

The Effect of Sarcopenia on Postoperative Outcomes Following Emergency Laparotomy: A Systematic Review and Meta-Analysis

N. Humphry¹, M. Jones¹, S. Goodison², B. Carter³, J. Hewitt⁴

1. School of Medicine, Cardiff University, United Kingdom; 2. Health Education Improvement Wales, United Kingdom; 3. Department of Biostatistics and Health Informatics, King's College London United Kingdom; 4. Division of Population Medicine, Cardiff University United Kingdom

Corresponding Author: Dr Nia Humphry, School of Medicine, Cardiff University, United Kingdom, HumphryNA1@cardiff.ac.uk, Telephone number: +447815913222

Abstract

Emergency laparotomy procedures have high rates of postoperative mortality and morbidity in older patient. Sarcopenia is associated with poor postoperative outcomes in elective surgeries and there is growing evidence for its use as a risk predictor in the emergency setting. The study aimed to evaluate the effect of sarcopenia on postoperative mortality and morbidity following emergency laparotomy. Five electronic databases were systematically searched (MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials, and Web of Science) from conception until the 14th February 2022. All prospective cohort studies were included. Risk of bias was assessed with the Newcastle-Ottawa score. Pooled meta-analyses were estimated using the Mantel-Haenszel and inverse-generic variance method for mortality and morbidity outcomes. Eleven retrospective cohort studies were included, of which ten were included in the meta-analysis comprising of 3492 patients (1027 sarcopenic, 2465 non-sarcopenic). The study level incidence of sarcopenia ranged from 24.6 to 50.3% with a median rate of 25.1%. Sarcopenia was associated with increased 30-day mortality (OR 2.36, 95% CI, 1.66, 3.37, I² = 43%), 90-day mortality (OR 2.51, 95% CI, 1.79, 3.52, I² = 0%), and length of hospital stay (in days) (MD 1.18, 95% CI, 0.42, 1.94, I² = 0%, P=0.002), but not incidence of postoperative major complications (OR 1.49, 95% CI, 0.86, 2.56, I² = 70%, P = 0.15). Sarcopenia predicts poor outcomes following emergency laparotomy. We suggest assessment of sarcopenia should be incorporated into acute surgical assessment to identify high risk patients and inform clinical decision-making prior to an emergency laparotomy.

Key words: Sarcopenia, emergency laparotomy, surgery.

Introduction

Emergency laparotomy (EL) describes a group of abdominal surgical procedures, performed at short notice, to investigate and manage potentially life-threatening conditions (1). There is a large diversity in terms of clinical presentation, underlying pathology, anatomical site of surgery, and perioperative management and an estimated 30,000–50,000 EL procedures are performed annually in the UK (2, 3). ELs carry one of the highest rates of short and long-term mortality in all surgical procedures - a consequence of the short time frame in which to plan and optimize the patient before surgery (4).

The National Emergency Laparotomy Audit (NELA) aims to enable improvements in the care of patients undergoing EL

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across England and Wales. NELA has demonstrated that older patients undergoing EL have worse outcomes; the fifth NELA report found that patients aged over 70 had a 30-day mortality of 14.5% following EL compared to 5.4% for those under 70 years old (5, 6). Further disparities in outcomes exist for older patients; increased rates of postoperative complications, longer-term hospital stays, increased readmissions to hospital and decreased rates of functional independence (7).

Sarcopenia can be defined as an age related, involuntary, loss of skeletal muscle mass and strength (8). Physiologically, the decline in the number and size of skeletal muscle fibres has several adverse health outcomes including reduced movement, loss of functionality and suboptimal breathing; it can be viewed as a mediator for frailty (9). Clinical definitions of sarcopenia vary - the European Working Group on Sarcopenia in Older People (EWGSOP) recommends identifying both the presence of low muscle mass and low muscle performance or strength, to accurately diagnose sarcopenia (9, 10). Muscle strength is widely assessed using measures of hand grip strength, however the nature of emergency surgery often renders this method impractical in clinical practice. Computerised tomography (CT) remains a gold standard technique for measuring muscle mass in research (10).

