load less than 1000 copies/ml, 19 (16%) participants had a viral load of more than 1000 copies/ml and 80 (66%) had not had a viral load measurement within the three months prior to enrolment. There were 68 (56%) participants who did not have their CD4 cell count measured within the last three months, 32 (26%) participants had a CD4 cell count less than 200/mm^3, 10 (8%) participants had CD4 cell counts between 200/mm^3 and 349/mm^3 and 11 (9%) participants had CD4 cell counts greater than or equal to 350/mm^3.

Table 1- Demographic and clinical characteristics of participants

	All N=244	HIV[1] negative n=123	HIV positive n=121
Gender, n (%)			
Male	111 (45)	65 (53)	46 (38)
Age, median [Q_1-Q_3]			
Years	37 [31-50]	36 [28-57]	37 [32-45]
Anthropometric measurements, median [Q_1-Q_3]			
Weight (kg)	62.5 [53.8-80.7]	68.1 [57.65-83.05]	57,4 [49.2-72.2]
Height (cm)	163 [156.8-169.3]	165.3 [159.1-170.1]	161,1 [155.9-168.0]
BMI[2] (kg/m^2)	23.61 [19.56-29.65]	25.15 [21.11-30.27]	22,41 [18.40-29.17]
Underweight[3], n (%)	41 (16.8)	9 (7.3)	32 (26.4)
Normal weight, n (%)	97 (39.8)	50 (40.7)	47 (38.8)
Pre-obese[4], n (%)	46 (18.9)	31(25.2)	15 (12.4)
Grade 1 obesity[5], n (%)	22 (9)	13 (10.6)	9 (7.4)
Grade 2 obesity[6], n (%)	18 (7.4)	10 (8.1)	8 (6.6)
Grade 3 obesity[7], n (%)	20 (8.2)	10 (8.1)	10 (8.3)
MUAC[8] (cm)	27.8 [24.5-32.0]	28.5 [26.5-32]	26 [22-31.5]
Confounders, n (%)			
Active TB[9]	39 (16)	4 (3)	35 (29)
Active phase of TB treatment	13 (5)	0(0)	13(11)
Continuation phase of TB treatment	15 (6)	1(1)	14(12)
Not on TB treatment	11(4)	3(2)	8(6)
Active cancer	7 (3)	4 (3)	3(2)
Unconfirmed cancer, being investigated	2 (1)	2(2)	0(0)
Recent admission[10]	42 (17)	16(13)	26(21)

[1] Human Immunodeficiency Virus
[2] Body mass index
[3] Underweight BMI<18.5 kg/m^2
[4] Pre-obese BMI=25.00−29.99 kg/m^2
[5] Grade 1obesity BMI=30.00−34.99 kg/m^2
[6] Grade 2 obesity BMI=35.00−39.99 kg/m^2
[7] Grade 3 obesity BMI≥40.00 kg/m^2
[8] Mid-upper arm circumference
[9] Tuberculosis
[10] Admitted in the last year for a week or longer

Intraclass Coefficient Correlation

The intraclass correlation coefficient using two-way mixed effects and absolute agreement model showed excellent interrater reliability, ICC=0,997 [95% CI 0.993-0.998].

Correlation of MUAC with weight and BMI

There was a statistically significant correlation between MUAC and weight in all the participants (r_s[244]=0.93, p<0.001, 95% CI: 0.90-0.95) and in HIV positive participants (r_s[121]=0.92, p<0.001, 95% CI: 0.88-0.95) presenting to the emergency centre (Figure 1). Furthermore, there was a statistically significant correlation between MUAC and BMI in all participants (r_s[244]=0.93, p<0.001, 95% CI: 0.91-0.95) and in HIV positive participants (r_s[121] =0.94 p<0.001, 95% CI: 0.91-0.96) presenting to the emergency centre (Figure 1).

External validation of existing MUAC-based method

The predicted weight using Cattermole's regression formula [kg=(3.8484xMUAC)−46.8585)] differed from the actual weight in both HIV negative (R^2=0.79) and in HIV positive (R^2=0.86) participants (Figure 2 Panel A). The predicted weights using Cattermole's simplified formula [kg=(4×MUAC)−50)] were also different to the observed weights in both the HIV negative participants (R^2=0.81) and in HIV positive participants (R^2=0.86) (Figure 2 Panel B).

Alternative formula for Khayelitsha population

The formula derived with linear regression using locally collected data was Wt.=(2,9306xMUAC)-15.939 for participants regardless of HIV status and Wt.=(2.9286xMUAC)-16.293 for HIV positive participants alone. The coefficients of these formulae were rounded to one significant figure, resulting in one simplified formula [Wt.= (3x MUAC)-16] to be used in all patients. The agreement between the predicted weight from the simplified formula against the actual weight is depicted in Figure 3. In HIV negative participants R^2=0.81, and in HIV positive participants R^2=0.86.

