Clinical and Biochemical diagnostic measures of sarcopenia in trauma and emergency laparotomy elderly patients. (PILOT STUDY)

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Research Article

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Abstract

Background:
Sarcopenia is the progressive decline in muscle quality and function attributed to aging. It is a prevalent global problem associated with worse morbidity and mortality outcomes. This risk is even higher in patients who have suffered a major trauma or those requiring an emergency laparotomy as a result of an intra-abdominal injury or to address an acute illness. Therefore, prompt diagnosis of sarcopenia is key to identifying high-risk patients for appropriate management planning and risk mitigation. Computed tomography (CT) remains the current gold standard diagnostic modality. This study aims to interrogate the utility of clinical and biochemical tests in identifying sarcopenia in elderly patients admitted to the hospital for trauma or emergency laparotomy. These measures may provide feasible, cost-efficient, and portable diagnostic tools, complementing or substituting the radiological measures established for diagnosing this condition.

Methods:

Forty eligible participants aged 65 years or older, admitted to Middlemore hospital for trauma or emergency laparotomy were included in the study. Clinical assessments performed included: midarm muscle circumference (MAMC), Appendicular skeletal muscle mass, handgrip strength (HGS), as well as 2 questionnaires. Thirteen biochemical markers were collected. For all patients who had a CT abdomen in the first week of their admission, the Total Psoas Major Cross-sectional area (TPMCSA) was assessed. The CT scans were conducted pre-operatively where possible as dictated by the patient's hemodynamic stability. Correlations between these measures and morbidity and mortality risks were assessed, in addition to correlations between the clinical and radiological measures.

Results:

Duke Activity Status Index questionnaire, free triiodothyronine, and Albumin levels correlated with the length of inpatient stay. Some clinical measures including HGS, and MAMC showed a positive correlation with TPMCSA. Similarly, biochemical measures including free triiodothyronine and Brain natriuretic peptide demonstrated correlations with TPMCSA.

Conclusion:

Some clinical and biochemical measures may prove to be useful surrogates to radiological scans in diagnosing sarcopenia to predict patients’ outcomes in trauma and emergency laparotomy settings.

Introduction:

Sarcopenia is defined by the European Working Group on Sarcopenia in Older People (EWGSOP) as a progressive generalised skeletal muscle disorder involving decreased muscle strength, mass, and quality resulting in increased adverse outcomes including falls, functional decline, frailty, and mortality (1).
Approximately, 24% of muscle mass is lost in healthy adults between the age of 40 and 70 years. This accelerates after 70 years, reaching 15% per decade (2). The reported prevalence of sarcopenia varies between 1–30% in community-dwelling adults, reflecting the inconsistencies in defining this condition (3–5). Sarcopenia is associated with poor morbidity and mortality outcomes reflected by physical disability, risk of falls and fractures, hospitalisation, and death (6–9). Much of the literature on sarcopenia thus far has focused on its impact on the geriatric population in the community. It is important to understand the impact of sarcopenia on acutely unwell patients, where a significant physiological insult has occurred, as exemplified by an acute abdominal surgery or a major trauma. Some studies have demonstrated higher morbidity and mortality in sarcopenic individuals undergoing abdominal surgery, more so in acute settings (10, 11). A 2018 literature review with meta-analysis reported that sarcopenic individuals had higher rates of 30-day mortality (RR = 2.15), 1-year mortality (RR = 1.97), total complications (RR = 2.07), and intensive care unit admission (RR = 1.38), compared to non-sarcopenic individuals undergoing emergency abdominal surgery (10). The American College of Surgeons National Trauma Database reported that 28% of trauma patients were aged ≥ 65 years old in 2014 and accounted for 44% of mortality (12). Similar findings have been reproduced locally in 2012, with a retrospective review of Auckland City Hospital’s Trauma Database, reporting that 20% of patients admitted for trauma were ≥ 65 years old but accounted for 38% of overall trauma mortality (13). These disparities in emergency laparotomy and major trauma outcomes pose great significance both in New Zealand and internationally, considering the large burden of emergency surgery (14). These disparities will likely grow in New Zealand, given the scale of its growing elderly population. Several measures have been proposed to assess sarcopenia, and can largely be classified into clinical biochemical, and radiological measures (15). Radiological measures such as computed tomography (CT) and magnetic resonance imaging (MRI) are the gold standard to diagnose sarcopenia. However, their applicability worldwide in resource-strained systems is limited given their high financial and time costs, low portability, and the need for highly trained personnel. Furthermore, using imaging modalities to diagnose sarcopenia often lacks any clinical indication. In contrast, biochemical and clinical measures, are less expensive and can be done at the bedside, making them more feasible (1).

