The relationship between computed tomography-derived body composition, systemic inflammation, and survival in patients with abdominal aortic aneurysm

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ABSTRACT

Objective: Patient selection and risk stratification for elective repair of abdominal aortic aneurysm (AAA), either by open surgical repair or by endovascular aneurysm repair, remain challenging. Computed tomography (CT)-derived body composition analysis (CT-BC) and systemic inflammation-based scoring systems such as the systemic inflammatory grade (SIG) appear to offer prognostic value in patients with AAA undergoing endovascular aneurysm repair. The relationship between CT-BC, systemic inflammation, and prognosis has been explored in patients with cancer, but data in noncancer populations are lacking. The present study aimed to examine the relationship between CT-BC, SIG, and survival in patients undergoing elective intervention for AAA.

Methods: A total of 611 consecutive patients who underwent elective intervention for AAA at three large tertiary referral centers were retrospectively recruited for inclusion into the study. CT-BC was performed and analyzed using the CT-derived sarcopenia score (CT-SS). Subcutaneous and visceral fat indices were also recorded. SIG was calculated from preoperative blood tests. The outcomes of interest were overall and 5-year mortality.

Results: Median (interquartile range) follow-up was 67.0 (32) months, and there were 194 (32%) deaths during the follow-up period. There were 122 (20%) open surgical repair cases, 558 (91%) patients were male, and the median (interquartile range) age was 73.0 (11.0) years. Age (hazard ratio [HR]: 1.66, 95% confidence interval [CI]: 1.28-2.14, $P < .001$), elevated CT-SS (HR: 1.58, 95% CI: 1.28-1.94, $P < .001$), and elevated SIG (HR: 1.29, 95% CI: 1.07-1.55, $P < .01$) were independently associated with increased hazard of mortality. Mean (95% CI) survival in the CT-SS 0 and SIG 0 subgroup was 92.6 (84.8-100.4) months compared with 44.9 (30.6-59.2) months in the CT-SS 2 and SIG ≥2 subgroup ($P < .001$). Patients with CT-SS 0 and SIG 0 had 90% (standard error: 4%) 5-year survival compared with 34% (standard error: 9%) in patients with CT-SS 2 and SIG ≥2 ($P < .001$).

Conclusions: Combining measures of radiological sarcopenia and the systemic inflammatory response offers prognostic value in patients undergoing elective intervention for AAA and may contribute to future clinical risk predication strategies. (J Vasc Surg 2023;78:937-44.)

Keywords: AAA; Sarcopenia; Body composition analysis; SIG; Systemic inflammatory response

Abdominal aortic aneurysm (AAA) remains an important health condition; the estimated UK prevalence is 1.5%, rising to approximately 4% in men aged over 65 years.[1] Intervention for AAA generally consists of either open surgical repair (OSR) or endovascular aneurysm repair (EVAR), with "complex aneurysms" repaired using fenestrated and branched EVAR. Patient selection for consideration of elective intervention is a key aspect to the management of AAA.

Sarcopenia is a chronic condition characterized by progressive loss of skeletal muscle volume and progressive reduction in skeletal muscle function (EWGSOP2 [European Working Group on Sarcopenia in Older People] definition) and is associated with increasing age and chronic illness.[2] Patients with sarcopenia are typically frail with associated poor functional status and inferior physiological reserve.[2,3] The use of computed tomography [CT]-derived body composition analysis (CT-BC) to measure sarcopenia has been widely performed in a range of patient cohorts, with majority of the literature based on patients with cancer.[4] In patients with AAA,

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the evidence base is plagued with heterogeneity;[5] however, we recently proposed novel sex- and disease-specific thresholds of CT-BC parameters, with the skeletal muscle index (SMI) at L3 appearing to offer superior prognostic value compared with other parameters.[6] CT-derived SMI and skeletal muscle density (SMD) have been combined into the CT-derived sarcopenia score (CT-SS), which appears to be associated with malnutrition, age, and prognosis in patients with cancer.[7]

Activation of the systemic inflammatory response (SIR) can be measured using routinely available systemic inflammation-based prognostic scoring systems, such as the modified Glasgow Prognostic Score (mGPS)[8] and neutrophil:lymphocyte ratio (NLR).[9] Activation of the SIR is an etiological factor in the diagnosis of malnutrition[10] and appears to be associated with sarcopenia.[11] mGPS and NLR have been recently combined into the more comprehensive systemic inflammatory grade (SIG), both in patients with AAA[12] and in patients with cancer.[13] Elevated magnitude of the SIG appears to confer inferior prognosis in elective cases in both of these patient groups.

A prognostic association between both CT-BC and the SIR has been described in patients with cancer,[14,15] though data in noncancer populations are lacking. Furthermore, CT-SS appears to be associated with the SIR in patients with cancer.[7] We hypothesize that patients with abnormal CT-BC and activation of the SIR are at risk of inferior long-term prognosis. The present study aimed to examine the associations and combined prognostic value of CT-BC parameters and systemic inflammation, measured by SIG, in patients undergoing elective intervention for AAA.

ARTICLE HIGHLIGHTS

- **Type of Research:** Multicenter, retrospective cohort study
- **Key Findings:** In 611 patients who underwent elective intervention for abdominal aortic aneurysm, elevated computed tomography-derived sarcopenia score (CT-SS) (hazard ratio: 1.58, 95% confidence interval: 1.28-1.94, $P < .001$) and elevated systemic inflammatory grade (SIG) (hazard ratio: 1.29, 95% confidence interval: 1.07-1.55, $P < .01$) were independently associated with mortality. Patients with CT-SS 0 and SIG 0 had 90% (standard error: 4%) 5-year survival compared with 34% (standard error: 9%) in patients with CT-SS 2 and SIG ≥2 ($P < .001$).
- **Take Home Message:** CT-derived body composition analysis may complement measures of systemic inflammation in developing novel clinical risk prediction tools.