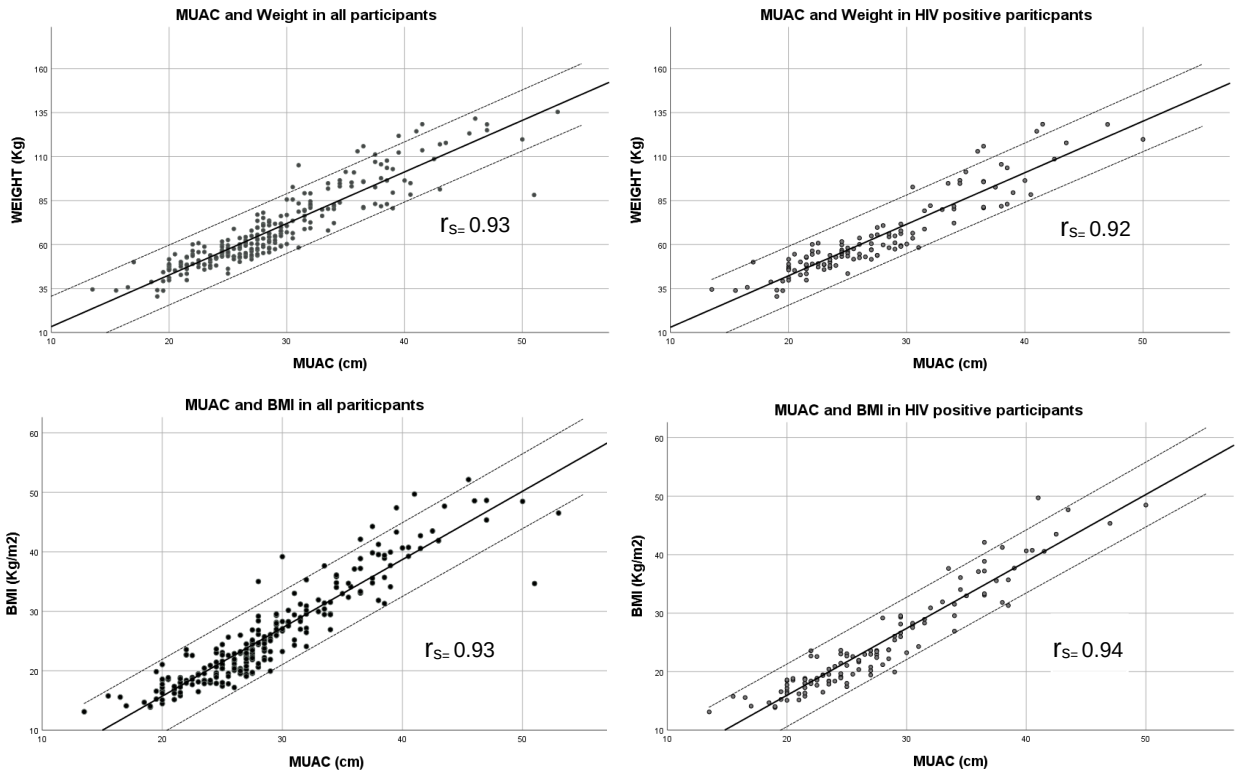

Figure 1- Correlation of MUAC with weight and BMI in all participants and HIV positive participants.

Dotted lines indicate 95% confidence intervals. BMI: Body mass index; HIV: Human immunodeficiency virus; MUAC: Mid-upper arm circumference

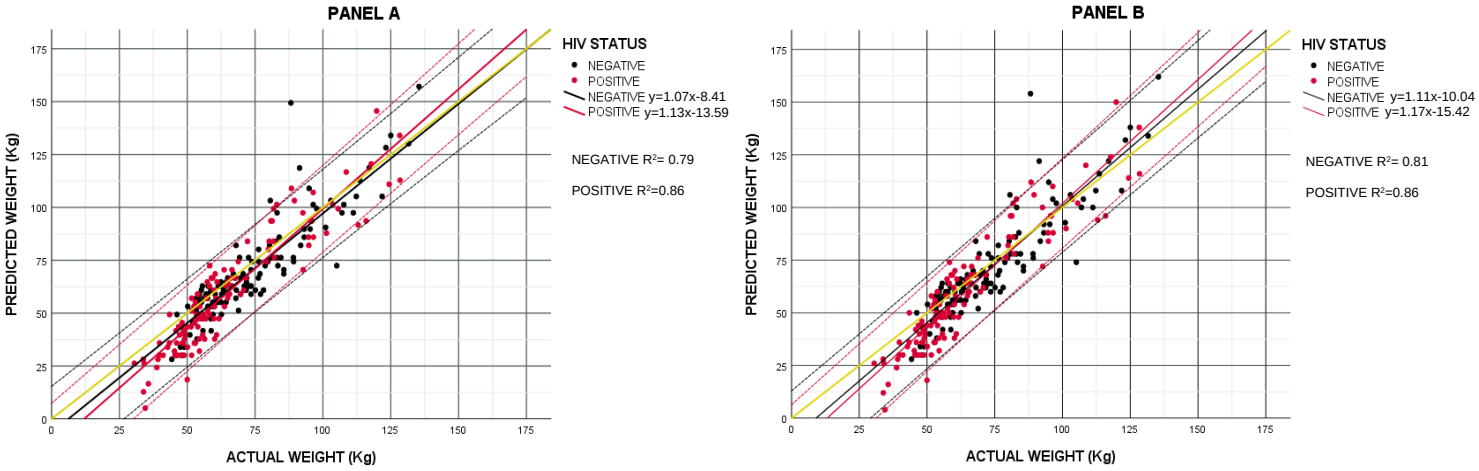

Figure 2- Actual weight compared to predicted weight using formulae developed by Cattermole et al.[12]

Panel A: Regression formula [kg=(3.8484xMUAC)−46.8585); Panel B: Simplified formula [kg=(4×MUAC)−50). Dotted line indicates 95% confidence intervals, gold line indicates y=x.

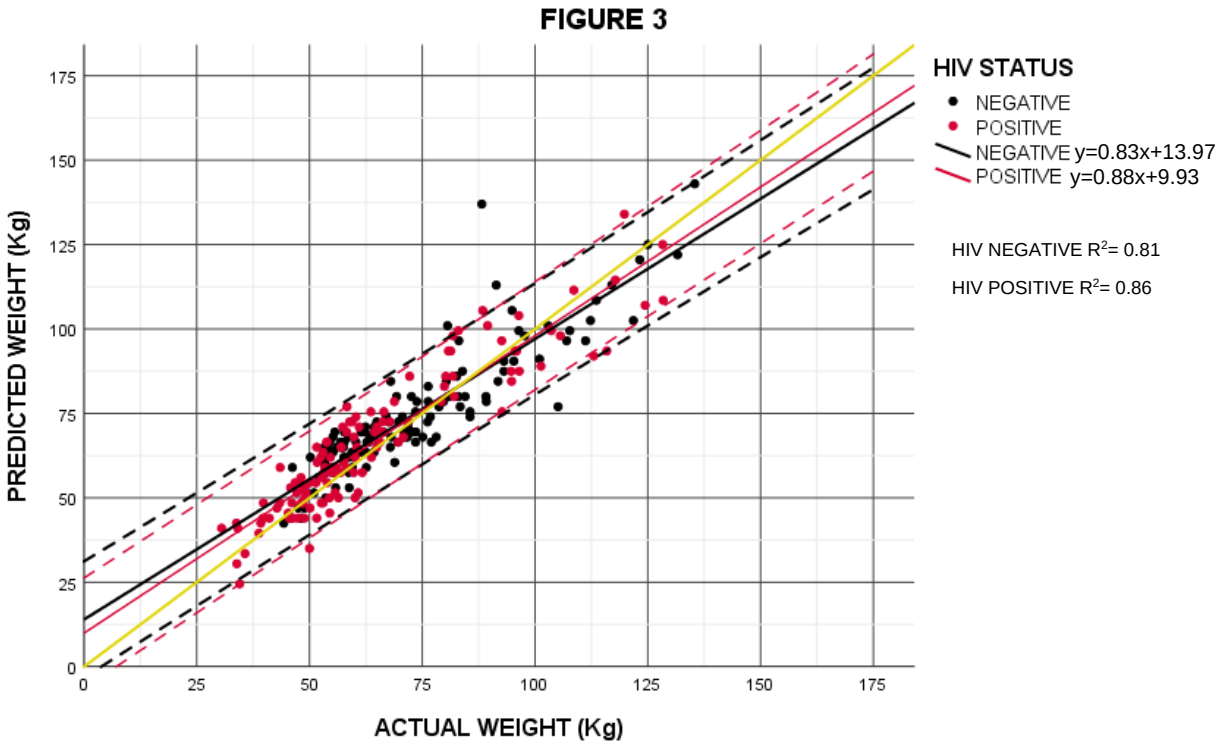

Figure 3- Actual weight compared to predicted weight using MUAC based on a simplified formula [Wt.= (3x MUAC)-16] developed from patients attending Khayelitsha Hospital.