NELA defines older patients as age 65 years and over, however biological age has greater relevance than chronological age in recognising high-risk patients (7). Sarcopenia associated with frailty reflects physiological vulnerabilities far better than the current surgical risk prediction tool of P-POSSUM (5, 11). In EL patients it may be more useful to use an objective radiological assessment of sarcopenia to assess perioperative risk and inform shared decision making. Indeed, CT assessment of sarcopenia may be the most pragmatic in an emergency setting given CT imaging of the abdomen forms a standard step in the EL pathway (5).

Aims & Objectives

In view of NELA's key recommendations, we aim to assess the risk of patient death and morbidity in relation to sarcopenia. Using a systematic review and subsequent meta-analysis, the objectives of this study were to evaluate the association of sarcopenia on: mortality, major complications and length of hospital stay (LOS) following EL.

Methods

Design

The systematic review was performed in accordance to the PRISMA guidelines (12) and the protocol registered with the PROSPERO database (13). Two independent authors (MJ, SG) performed all aspects of the literature retrieval and quality assessment. When results were compared, disagreement was reviewed by a third independent author (JH).

Included Study Designs

Included study designs were randomised controlled trials (RCTs), case-control and retrospective cohort studies of patients undergoing EL. Excluded studies included those conducted in an elective setting, studies with cohorts of emergency abdominal surgery patients where EL was not the sole procedure investigated, review studies and case-reports. Non-English language studies were excluded.

EL was the only procedure of interest and the definition for eligibility was consistent with that of National Confidential Enquiry into Patient Outcome and Death (NCEPOD); “An expedited, urgent or emergency unscheduled abdominal surgery via a midline abdominal incision or laparoscopic approach including laparoscopic converted to open or laparoscopic assisted procedures.” This excluded elective procedures and surgeries defined as uncomplicated cholecystectomy, pancreatotomy and appendectomy, as well as gynaecological laparotomy, vascular surgery, and organ transplantation (14, 15). The inclusion criteria was therefore patients aged over 16 undergoing an EL.

Definition of exposure

The diagnosis of sarcopenia compared to no sarcopenia was considered the exposure. Diagnosis was assessed using measurement of psoas muscle area (PMA) at level L3 or L4 on preoperative CT scan.

Search strategy and study selection

Literature searches were conducted across five multi-disciplinary electronic databases: MEDLINE (Ovid), EMBASE (Ovid), CINAHL (Embase), Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science (Thompson Reuters). The last search was conducted on the 14th February 2022. Databases were searched using appropriate Medical Subject Headings (MeSH) and keyword searches. Terms relating to ‘sarcopenia’, ‘emergency laparotomy’ and ‘association’ allowed us to utilize a concept-based approach. All types of emergency abdominal surgery were incorporated into our initial search terms ensuring the search was sufficiently comprehensive. In the same way, we deemed it inappropriate to use a filtering term for mortality or morbidity at the risk of excluding relevant literature associated with other relevant

outcomes. The full search strategy conducted in Ovid MEDLINE is shown in Appendix. 1.

Citation lists of all included studies and relevant reviews were investigated alongside the contents lists of relevant journals within the field; Age and Ageing and British Journal of Surgery (BJS). Once duplicates were removed, the retrieved studies underwent title and abstract screening to identify studies to undergo full-text review. Here the inclusion and exclusion criteria were applied, and the articles were selected for inclusion.

Risk of Bias (RoB) and Quality Assessment (QA)

Included studies were quality assessed using the Newcastle-Ottawa Scale (NOS) (16). This assessment tool for observational studies evaluates quality over the three domains of selection, comparability and either exposure (case-control) or outcome (cohort); overall comprising eight distinct categories. We considered each domain separately to conclude whether studies were of good, fair or poor quality. A risk of bias table was produced to illustrate the implementation of the NOS to the included studies, see Appendix 2.

Included Studies Characteristics

Information relating to the characteristics of the included studies were extracted by both authors. This included data regarding the country of population origin, journal of publication, study design, sample size, sarcopenia criteria applied, mortality assessment timeframe, mortality rates, morbidity outcomes identified and associated data, and characteristics of populations where available (male: female ratio and age range).

