



Chowdhury, M. M., Ambler, G. K., Al Zuhir, N., Walker, A., Atkins, E. R., Winterbottom, A., & Coughlin, P. A. (2018). Morphometric Assessment as a Predictor of Outcome in Older Vascular Surgery Patients. *Annals of Vascular Surgery*, 47, 90-97. <https://doi.org/10.1016/j.avsg.2017.08.002>

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Morphometric Assessment as a Predictor of Outcome in Older Vascular Surgery

Patients.

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ABSTRACT

Introduction

Frailty is a recognised predictor of poor outcome in patients undergoing surgical intervention. Frailty is intricately linked with body morphology, which can be evaluated using morphometric assessment via computerised tomographic (CT) imaging. We aimed to assess the predictive power of such objective assessments in a broad cohort of vascular surgical patients.

Patients and methods

A consecutive series of patients aged over 65 years admitted to a vascular unit, who had undergone CT imaging of the abdomen, were analysed.

Demographic and patient specific data was collated alongside admission relevant information. Outcomes included mortality, length of stay, healthcare related costs and discharge destination. Images were analysed for four morphometric measurements: i) psoas muscle area, ii) mean psoas density, iii) subcutaneous fat depth and iv) intra-abdominal fat depth, all taken at the level of the fourth lumbar vertebra.

Results

Two hundred and ten patients were initially analysed. Forty four patients had significant retroperitoneal and abdominal abnormalities that limited appropriate CT analysis. Decreased subcutaneous fat depth was significantly associated with mortality, readmission within 12 months and increased cost of healthcare ($P < 0.01$ –

adjusted for confounders). Psoas muscle area was significantly associated with readmission-free survival.

Conclusions

Morphometric analysis predicts poorer outcome in a broad cohort of vascular surgery patients. Such assessment is likely to enhance patient counselling regarding individual risk as well as enhancing the ability to undertake risk modified surgical audit.

Keywords: morphometric analysis, vascular surgery

INTRODUCTION

The population worldwide is aging, with this observed trend of an aging population predicted to continue over the next 20 years^{1,2}. For example, the proportion of people over the age of 85 years within the UK set to increase by 109%, compared to a 7% increase in the population of 15-64 year olds¹. These predicted population statistics will have major impact upon healthcare provision and associated socioeconomic costs. Indeed, although current life expectancy has increased, this has not been associated with a decline in mild to moderate disability rates², which is in part likely due to an increased burden of multiple chronic diseases.

Ageing is defined as the accumulation of changes in a human being over time³. This encompasses physical changes, a result of damage at a molecular and cellular level, psychological and social changes. However, these changes are neither linear with increasing age nor consistent between two people of the same age.

Vascular disease has a strong association with age. This is common to all territories, including the arterial and venous systems. Indeed, more than 20% of patients aged 80-89 and 30% of patients aged 90-99 have disease in at least one vascular territory⁴. As the population ages, this will cause a corresponding increase in demand for vascular surgical intervention. Allied to this, continued improvements in minimally invasive technology means that more older patients have the potential to be treated.

Frailty is a phenotype often seen within the older population. It is characterised by reduced homeostatic reserves, leading to increasing vulnerability. It increases risk for

hospitalisation, falls, disability and mortality⁵ and previous studies have shown increasing frailty predicts poorer outcome in surgical patients^{6,7,8,9,10}.

Morphometric measures have long been used to predict outcomes in surgery^{11,12,13}, and the increasing role of cross sectional imaging within secondary care increases the availability of such data. Yet the evidence with regard to such factors is limited, specifically within the high-risk group of vascular surgical patients.

As such, the aim of this study was to determine whether standard morphometric data was able to predict short and mid term patient related adverse outcomes in older vascular surgical patients, with a primary outcome of survival during follow-up and secondary outcomes including length of in-hospital stay, discharge destination and readmission-free survival.