Dotted line indicates 95% confidence intervals, gold line y=x.

The simplified Khayelitsha derived formula predicted 98.4% of weight estimates within 30% of the actual weight for participants with any HIV status and 97.5% for HIV positive participants (Table 2). Difference plots for Cattermole's original regression formulae and the Khayelitsha model are depicted in additional figures [see Additional file 1].

Table 2- Percentage of estimates lying within actual weight with different formulae based on MUAC.

		Percentage of estimates lying within x% of actual weight		
		10%	**20%**	**30%**
Cattermole original formula [kg=(3,8484xMUAC)-46,8585]	**All**	43.9	77.5	90.2
	HIV positive	33.1	69.4	85.1
Cattermole simplified formula [kg=(4xMAUC)–50]	**All**	46.7	77.5	89.8
	HIV positive	35.5	70.2	85.1
Khayelitsha original formula	**All [kg=(2,9306xMUAC)-15,939]**	57.8	91.8	98
	HIV positive [kg=(2,9286xMUAC)-16,293]	53.7	91.7	97.5
Khayelitsha simplified formula [kg=(3xMUAC)-16]	**All**	59.0	88.5	98.4
	HIV positive	53.7	87.6	97.5

Discussion

This study indicates that MUAC is highly correlated with weight and BMI in adults presenting to the Khayelitsha emergency centre independent of HIV status. Cattermole's regression formula (kg=(3.8484×MUAC)−46.8585) and simplified version (kg=(4xMUAC)-50) were not accurate in the study population. The regression formula derived from study data (kg=(3xMUAC)-16) better estimated weight in the local population.

The study population demographics are quite similar to those found in the 2003 South African Demographic and Health survey. The average height of our patients was 163cm, which fell within the range of 157cm in women and 168cm in men that was found in the survey.[23] The average weight (62.5kg) and BMI (23.61kg/m^2) of our study population was similar to the African male weight (64.6kg) and BMI (22.9kg/m^2), but slightly less than the female weight of 68.5kg and

27.2kg/m^2.[23] Although body mass index is a widely accepted anthropometric measure used as a measure of obesity and nutrition[3] and its ease of use in large populations is relatively cost effective and practical, it cannot be used in bed bound, immobile patients where heights cannot be measured. In addition, BMI and its relationship with body composition components differ with different ages, sex, ethnicity, and body shapes.[1] Furthermore, the extremes of weights seen in HIV positive patients make defining obesity with standard anthropometry such as BMI inaccurate.[5] Although urbanisation and lack of exercise are associated with increasing obesity prevalence,[23] the data from the 1998 and 2003 South African survey shows that there hasn't been any major changes in BMI over the five years measured.[23]

MUAC correlates well with both weight and BMI and this is similar to previous findings.[12,14,24–27] Cattermole et al.[7] noted that MUAC correlates better to weight compared to other anthropometric measurements such as height, waist circumference and abdominal circumference. Some evidence demonstrates that MUAC is a better indicator of nutritional status than BMI due to its ease of use and cost effectiveness.[24,26,28–30] Moreover, MUAC cut-offs have been suggested in place of BMI to screen for nutritional status in adults.[24,25,31–33] The strong correlation between MUAC and both weight and BMI supports the idea that MUAC is a suitable tool to estimate weight and nutritional status.

Cattermole's MUAC-based formulae estimated weight poorly in this study. Even though the goodness of fit of Cattermole et al.'s simplified formula was the same as the simplified Khayelitsha formula, when percentages of estimates lying withing a certain percentage of actual weight was compared, the simplified Khayelitsha formula fared better. This finding echoes Opdam et al.[15] where the simplified formula was also inaccurate in the elderly Dutch population. Opdam et al.[10] suggested the reason for conflicting results were due to body composition differences between the Dutch and American elderly. Body composition differences could also be the reason the formulae were inaccurate in our population. There are significant differences in the distribution of subcutaneous fat, muscularity, and the length of limbs relative to the trunk between black African and white populations.[34,35] Black Africans also deposit relatively less subcutaneous fat on the front of the body and extremities, and more on the trunk and back.[34] These differences can result in different populations having varying relationships between percentage body fat, BMI and waist circumferences.[34] Moreover, racial differences in fat patterning could produce errors in the assessment of the prevalence of obesity, skin fold thickness [34,35] and quite possibly, MUAC.

In the HIV positive population, MUAC correlated well with weight and BMI, but Cattermole's formulae only estimated 33 to 35% of weights estimated within 10% of actual weight in this subset

of participants. Cattermole et al.[12] found that their formulae perform poorly in severely underweight individuals (less than 30kg) or in MUAC readings less than 20cm. Although some HIV positive participants in the current study were underweight (26.4%) and nine (7%) participants had MUAC readings less than 20cm, this is insufficient to account for the inaccuracy of the formulae in all of the HIV positive participants. A possible reason the formulae performed poorly could be the above-mentioned difference in body composition between Americans and South Africans. However, there are also added body composition differences between HIV positive individuals and their negative counterparts. HIV positive individuals have lower fat and lean masses, and percentage body fat than their HIV negative counterparts.[36] Furthermore, ART use may predispose to lean body fat, skeletal muscle and weight changes.[37,38] ART themselves may lead to lipodystrophy,[38,39] decreased lean tissue mass, fat mass atrophy and reduced bone mineral content.[40] Thus, in the HIV positive participants, over and above the differences in body compositions between the two countries, HIV seropositive status in itself could also contribute to formulae inaccuracy in this subset of patients.

The MUAC-based formula derived from the study data was more suitable for the local population. This study was performed in a single centre, fairly homogenous population in Khayelitsha with a high HIV prevalence and our formula better estimated weight in this population compared to Cattermole's. However, more research will be required to validate this formula in different South African settings with different populations and HIV prevalence.

It is uncertain what measures are best to validate anthropometric weight estimation tools and unfortunately there is no agreement on the amount of error that is tolerable[12]. Little is known as to what percent difference of actual weight will adversely affect a patient as this has not been studied. Cattermole et al.[12] believe that emergency medicine physicians would be comfortable with estimating weights within ten percent of actual weight and would not be comfortable differing more than 30% from actual weight, and thus chose to use 10%, 20% and 30% of actual weight to demonstrate how precisely one can estimate weight in adults. Furthermore, they reasoned that 33% error of an "average" 75kg patient would result in a conservative adult range of 50 to 100 kilograms. Unfortunately, the precision of weight estimation required for drugs with different therapeutic ranges is not known and until this has been investigated, the amount of error tolerable for an anthropometric weight estimation tool cannot be decided upon.