Outcomes

The primary outcome was mortality following the EL procedure at 30, or 90-days.

Secondary outcomes were: LOS and major complications following EL reported as \geq IIIb on the Clavien-Dindo Classification (CDC) - a widely adopted measure of surgical outcomes, categorising outcomes based on the type of therapy required to treat the complication (18).

Data Synthesis & Analysis

Due to the contextual heterogeneity of non-randomised designs, each study was described narratively (Table. 1) in terms of their design. Only studies that were clinically homogeneous with respect to population and sarcopenic definition were considered for pooling into meta-analysis (18). Meta-analysis was undertaken when two or more studies examined the same outcome. Outcome variables that were categorical and dichotomous in nature, were pooled as estimated odd ratios (ORs). LOS was summarised as a mean difference (MD) between those with sarcopenia and those without. Pooled results were estimated using the software

package Review Manager 5.3; the Mantel-Haenszel estimator calculated relative risks (RR) and the inverse-generic variance method calculated pooled MD estimates. All meta-analyses were subsequently represented visually using forest plots with 95% confidence intervals (CIs).

Statistical heterogeneity and Subgroup analysis

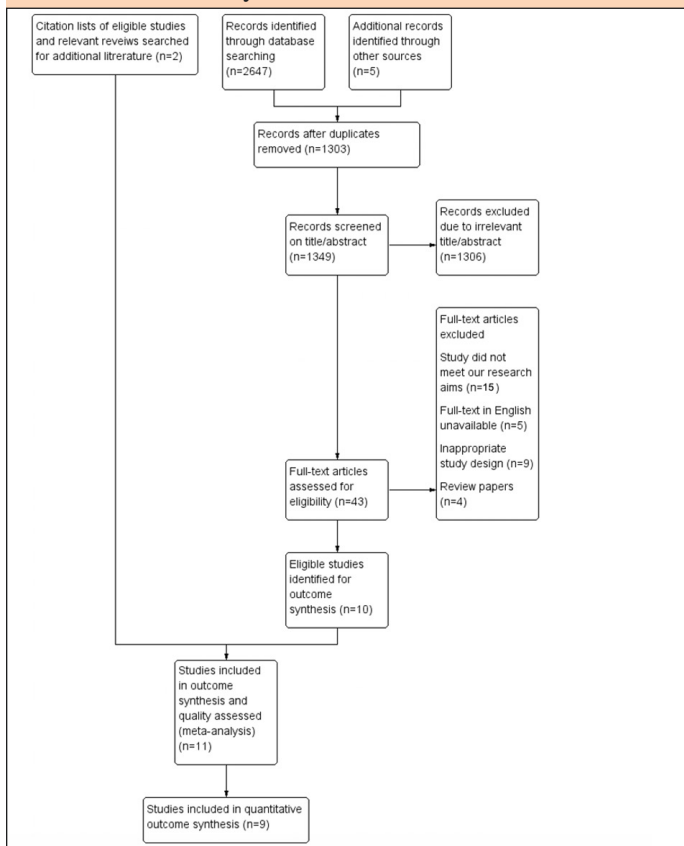
Statistical heterogeneity was evaluated amongst the studies by visual inspection and calculation of the Higgins I2 statistic. Heterogeneity measured above 75% was considered high and would undergo further subgroup analysis. Subgroups used to explore heterogeneity were: study design (surgical procedure of interest), median age, and sarcopenic definition utilised in study. Repeating the primary analysis when we removed one study at a time allowed us to further assess the robustness of our results (18).

Results

Search results

2,647 articles were retrieved. Following removal of duplicates, 1,349 studies were screened of which 43 met inclusion criteria and underwent full-text review. Eleven studies were included within the review and underwent quality assessment; nine of these were included in meta-analyses (Figure. 1).