METHODS

All patients admitted between 1 January 2012 and 31 December 2012 to the Cambridge Vascular Unit were screened for inclusion. The cohort of patients analysed was a subset of a database previously described by our group¹¹. In addition to the inclusion criteria of age at least 65 years and length of hospital stay two or more days, which were used in previous work, we also included only those patients who had had a computerised tomographic (CT) scan of the abdomen either during the index admission or within the previous six months from the date of admission. Patients were included irrespective of whether they underwent a surgical procedure or not. Patients were followed up until 31st December 2013 with no deviation from standard follow up requirements which varied for each patient. No data was collected after the 31st December 2013. Data available included basic demographic information, mode of admission, diagnosis, management, prolonged length of stay (defined as greater than or equal to one week), discharge destination (whether to the patient's own home, a nursing/residential home, or another hospital), mortality and readmissions (including readmission to the base hospital and other hospitals within the vascular network). In addition we measured various frailty-specific factors detailed previously¹¹. These included age, sex, independent mobility on admission, living alone, Katz score, Charlson comorbidity index, Waterlow score, history of depression, previous admission to intensive care, primary admission diagnosis, number of medications on admission, visual or hearing impairment, cognitive impairment on admission, history of two or more falls in the past 12 months, anaemia, evidence of malnutrition, and whether the admission was planned or emergent. The hospital electronic records system is linked to the United Kingdom Office for

National Statistics for collection of mortality data. Data were collected as part of routine service evaluation and no patient identifiable data are presented, so it was not deemed necessary to seek ethical approval or retrospective consent for the study.

Morphometric analysis

CT images of the abdomen and pelvis were evaluated using GE Life Sciences™ workstations. Morphometric measurements were made independently by two operators (NAZ and AWa), and the results averaged to improve accuracy.

Four measurements were determined for this study: psoas muscle area (PMA, mm²) psoas muscle mean density (PMD, measured in Hounsfield units – Figure 1), subcutaneous fat depth (SCF, mm) and intra-abdominal fat depth (IAF, mm – Figure 2).

Axial cross-sectional areas and densities of the left and right psoas muscles on axial section at mid fourth lumbar vertebra (L4) level were processed using multi-planar reconstruction (MPR). Outlines of the psoas muscles were traced using the area calculation tool and densities were measured within the traced area using the region-of-interest (ROI) tool. Fat thickness values were measured using the distance tool. Subcutaneous fat depth measurements were made from the anterior abdominal wall fascia to the skin, and IAF was measured from the L4 anterior vertebral body to the anterior abdominal wall fascia. Patients with significant retroperitoneal or abdominal abnormalities on the reference CT were excluded owing to the difficulty in accurately assessing psoas area and density.

Statistical analysis

Analysis was performed using R statistical software version 3.1.1 (<http://www.r-project.org/foundation>). The association between the four morphometric measurements and the primary and secondary outcomes were assessed using both univariate analysis and also multivariate analysis to allow correction for potential confounders. For univariate analysis we used the Mann-Whitney U test for prolonged length of stay and discharge destination, and the log-rank test for survival and readmission-free survival. Confounder adjustment was performed by allowing all measured covariates to be present in multivariate models and using stepwise minimisation of Akaike's Information Criterion¹⁴ to prevent overfitting. Measured covariates were age, sex, independent mobility on admission, living alone, Katz score, Charlson comorbidity index, Waterlow score, history of depression, previous admission to intensive care, primary admission diagnosis, number of medications on admission, visual or hearing impairment, cognitive impairment on admission, history of two or more falls in the past 12 months, anaemia, evidence of malnutrition, and whether the admission was planned or emergent which have all been defined previously¹¹. Prolonged length of stay and discharge destination were modelled using logistic regression¹⁵, whereas survival and readmission-free survival was modelled using Cox' proportional hazards¹⁶. Correlation was determined using the Spearman's Rank Correlation¹⁷.

RESULTS

Between January 1st and December 31st 2012, 823 patients were admitted to the Vascular Unit, of whom 210 satisfied the three inclusion criteria of age, duration of admission and availability of CT imaging. The median age was 76 (range 65-94), and follow-up was for a median of 18 months (range 12-24). One hundred and fifty seven were male, and 53 were female with 87 being emergency admissions.