Darnis et al.[41] found that anthropometric measures to estimate body weight were not accurate. They compared the Lorenz formula (based on height, waist, and hip circumference), the Crandall formula (based on height and MUAC) and the average of two pharmacy intern's visual estimates

of actual body weights. They found estimates of actual body weight based on height and MUAC to be poor and supported the need for equipment to accurately weigh unconscious, immobile patients.[41] However, despite Cattermole's formulae being inaccurate in the study population, these formulae could still fare better than health care practitioner's estimating patient's weights. Health care providers are inaccurate when estimating weight [9–11] and only 10% of observers are able to correctly estimate weight within 25% of actual values[11], whereas at the worst estimates, all formulae found in this study accurately estimated at least 69.4% of weights within 20% of actual weights. Further in-depth studies will be required to compare anthropometric based formulae with health care practitioner's estimations with a consistent definition of what amount of error is tolerable for an anthropometric tool. Although MUAC is a good substitute for BMI and most likely can accurately estimate weight, it is unlikely that a universal formula will be found due to the differences in body compositions in different populations.

Strengths and Limitations

The validity and reliability of the study findings were enhanced by using a single trained investigator to do the measurements with a subsequent, independent re-measurement in 10% of included participants.

However, the study still had many limitations. Only patients that could stand independently were included. This might have biased the results away from underweight participants, especially in the chronically ill or malnourished population. Furthermore, a large proportion of the HIV positive participants did not have CD4 cell counts or viral loads done in the last three months. This limits our understanding on the staging of HIV disease in the HIV positive participants and the potential confounding factor of weight loss or gain due to HIV disease. Some potential confounders which could have influenced the accuracy of MUAC measurements and weight were not included. These include comorbidities (e.g., chronic heart failure, chronic renal disease), the presence of oedema, socioeconomic status and whether upper arm muscles were frequently exercised. A higher HIV prevalence was noted than was found in previous studies. This could likely be due to a small sample size that does not accurately reflect the population's HIV prevalence. Furthermore, there are different cultural and ethnic groups within South Africa and this small sample size likely does not reflect the true diverse cultural and ethnic background of black South Africans. Furthermore, there could be a different body habitus between those living in urban and rural areas in South

Africa and this small, urban sample size likely does not adequately represent the true South African population.

Conclusions

MUAC is highly correlated to weight and BMI in participants presenting to the emergency centre regardless of HIV status and should be considered as a weight estimation tool in emergency centres. In this high HIV prevalent setting, this study population's weight can be estimated using the formula [Kg=(3xMUAC)-16]. It is likely that no universal formula is applicable to all populations and that the formulae are dependent on the body compositions of different populations.

Future directions

The weight estimation formula derived in this study needs to be validated in different settings and populations with a different HIV prevalence to assess for its validity in a population that better represents the diverse South African population. Future research can be directed at different settings with larger study populations such as community health care centres and in the community to assess whether the formula is applicable beyond our local population. Extra effort should be made in future studies to include non-mobile, very ill patients and perhaps measure their weights with a bed scale, as this weight estimation tool will mostly likely affect their management the most. Furthermore, future studies can explore health care workers' perceptions of weight measurement and its associated barriers.

List of abbreviations

ART	Antiretroviral therapy
ARV	Antiretrovirals
BMI	Body mass index
CD4	Cluster of Differentiation 4
CED	Chronically energy deficient
CI	Confidence Interval
Cm	Centimetre
CT	Computed tomography
CVD	Cardiovascular disease
HIV	Human Immunodeficiency Virus
HR	Hazards ratio
ICC	Intraclass correlation coefficient
Kg	Kilogram
MRI	Magnetic Resonance Imaging
MUAC	Mid-upper arm circumference
NCD	Non-communicable disease
NHANES	United States Nation Health and Nutrition Examination Survey
SD	Standard deviation
TB	Tuberculosis
UCT	University of Cape Town
VL	Viral Load
WC	Waist circumference
WHO	World Health Organisation
Wt.	Weight

Declarations

Ethics approval and consent to participate

Ethical approval was obtained from the University of Cape Town, Faculty of Health Sciences Human Research Ethics Committee (HREC REF: 640/2019). All participants gave written consent to partake in the research.

Availability of data and materials

The dataset used during the current study are available from the corresponding author on reasonable request and pending further ethical approval.

Competing interests

The authors have no competing interests to declare.

Funding

This study was self-funded.

Author's contributions

EC and DJvH conceptualised the original idea. All authors contributed to the planning of the study. EC collected the data and EC and DJvH did the analyses. All authors interpreted the results. EC drafted the manuscript and DJvH and CS provided critical insights. All authors read and approved the final manuscript.

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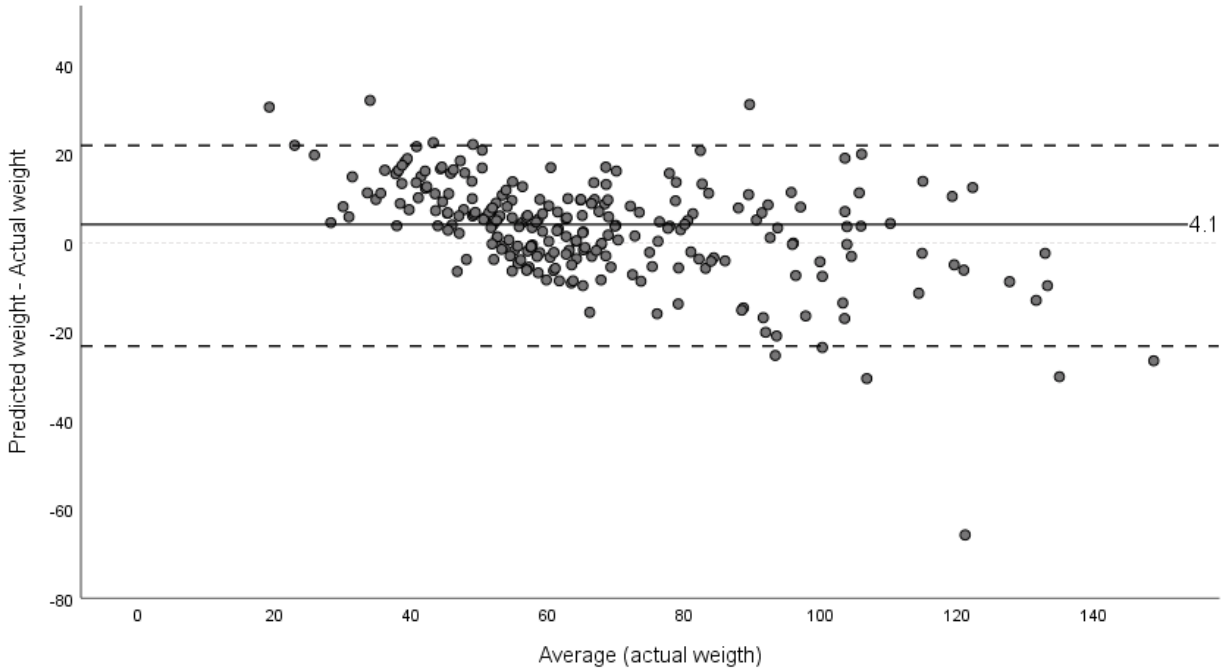
Thank you to enrolled nurse NI Nyembezi for assisting with the enrolment of participants and translations into IsiXhosa when required. Thank you to Dr JC King for measuring the second set of MUACs on participants to determine interrater reliability. Thank you to Scales Incorporated® for providing the scale free of charge.