Seven biochemical measures of sarcopenia have been studied in the setting of emergency surgery or trauma: low 25(OH) Vitamin D, free triiodothyronine (FT3), alanine aminotransferase (ALT), albumin, high C-terminal agrin fragment (CAF), and interleukin-6 (IL-6) (16–22). Brain natriuretic peptide (BNP), a biomarker of heart failure, has been associated with sarcopenia in individuals with type 2 diabetes mellitus with no heart failure (23). Similarly, four clinical measures of sarcopenia were reported: hand-grip strength (HGS), gait speed, and appendicular skeletal mass (ASM), with the lattermost measure calculated from anthropometry and bioelectrical impedance analysis (BIA) (1, 16, 24, 25). Furthermore, questionnaires such as SARC-F and the Duke Activity Status Index (DASI), have been validated as tools useful in assessing elderly patients’ functional status and predicting their outcomes (26, 27). SARC-F score > 4 correlates with functional deficits, low HGS test, as well as mortality (28). Higher DASI scores, on the other hand, reflect higher functional status. Although some of these measures have demonstrated value in diagnosing sarcopenia and predicting patients’ outcomes, they have been under-investigated in
surgical patients. A recent literature review collating the body of published studies on sarcopenia in different populations, highlights that less than a third of these studies investigate the impact of sarcopenia on surgical outcomes (29). In this pilot study, a sample of 40 participants admitted for trauma or an emergency laparotomy were investigated clinically, biochemically, and radiologically. This study aims to investigate the correlation between biochemical and clinical measures with the radiological measures of sarcopenia and to determine their prognostic value in the emergency laparotomy or trauma setting.

Methods:

Study subjects: Middlemore hospital is a major trauma centre established in 1947 to accommodate the afflicted servicemen from World War II in the Pacific. Today, it has about 800-bed capacity and serves a population of over 600,000 people with the busiest emergency department in Australasia. 28% of this population is over 65 years of age. Study participants were admitted to Middlemore Hospital during the study period of 17 August 2020 to 18 August 2021. Patients ≥65 years old with trauma injury severity score (ISS) > 12 AND / OR an indication for emergency laparotomy were included. The ISS is an anatomical scoring system used to grade the severity of injuries in the setting of polytrauma. A score of >12 is considered a major trauma according to the New Zealand Major Trauma Database definition (30). An emergency laparotomy was defined by the Australia and New Zealand Emergency Laparotomy Audit as a laparotomy procedure booked with urgency for surgical intervention of < 24 hours (31). Patients who had cognitive impairment, psychiatric illness, Glasgow Coma Scale of ≤14, or severe uncontrolled pain precluding consent were excluded from the study.

Protocol:

This prospective cohort study received ethics approval from the Auckland Health Research Ethics Committee (AH1076). Eligible participants aged 65 years or older, were recruited and assessed within the first 48 hours of admission. Those who underwent surgery before recruitment were assessed 24 hours post-surgery. After informed consent was obtained, biochemical, clinical, and radiological sarcopenia assessments were collated. Participants’ admission blood tests were utilized to prevent additional blood draws. Where tests required for this study had not been performed, the tests were added to laboratory-stored admission samples. The clinical assessment consisted of mid-arm muscle circumference (MAMC) by a standardised technique and formula, appendicular skeletal mass assessment with a bioelectrical impedance analysis scale (ASM-BIA), hand grip strength assessment with a Jamar Hydraulic Hand Dynamometer (32-34), a Duke Activity Status Index (DASI) and a SARC-F questionnaire (35,36). These measurements were obtained as early as possible in the admission in an attempt to exclude postoperative complications as a confounder. Radiological data were collected for patients who had a CT abdomen and pelvis within the first week of admission, using ImageJ software to assess total psoas major cross-sectional area (TPMCSA) at the mid-level of the L3 vertebra (Table 1). The primary outcomes measured were mortality at 24 hours, 30 days, and 90 days from admission. Secondary outcomes are summarised in table 2 (Table 2).
Statistical Analysis:

Descriptive statistics summarised patients’ characteristics using mean, standard deviation (SD), and count (%) as appropriate. The Spearman correlation analysis was performed to examine the relationships among variables of interest. The chi-square tests of independence were performed on variables to examine the relationships among them. The level of the p-value was set at 0.05. All statistical tests were performed using IBM SPSS Statistics 28 (SPSS, Chicago, IL, USA). All graphs were created using R (version 4.0.3).

Results:

Descriptive statistics

Forty patients (16 females [40 %], 24 males [60%]) were enrolled with a mean age of 76.0 ± 7.2 for males, and 73.6 ± 7.1 for females. 28 (70%) were of European ethnicity, 7 (17.1) were Asian, 3 patients identified as Māori (7.5%), and 2 as Pacifica (5%). No correlations were identified between ethnicity and any of the clinical, biochemical, or radiological measures of sarcopenia. The mean BMI of male patients was 26.1 ± 4.7, 28.0 ±7.2 for females. A statistically significant negative correlation (r (40) = -0.421, p = .007) was observed between age and BMI. 15 patients (37.5%) underwent an emergency laparotomy, and 25 patients (62.5%) were admitted for trauma. The most common mechanism of trauma injury was falls (29.3%), and road traffic crashes (24.4%). The most severe injury was facial in 32.5% of patients, Chest in 32.5%, Abdomen in 35%, and extremities in 40% of the patients. The mean injury severity score scale was 16.4 ± 5.2. In our cohort, 60% had a CT scan allowing measurement of TPMCSA. ASM-BIA assessment was limited by patients’ ability to weight bear safely, only 47.5% of patients completed this test with an average result of 51.9 kg. 92.5% of the patients completed the hand grip strength test, and 7.5% of patients could not complete this test due to hand injuries, and the average score was 23.8 kg. MAMC testing was completed for all patients with an average score of 20.7 cm. All patients were able to complete the SARC-F and DASI questionnaires.

The prevalence of sarcopenia in this study cohort

The EWGSOP proposes that sarcopenia can be diagnosed using the HGS test with cut-off points of < 27 kg for males and < 16 kg for females. As for BIA estimates of body muscle mass, the diagnostic threshold was determined to be < 7.0 kg/m² for males and < 5.5 kg/m² for females (37). When these thresholds were applied to our patient population, 37.5% of the participants met the criteria for diagnosing sarcopenia using the HGS test with means of 28.6 ± 12.9 kg, and 17.9 ± 4.5kg for males and females respectively. Conversely, the estimated body muscle mass as adjusted for height, weight, and gender, indicated that none of the participants meet the EWGSOP threshold for diagnosing sarcopenia, with means of 28.6 ± 12.9 kg/m² for males and 17.9 ± 4.5 kg/m² for females. Multiple cut-off points have been proposed for identifying sarcopenia on L3 TPMCSA, varying dramatically from 49 cm² to 144 cm² for males, and 31 cm² to 92 cm² for females, as influenced by the ethnic background of the investigated
population (38,39). The lowest suggested cut-off point was applied to our cohort with 49 cm$^2$ and 31 cm$^2$ for males and females respectively. Surprisingly, it was found that 100% of participants who underwent a CT scan, met the radiological diagnostic threshold for sarcopenia with a mean TPMCSA of 17.9 ± 3.8 cm$^2$ for males, and 10.0 ± 3.1 cm$^2$ for females. Although no consensus has been reached on the diagnostic threshold of SARC-F and the DASI questionnaires, a SARC-F total score of >4 has been suggested as indicative of sarcopenia (36). 20% of the studied population had a SARC-F score reflective of this. Similarly, a cut-off point of <32 on the DASI questionnaire was suggestive of poor functional capacity in stroke patients (40). Applying this threshold to our study population resulted in 51.2% reflecting a poor functional state.