Thirty-one patients died within 12 months of admission, and a further seven died during the second year of follow-up. Eight deaths were on the index admission. The median length of stay was 6 days (range 2-93). The overall median readmission free survival was 318 days (range 1-669).

In 44 of the patients, abdominal CT was unsuitable for morphometric measurements due to significant abnormalities. These abnormalities precluded assessment of the psoas muscle and as such this cohort were excluded from subsequent analysis resulting in a final cohort of 166 patients. Reasons for CT related exclusions included inflammatory intra-abdominal conditions and retroperitoneal haematoma (often related to ruptured abdominal aortic aneurysms), making it impossible to accurately record the size and density of the psoas muscle.

Of the 166 patients, 48 were female and the median age was 76 years with 64 patients being emergency admission. Median length of stay was 11 days (range 2-74 days).

The admitting diagnosis for the 144 patients were as follows: 9 patients with lower limb ulceration, 41 patients with chronic lower limb ischaemia, 6 patients with acute lower limb ischaemia, 74 patients with AAA treated with EVAR, 15 patients with AAA treated with open repair and 21 patients with other miscellaneous diagnoses.

Surgical interventions were as follows, EVAR 75, open AAA repair 15, major lower limb amputation 5, infrainguinal lower limb bypass 20, common femoral endarterectomy 5 and lower limb embolectomy in 4. The remaining 42 patients underwent diagnostic / conservative management. The frailty specific factors are tabulated in table 1. The overall median readmission free survival was 315 days.

Morphometric analysis

Overall values for the PMA, PMD, SCF and IAF are shown in Table 2.

Increased SCF depth was a significant predictor of survival in this cohort of patients ($P < 0.001$ – Table 3), and this association persisted after adjustment for confounders ($P < 0.01$ – Table 4). After adjustment for overfitting, significant confounders for survival were patient age, Katz score, Charlson comorbidity index, Waterlow score, emergent admission, frequent falls (at least 2 in the past 12 months), a history of depression, and hearing impairment. When the SCF depth was split into quartiles the lowest quartile was associated with the poorest outcome ($P < 0.001$ – Figure 3). Median values of SCF for the four quartiles (Q1 – Q4) were 11, 15, 20 and 28 mm respectively. None of the remaining three morphometric measurements were significantly associated with survival.

Increased SCF depth was also associated with improved readmission-free survival ($P = 0.04$ – Table 3), as was reduced average psoas muscle area ($P = 0.04$ – Table 3), and these associations also persisted following adjustment for confounding variables ($P = 0.004$ and $P = 0.02$ respectively – Table 4). After adjustment for overfitting, significant confounders for readmission-free survival were patient sex, Katz score, admission for a limb-related problem, and independent mobility on admission. No

morphometric measurements were associated with either prolonged length of stay or discharge to a care facility.

Decreased SCF depth was also implicated in increased cost of healthcare ($P < 0.01$), remaining significant after adjustment for confounders. After adjustment for overfitting, significant confounders for cost of healthcare were patient sex, Katz score, Waterlow score, emergent admission, primary admission diagnosis, previous admission to intensive care, visual or hearing impairment and evidence of malnutrition on admission. None of the morphometric measurements were associated with prolonged LOS or discharge destination.

When assessing correlations between the morphometric factors assessed we found a positive correlation between psoas muscle area and intra-abdominal fat depth and a weak negative correlation between psoas muscle mean density and intra-abdominal fat depth (Table 5).

DISCUSSION

The data from this study suggests that vascular surgery patients with lower levels of subcutaneous fat have an increased mortality rate, lower readmission free survival rates with associated increased associated healthcare costs. Over the last one to two decades body composition has been increasingly investigated and shown to predict outcome in numerous patient groups. Data such as presented here is thus increasingly relevant to vascular surgery as the population continues to age.

