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The prevalence of sarcopaenia in a vascular surgical patient cohort and its impact on outcome

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ABSTRACT

Background: Sarcopaenia, loss of lean muscle mass and quality, has prognostic significance and can be used to guide the management of oncology patients.[1] However, there is limited research into the prevalence and effect of sarcopaenia in vascular populations. We aim to investigate the prevalence of this measure of physiological reserve in a vascular patient group.

Methods: All patients admitted to a tertiary vascular unit in a single year were considered for the study. Patients with an abdominal CT scan (available for analysis) within 12 months of admission were included. Patient data were extracted from electronic patient records and hospital case notes. CT scans were analysed at L3 vertebral body to calculate body composition indices, as previously described.[1] Sarcopaenia was defined as skeletal muscle index of <41 cm^2/m^2 in female patients and non-obese males and <53 cm^2/m^2 in obese males. Outcome at 3-years was ascertained.

Results: Of 314 patients, 129 (41.1%) were sarcopaenic. Female patients were more likely to be sarcopaenic ($p < 0.0001$). The prevalence of sarcopaenia increased with age ($p < 0.001$). Rates of sarcopaenia didn't differ between occlusive and aneurysmal diagnoses. In a potentially unique finding in vascular literature to date, mortality and non-home discharge were not significantly different between the groups. On multivariate analysis, sarcopaenia was not significantly associated with earlier death ($p = 0.55$).

Conclusions: Sarcopaenia is highly prevalent in vascular surgical patients. In our analysis, sarcopaenia was not independently associated with mortality. Potentially the associated cardiovascular risk of patients with end stage vascular disease may negate the additional risk of altered body composition.

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Introduction

Sarcopaenia may be defined as loss of lean muscle mass and quality.[2,3] In recent years there has been increasing interest in the use of sarcopaenia as a surrogate measure of frailty.[4] It has been used as a predictor of post-operative complications and outcomes within the general surgical literature.[4–7] In surgical oncology populations, the presence of sarcopaenia has been shown to be an independent risk factor for mortality[8–19] and post-operative complications.[20–23] There is limited literature regarding sarcopaenia in vascular patients.

Muscle mass can be accurately assessed on CT imaging. Several methods of assessing sarcopaenia radiologically have been described including: skeletal muscle index,[1] Hounsfield unit average of psoas,[24] intramuscular adipose content,[25,26] total psoas volume[27] and dorsal muscle group area.[28] These indirect measures of sarcopaenia are advantageous in that they can be assessed on imaging already undertaken without subjecting the patient to additional testing. Furthermore, sarcopaenia has been shown to have a greater predictive value than some traditional frailty scores, such as the modified frailty index, in identifying patients at high risk of adverse events.[4] It has therefore been proposed as a useful tool for pre-operative risk stratification.[29]

To date, by far the greatest volume of research into sarcopaenia has been in oncological populations. It has been identified as a significant independent risk factor for post-operative mortality following resection of a range of different malignancies.[9–15,30,31] Sarcopaenic groups have been shown to have an increased mortality risk even when controlling for poor differentiation, margin status and lymph node status of tumour.[31] Decreased muscle mass does not, however, occur only in the context of cancer but also in benign pathologies and in the general populace. Indeed, using one definition of sarcopaenia, its estimated prevalence amongst an English cohort of elderly patients in the community was 4.6% in men and 7.9% in women.[32] However, the prevalence of sarcopaenia, and its influence on outcome, in patients admitted to a vascular surgery ward remains unclear. The presence of sarcopaenia is not only predictive of mortality, but also of complications following surgery.[20,22,23] It is also significantly associated with increased likelihood of non-home discharge, for example to a nursing home or rehabilitation hospital.[33–37] This effect is seen even following adjustment for complexity of intervention and comorbidities and may partly explain why sarcopaenia is an independent predictor of high resource utilisation[38] and increased costs of care for patients.[33,39,40]

Although sarcopaenia has been the focus of much research in surgical patients, there is little literature available evaluating the prevalence and significance of sarcopaenia in vascular patient groups.[41,42] There have, however, been studies showing that frailty predicts poorer outcomes and discharge to a non-home environment in surgical populations.[43–48] Frailty is a difficult and subjective parameter to assess. Therefore there has been recent interest as to whether more objective measures of physiological reserve, such as sarcopaenia, are as predictive for outcomes in vascular patients. In this study we focus on sarcopaenia and aim to ascertain its prevalence in this patient group. We also aim to establish if the presence of sarcopaenia is predictive for poorer outcomes in vascular patients.