PATIENTS AND METHODS

Patient selection. Patients who underwent elective intervention for AAA were retrospectively identified from theatre records at three large tertiary referral centers in Scotland, UK, representing cases drawn from three health boards (NHS Grampian, NHS Lanarkshire, and NHS Tayside). Specific procedural techniques were at the discretion of each institution, though practice was broadly similar between sites throughout the study period. Consecutive cases undergoing EVAR, fenestrated and branched EVAR, or OSR to treat aortic aneurysmal disease between January 1, 2015, and January 10, 2021, were screened for inclusion. Patients with active malignancy, active infection, isolated iliac aneurysms, aortic dissection, penetrating aortic ulcer, incomplete clinical or follow-up data, or emergency/urgent cases were excluded. Patients without CT-SS (eg, due to corrupted CT imaging, missing height for normalization) or without SIG (eg, due to incomplete preoperative blood work) were excluded. Clinical, demographic, and comorbidity data were recorded from electronic case records and patients' community health records. Comorbidity was summarized using American Society of Anesthesiologists (ASA), which was extracted from anesthetic charts (recorded by vascular anesthetists) and subgrouped (≤2/>2) in keeping with previous literature.[16] Age (<65, 65-75, and >75 years) and body mass index (BMI) (<25 kg/m^2 and ≥25 kg/m^2) were considered as categorical variables. In all patients, the date of follow-up was more than 2 years from the date of surgery. West of Scotland Research Ethics Committee approval was obtained for this study (reference 21/WS/0146; approval granted November 23, 2021).

Outcomes of interest. The primary outcome was overall mortality during the follow-up period. The secondary outcomes were 5-year mortality and sac regression at planned 12-month follow-up, defined as the reduction in the sac size on surveillance imaging of ≥5 mm from baseline. Outcome data were obtained from the Community Health Index registry, a routinely available registry maintained at a national health board level and populated from both primary and secondary care data. The specific cause of death was not available from this registry.

Body composition analysis. Body composition analysis was performed using established methodology. Briefly, preoperative CTs at the L3 vertebral level were used for body composition analysis. Subcutaneous fat area, visceral fat area, skeletal muscle area, and SMD were manually measured using the ImageJ v1.53 software (National Institutes of Health) using muscle tissue thresholds of −29 to +150 Hounsfield units and adipose tissue thresholds of −190 to −30 Hounsfield units. The areas obtained were normalized to height^2 to generate subcutaneous fat index, visceral fat index, and SMI, whereas SMD was not normalized. Sex-specific thresholds of VFI/

SFI/SMI/SMD derived from a previously reported cohort of patients with AAA[6] were used to dichotomize these continuous parameters in keeping with prior studies.[4] CT-SS was calculated based on SMI/SMD as per McGovern et al,[7] with each parameter assigned an integer value of 0 (high SMI/SMD) or 1 (low SMI/SMD) and the combined score (range: 0-2) calculated, with analyses between subgroups of CT-SS performed.

Inflammatory profiling. mGPS (from C-reactive protein and albumin) and NLR (from absolute neutrophil and lymphocyte counts) were calculated based on preoperative blood investigations using previously described methodology.[8,9] Institutional policy during the study period was to admit patients to hospital on the evening before surgery, where preoperative blood work was routinely performed as part of existing patient care. mGPS and NLR were then combined into SIG as previously reported,[12,13] which was chosen as the parameter of interest as it describes a more comprehensive assessment of the SIR incorporating both acute phase (mGPS) and differential white cell (NLR) responses. Outcomes were compared between the groups of SIG 0 (considered "noninflamed") vs SIG 1 (considered "mildly inflamed") vs SIG ≥2 (considered "inflamed").

Statistical analyses. Differences between continuous variables were assessed using the Kruskal-Wallis and Mann-Whitney tests, and differences between categorical variables using the χ^2 test, with linear-by-linear P values reported. To examine the relative contributions of CT-SS and SIG to prognosis, 5-year survival rates and percentage standard error (SE) were compared between the subgroups. The association between covariates and overall survival was assessed using a Cox proportional hazards model; covariates were initially interrogated in univariate analysis and those with univariate $P < .05$ were included in a multivariate model. Covariates with multivariate significance were further investigated using time-to-event analyses. Time-to-event analyses were calculated using the Kaplan-Meier method, with differences between cohorts assessed using the log-rank t test. Where time-to-event survival data did not reach a median survival, the mean (95% confidence interval [CI]) values were reported. Multivariable logistic regression was performed to generate two propensity-matched cohorts for comparison based on variables of interest; the match tolerance was 0 for both matching algorithms, and satisfactory matching was confirmed based on visual inspection of propensity score histograms and pairwise comparisons of factors of interest. CT-SS (0/1 vs 2) was matched 1:1 based on age, sex, BMI, and SIG. SIG (0/1 vs ≥2) was matched 1:1 based on age, sex, BMI, and CT-SS. To account for potential selection bias, excluded patients were compared with the final study cohort. The association between factors of interest and sac regression ≥5 mm was examined by binary logistic regression. All analyses were performed using IBM SPSS 28.0 (IBM Corp). P values <.05 were considered statistically significant.