It is well recognised that as aging progresses there is age-related fat redistribution with a reduction in subcutaneous fat mass yet an associated increase in overall fat mass¹⁸. Traditional teaching has suggested that obesity is a predictor of poor outcome in general yet, the “obesity paradox”, a somewhat counterintuitive medical hypothesis, suggests that obesity may actually be protective with associated increased survival specifically in older patients and patients with chronic diseases such as renal and cardiac failure^{19,20,21}. Such a phenomenon is seen within vascular surgery patients as a whole^{22,23,24} and specifically in lower limb surgical and endovascular revascularisation^{25,26} and carotid surgery²⁷, although not in aneurysm surgery^{28,29,30}.

While body mass index is suitable for population-based studies, it has well recognised limitations when assessing individual patients including poor differentiation between fat and muscle and an inability to determine fat distribution (e.g. central vs peripheral). Morphometric analysis is able to analyse body composition in part due to increasingly widespread used of computerised tomography (CT) in the diagnosis and follow up of surgical patients. Such techniques have been well validated within the surgical literature³⁷.

The majority of such data is in patients undergoing abdominal surgery including surgery for intra-abdominal malignancy. Fat distribution has been shown to predict poorer outcomes with fat composition predicting infective complications post Crohn's resection as well as following midline laparotomy^{31,32}. Psoas muscle characteristics predict both survival, length of stay and complication rates in a number of patients groups³³ undergoing abdominal surgery^{34,35}. Specifically, sarcopenia is associated with higher healthcare costs^{36,37}. Potential links between sarcopenia and potential overall function in older, more vulnerable patients have been examined and one study found that psoas characteristics predicted reduced mobility, poorer functional performance with allied cognitive impairment in this specific cohort of patients³⁸.

Sarcopenia is the loss of skeletal muscle mass and strength as a result of ageing and morphometric analysis allows quantitative evaluation specifically of muscle composition. As such, morphometric analysis has been increasingly used to determine both skeletal muscle mass as well as fat distribution using CT scans as the primary imaging technique^{14,15,16,39}.

Sarcopenia specific studies (as apposed to BMI related studies) on vascular surgical patients are somewhat sparse. One study published by Maturbara *et al* suggested that a binary diagnosis of sarcopenia (defined using muscle mass) predicted longer-term mortality in patients with critical limb ischaemia⁴⁰. A further study by Lee *et al* specifically analysed a cohort of patients undergoing abdominal aortic aneurysm (AAA) repair. They found that there was a significant association between psoas muscle area and postoperative mortality in a cohort of 262 patients with a mean follow up of 2.3 years⁴¹. This study is the first to examine such characteristics in a broader vascular surgical cohort representative of everyday practice and given the

association in elderly patients, we specifically analysed patients over the age of 65 years.

The sarcopenia specific results from our study (reduced PSA associated with increased readmission free survival) do not reflect the data from previous studies. This may be due to the more heterogeneous group of patients analysed (ie. not procedure of diagnosis specific) or may be location specific (a “healthier” set of patients) but these require further exploration.

There are recognised limitations and possible areas of bias within this type of study. Primarily this relates to the types of patients undergoing CT examination. Firstly the study cohort was naturally restricted to those patients who had undergone a CT scan, generally endovascular / open aortic repair and patients requiring more comprehensive imaging prior to lower limb revascularization, yet this is reflective of “real world” care. Furthermore, not all CT examinations were suitable for inclusion – namely those patients with a ruptured AAA or large AAA’s that distort the outline of the psoas muscle. Exclusion criteria were as per a previously published study and were determined so as to exclude patients admitted overnight for observation after minor procedures such as angioplasty or varicose vein procedures. The definition of prolonged LOS as greater than or equal to one week, irrespective of diagnosis, was chosen firstly as the median LOS within the whole patient cohort was 6 days, and secondly as this was considered to be more than would be expected for the majority of admissions. Similarly, we performed little subgroups analysis, specifically with regard to admission diagnosis, as the number of patients in each group was too small to make sound statistical analysis. Readmission was felt to be an appropriate outcome measure as geriatric syndromes are well recognised cause of readmission which are

also associated with increased morbidity and higher costs and given the inclusion criteria, such readmission were likely to be significant. Finally, while this study suggests association between these morphometric findings and outcome it does not show causality which requires more complex prospective longitudinal investigation.