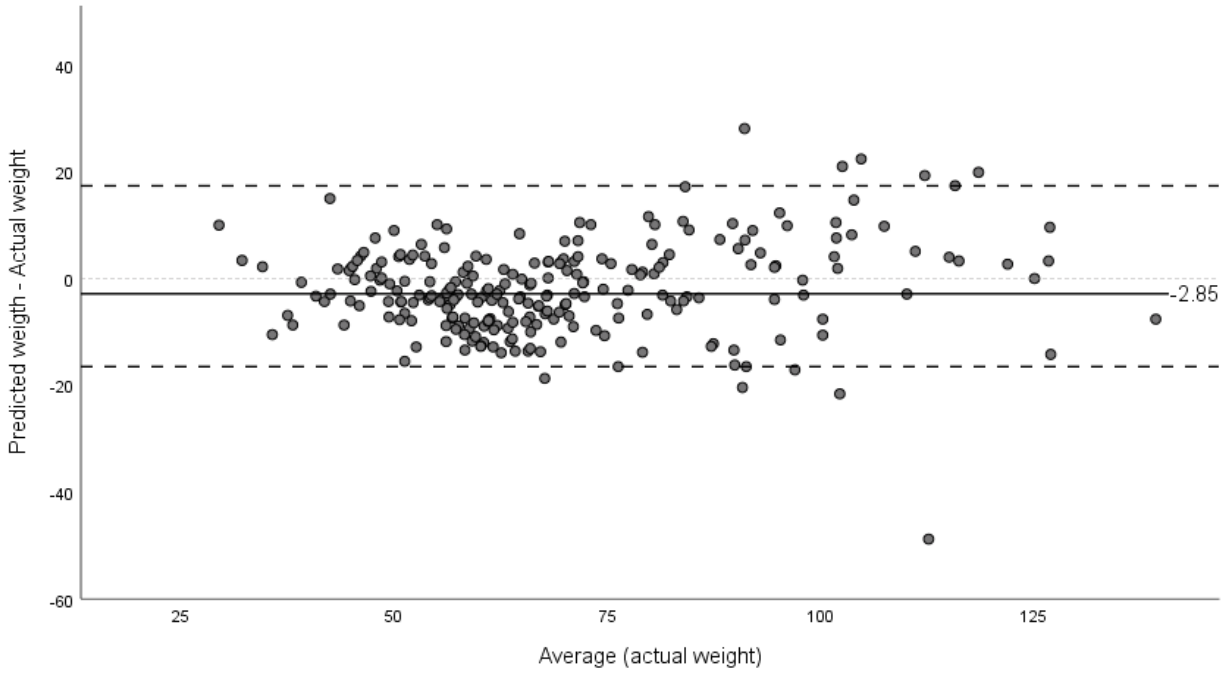
Additional files

Additional file 1



Difference plot indicating the average difference between actual weight and the simplified MUAC-based formula [kg=(4×MUAC)−50)] developed by Cattermole et al.(12) (solid line = median; broken lines = 2.5th and 97.5th percentiles)

Additional file 2



Difference plot indicating the average difference between actual weight and the MUAC-based formula [kg=(3x MUAC)-16] developed using local data (solid line = median; broken lines = 2.5th and 97.5th percentiles)

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PART C. APPENDICES

Appendix 1. Instruction to Authors (International Journal of Emergency Medicine)

This manuscript was formatted for submission to *International Journal of Emergency Medicine*; an open-access, peer-reviewed journal accredited by the South African Department of Higher Education and Training.

The instructions for authors are available at https://intjem.biomedcentral.com/submission-guidelines/preparing-your-manuscript/original-research

Appendix 2. Research Protocol

RESEARCH PROPOSAL

THE VALIDATION OF THE MID-UPPER ARM CIRCUMFERENCE MEASUREMENT AS A WEIGHT ESTIMATION TOOL IN A HIGH HIV PREVALENCE SETTING

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University of Stellenbosch

This study is in partial fulfilment of the MMed degree

Contents

Declaration

I, Emily Chen, hereby declare that the work on which this proposal is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

I authorise the University to reproduce for the purpose of research either the whole or any portion of the contents in any manner whatsoever.

Introduction

Background

Malnutrition, ranging from underweight to overweight and obesity, affects countries worldwide. Globally, the prevalence of obesity has nearly tripled from 1975 to 2016.[1] In 2016, more than 1.9 billion adults were overweight, of which 650 million were obese.[1] Being overweight is associated with a higher prevalence of cardiovascular diseases, diabetes and cancer.[2] Complications of obesity include fatty liver disease, mechanical complications of joint pain and arthritis, increased obstetric risk and sleep apnoea.[3] It may also affect mental health, partly due to stigmatisation.[3]

On the other hand, 462 million people in the world are underweight[4]. Undernutrition accounts for 11 % of the global burden of disease and is considered the number one risk to health worldwide.[5] Malnutrition in all its forms result in diet-related non communicable diseases and its impact on individuals, their families and communities economically, socially and medically are serious and long lasting.[4]

In sub-Saharan Africa, the proportion of patients reaching more than 60 years of age is increasing.[6] Up to half of elderly Africans are underweight (6-48%) and almost a quarter (2.5-21%) are overweight, while 56% of older South Africans are obese.[6] Poverty, HIV/AIDS, and complex humanitarian emergencies are major determinants of undernutrition in sub-Saharan Africa.[6]

Human Immunodeficiency Virus (HIV) is a global pandemic. As of 2017, there were 36.9 million people living with HIV worldwide.[7] South Africa has one of the largest HIV epidemics in the world. In 2018, an estimated 7.5 million South Africans were living with HIV.[8] Of these patients, approximately 4.4 million were on antiretroviral therapy (ART) and only 47% of them were immunosuppressed.[9] The burden of HIV in South Africa is high and thus doctors working in emergency centres commonly manage patients who are HIV positive. It is estimated that 12 to 23% of patients presenting to emergency centres in South Africa are infected with HIV.[8,10]

HIV infected patients can present with two extremes of weight. In Sub Saharan Africa, the most common presentation is the HIV wasting syndrome.[11] HIV wasting syndrome is characterized by more than 10% involuntary weight loss (both fat and lean body mass) and is often accompanied by muscle fatigue and weakness.[12,13] Since the availability of ARTs, the incidence of wasting has decreased dramatically.[14] However, the initial lean body mass loss may not be fully restored with effective immunosuppression after ART initiation and a high incidence of wasting has still been noticed in some populations during the ART era.[15-19]

In rural South Africa, the body mass index (BMI) of HIV-positive people both on and not on ART are on average lower than the HIV-negative population.[20] The HIV-positive ART naive group are lighter, have a lower BMI, lower fat, lean mass and lower percentage body fat than their HIV-negative counterparts.[21] In HIV-positive patients, being underweight prior to ART was associated with more than double the rate of Acquired Immunodeficiency Syndrome (AIDS) deaths.[22] This extreme underweight body habitus of HIV-positive patients is one that is commonly seen in South African emergency centres and estimation of weight in these patients can prove to be difficult.