RESULTS

A total of 829 patients were screened for inclusion into the study. Of these, 218 patients were excluded: 66 patients who underwent emergency or urgent repair for ruptured or symptomatic AAA, 3 patients due to hematological malignancy, 1 patient due to mycotic aneurysm, 20 due to missing CT-SS, and 128 due to missing SIG (Supplementary Fig 1, online only). This resulted in 611 elective patients who were eligible for inclusion into the final study cohort. There were 122 (20%) OSR cases, 558 (91%) patients were male, and the median (interquartile range) age was 73.0 (11.0) years. Median (interquartile range) follow-up was 67.0 (32) months, and there were 194 (32%) deaths during the follow-up period. Mean (95% CI) survival in the entire study population was 87.1 (81.4-92.9) months.

The characteristics of the study cohort when subgrouped by CT-SS are shown in Table I. There were 138 patients (23%) with CT-SS 0, 283 patients (46%) with CT-SS 1, and 190 patients (31%) with CT-SS 2. Patients with elevated CT-SS were older ($P < .001$), with a lower proportion of females ($P < .001$), were more likely to undergo EVAR ($P < .01$), and had a lower BMI ($P < .01$). SIG was similar between subgroups of CT-SS. Five-year survival was lower in patients with elevated CT-SS: CT-SS 0 (86%) vs CT-SS 1 (72%) vs CT-SS 2 (63%) ($P < .001$).

The association between baseline covariates, CT-SS, SIG, and mortality is shown in Table II. On univariate analysis, age ($P < .001$), elevated CT-SS ($P < .001$), and elevated SIG ($P < .01$) were associated with increased hazard of mortality. On multivariate analysis, age (hazard ratio [HR]: 1.66, 95% CI: 1.28-2.14, $P < .001$), elevated CT-SS (HR: 1.58, 95% CI: 1.28-1.94, $P < .001$), and elevated SIG (HR: 1.29, 95% CI: 1.07-1.55, $P < .01$) were independently associated with increased hazard of mortality. A sensitivity analysis on patients aged <80 years with preoperative AAA diameter ≤6.0 cm (n = 261, 65 deaths) was performed; CT-SS (HR: 1.63, 95% CI: 1.14-2.33, $P < .01$) remained associated with mortality, but age (HR: 1.19, 95% CI: 0.74-1.90, $P = .47$) and SIG (HR: 1.23, 95% CI: 0.89-1.70, $P = .22$) were not.

Five-year survival in patients stratified by CT-SS and SIG is shown in Table III. Patients with CT-SS 0 and SIG 0 had 90% (SE: 4%) 5-year survival compared with 34% (SE: 9%) in patients with CT-SS 2 and SIG ≥2 ($P < .001$). In the CT-SS 2 subgroup, there was a trend toward inferior survival with increasing SIG ($P < .05$), and in the SIG 0 and ≥2 subgroups, there were trends toward inferior survival with increasing CT-SS ($P < .05$).

Figs 1, 2 and 3 display Kaplan-Meier survival plots for subgroups of CT-SS (Fig 1), SIG (Fig 2), and age (Supplementary Fig 2, online only). Regarding CT-SS,

Table I. The relationship between baseline clinical characteristics, preoperative CT-derived body composition parameters, systemic inflammation, and 5-year survival in patients undergoing elective intervention for AAA (N = 611)

	CT-SS 0 (n = 138)	CT-SS 1 (n = 283)	CT-SS 2 (n = 190)	*P* value
Age, years				
<65	21 (15)	17 (6)	7 (4)	
65-75	81 (59)	161 (57)	75 (39)	
>75	36 (26)	105 (37)	108 (57)	**<.001**
Sex				
Male	108 (78)	268 (95)	182 (95)	
Female	30 (22)	15 (5)	8 (4)	**<.001**
Repair type				
Open	34 (25)	63 (22)	25 (13)	
EVAR	104 (75)	220 (78)	165 (87)	**<.01**
BMI, kg/m^2				
<25	23 (17)	51 (18)	53 (28)	
≥25	115 (83)	232 (82)	137 (72)	**<.01**
ASA				
≤2	74 (54)	150 (53)	100 (53)	
>2	62 (46)	132 (47)	90 (47)	.76
High SFI				
Yes	109 (86)	244 (90)	161 (87)	
No	18 (14)	28 (10)	25 (13)	.98
High VFI				
Yes	91 (66)	217 (77)	136 (72)	
No	47 (34)	66 (23)	54 (28)	.37
SIG				
0	75 (54)	149 (53)	96 (51)	
1	42 (30)	96 (34)	63 (33)	
≥2	21 (16)	38 (13)	31 (16)	.51
5-year survival				
Yes	119 (86)	204 (72)	120 (63)	
No	19 (14)	79 (28)	70 (37)	**<.001**

AAA, Abdominal aortic aneurysm; *ASA*, American Society of Anesthesiologists; *BMI*, body mass index; *CT-SS*, computed tomography-derived sarcopenia score; *EVAR*, endovascular aneurysm repair; *SFI*, subcutaneous fat index; *SIG*, systemic inflammatory grade; *VFI*, visceral fat index.
Data are presented as number (%). Boldface *P* values represent significance $P < .05$.
P values generated through linear-by-linear χ^2 analyses comparing proportion of each covariate within each CT-SS subgroup.

mean (95% CI) survival in the CT-SS 0 vs CT-SS 1 vs CT-SS 2 subgroups was 98.1 (88.5-107.7) vs 87.3 (82.0-92.7) vs 72.4 (64.7-80.0) months, respectively ($P < .001$). Regarding SIG, mean (95% CI) survival in the SIG 0 vs SIG 1 vs SIG ≥2 subgroups was 89.9 (82.6-97.1) vs 85.5 (77.9-93.1) vs 71.5 (62.4-80.6) months, respectively ($P < .05$). Regarding age, mean (95% CI) survival in the age <65 vs age 65-75 vs age >75 subgroups was 97.8 (87.1-108.4) vs 94.3 (86.8-101.8) vs 72.7 (66.3-79.1) months, respectively ($P < .001$). Mean (95% CI) survival in the CT-SS 0 and SIG 0 subgroup was 92.6 (84.8-100.4) months compared with 44.9 (30.6-59.2) months in the CT-SS 2 and SIG ≥2 subgroup ($P < .001$, Fig 3).