The unique factors associated with an aging population means that there is a need for reliable quantification of operative and non-operative risk specifically with regard to enhancing our ability to predict both morbidity and mortality. Frailty itself is without an all-encompassing definition and there is no single “gold standard” test. The retrospective nature of this study has limited a comparison between various measures of frailty. CT examination is becoming a more frequent medical investigation and it is likely that although morphometric analysis on its own will not be the panacea when determining patient outcome it is more likely to be used as part of a battery of assessments that will ultimately predict short and longer term outcome. This will need further assessment using large prospectively collated databases. Furthermore, it may be that some of these predictors can be positively modified either prior to or on admission to improve outcome and as such this study ultimately strengthens the evidence for the need of in hospital multidisciplinary teams to address frailty incorporating medical, nursing and allied health professionals. Finally, such markers of sarcopenia may allow for appropriate patient counselling about individual risk yet again prospective studies are required to confirm general applicability but further data may strengthen surgical audit given the increasing drive towards publication of surgeon-specific outcomes.

ACKNOWLEDGEMENTS

Nil acknowledgments need to be made for this paper.

SOURCES OF FUNDING

No funding was provided for this paper

CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose

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FIGURES

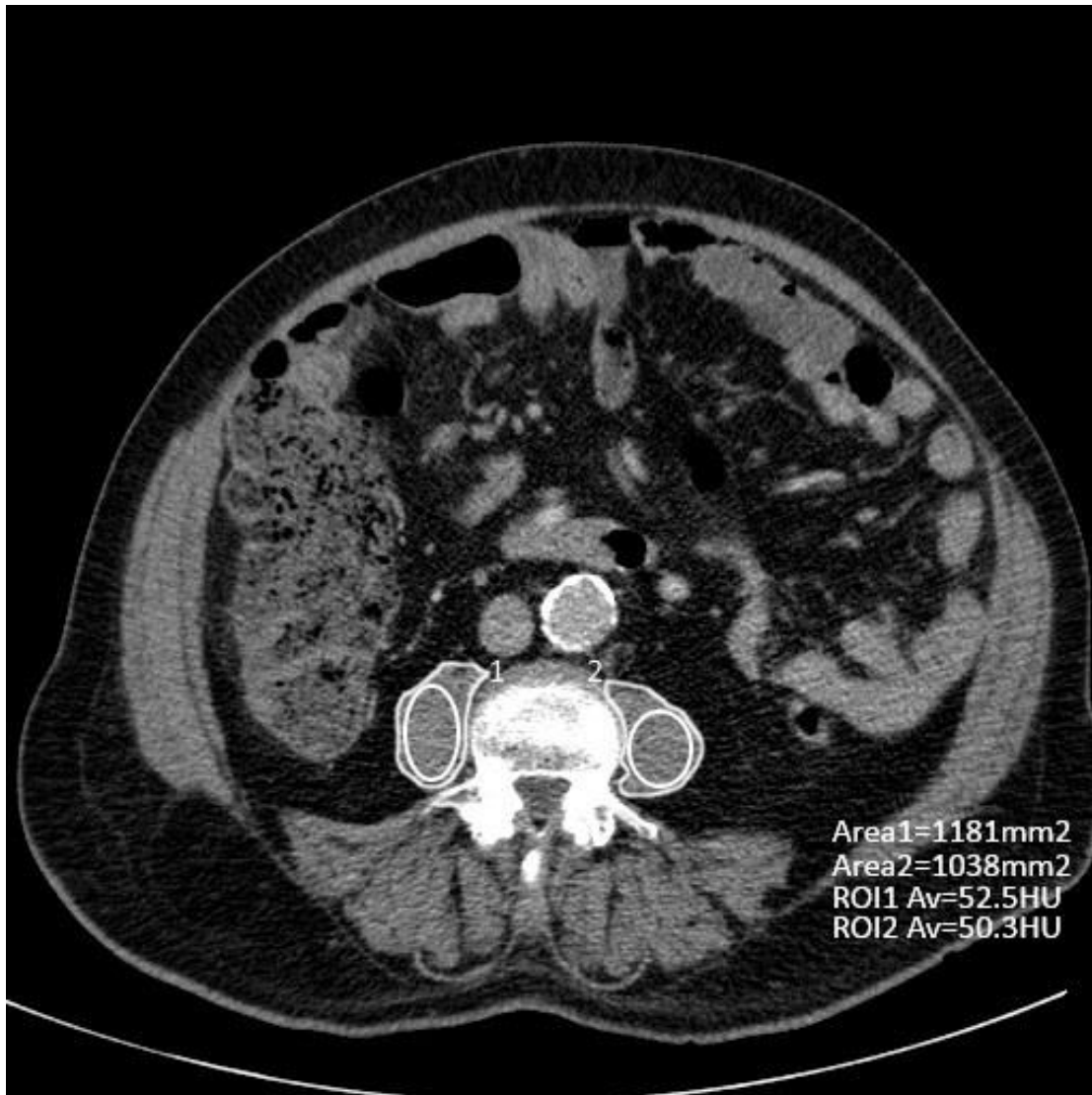


Figure 1. Psoas muscle area and mean density measurements using GE-Solutions™ workstation volume-viewer. At the level of L4 vertebral body, an area marker is drawn around the borders of the psoas muscle which represents the psoas area in mm². A region of interest (ROI) is marked inside the psoas area which represents the average density of the psoas muscle area in Hounsfield Units (HU).