The other extreme of weight relates to a higher prevalence of obesity. This new phenomenon is a result of HIV patients living longer and gaining weight due to the advent of ARTs.[23-25] In the United States, obesity was more prevalent than wasting in their HIV-positive patients.[26] Almost half of the patients were overweight or obese at ART initiation and 1 in 5 patients moved to a BMI in the overweight category within two years of ART initiation.[27] The prevalence of obesity in one South African sample of both HIV-positive and HIV-negative patients was approximately 59%.[21] In KwaZulu-Natal, the prevalence of obesity and hypertension were still both very high despite the high prevalence of HIV.[28]

Accurate weight assessment in the emergency centre is important as many decisions are based on a patient's weight, such as ventilator settings, drug dosages and fluid regimens. Furthermore, it correlates with metabolic syndrome and identifies patients at cardiovascular risk.[29] It has been shown that doctors and nurses are inaccurate when estimating a patient's body weight and when compared to patients estimating their own weights, doctors fair worse.[30-32] Anthropometric measurements that can be taken in the emergency centre include measuring weight, height, mid-upper arm circumference (MUAC), waist circumference, hip circumference, thigh circumference, calculated BMI, body adiposity index, waist to hip ratio and waist to thigh ratio.[33]

MUAC has been researched in paediatrics as a tool to estimate nutritional status and weight but only recently has its use for weight estimation expanded to adults and adolescents.[34] The MUAC is a much simpler anthropometric measure than BMI or weight, as its use eliminates the need for height charts, calibrated scales and relevant calculations. It is also much easier and faster to perform on a patient who is acutely unwell, bed bound or sedentary, making it ideal for the emergency centre setting. Furthermore, a simple measuring tape would be more cost effective than expensive charts and scales and would therefore be preferred in resource limited settings.

South Africa is a diverse country with a population different to that of high-income countries due to its marked burden of HIV. Little is known whether MUAC is a valid tool to estimate weight and BMI in the South African population, specifically with the extremes of weight seen in the HIV

positive population. In resource limited settings like South Africa, the MUAC's ease of use and cost effectiveness could be very beneficial to estimate weight in emergent, sick, often bedbound patients.

Aim and objectives

The aim of the study is to assess whether mid-upper arm circumference measurement is a valid tool to estimate weight in patients presenting to the emergency centre situated in a high HIV prevalence setting.

The objectives are:

i. To assess the correlation between the MUAC and weight in all patients presenting to the emergency centre of Khayelitsha Hospital.
ii. To assess the correlation between the MUAC and weight in HIV-positive patients presenting to the emergency centre of Khayelitsha Hospital.
iii. To assess the correlation between the MUAC and BMI in all patients presenting to the emergency centre of Khayelitsha Hospital.
iv. To assess the correlation between the MUAC and BMI in HIV-positive patients presenting to the emergency centre of Khayelitsha Hospital.
v. To externally validate an existing MUAC-based method for weight estimation in all patients presenting to the emergency centre of Khayelitsha Hospital.
vi. To externally validate an existing MUAC-based method for weight estimation in HIV-positive patients presenting to the emergency centre of Khayelitsha Hospital.

Methods

Study design

A cross sectional diagnostic study

Sample size

A convenience sample of 240 participants will be included, of which 50% (n=120) will be HIV-positive in order to test the tool in all patients and in an HIV-positive subgroup. This is more than the minimum effective sample size (n=100) needed for external validation[35]. It is also more than Green's rule-of-thumb for multiple correlation (n ≥ 50 + 8(number of variables)) and partial

correlation (n ≥ 104 + number of variables),[36] since the original model only includes one predictor variable.[34]

Study setting

The study will be done at Khayelitsha Hospital, a 300-bed hospital situated in the township of Khayelitsha, Cape Town. It serves a health district with a population of more than 390 000, where the population is predominantly black African (99%) with high levels of unemployment (38%).[34] There is a tremendous burden of disease related to HIV, tuberculosis (TB) and interpersonal violence.[37] Khayelitsha Hospital provides inpatient services such as surgical, medical, paediatric and obstetric care.[38] It has a large emergency centre, which is 30% larger than that of a standard district hospital trauma unit.[38]

Study population

All patients presenting to the emergency centre of Khayelitsha Hospital will be eligible to participate. HIV testing will not be conducted as part of the study. After consent has been obtained from the patient to disclose their status to researchers, their HIV status will be confirmed from clinical notes using either a documented previous HIV diagnosis or a current diagnosis on the index admission (opt-out HIV testing and counselling is routinely offered in the emergency centre at the hospital) or results obtained on NHLS.

Inclusion criteria

1. Patients ≥ 18 years of age

Exclusion criteria

1. Pregnancy
2. Previous trauma / illnesses to the non-dominant arm that will influence the MUAC measurement (e.g., circumferential burns, polio etc.).
3. Patients who are unable to get onto a scale due to their illness, for example femur fractures on traction or severely respiratory distressed patients.
4. Patients whose HIV statuses are not known.
5. Informed consent not obtained.

Recruitment and enrolment

The procedure developed for enrolment is aimed at minimising selection bias. Consecutive patients admitted to the emergency centre will be screened for potential eligibility. Potential participants will be stable patients that do not require emergent, resuscitative care. Patients who have received emergent care and have stabilised will be offered the opportunity to partake in the study. Patient screening will take place between 08h00 and 15h00. We foresee that twelve days would be enough to enrol the required sample size. Patients will receive the same standard of care should they decline to take part in the study.

All stable, ambulatory patients presenting to the emergency centre will be eligible. Individual patients will be taken to a single room within the emergency centre one at a time. A member of the study team (research assistant) will explain the research study and that knowledge of the patient's HIV-status is a requirement for the study. Patients choosing not to disclose their HIV-status, partake in the study or refuse that the study team member access their patient records will be excluded. The patients who agree to disclose their HIV status and who verbally agree to a study team member accessing their HIV-status will thus be enrolled into the study and consent be taken for HIV disclosure and participation in the study.

Research procedures

We will prospectively enrol 240 patients. Index variables to be collected include demographics (age, gender); ART status and CD4 count; recent hospital admissions; previous and/or current TB status; previous and/or current cancer diagnoses; weight; height; MUAC. The MUAC will be measured midway between the olecranon of the elbow and the acromion process of the shoulder of the non-dominant arm. A standard measuring tape will be used. The lead investigator will perform the measurements. The MUAC measurement will be double-checked in 10% of the study sample by a different research team member blinded to the initial measurement (randomly selected using a computer-generated random number list).

The outcome variable will be the weight of the participant, measured to the nearest 0.1kg as well as height, measured to the nearest 0.1cm. Participant's weight will be taken with a calibrated scale, dressed in clothes similar to a dressing gown and underwear. All assessments will be done on the same day.