Methods

Inclusion criteria

All patients admitted to a tertiary vascular unit in 2012 and having had CT scans within a year of their admission were identified using ward admissions data. This allowed for a minimum of three years follow-up at censorship.

The CT scan had to include the L3 vertebral transverse area in order to analyse for the presence or absence of sarcopaenia. Therefore patients who had not had such a CT were excluded. Data was unavailable for patients admitted under other specialties therefore they also were excluded.

Data collection

Patients were identified via a ward admissions database. Data was then collected retrospectively from electronic patient records to establish (at time of admission): height, weight, Body Mass Index (BMI), age, gender, diagnosis, operations (if any during admission), admission bloods, co-morbidities and smoking status. Co-morbidity data were utilised to calculate the Charlson comorbidity index[49] for each patient. Data on outcome measures, including length of stay and mortality as of January 2016, were also collected.

Technique for diagnosing sarcopaenia

For each patient, a transverse computed tomography (CT) slice at the level of the third lumbar vertebral body (L3) was analysed using ImageJ, (National Institutes for Health Image J version 1.47, http://rsbweb.nih.gov/ij/). Conventional Hounsfield Unit (HU) thresholds were applied for skeletal muscle (−29 to 150) and adipose tissue (−190 to −30). A region of interest (ROI) was manually traced around each compartment to calculate skeletal muscle area (SMA) in cm^2 (Fig. 1). This has been previously described.[1]

SMA was normalised for height by dividing the measured area by the patient's height[2] to give skeletal muscle index (SMI, cm^2/m^2). Previously defined cut-off values were then used to categorise the body composition parameters that were used for analysis, which are as follows: Sarcopaenia was defined by SMI thresholds of <53 cm^2/m^2 for overweight and obese male patients and <41 cm^2/m^2 for female patients and non-obese male patients.[1]

Statistical methods

Data were analysed using SPSS v24 (IBM, New York). For binary variables a chi-squared test with continuity correction was used to compare groups by sarcopaenia status. The chi-squared test for trend was used for ordered categorical variables and the Mann–Whitney test for continuous variables that were not normally distributed. A Cox proportional hazards model was developed to examine factors associated with

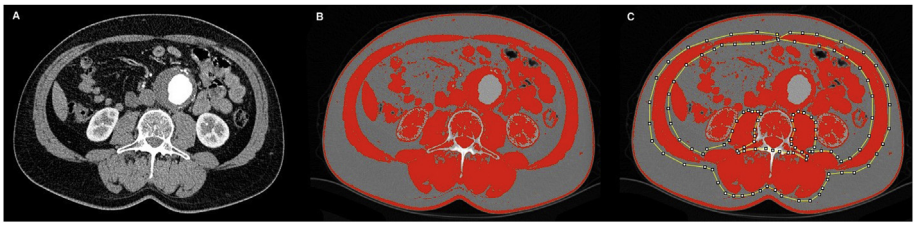

Fig. 1 – A) Transverse CT slice at L3 level prior to analysis. B) Image with skeletal muscle HU threshold applied (−29 to 150 HU-muscle seen in red). C) skeletal muscle area manually selected as the region of interest to allow measurement.

time to mortality and a logistic regression model used to compare factors associated with discharge to a nursing home or death in hospital.

Results

Of 622 admissions in 2012, a total of 314 patients were included. Patients were excluded if: they had not had a CT including the L3 vertebral level (n = 261), the scan was unavailable for analysis (n = 9), the scan was of too poor a quality for analysis (n = 3), a contemporaneous patient height was unavailable therefore calculation of SMI was rendered impossible (n = 20) or the patient had active malignancy at the time of admission (n = 14). A further patient was omitted as, due to obesity, the skeletal muscle area was larger than the CT field of view.