Figure 1. PRISMA flowchart: Study selection for systematic review and meta-analysis



Study characteristics

All included studies utilized a retrospective cohort study design; the main characteristics of the eleven included studies are outlined in Table. 1. A total of 3492 patients were studied (1027 sarcopenic, 2465 non-sarcopenic) - sarcopenia was reported in 24.6 to 50.3% of patient cohorts within the studies, with a median percentage of 25.1%. The median age of all patients within studies ranged from 49 to 82 years and sarcopenic patients had a higher median age than their non-sarcopenic counterparts in all except one study, where the two cohorts were compared. There were more female than male patients (1,684 male and 1,808 female). All studies diagnosed sarcopenia by evaluating PMA:L3/4 on preoperative computed tomography, however sarcopenic definition varied between studies. Four studies applied pre-defined psoas area ranges (19-22) and seven studies considered the lowest PMA:L3/4 quartile or tertile to diagnose sarcopenia (23-28).

Quality assessment

The results of the quality assessment of the eleven included studies is summarised in Appendix 2. Five studies were deemed to be good in quality (19, 22, 25, 27, 28) and six studies fair in quality (20, 21, 23, 24, 26). Three studies lost points for selection by limiting their respective cohort to specific age groups. Six studies lost points in comparability where insufficient detail in the characteristics between the sarcopenic and non-sarcopenic cohorts.

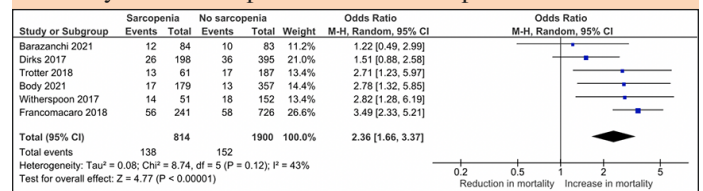
Outcome synthesis

Four meta-analyses were conducted evaluating the predictive value of sarcopenia for 30-day mortality, 90-day mortality, major complications and LOS; 30-day mortality, 90-day mortality and LOS meta-analyses were statistically significant.

30-day mortality

Six studies were included with a total of 2,714 patients (19, 20, 25, 26, 28). Sarcopenia showed statistically significant association with increased 30-day mortality (OR 2.36, 95% CI, 1.66, 3.37, I2 = 43%).

Figure 2. The number of participants experiencing 30-day mortality in the sarcopenia and non-sarcopenia cohorts



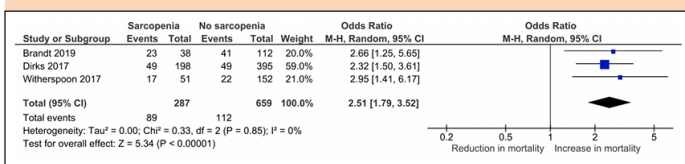
90-day mortality

Three studies were included with a total of 946 patients (27, 28). Sarcopenia showed statistically significant association with increased 90-day mortality (OR 2.51, 95% CI, 1.79, 3.52, I2 = 0%).