Patients with CT-SS 0 and SIG 0 were younger than those with CT-SS 2 and SIG ≥2 (median age 68 vs 79 years, $P < .001$). To account for this, a sensitivity analysis on patients aged 65-75 years in the CT-SS 0 and SIG 0 and CT-SS 2 and SIG ≥2 subgroups was performed (n = 53). On both univariate Cox proportional hazards model ($P < .001$) and time-to-event ($P < .001$) analyses, patients with CT-SS 2 and SIG ≥2 had inferior survival outcomes.

Baseline variables in propensity-matched cohorts are shown in Supplementary Table I (online only), and histograms of propensity score distributions are shown in Supplementary Fig 3 (online only). The matched CT-SS 0/1 (n = 183) vs CT-SS 2 (n = 190) cohorts were well matched for all variables other than a higher proportion of patients with CT-SS 2 undergoing OSR ($P < .01$). In these matched cohorts, CT-SS 2 was associated with inferior survival on univariate analysis (HR: 1.60, 95% CI: 1.14-2.23, $P < .01$), and mean (95% CI) survival in the

Table II. The association between baseline clinical characteristics, preoperative CT-derived body composition parameters, systemic inflammation, and mortality in patients undergoing elective intervention for AAA (N = 611)

	Univariate			Multivariate		
Covariate	HR	95% CI	*P* value	HR	95% CI	*P* value
Age (<65/65-75/>75)	1.91	1.48-2.45	**<.001**	1.66	1.28-2.14	**<.001**
Female sex	1.09	0.67-1.77	.73	–	–	–
Open repair	0.73	0.49-1.08	.12	–	–	–
BMI ≥25 kg/m^2	0.78	0.56-1.08	.14	–	–	–
ASA >2	1.24	0.93-1.65	.14	–	–	–
High SFI	0.73	0.49-1.10	.13	–	–	–
High VFI	0.82	0.60-1.11	.20	–	–	–
CT-SS (0/1/2)	1.73	1.41-2.12	**<.001**	1.58	1.28-1.94	**<.001**
SIG (0/1/≥2)	1.30	1.08-1.57	**<.01**	1.29	1.07-1.55	**<.01**

AAA, Abdominal aortic aneurysm; *ASA*, American Society of Anesthesiologists; *BMI*, body mass index; *CI*, confidence interval; *CT-SS*, computed tomography-derived sarcopenia score; *HR*, hazard ratio; *SFI*, subcutaneous fat indices; *SIG*, systemic inflammatory grade; *VFI*, visceral fat indices.
Boldface *P* values represent significance $P < .05$.
HR: hazard ratio describing hazard of all-cause mortality during the follow-up period generated through Cox proportional hazards analysis. For covariates with >2 subgroups, the first category was considered as the reference category.

Table III. Percent 5-year survival in patients undergoing elective intervention for abdominal aortic aneurysm (AAA) stratified by the computed tomography-derived sarcopenia score (*CT-SS*) and systemic inflammatory grade (*SIG*) subgroups (N = 611)

	CT-SS 0		CT-SS 1		CT-SS 2		
	n	%5yrOS (%SE)	n	%5yrOS (%SE)	n	%5yrOS (%SE)	
SIG 0	75	90% (SE 4%)	149	77% (SE 4%)	96	66% (SE 5%)	***P* < .01**
SIG 1	42	83% (SE 6%)	96	66% (SE 5%)	63	73% (SE 6%)	$P = .51$
SIG ≥2	21	79% (SE 9%)	38	66% (SE 8%)	31	34% (SE 9%)	***P* < .01**
		$P = .32$		$P = .24$		***P* < .001**	

%5yrOS, % 5-year overall survival; *SE*, standard error.
Boldface *P* values represent significance $P < .05$.

CT-SS 0/1 vs CT-SS 2 cohorts was 79.5 (74.0-84.9) vs 72.4 (64.7-80.0) months ($P < .01$). The matched SIG 0/1 (n = 89) vs SIG ≥2 (n = 90) cohorts were well matched for all variables other than a higher proportion of patients with SIG ≥2 undergoing OSR ($P < .01$) and having a higher ASA ($P < .001$). In these matched cohorts, SIG ≥2 was not associated with inferior survival on univariate analysis (HR: 1.36, 95% CI: 0.86-2.15, $P = .19$), and mean (95% CI) survival in the SIG 0/1 vs SIG ≥2 cohorts was 72.6 (66.3-78.9) vs 71.4 (62.3-80.6) months ($P = .19$).

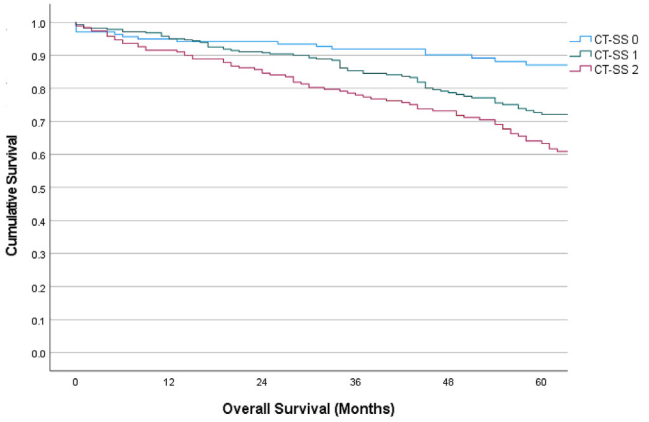
In patients who underwent EVAR, 431 (88%) had data available on sac size at planned 12-month follow-up. Of these, 202 (47%) were noted to have ≥5 mm sac regression. Neither CT-SS (odds ratio: 0.98, 95% CI: 0.75-1.26, $P = .84$) nor SIG (odds ratio: 0.84, 95% CI: 0.65-1.10, $P = .20$) was associated with sac regression.