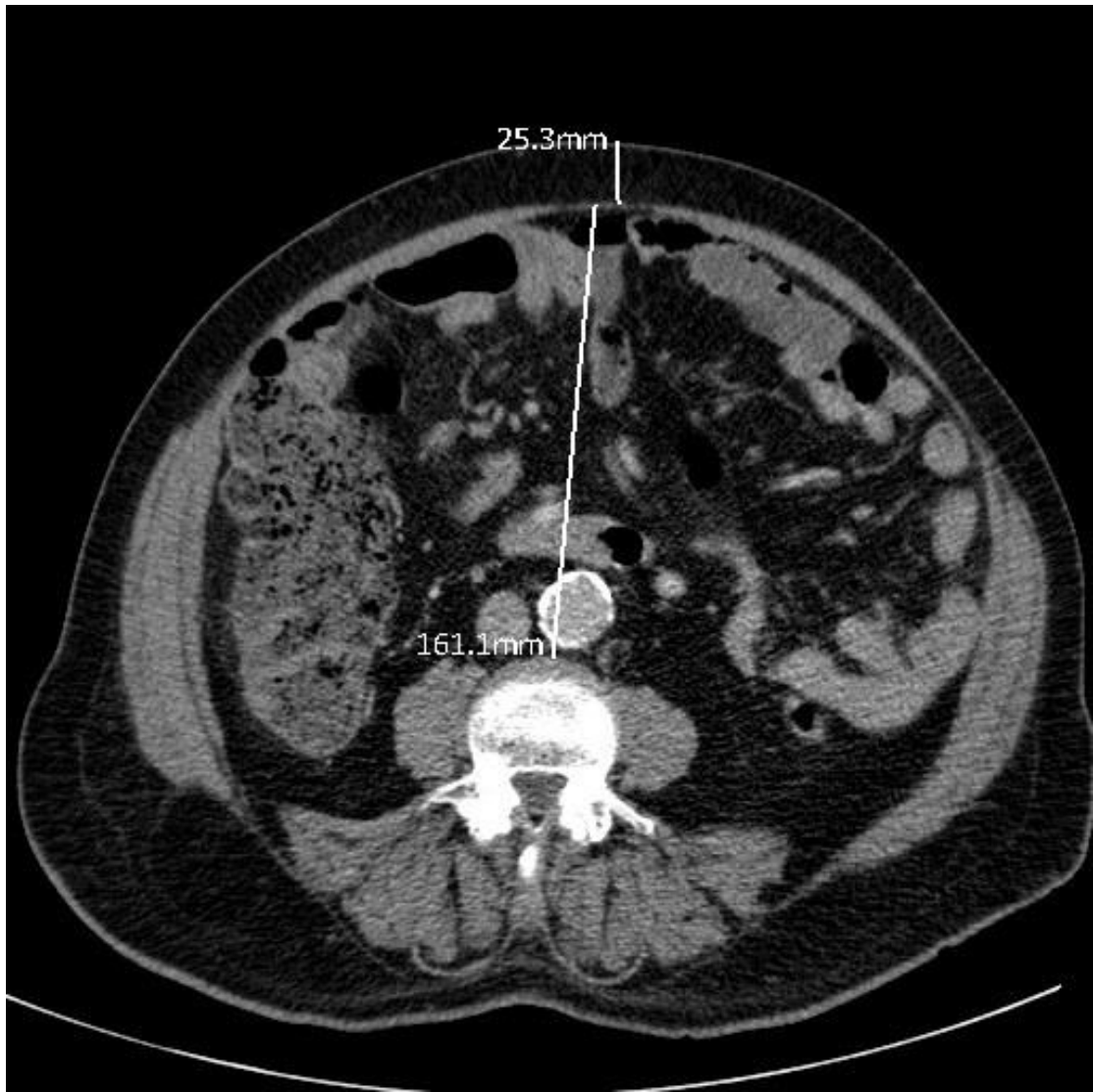


Figure 2. Subcutaneous and intra-abdominal fat measurement using GE-Solutions™ workstation volume-viewer. At the level of L4 vertebral body, a measurement line is drawn from the anterior abdominal skin surface to the linea alba which represents subcutaneous fat thickness in mm. A second line is drawn from the linea alba to the anterior surface of the vertebral body which represents intra-abdominal fat thickness in mm.