Of the resulting 314 patients included, 196 (62.4%) were male and 140 (44.6%) were admitted electively. The mean age of the cohort was 70.8 years. Occlusive disease was diagnosed in 230 (73.3%) patients. A total of 129 (41.1%) patients were diagnosed as sarcopaenic.

Table 1 depicts the demographic characteristics and admission blood results of the sarcopaenic and non-sarcopaenic groups. Sarcopaenic patients were more likely to be older ($p < 0.001$) than non-sarcopaenic patients and rates of sarcopaenia were higher in female patients. There was no significant difference in co-morbidity score between the two groups. The only admission blood test that was statistically significantly different between the two groups was serum albumin level, although the median value of this test was within the normal range in both groups.

Table 2 depicts the operations and procedures, if any, undergone by patients in both the sarcopaenic and non-sarcopaenic groups. Some patients were elected to be managed conservatively (n = 48), whereas others were not medically fit for the intervention required (n = 12). There was no significant difference ($p = 0.28$) between the sarcopaenic and non-sarcopaenic groups in terms of procedures undergone.

Frail patients are more likely to be discharged to a non-home environment,[44] i.e. to a hospital rehabilitation facility, nursing home or to die prior to discharge. As sarcopaenia is a potential substitute marker of frailty, we investigated patient discharge destination in our cohort. On this analysis, sarcopaenic patients were more likely to have a non-home discharge but this was not statistically significant ($p = 0.10$). Furthermore, sarcopaenic patients stayed in hospital for a median of one more day than non-sarcopaenic patients (Table 3).

On Kaplan–Meier analysis of mortality, sarcopaenia was not significantly predictive of adverse outcome in this cohort ($p = 0.22$) (Fig. 2).

Multivariate analysis was performed to determine which factors in our cohort were independently predictive for mortality (Table 4) and non-home discharge (Table 5). There was evidence from the Cox regression model that older age (HR

Table 1 – Demographic and baseline information.[a]

Demographic	Sarcopaenic (n = 129)	Non-sarcopaenic (n = 185)	p-Value
Smoking status (N (%))			
Non-smoker	18 (15.3%)	31 (18.0%)	0.56
Ex-smoker	71 (60.2%)	86 (50.0%)	
Smoker	29 (24.6%)	55 (32.0%)	
Unknown	11	13	
Gender (N (%))			
Female	54 (41.9%)	64 (34.6%)	N.A[a]
Male	75 (58.1%)	121 (65.4%)	
Admission (N (%))			
Elective	50 (39.1%)	90 (48.9%)	0.11
Emergency	78 (60.9%)	94 (51.1%)	
Unknown	1	1	
Diagnosis (N (%))			
Occlusive	90 (70.3%)	140 (78.2%)	0.0576[b]
Aneurysm	38 (29.7%)	35 (19.6%)	
Mixed	0	4 (2.2%)	
Charlson Comorbidity Index (CCI) Median Score (IQR)	5 (4–7)	5 (3–6)	0.94
Age (years)	75.3 (67.5, 82.5)	68.6 (61.7, 77.9)	<0.001
BMI (kg/m^2)	26.4 (22.5, 29.4)	26.7 (23.3, 30.8)	N.A[a]
Hb (g/l)	127 (98,156)	132 (103,161)	0.31
WCC ($\times 10^9$/l)	8.8 (7.2, 12.6)	8.7 (7.0, 11.5)	0.32
Neutrophils ($\times 10^9$/l)	6.3 (4.7, 9.6)	5.9 (4.4, 8.9)	0.11
Lymphocytes ($\times 10^9$/l)	1.5 (1.1, 2.0)	1.6 (1.1, 2.2)	0.20
Albumin (g/l)	42.0 (38.0, 44.0)	43.0 (40.0, 45.0)	0.004
CRP (mg/l)	19.0 (3.0, 54.5)	14.0 (3.0, 58.0)	0.58

[a] As Gender and BMI are used in the definition of sarcopaenia, hypothesis testing was not undertaken. Data are presented as number of patients (as a percentage) where stated, otherwise presented as median (interquartile range).
[b] Comparison between aneurysmal and occlusive disease.