In order to account for selection bias due to patients with missing preoperative CT-SS or SIG, patients who were excluded on this basis were compared with the final study cohort (Supplementary Table II, online only). Compared with patients who were excluded, the final study cohort had a higher proportion of females (9% vs 2%, $P < .01$) and a higher proportion of patients with ASA >2 (47% vs 36%, $P < .05$), whereas other characteristics were similar. Survival analysis was performed on this subgroup and compared with the final study cohort; mean (standard deviation) survival in the excluded subgroup was 98.2 (85.7-110.7) months, comparable to the final study cohort ($P = .74$).

DISCUSSION

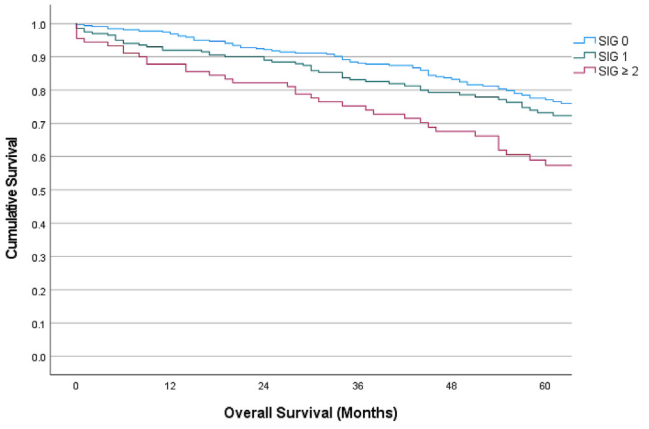
The results of the present study highlight the independent prognostic association of body composition and systemic inflammation in patients undergoing elective intervention for AAA. These associations have been explored separately in prior studies[6,12]; however, to our knowledge, this is the first study to demonstrate the combined prognostic value in this patient group. Furthermore, we add the novel observation of the prognostic value of the combined CT-SS in patients with AAA.

Optimal prognostication in patients undergoing elective intervention for AAA is a clinically relevant and important area for service improvement. The landmark EVAR-2 trial failed to demonstrate a survival advantage



	Number at Risk					
Months	0	12	24	36	48	60
CT-SS 0	138	131	128	118	98	77
CT-SS 1	283	271	251	214	164	119
CT-SS 2	190	174	158	139	112	84

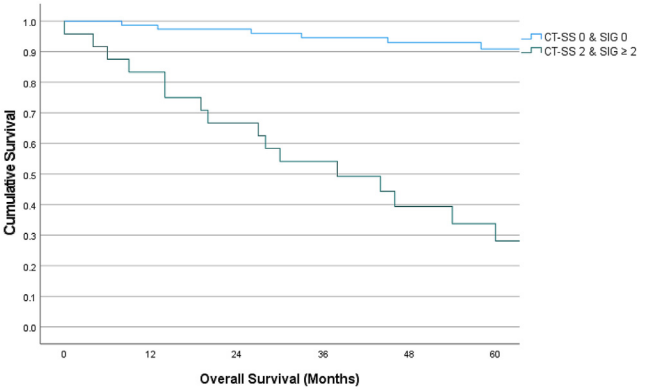
Fig 1. Kaplan-Meier survival plots and life table for computed tomography-derived sarcopenia score (*CT-SS*) (0/1/2) subgroups in patients undergoing elective intervention for abdominal aortic aneurysm (AAA). $P < .001$ (log-rank method).



	Number at Risk					
Months	0	12	24	36	48	60
SIG 0	320	312	289	262	210	154
SIG 1	201	185	174	147	112	89
SIG ≥ 2	90	79	74	62	52	37

Fig 2. Kaplan-Meier survival plots and life table for systemic inflammatory grade (*SIG*) (0/1/≥2) subgroups in patients undergoing elective intervention for abdominal aortic aneurysm (AAA). $P < .05$ (log-rank method).

in performing EVAR vs no treatment in patients unfit for OSR,[17] although these findings have recently been challenged by a contemporary series.[18] Moreover, the recent preliminary observations from the UK-COMPASS study (where poor midterm survival was observed in the endovascular subgroup)[19] emphasize the need for validated



	Number at Risk					
Months	0	12	24	36	48	60
CT-SS 0 & SIG 0	75	74	73	67	54	40
CT-SS 2 & SIG ≥ 2	24	20	16	12	8	6

Fig 3. Kaplan-Meier survival plots and life table for computed tomography-derived sarcopenia score (*CT-SS*) 0 and systemic inflammatory grade (*SIG*) 0 vs CT-SS 2 and SIG ≥2 subgroups in patients undergoing elective intervention for abdominal aortic aneurysm (AAA). $P < .001$ (log-rank method).

prognostic factors to identify those patients who are likely to benefit from prophylactic aneurysm repair, thereby optimizing patient selection and resource allocation. Prognostic tools in this patient cohort have been previously explored, though there remains heterogeneous uptake and a lack of implementation into guidelines.[20] Although rapid calculation and routinely available parameters make SIG an attractive candidate for clinical risk prediction, CT-BC analysis is more time intensive. Feasibility studies of the implementation of CT-BC analysis into preoperative AAA pathways are lacking and may help to resolve the concerns around resource use. A benefit of CT-SS is in its simple scoring system allowing for easy stratification. Direct comparisons between CT-SS, SIG, and other risk prediction tools or frailty assessment scores may allow the optimal strategy to be defined.