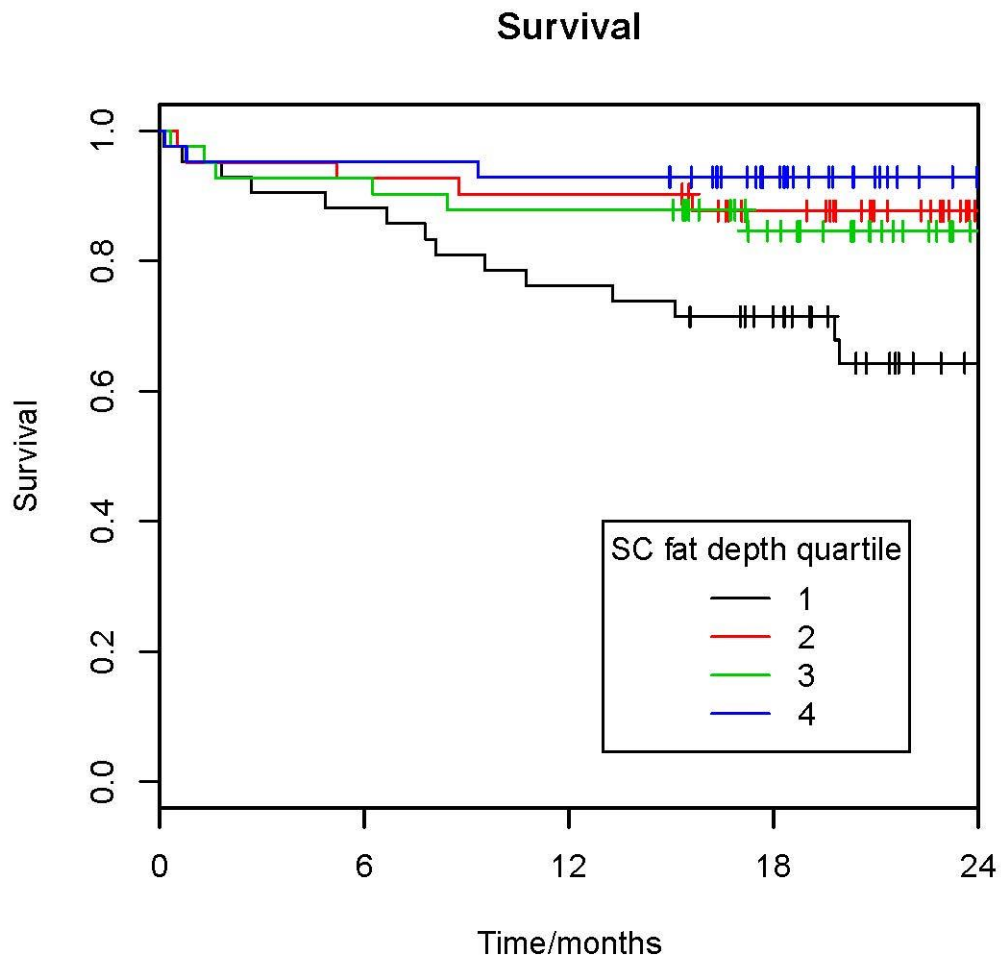


Figure 3. Kaplan-Meier survival curves for quartiles of subcutaneous fat depth.

TABLES

Frailty specific factor (n=166)	
Independent on admission*	128
Living alone*	52
Katz score	6 (6-6)
Charlson morbidity index	2 (1-4)
Waterlow score on admission	12 (9-15)
Depression*	13
Number of medication on admission	7 (1-10.75)
Visual impairment*	12
Hearing impairment*	15
Cognitive impairment*	6
Haemaglobin	12 (10.5 - 13.6)
Malnutrition*	19
More than 2 falls within the preceding 12 months*	17

Table 1: Frailty specific factors analysed in the cohort of 166 patients with a Ct deemed suitable for morphometric analysis. * number of patients. Other values are median and interquartile range. Appropriate definitions of each factor can be found at reference 11.

	Median	Interquartile range
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Subcutaneous fat depth (mm)	17.5	12.8 – 22.7
Intra-abdominal fat depth (mm)	108	88.5 – 133.2
Psoas muscle area (mm ²)	2253	1836 – 2717
Mean psoas density (HU)	41.7	37.7 – 45.8

Table 2. Median and interquartile ranges for the four morphometric measurements. HU: Hounsfield Units.

	Survival	Readmission-free survival	Prolonged LOS	Discharge to Care
Subcutaneous fat	0.0008	0.04	0.96	0.55

Intra-abdominal fat	0.30	0.33	0.26	0.15
Psoas muscle area	0.27	0.04	0.39	0.44
Mean psoas density	0.18	0.16	0.95	0.75