**Correlations among variables of interest**

**Correlations with patient outcomes**

No correlation was observed between most clinical, biochemical, and radiological measures of sarcopenia and the patient outcomes due to sample size. SARC-F questionnaire correlated positively with the length of admission ($r (40) = .427, p = <0.01$). DASI scores, on the other hand, negatively correlated with the length of admission ($r (40) = -.337, p = <0.05$) (Table 3). Some biochemical measure showed statistically significant correlation with hospital length of admission, including: FT3 and Albumin levels negatively correlated with length of admission ($r (39) = -.324, p = <0.05$), ($r (40) = -.361, p = <0.05$) respectively. Albumin levels were associated with decreased mortality at 90 days ($r (40) = .379, p = <0.05$). Positive correlation was observed between the SARC-F total score and BNP ($r (39) = .47, p = .002$) and a negative correlation seen between SARC-F and Albumin ($r (40) = -0.30, p = .053$). DASI score, however, correlated negatively with BNP ($r (39) = -0.37, p = .02$) and positively with ALT ($r (37) = 0.40, p = .015$) (Table 4).

**Correlations with Radiological measures**

Of the clinical assessments, HGS correlated positively with TPMCSA ($r (21) = 0.49, p = .024$) and MAMC also correlated positively with TPMCSA ($r (24) = 0.69, p = <.001$) (Table 5). Biochemical measures such as BNP demonstrated a negative correlation with TPMCSA ($r (23) = - 0.461, p = <0.05$), whereas FT3 showed positive correlation with TPMCSA ($r (23) = 0.497, p = <0.05$) (Table 6).

**Discussion And Conclusion:**

Identifying undemanding, reliable, and cost-efficient diagnostic and prognostic measures of sarcopenia is pivotal for appropriate clinical decision-making. This is challenged by the lack of consensus on the most reliable diagnostic modality and the lack of clear cut-off thresholds to ensure accurate diagnosis (41). This explains the variable reports of sarcopenia prevalence both in community-dwelling and hospitalised populations. Currently, TPMCSA is considered the gold standard diagnostic test of sarcopenia. It has been reported to be a reliable marker enabling the identification of sarcopenia to predict the prolonged length of hospital stay, postoperative complication rate, readmission rate, and discharge to care facilities.
in surgical patients (42). It also has a proven value in personalising management plans in patients with haematological malignancies (43). CT scans, however, are not routinely indicated for hospitalised patients, they’re associated with high cost, the need for trained personnel, and the additional time required to analyse the scans for psoas muscle measurements, particularly when the thresholds for diagnosing sarcopenia are not clear, varying from 49 cm$^2$ to 144 cm$^2$ for males, and 31 cm$^2$ to 92 cm$^2$ for females (38,39). In our diverse patient population applying the highest threshold, indicated that all participants are sarcopenic which contradicted the results from the clinical measures. This raises the question of whether TPMCSA's utility in identifying sarcopenia, is dependent on establishing population-specific cut-off points adjusted for sex, ethnicity, and age group. The significant correlations observed in this study, between MAMC, HGS, BNP, F3, and TPMCSA highlight their potential value as surrogate markers of sarcopenia or their additive value in affirming the diagnosis. They are feasible, cost-efficient, and portable measures that may obviate the need for radiological diagnostic modalities. This is in keeping with other studies highlighting their importance in assessing muscle quality and functionality which predicted hospitalization and overall mortality (44,45). Furthermore, the positive correlation between DASI scores, HGS, and MAMC, eludes to the value of combining clinical measures with questionnaires as diagnostic tools for sarcopenia. Similarly, SARC-F questionnaires have been validated in studies investigating the pre-operative risk for patients undergoing cardiac surgery and have been proposed as a useful screening tool for sarcopenia (46,47). Lin Et al found a significant negative correlation between SARC-F and MAMC, calf circumference, and handgrip strength (48). This pilot study, reproduced some of these findings with a negative correlation between SARC-f and MAMC, indicating that both tools may be useful in affirming the diagnosis.