Subgroup analyses showed a significantly inferior prognosis in patients with both elevated CT-SS and elevated SIG. The observation of a mean survival of 44.9 months in this subgroup draws into question the merit of elective intervention in such patients, particularly those with aneurysms only modestly above threshold, given recent data suggesting a lower than expected rate of rupture in 55 to 60 mm aneurysms.[21] Absolute numbers in these subgroups may limit the validity of conclusions drawn; however, we describe a potentially "high-risk" patient cohort who may be exposed to substantial long-term cardiovascular morbidity. Although this "high-risk" cohort was older than the "low-risk" patients, steps were taken

to adjust for this and similar trends observed. Further validation of these findings is required; however, the potential clinical utility of CT-SS and SIG, in combination with existing risk predication measures, is highlighted by these results.

The mechanism by which low skeletal muscle mass and density confer inferior prognosis is incompletely described. Of particular interest, on visual inspection of CT-SS survival plots, the divergence between subgroups initially occurs between 18 and 24 months and is sustained throughout later follow-up intervals. This suggests that the predominant survival advantage occurs later in the postoperative period. Repeated follow-up of the present patient cohort with a longer follow-up interval may clarify the nature of the prognostic value of CT-SS in patients with AAA. To better define the benefit of AAA repair in these cohorts, a comparative study investigating CT-SS and SIG in patients who did not undergo repair would be of interest; however, this was outwith the scope of the present study.

Similarly, the mechanism underlying inferior prognosis in relation to chronic activation of the SIR in this patient group is incompletely understood. Inferior short-term survival has been reported in patients who experience a significant inflammatory response both before and after EVAR.[12,22] Chronic inflammation appears to predispose patients to cardiovascular events, and cytokine blockade (interleukin [IL]-1β) has been shown to reduce cardiovascular morbidity in a large trial of patients with coronary artery disease.[23] Patients with AAA typically have a high prevalence of synchronous atherosclerotic disease, indicating a potential susceptibility to cardiovascular events, which may explain the increased mortality conferred by chronic activation of the SIR in this patient group. Furthermore, an association between clinical frailty and inflammation has been described.[24] The presence of both abnormal skeletal muscle and chronic inflammation may have a composite effect on physical function and performance status, impairing physiological reserve and predisposing to inferior outcomes.

The present study did not observe an association between elevated CT-SS and magnitude of SIG. This is in contrast to studies from patients with cancer, which observed the association between activation of the SIR and both SMI and SMD.[25–27] There appears to be an association between the presence of a tumor and elevated magnitude of systemic inflammation.[28,29] Chronic activation of the SIR may result in a proteolytic catabolic state, mediated by cytokines such as tumor necrosis factor, IL-6, and IL-1β,[30,31] which may be responsible for altered skeletal muscle volume and function. It may be that this relationship is less marked in patients with AAA due to the lower magnitude of systemic inflammation as compared with patients with colorectal cancer. This complex mechanistic pathway requires further prospective characterization, with interventional studies performing longitudinal CT-BC analysis, a potential route to a more comprehensive understanding. Upcoming studies[32] investigating the effect of immunomodulation in patients with coronary artery disease are eagerly awaited and may be reproducible in other cardiovascular patient groups, particularly those with AAA.

The present study did not observe an association between elevated CT-SS or SIG and sac regression at 12 months. Although prior series have demonstrated an association between early postoperative inflammation and sac dynamics,[22] these observations are not widely reported, and this potential relationship requires further prospective evaluation.

Limitations. The present study is limited by retrospective study design and the use of data-derived thresholds for CT-BC analysis, which are a potential source of bias and require external validation. There were a considerable number (19%) of potentially eligible patients who were excluded because of missing data; however, steps were taken to mitigate the potential risk of bias through comparative analyses of excluded patients. Low absolute numbers in some subgroups of CT-SS and SIG limit the conclusions drawn. The observations may have been strengthened through reporting of perioperative/30-day mortality; however, the low rate (0.8%) precluded meaningful comparisons between subgroups. Ideally, a "disease-free" control group for comparison would strengthen the present study by allowing us to investigate whether the survival differences seen are present independent of disease state. However, this is not feasible given the need to obtain CT imaging and the inherent risks associated with exposure to contrast medium and ionizing radiation. Moreover, the results of the present study contribute to the growing body of evidence describing inferior prognosis in sarcopenic, inflamed patients across a range of disease states. Although we infer that the major cause of mortality is cardiovascular, given that specific cause of death is not available, this is a potential source of bias. The lack of in-hospital complication data may limit the clinical utility of the present study and requires further investigation.

CONCLUSIONS

The results in the present study describe a potential novel prognostic role for CT-BC and SIG in patients with AAA undergoing elective intervention. The use of these measures to identify patients at a high risk of poor outcome may allow for the development of targeted therapies or expectant management of certain high-risk groups. Further prospective analysis of AAA cohorts is required, including to externally validate the thresholds used by the present study.