Data collection

Data will be abstracted onto standardised hardcopy data capture forms (Appendix A). Data will be imported onto an electronic data platform (Microsoft Excel®) curated by the lead investigator.

Data safety and monitoring

Each participant will have a unique identifying study number, and this will be recorded together with the patient's name and hospital folder number in a study log. The study log (and all the patients' data capture forms in a study folder) will be kept in a locked cabinet in a limited-access office at Khayelitsha Hospital. The anonymised patient study folders will be transported to one of the supervisors' offices within the Division of Emergency Medicine. Laboratory results will be obtained from the NHLS Laboratory.

All data will be entered by the lead investigator onto an electronic database on the lead investigators' password protected private computer. Back-up will occur daily. All data on the database will be anonymised. The hard copies of the data sheets will then be shredded and destroyed.

Upon completion of the study, we will ensure that two copies of the anonymised electronic database are backed-up and stored for five years: one on a UCT server, and one on an external hard-drive that the lead investigator will keep secure.

Data analysis

Summary statistics will be used to describe the variables. Reproducibility of 10% of the study sample will be measured using κ statistics with 95% confidence intervals. The κ statistics will be interpreted as previously described.[39]

Correlation of MUAC with weight and BMI will be determined using correlation coefficients (Pearson's or Spearman's depending on distribution of the data) with 95% confidence intervals.

Predictions will be calculated from a previously developed model (regression model: kg=[3.8484×MAUC in cm]−46.8585; simplified model: kg=(4×MAUC)−50)).[34] The agreement between the predicted and observed weights (calibration) will be graphically assessed with a calibration plot (perfect predictions should be on the 45° line). Bland-Altman plots will be constructed to examine limits of agreement between the predicted and measured weights.[40] SPSS Statistics for Windows, Version 25.0 (IBM Corp. Released 2017. Armonk, NY: IBM Corp.) will be used.

Reporting of this study will be guided by the TRIPOD statement (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis),[41] although it is mainly applicable to models with binary outcomes.

Ethical considerations

Risks and benefits

There is no direct benefit for study participants. However, there is an indirect benefit to the study population. Should the MUAC be an effective tool to measure weight in adults, the benefits for its use in this population would be seen in the emergency centre as appropriate care can be provided with an accurate weight and correct drug dosages and ventilator settings etc can be calculated. Furthermore, time spent mobilising and weighing patients and searching for scales would be saved. In resource limited environments, there is also a potential cost benefit as a measuring tape is less expensive than scales and need not be calibrated.

The risk to the participant in this study is low and injury is unlikely to occur. Minimal discomfort will be experienced during measurements. Great effort will be placed in preventing the patient's participation in the study from interfering with clinical care, any severely ill patient requiring emergency care will not have their management delayed due to this study and will not be recruited unless they become well and stable enough to give consent and can mobilise.

HIV-positive patients are a particularly vulnerable population due to the stigma surrounding HIV and thus caution will be taken to maintain their confidentiality. Confidential information will need to be used during this study and this could pose a risk to the participant should the data get lost, as this will constitute a breach of confidentiality. However, precautionary measures (as described above) will minimise this risk; including de-identifying the data once collected and destroying hard copies of data as soon as possible. The study log containing the identifiers will be kept separate from the de-identified data.

Informed Consent

Process

A study team member will approach patients in the emergency centre. Every effort will be made to make the space as confidential as possible, i.e., draw curtains around the bed, look for a side

room if patient is well enough to mobilize. The informed consent process will be delegated to the trained research assistant. The lead investigator will support the process. The Principal Investigator will provide training of the study-specific informed consent process and monitor that informed consent is being taken that fulfils Good Clinical Practice (GCP) requirements throughout the study.

The informed consent document (Appendix B) will be discussed with the patient in detail in their language of choice (Xhosa or English). The informed consent document will be available in both languages. The patient will be given time to consider the study and time to discuss with their relatives if they are present. The patient will be given time to ask questions. It will also be emphasised to the patient that should he or she decide not to participate in the study, their medical treatment will not be affected in any way and their confidentiality will still be maintained - they will not be disadvantaged in any way.

Comprehension of information

Patient's understanding will be tested with standard questions prior to signing the informed consent documents.

Withholding information

No information regarding the study will be withheld from participants.

Privacy and confidentiality

Each participant will have a unique identifying study number, and this will be recorded together with the patient's name and hospital folder number in a study log. The study log will be kept in a locked cabinet in a limited-access office at Khayelitsha Hospital. Only the study team will have access to these records. All data on the electronic database will be anonymised.

Reimbursement for participation

Participants will not be reimbursed for participating in the study.

Emergency care and Insurance for research-related injuries

This is a low-risk study, and no research related injuries are reasonably anticipated.

Formal provincial permission will be obtained from the Western Cape Government Health Impact Assessment Unit once ethics permission has been obtained and prior to commencing the study.

Study timeline

EMDRC submission	HREC approval	WCG Health approval	Data collection	Data analysis	Write up
August 2019	October 2019	December 2019	January-February 2019-2020	March-April 2020	May-July 2020

Budget

Consumables	Cost
Measuring tape	R30
Printing data sheets and consent forms	R2000
Calibrated scale	R400
Research assistant	R5000
Travel to research site Twelve visits @ R74.10 (R1.30 /km; Return distance between UCT and Khayelitsha Hospital = 57km)	R890
Total	**R8320**

The project will be self-funded.

Limitations

Bedridden patients who are too sick to be weighed or unable to mobilise will be excluded from the study and cannot be included due to resource constraints and unnecessary exposure to harm.

There is a possibility of measurement errors when the investigator measures the MUAC. However, as described above, the MUAC measurement will be double-checked in 10% of the study sample by a different research team member blinded to the initial measurements.

Reporting and implementation of results

Publication as an original article or short report in a peer reviewed journal is anticipated. The study results will also be distributed to the management team of Khayelitsha Hospital Emergency Centre and hospital administration.

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Appendix A. Data capture form

Study screening no: _____

Name and Surname	
Folder number	
Date of birth	
Gender	
Handedness (right or left)	

HIV STATUS

- □ Positive
- □ Negative

CD4 count _____ Date of result (__DD__/_MM__/_YYYY__)

Viral Load _____ Date of result (__DD__/_MM__/_YYYY__)

ART use: YES / NO / DEFAULTED

If yes, when initiated? (_MM__/_YYYY__)

Which ART? FIXED DOSE REGIMEN / OTHER

If other, please specify:

_____

TB STATUS

Currently have TB? YES / NO

If yes: ONCE / MORE THAN ONCE

On TB treatment? YES / NO / DEFAULTED

PAST MEDICAL HISTORY

Recent admission: YES / NO

Date of admission (__DD__/_MM__/_YYYY___) until (__DD__/_MM__/_YYYY___)

Reason for admission

_____

_____

_____

Currently diagnosed with cancer? YES / NO

Is cancer active or in remission? ACTIVE / REMISSION

Has participant recently eaten in last 6 hours? YES / NO

If so, what was eaten and how much?