Table 1. Main characteristics of included studies

Author	Country	Study design	Sample size (sarcopenic population)	Location of sarcopenic assessment	Criteria for diagnosing sarcopenia	Mortality assessment post-surgery	Morbidity outcome measures	Median age in years Sarcopenia/ no sarcopenia	Sex Ratio M:F % Sarcopenia/ no sarcopenic %	Quality Evaluation
(Barazanchi et al. 2021)	New Zealand	Retrospective cohort study	167 (84)	Psoas area at L3 level on preoperative computed tomography	Pre-defined values	30-day 1-year	LOS Major complication	75.6 76.2/74.9	50.9/49.1 41.7: 58.3/ 60.2: 39.8	Good
(Body et al. 2021)	UK	Retrospective cohort study	609 (179)	Psoas area at L3 level on preoperative computed tomography	Lowest quartile of cohort	30-day 1-year	LOS Major complication	71 75/68	46.5: 53.5 45.8: 54.2/ 45.9: 54.1	Fair
(Brandt et al. 2019)	Denmark	Retrospective cohort study	150 (38)	Psoas area at L3 level on preoperative computed tomography	Lowest quartile of cohort	90-day	n/a	82 n/a	39.3: 60.7 n/a	Good
(Dirks et al. 2017)	USA	Retrospective cohort study	593 (198)	Psoas area at L4 level on preoperative computed tomography	Lowest tertile of cohort	30-day 90-day	LOS	61 n/a	49:51 n/a	Good
(Francomacaro et al. 2018)	USA	Retrospective cohort study	967 (241)	Psoas area at L3 level on preoperative computed tomography	Predefined values	30-day	LOS	n/a 70.3/61.2	n/a 48.5:51.5 / 48.6:51.5	Fair
(Kubo et al. 2018)	Japan -	Retrospective cohort study	103 (50)	Psoas area at L3 level on preoperative computed tomography	Pre-defined values	In-hospital mortality	LOS	n/a 67.6 / 68.6	n/a 34:64 / 58: 42	Fair
(Matsushima et al. 2017)	USA	Retrospective cohort study	89 (32)	Psoas area at L3 level on preoperative computed tomography	Predefined values	In-hospital mortality	Major complication LOS	49 54/44	68:32 50:50 / 78.9:21.1	Good
(McQuade et al. 2021)	Ireland	Retrospective cohort study	80 (20)	Psoas area at L3 level on preoperative computed tomography	Lowest quartile of cohort	90-day	n/a	n/a 67.5/60 years	47.5:52.5 n/a	Fair
(Salem et al. 2020)	Israel	Retrospective cohort study	283 (73)	Psoas area at L3 level on preoperative computed tomography	Lowest quartile of cohort	30-day	LOS	77.9 n/a	43.1: 56.9 49.3: 50.7/ 41.0: 59.0	Fair
(Trotter et al. 2018)	UK	Retrospective cohort study	248 (61)	Psoas area at L3 level on preoperative computed tomography	Lowest quartile of cohort	30-day and 1-year	LOS	n/a 72/70	n/a 49.1:50.9 / 48.1:51.9	Good
(Witherspoon. 2017)	UK	Retrospective cohort study	203 (51)	Psoas area at L3 level on preoperative computed tomography	Lowest quartile of cohort	30-day and 90-day.	LOS	68 n/a	50.4: 49.6 n/a	Fair

Figure 3. The number of participants experiencing 90-day mortality in the sarcopenia and non-sarcopenia cohorts



Major complications (≥IIIb on CDC)

Four studies were included with a total of 1,783 patients (19-21, 26). Sarcopenia did not show statistically significant association with incidence of major complications (MC) (OR 1.49, 95% CI, 0.86, 2.56, I² = 70%, P = 0.15).

LOS

Six studies reported were included with a total of 2110 patients (19-22, 25-26). Sarcopenia showed a statistically significant association with a longer LOS (days) (MD 1.18, 95% CI, 0.42, 1.94, I² = 0%, P=0.002).

Sensitivity analyses & publication bias

None of the meta-analyses had a high level of heterogeneity and therefore subgroup analysis did not need to be conducted. Moreover, removing one study at a time did not alter the direction of the effect size. Due to the limited number of included studies, publication bias was not assessed using a funnel plot; Witherspoon. 2017 was an unpublished study.

Figure 4. The number of participants experiencing major complications (≥IIIb on CDC) in the sarcopenia and non-sarcopenia cohorts

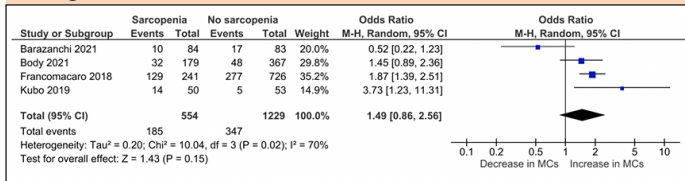
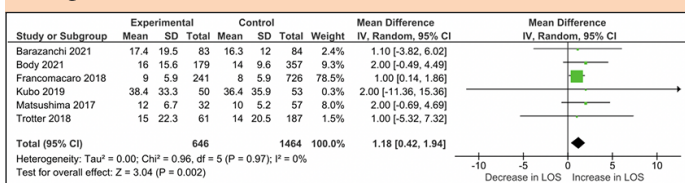


Figure 5. The mean length of LOS in the sarcopenia and non-sarcopenia cohorts



Discussion

Findings

This is the first review to assess the effect of sarcopenia on mortality following an EL procedure, which identified eleven retrospective cohort studies comprising of 3,492 patients. The quality of the included studies was varied between fair and good with only five studies being assessed as good in quality. Sarcopenia was strongly associated with increased mortality (at both 30 and 90 days), and longer length of stay. However, sarcopenia did not have a statistically significant association with major complications following EL. A greater understanding of how sarcopenia affects postoperative outcomes will allow the identification of high-risk surgical patients, to target subsequent health interventions and resources (7).