ASM-BIA is another useful modality, Low ASM is a key feature in geriatric syndromes, such as sarcopenia and geriatric cachexia (1,49). Novel anthropometric prediction equations against DEXA estimating ASM were designed for older orthopaedic patients. They show that ASM-BIA is useful as an alternative to DEXA in diagnosing skeletal muscle wasting syndromes (50). This measure, however, is limited by the weight-bearing status, less than 50% of our recruited participants were able to complete this test. It is, therefore, unsurprising that it was of a low diagnostic yield in this study population and demonstrated no statistically significant correlations with patients’ outcomes.

In this study, the value of chemical measures of sarcopenia was corroborated. BNP levels were reported to be significantly higher in acutely decompensated heart failure patients with sarcopenia than in those without sarcopenia (1666 versus 429 ng/mL, p< 0.0001). High BNP levels were considered an independent predictor of sarcopenia in the same group of patients (OR = 18.4; p = 0.013) (51). The combination of high SARC-F and BNP scores identified patients with a significantly higher risk of cardiac events (52). Albumin has also been implicated; low serum albumin levels synergistically increase the risk of morbidity expressed as incident disability (53,54). This is in keeping with this study's findings of a positive correlation between SARC-F and BNP, and a negative one with albumin. These findings also correlated with increased length of inpatient stay.
This study has some limitations, including the small sample size and the single-center setting, which may hinder the generalizability of the findings. The population investigated includes trauma patients who are limited in their ability to complete some of the clinical assessments. HGS test is influenced by hand dominance state; however, we only reported overall HGS.

In conclusion, despite the developments in defining sarcopenia, there is lacking evidence on the best diagnostic modality and the diagnostic thresholds for these modalities. This study presents evidence suggesting several clinical and biochemical measures which may prove to be useful as surrogates to radiological measures for diagnosing sarcopenia. Upon completion of the study, stronger correlations between these measures and patients’ outcomes will enable a proposition on the most reliable, cost and time-efficient combination of tests for accurate detection of sarcopenia and assessment of outcomes in elderly surgical patients.

**Abbreviations:**

<table>
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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
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<tr>
<td>MAMC</td>
<td>Midarm Muscle Circumference</td>
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<td>HGS</td>
<td>Handgrip Strength</td>
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<td>TPMCSA</td>
<td>Total Psoas Major Cross-Sectional Area</td>
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<td>EWGSOP</td>
<td>European Working Group On Sarcopenia In Older</td>
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<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
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<td>FT3</td>
<td>Free Triiodothyronine</td>
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<td>ALT</td>
<td>Alanine Aminotransferase</td>
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<tr>
<td>CAF</td>
<td>C-Terminal Agrin Fragment</td>
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<td>IL-6</td>
<td>Interleukin-6</td>
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<td>BNP</td>
<td>Brain Natriuretic Peptide</td>
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<tr>
<td>ASM</td>
<td>Appendicular Skeletal Mass</td>
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<tr>
<td>BIA</td>
<td>Bioelectrical Impedance Analysis</td>
</tr>
<tr>
<td>DASI</td>
<td>Duke Activity Status Index</td>
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<tr>
<td>ISS</td>
<td>Injury Severity Score</td>
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<tr>
<td>ASM-BIA</td>
<td>Bioelectrical Impedance Analysis Scale</td>
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<tr>
<td>SD</td>
<td>Standard Deviation</td>
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**Declarations:**
- **Ethical Approval and Consent to participate:**

This prospective cohort study received ethics approval from the Auckland Health Research Ethics Committee (AH1076). All participants completed an informed consent form as per good clinical practice.

- **Consent for publication:**

Consent for publication has been obtained from participants and authors involved with this project.

- **Availability of data and materials:**

Data is available for review upon request.

- **Competing interests:**

Authors confirm no conflict of interest.

- **Funding:**

No funding was provided or required for this study.

- **Authors' contributions:**

This is to confirm that all authors had a substantial contribution on the conceptualisation, data collection, analysis, writing and editing this project.

- **Acknowledgements:**

Not applicable

**References:**


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Tables:

Table 1-6 are available in the Supplemental Files section.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- table1.docx
- table2.docx
- table3.docx
- table4.docx
- table5.docx
- table6.docx