_____

_____

Has participant recently had something to drink in last 4 hours? YES / NO

If yes, what did he or she drink and how much?

_____

_____

MEASUREMENTS

Arm LEFT / RIGHT

MUAC (in cm) _____

Height (cm) _____

Weight (kg) _____

Appendix B. Informed Consent Document

PARTICIPANT INFORMATION LEAFLET AND CONSENT FORM

TITLE OF THE RESEARCH PROJECT: THE VALIDATION OF THE MID-UPPER ARM CIRCUMFERENCE MEASUREMENT AS A WEIGHT ESTIMATION TOOL IN IN A HIGH HIV PREVALENCE SETTING

PRINCIPAL INVESTIGATOR: Dr Colleen Saunders

INVESTIGATOR: Dr Emily Chen

You are being invited to take part in a research project. Please take some time to read the information presented here, which will explain the details of this project. Please ask the study staff or doctor any questions about any part of this project that you do not fully understand. It is very important that you are fully satisfied that you clearly understand what this research entails and how you could be involved. Also, your participation is **entirely voluntary,** and you are free to decline to participate. If you say no, this will not affect you negatively in any way whatsoever. You are also free to withdraw from the study at any point, even if you do agree to take part now.

This study has been approved by the Human Research Ethics Committee at the University of Cape Town (HREC Ref 640/2019).

What is this research study all about?

We are assessing if the arm circumference measurement (the distance around your upper arm) can be used to accurately predict a person's weight. The study will be conducted at Khayelitsha Hospital. The lead researcher is Dr Emily Chen from the University of Cape Town who is specialising in emergency medicine.

Background:

When you come to an emergency centre, the treatment given to you is mostly based on your weight and so it is important to accurately determine your weight so that doctors can give you the correct dose of treatment. Sometimes patients are too sick to stand on a scale or cannot move because of a disability (e.g., a broken bone) and so we cannot measure your weight and only an estimation of your weight is used. We would like to know if we can use your arm width measurements to accurately estimate your weight so that your weight can be measured correctly without standing on a scale. We also specifically want to know if a person's HIV status has an impact on their weight. HIV is a virus infection which slowly damages the immune system (the body's response to illnesses) and makes your body weak. People who are HIV positive have different weights, ranging from underweight to overweight and this weight difference can maybe affect the accuracy of the arm measurements.

We are aiming to include 240 patients in this study who already know their HIV status. We will not be retesting your HIV status. We will ask you some personal questions regarding your HIV status, TB and medical history and then ask you to change into light clothing so that we can do the measurements. After we have recruited all the patients and collected the data, we will then determine if we can estimate your weight based on your arm width.

Benefits and risks:

Taking part in the study may not benefit you directly. However, if this study finds that we can use the arm width to estimate weight, this will help all patients in the future who come to the emergency centre to get their correct weights measured and have the correct weight-based treatment.

There are very minimal risks for taking part in the study. We will ask you to dress in clothes similar in weight to a gown and have your arm width measured and your weight taken. There will be no pain during the measurements.

Furthermore, we understand the importance of keeping your HIV status confidential and that there is always a risk that this confidentiality can be breached. We will minimise this risk by only speaking to you in the comfort of a private room and we will not be sharing your information with anyone that is not involved in the study. We will take precautionary measures to ensure that all the data we have collected is kept in a secure place. We will also shred all hard copies of your information once it is stored as de-identified data on a password protected computer.

If you choose not to participate in the study, you will still receive standard of care treatment for your medical condition.

Confidentiality:

Information that you shared with us will be kept confidential. Once all the data has been collected, your identifying information will be erased, and we will only work with anonymous data. After the study, we will compare our results with other studies and the results may be published in an academic journal, but your identity will not be made known in any publications or presentations. The university may review your records for the study to make sure it is correct, of good quality and that the study is being done in the correct way.

Study costs/compensation:

You will not be paid for allowing the researchers to take your arm and weight measurements.

Alternatives to participation:

You can decide to not take part in the study. Even if you give your permission now, you can change your mind later. Your decision will not affect your treatment or future relations with the hospital or university.

You now have two choices:

1) You may choose to NOT take part in the study and continue to receive care at the hospital.
2) You may choose to take part in the study and let the researchers ask you some questions and take your measurements.
3)

Contacts and Questions

You may ask any questions you have now, and for future questions, you are encouraged to contact:

Colleen Saunders on phone number **(021) 650 4842** or c.saunders@uct.ac.za

In case of any questions regarding your welfare and rights, you can contact the UCT Research Ethics Committee at **021 406 6492**.

Before signing this form, make sure you understand the following information:

1. Your doctors will know your HIV status, but will not be testing you again for HIV.
2. For this study, we would like to ask you some personal questions regarding HIV, TB, and cancer. We will then measure your arm and your weight and record the measurements.

If you would like to participate, please complete below:

By signing this document, I confirm the following:

- I have had time to read this information and think about the study and my questions have been answered properly.
- I agree to take part in this research study.

I agree that the research team may know my HIV-status and that they will do their utmost to keep my status confidential.	**Yes** ☐ **No** ☐

Participant name (Printed) _____

Participant signature _____

Date signed _____

OR Thumb Print

SIGNATURE OF INDEPENDENT WITNESS:

(if participant or person signing consent unable to read/write): _____

Name of witness (Printed) _____

Date: _____

PERSON ADMINISTERING INFORMED CONSENT:

I confirm that the participant (or parent/guardian or representative) signing consent above had enough time to consider this information, had an opportunity to ask questions, and voluntarily agreed to participation of the participant in the study.

Signature of person who administered informed consent _____

Name of person who administered informed consent (Printed) _____

Date: _____

Appendix 3. Ethics approval letter

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E53-46 Old Main Building
Groote Schuur Hospital
Observatory 7925
Email: hrec-enquiries@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

02 December 2019

HREC REF: 640/2019

Dr Colleen Saunders
Depart of Surgery
Division of Emergency Medicine
F51, OMB

Dear Dr Saunders

PROJECT TITLE: THE VALIDATION OF THE MID-UPPER ARM CIRCUMFERENCE MEASUREMENT AS A WEIGHT ESTIMATION TOOL IN A HIGH HIV PREVALANCE SETTING (MASTERS - DR EMILY CHEN)

Thank you for submitting your response to concerns raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 November 2020.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period. (Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledges that the student: Dr Emily Chen will also be involved in this study.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC REF in all your correspondence

Yours sincerely

pp **PROFESSOR MARC BLOCKMAN**
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
NHREC-registration number: REC-210208-007

HREC/ref: 640/2019
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Appendix 4. Differences between protocol and study

The actual study deviated slightly from the original approved protocol. Firstly, the intraclass correlation coefficient was used to determine inter-rater reliability instead of kappa statistics. Secondly, Bland-Altman plots were not constructed to determine the limits of agreements between the predicted and measured weights as the data acquired was nonparametric and thus not comparable using Bland-Altman plots.