Table 2 – Operations/procedures undergone by patients in sarcopaenic and non sarcopaenic groups.

Operation/procedure	Sarcopaenic group (n = 129)	Non-sarcopaenic group (n = 185)	Totals (n = 314)
AAA repair (open/Endovascular)	20 (15.5)	34 (18.4)	54 (17.2)
ABG (Aorto-bifemoral graft)	5 (3.9)	7 (3.8)	12 (3.8)
Amputation	14 (10.9)	17 (9.2)	31 (9.9)
Embolectomy	6 (4.7)	4 (2.2)	10 (3.2)
Endovascular lower limb (i.e. angioplasty)	13 (10.1)	28 (15.1)	41 (13.1)
Lower limb bypass	30 (23.3)	58 (31.4)	88 (28)
Other interventional procedure	9 (7.0)	9 (4.9)	18 (5.7)
Conservative management	25 (19.4%)	23 (12.4)	48 (15.3)
Patient not fit for intervention	7 (5.4)	5 (2.7)	12 (3.8)

Figures presented as n (% of patient group), to 1 decimal place. p = 0.28.

Table 3 – Discharge destination and length of stay.

	Sarcopaenic (n = 129)	Non-sarcopaenic (n = 185)
Discharge destination		
Home	100 (77.5%)	159 (85.9%)
Nursing Home	22 (17.1%)	22 (11.9%)
Mortality in Hospital	6 (4.7%)	4 (2.2%)
Unknown	1	0
Length of stay in days (Median (IQR))	9 (5, 19)	8 (4, 16)

1.068; p < 0.001) and emergency admission (HR 2.017 p = 0.001) were independent risk factors of earlier death. The logistic regression model suggested that female patients (p = 0.02) and those admitted in an emergency manner (p = 0.001) were more likely to be discharged to a nursing home or die in hospital. There was no evidence that sarcopaenia status was associated with either mortality or discharge destination.

Discussion

To our knowledge, this is the largest vascular group in the literature assessed for the presence of sarcopaenia. We have shown that, using previously established techniques and definitions of diagnosis,[1] a striking proportion of patients admitted to a vascular surgery unit are sarcopaenic (41%). Indeed, it should be highlighted that a UK cohort study in community dwelling elderly people (albeit determining sarcopaenia by a different radiological method) estimated the prevalence of sarcopaenia to be 4.6% in men and 7.9% in