Table 3. Univariate P-values assessing the association between morphometric measurements and outcomes. Prolonged LOS: Length of Stay at least 7 days; Discharge to Care: Patient either discharged to another hospital for rehabilitation, or discharged to a care facility.

	Survival	Readmission-free survival	Prolonged LOS	Discharge to Care
Subcutaneous fat	0.009 (HR 0.92 95% CI 0.86-0.98)	0.004 (HR 0.96 95% CI 0.93-0.99)	0.40	0.35

Intra-abdominal fat	0.39 (HR 1.01 95% CI 0.99-1.02)	0.71 HR 0.99 95% CI 0.99-1.01)	0.96	0.50
Psoas muscle area	0.18 (HR 0.99 95% CI 0.99-1.01)	0.02 (HR 1.00 95% CI 1.00-1.01)	0.84	0.10
Mean psoas density	0.27 (HR 1.03 95% CI 0.98-1.09)	0.18 (HR 0.98 95% CI 0.95-1.01)	0.13	0.85

Table 4. Multivariate P-values after confounder adjustment assessing the association between morphometric measurements and outcomes. Prolonged LOS: Length of Stay at least 7 days; Discharge to Care: Patient either discharged to another hospital for rehabilitation, or discharged to a care facility. HR: Hazard ratios, CI: confidence intervals

	Intra-abdominal fat depth	Psoas Muscle Area	Psoas Muscle Mean Density
Subcutaneous fat depth	-0.04	0.09	0.04
Intra-abdominal fat depth		0.55 ^a	-0.16 ^b
Psoas Muscle Area			0.02

Table 5. Correlation between morphometric variable assessed in this patient cohort. ^a $P = 1.2 \times 10^{-14}$; ^b $P = 0.045$ (Spearman Rank Correlation).