A similar review (29) investigated the effect of sarcopenia in relation to all emergency abdominal surgery (EAS) and reported consistent results; a positive risk ratio for 30-day mortality in sarcopenic patients. Comparison confirms the predictive value of sarcopenia in EL as a subtype of EAS, albeit with one overlapping study (25).

Clinical mechanisms

A loss of lean skeletal muscle mass and functional strength seen in sarcopenic patients is an indicator of frailty. Its development is multimodal in nature; malnutrition, functional status and comorbidity all contribute to an overall vulnerability to physiological stressors (30). Indeed, the subsequent lack of physiological reserve has been evidenced by an independent predictor of adverse surgical outcomes (31).

Across surgical studies of frail older adults it has been shown that outcomes are universally poorer (32, 33). This includes mortality both short (30 days) and longer term (90 days), length of hospital stay and readmission to hospital. The findings from this study are consistent with those. It was then surprising that postoperative complications were not increased in this study, although there was a trend towards that outcome the failure to reach significance may reflect the degree of heterogeneity (I²=70%). Frailty and sarcopenia are invariably linked - we suggest the identification of sarcopenia accurately identifies the frail cohort of patients and predicts those who are likely to have poor short and long-term outcomes following EL.

Strengths & limitations

There was a consistent direction of effect across ten of the eleven included studies; all but one study associated sarcopenia with an increased risk of poor outcomes. Due to the nature of EL and the subsequent literature, pooling of non-randomised studies was the only method to address of research objectives and incurred inherent bias (18). Many studies failed to control for additional confounders in the basis of their design or analysis; adjustment for differences in age or surgical procedure between cohorts was seldom undertaken.

Sarcopenia was defined inconsistently - four studies employed pre-defined objective measurements and seven studies assigned a diagnosis by considering an individual's measurements in respect of the overall cohort. The number of sarcopenic patients in these studies is likely to have been over- or underestimated incurring further selection bias. Moreover, insufficient detail was documented regarding the diagnoses or surgical procedures of the respective cohorts.

Impact of these findings on clinical practice and research

NELA recognises the need to assess the risk of mortality and morbidity to identify high-risk surgical patients preoperatively. The risk of a general surgical patient can be stratified with the use of the P-POSSUM tool or the NELA Risk Calculator (34, 35), however this fails to consider the impact of frailty or sarcopenia in its evaluation. Since a large proportion of high-risk patients are older in age, recent evidence has focused upon the adoption of frailty assessment prior to EL. NELA reports that 55.4% of EL patients are over the age of 65. It recommends perioperative geriatrician input for all age 80 and over and those age 65 or more who are living with frailty, however only 27.1% of these patients receive such input (6). Pre-operative frailty assessment can be challenging owing to a lack of patient compliance and time-constraints in emergency settings (36).

Sarcopenia assessment offers an additional tool to reliably predict risk in the elderly; sarcopenia can be objectively measured as part of the standard pathway of care and does not require additional investigations. Since preoperative contrast-enhanced computed tomography imaging is recommended in all older EL patients its assessment should not delay subsequent treatment, although our research does not consider its practical utility (37). Future research should consider whether this imaging technique as a measure of sarcopenia is feasible in differing healthcare settings, where technical equipment and staffing resources may present a logistical challenge. Further, contrast-enhanced computed tomography may not be available in healthcare settings in the developing world, making the practical recommendations only applicable to first world settings.

Conclusion

Sarcopenia was associated with mortality, and longer length of hospital stay. Sarcopenia may be used to identify patients at high-risk of deterioration in conjunction with current prediction tools such as P-POSSUM, which have limited accuracy in emergency settings. We suggest sarcopenia assessment should be considered for inclusion in current risk prediction tools to help inform shared decision making between patient and clinician preoperatively.

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Conflicts of Interest: None.

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