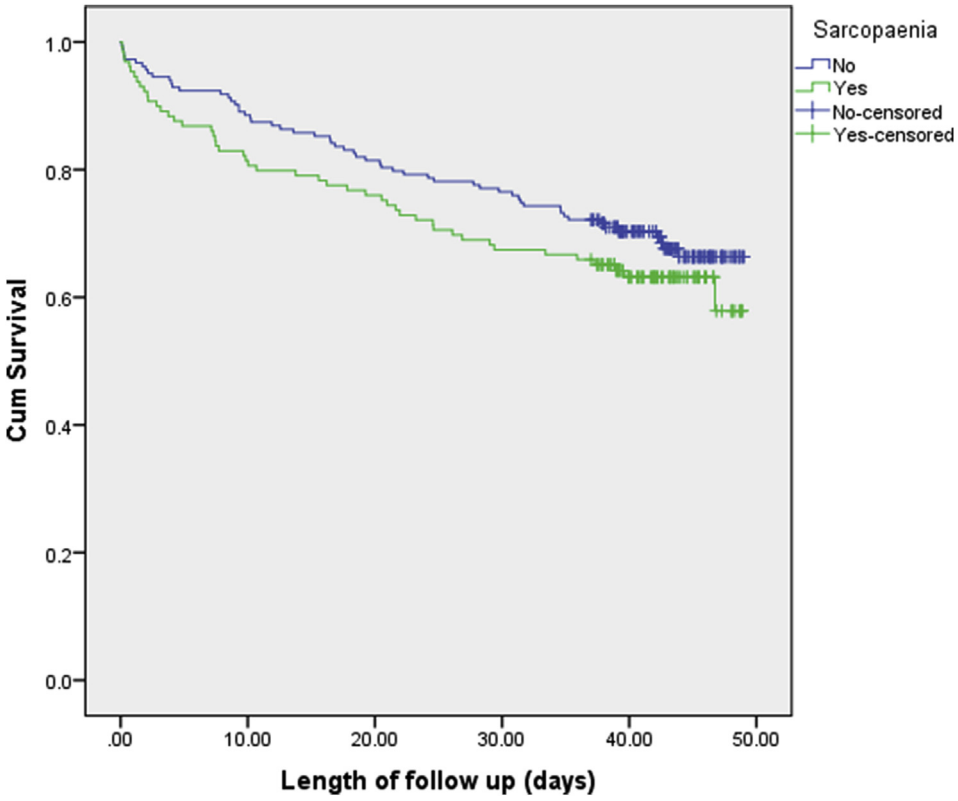

Fig. 2 – Kaplan–Meier analysis of death.

Table 4 – Results of Cox regression analysis predicting time to death.

	HR (95% CI)	p-Value
Age	1.068 (1.046, 1.090)	<0.001
Gender		
Female	1	0.17
Male	0.758 (0.511, 1.124)	
Admission		
Elective	1	0.001
Emergency	2.017 (1.339, 3.038)	
Sarcopaenia		
No	1	0.55
Yes	0.887 (0.595, 1.321)	

HR: Hazard ratio, CI: confidence interval.

Table 5 – Results of logistic regression predicting discharge to nursing home/death in hospital versus discharge to home.

	OR (95% CI)	p-Value
Age	1.025 (0.997, 1.054)	0.08
Gender		
Female	1	0.02
Male	0.491 (0.264, 0.912)	
Admission		
Elective	1	0.01
Emergency	2.302 (1.185, 4.472)	
Sarcopaenia		
No	1	0.35
Yes	1.352 (0.720, 2.541)	

OR: Odds ratio, CI: confidence interval.

women.[32] This indicates that the level of sarcopaenia in vasculopaths may be up to a factor of 10 times higher than in the general population. Indeed, the rate of sarcopaenia in our cohort was comparable to that seen in Martin's flagship paper,[1] which studied 1500 oncological patients, and found a prevalence of sarcopaenia (also diagnosed via SMI) of 41%. Such a high level of muscle wasting and low muscle quality is perhaps intuitive given the exercise inhibition associated with many vascular pathologies, but it is surprising that the level of sarcopaenia in vascular patients is comparable to that seen in an oncological population.

As loss of muscle mass is a factor in the aging process,[50] it is unsurprising that the sarcopaenic group was significantly older than the non-sarcopaenic group. However, we were surprised to discover that there was no evidence that sarcopaenia predicted mortality, either on univariate or multivariate analysis. This is in contrast to previous publications on sarcopaenia in the oncology literature[8,10–18,31,51] and indeed in previous smaller investigations into body composition in vascular patients. Therefore our results may represent a unique finding in the literature. The vascular studies include one into patients with critical limb ischaemia[52] and two in those undergoing abdominal aortic aneurysm repair.[42,41] Our cohort did not select for specific diagnoses and demonstrates that sarcopaenia cannot be used uniformly as identifying higher risk patients. It is possible that the variety of methods used to identify sarcopaenia, both radiologically and clinically, has resulted in such variations in results in the literature, as well as hindering literature reviews in this subject. For example, some studies looked at skeletal muscle area, without correction for height.[42,52] Others used psoas muscle area,[41] or total psoas volume. Clinical methods of diagnosing sarcopaenia, such as walking speed and skin fold thickness, have also been used. The definitions and SMI cut-off values for used in our analysis have been widely accepted as a valid assessment of sarcopaenia.[1] Although other methods for diagnosing sarcopaenia from cross sectional imaging are available, analysis of SMI has been undertaken in large cohorts.[1] This previous analysis identified specific threshold values for SMI below which there was a statistically significant association with low survival, and therefore were identified as limits for diagnosing sarcopaenia. This method is also cost effective, as it uses scans already done in routine clinical practice and, in our experience, only adds around 5 min to the reporting of these scans.