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AUTHOR CONTRIBUTIONS

Conception and design: NB, CR, DM, GG
Analysis and interpretation: NB, GG
Data collection: NB, A Walter, A Wilson, TS
Writing the article: NB, A Walter
Critical revision of the article: A Wilson, TS, CR, DM, GG
Final approval of the article: NB, A Walter, A Wilson, TS, CR, DM, GG
Statistical analysis: NB, A Walter
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Overall responsibility: GG

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Supplementary Table I (online only). The comparison between clinical parameters, CT-BC parameters, and systemic inflammation in subgroups propensity matched for computed tomography-derived sarcopenia score (*CT-SS*) and systemic inflammatory grade (*SIG*)

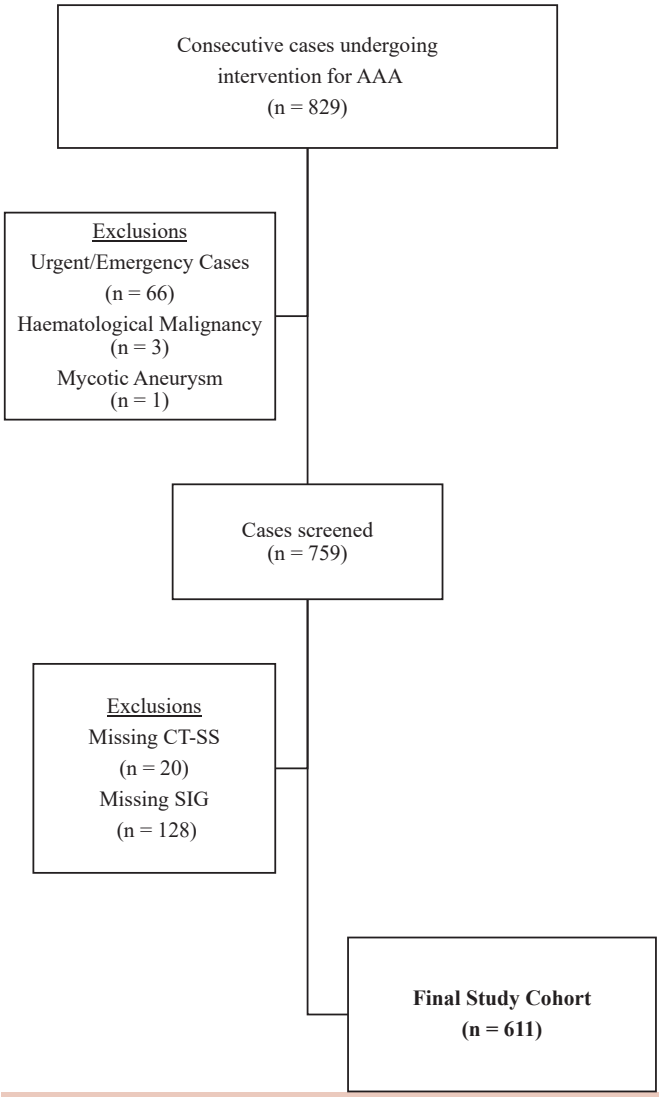
	CT-SS 0/1 (n = 183)	CT-SS 2 (n = 190)	*P* value	SIG 0/1 (n = 89)	SIG ≥2 (n = 90)	*P* value
Age, years						
<65	7 (4)	7 (4)		4 (4)	4 (5)	
65-75	75 (41)	75 (40)		39 (44)	40 (44)	
>75	101 (55)	108 (56)	.76	46 (52)	46 (51)	.95
Sex						
Male	175 (96)	182 (96)		81 (91)	81 (90)	
Female	8 (4)	8 (4)	.94	8 (9)	9 (10)	.82
Repair type						
Open	8 (4)	25 (13)		1 (1)	16 (18)	
EVAR	175 (96)	165 (87)	**<.01**	88 (99)	74 (82)	**<.001**
BMI, kg/m^2						
<25	46 (25)	53 (28)		23 (26)	24 (27)	
≥25	137 (75)	137 (72)	.55	66 (74)	66 (73)	.90
ASA						
≤2	107 (59)	100 (53)		60 (68)	37 (42)	
>2	75 (41)	90 (47)	.23	28 (32)	52 (58)	**<.001**
High SFI						
Yes	153 (85)	161 (87)		75 (86)	73 (86)	
No	27 (15)	25 (13)	.67	12 (14)	12 (14)	.95
High VFI						
Yes	126 (69)	136 (72)		61 (68)	58 (64)	
No	57 (31)	54 (28)	.57	28 (32)	32 (36)	.56
CT-SS						
0	–	–		21 (24)	21 (23)	
1	–	–		37 (42)	38 (42)	
2	–	–	–	31 (34)	31 (35)	.99
SIG						
0	93 (51)	96 (51)		–	–	
1	61 (33)	63 (33)		–	–	
≥2	29 (16)	31 (16)	.92	–	–	–

ASA, American Society of Anesthesiologists; *BMI*, body mass index; *CT-BC*, computed tomography-derived body composition analysis; *EVAR*, endovascular aneurysm repair; *SFI*, subcutaneous fat index; *VFI*, visceral fat index.
Data are presented as number (%). Boldface *P* values represent significance $P < .05$.
P values generated through linear-by-linear χ^2 analyses comparing proportion of each covariate within each subgroup.

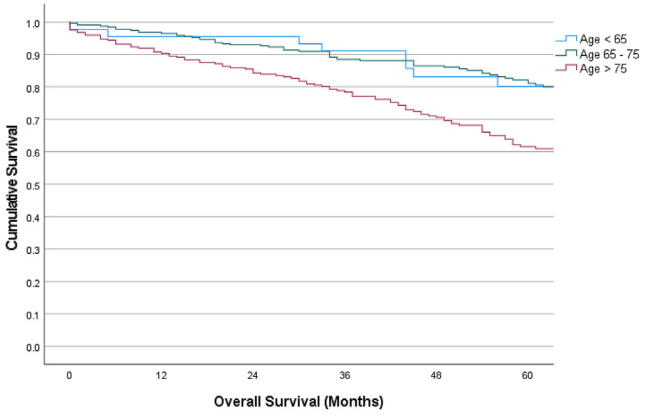
Supplemental Table II (online only). The comparison between the final study cohort and patients excluded from the study on the basis of missing computed tomography-derived sarcopenia score (*CT-SS*) or systemic inflammatory grade (*SIG*)