Our study demonstrates the ability to determine the prevalence of sarcopaenia in vascular inpatients; the primary aim of this work. It also highlights the increased risk of adverse outcomes in emergency patients and the elderly. Interestingly, in this cohort, female gender was predictive of both mortality and non-home discharge, which warrants further investigation in future works. We speculate that the reasons why sarcopaenia did not predict survival in our cohort are multifactorial. Firstly, our definition of sarcopaenia was taken from a large Canadian cohort study[1] which included more than 1500 oncology patients. It is therefore possible that this cohort does not correlate with ours in terms of geographical location and disease pathophysiology. In addition, those patients who have vascular pathologies warranting in-patient admission have higher physiological risk - perhaps observed by the high rate of sarcopaenia identified in this cohort and the low three-year survival rates observed. Previous studies have assessed all cancer patients and therefore included a wider age-range and physiological range of patients. It may be that by having a vascular pathology and associated high cardiovascular risk, the additional risk of altered body composition is obsolete in risk stratification. Finally, our findings may be as a result of a type 2 error, and study into further cohorts in the future would help to clarify this hypothesis.

It is interesting that commonly considered surrogate markers of nutrition such as BMI were similar between the two study groups. Moreover, although serum albumin levels were significantly lower in the sarcopaenic group, this was not below the normal range for our laboratory (35–50 g/l). Thus, CT provides a radiological means by which sarcopaenia can be readily identified, even where standard measures such as BMI and albumin may be misleading. Sarcopaenic obesity is an increasingly recognised phenomenon, where, despite a high BMI, patients have a lack of lean muscle mass. This combination of adverse factors has been shown in some studies to have an even greater detrimental effect on outcome than either in isolation.[53] Our analysis is able to identify these patients. However, outcomes in our cohort were not affected by this phenomenon.

This study has several strengths. We utilised a patient group from a prospectively collected database and a single analyser reviewed all scans thereby reducing inter-observational error. We acknowledge that the data in this cohort are real world and therefore patients with underlying conditions that may contribute to sarcopaenia are not excluded. However, active malignancy was an exclusion criterion and median comorbidity score, in the form of the Charlson index, was 5 in both groups, suggesting both groups to be highly, but equally, comorbid. Only those vascular patients who had a CT scan covering the L3 region were included, therefore certain groups, for example carotid endarterectomy patients, were largely not included. Although the admissions database is prospectively maintained, the outcome data was retrospectively collated, therefore we have used markers such as length of stay and discharge destination as outcome measures rather than postoperative complications, which can be challenging to accurately ascertain retrospectively.

This study has highlighted several areas for future work. For instance, it would be interesting to see if higher Fontaine stage or Rutherford grade of chronic limb ischaemia altered the prognostic value of sarcopaenia, as sadly we did not have access to this information for our cohort and therefore couldn't include it in our study. There has been a wealth of recent research into frailty indices, such as that used in comprehensive geriatric assessment, or the shorter Edmonton Frailty Index. Further work is required to see if these frailty scores correlate with sarcopaenia, perhaps especially in vascular patients.

Conclusion

Sarcopaenia is extremely prevalent in patients admitted to our unit. However, to our surprise, there was no significant difference in mortality rate between the sarcopaenic and non-sarcopaenic patient groups. Non-home discharge, again, was not influenced by sarcopaenia. This is contrary to other reports in the vascular literature on this subject and highlights that sarcopaenia cannot be used as a blanket marker of frailty in a heterogeneous vascular population. It may be that the associated cardiovascular risk of patients with end stage vascular disease negates the additional risk of altered body composition and as such, all vascular patients continue to require intensive pre and post operative support as risk stratification only via muscle mass analysis on CT was not possible in this all-comers vascular cohort.

Conflicts of interest

None.

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