	Excluded patients (n = 148)	Final study cohort (n = 611)	*P* value
Age, years			
<65	8 (5)	45 (7)	
65-75	90 (61)	317 (52)	
>75	50 (34)	249 (41)	.21
Sex			
Male	145 (98)	558 (91)	
Female	3 (2)	53 (9)	**<.01**
Repair type			
Open	33 (22)	122 (20)	
EVAR	115 (78)	489 (80)	.53
BMI, kg/m^2			
<25	31 (22)	127 (21)	
≥25	112 (78)	484 (79)	.81
ASA			
≤2	94 (64)	324 (53)	
>2	53 (36)	284 (47)	**<.05**
High SFI			
Yes	101 (84)	514 (88)	
No	20 (16)	71 (12)	.19
High VFI			
Yes	101 (73)	444 (73)	
No	37 (27)	167 (27)	.90
CT-SS[a]			
0	27 (22)	138 (23)	
1	64 (51)	283 (46)	
2	34 (27)	190 (31)	.68
SIG[a]			
0	11 (55)	320 (52)	
	6 (30)	201 (33)	
≥2	3 (15)	90 (15)	.89
5-year survival			
Yes	110 (74)	440 (72)	
No	38 (26)	171 (28)	.84

ASA, American Society of Anesthesiologists; *BMI*, body mass index; *EVAR*, endovascular aneurysm repair; *SFI*, subcutaneous fat index; *VFI*, visceral fat index.
Data are presented as number (%). Boldface *P* values represent significance $P < .05$.
P values generated through linear-by-linear χ^2 analyses comparing proportion of each covariate within each subgroup.
[a]Some missing data in the excluded subgroup.

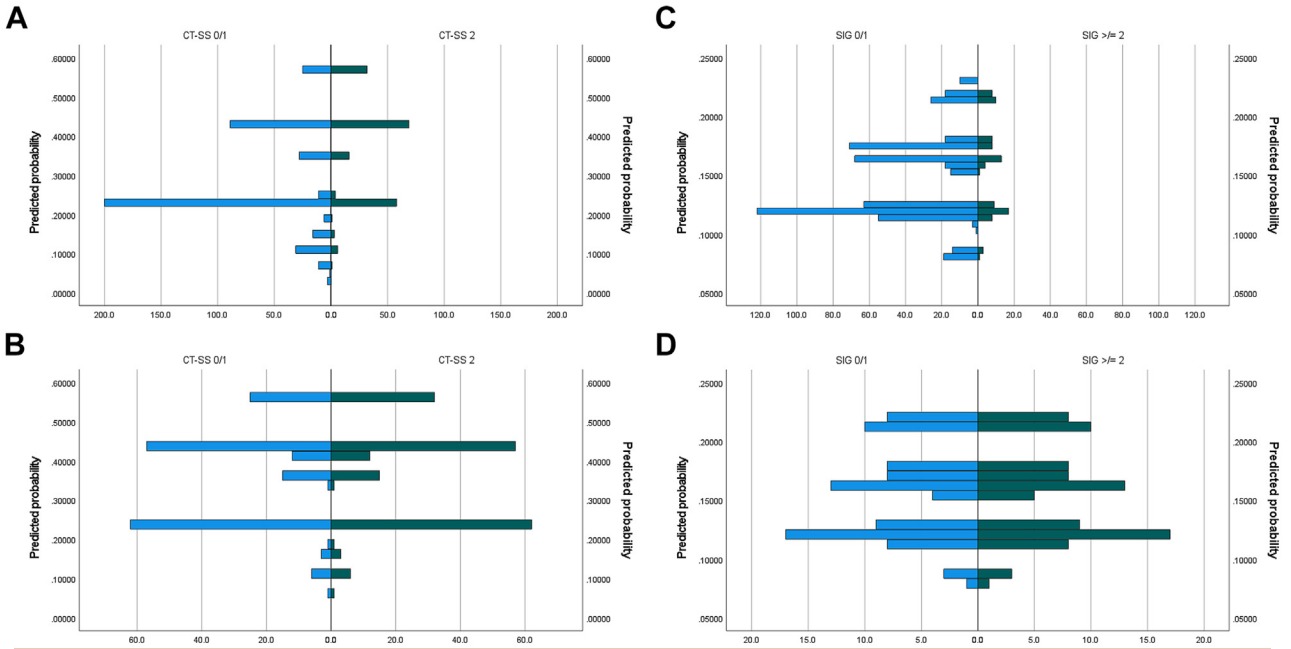


Supplementary Fig 1 (online only). Patient selection into the study. *AAA*, Abdominal aortic aneurysm; *CT-SS*, computed tomography-derived sarcopenia score; *SIG*, systemic inflammatory grade.



	Number at Risk					
Months	**0**	**12**	**24**	**36**	**48**	**60**
Age < 65	45	43	43	41	30	23
Age 65 - 75	317	307	284	251	196	156
Age > 75	249	226	210	179	148	101

Supplementary Fig 2 (online only). Kaplan-Meier survival plots and life table for age (<65/65-75/>75 years) subgroups in patients undergoing elective intervention for abdominal aortic aneurysm (AAA). $P < .001$ (log-rank method).



Supplementary Fig 3 (online only). Distribution of propensity scores in the unmatched and matched cohorts: **(A)** computed tomography-derived sarcopenia score (*CT-SS*) prematch, **(B)** CT-SS postmatch, **(C)** systemic inflammatory grade (*SIG*) prematch, and **(D)** SIG postmatch.