RESEARCH LETTER

Low Subcutaneous Adipose Tissue is Associated with Poor Prognosis for Aged Patients with Cutaneous Angiosarcoma: A Retrospectiv e Cohort Study

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Submitted Sept 28, 2025. Accepted after revision Dec 8, 2025
Published Feb 11, 2026. DOI: 10.2340/actadv.v106.adv-2025-0058 Acta Derm Venereol 2026; 106: adv-2025-0058.

To the Editor,

Cutaneous angiosarcoma is a highly malignant sarcoma derived from vascular endothelium. It frequently develops on the scalp of the elderly, and the outcomes remain dismal. Low body weight adversely affects the prognosis of cancer patients (1). To investigate which components of body mass index (BMI) are associated with prognosis, we addressed body composition. Adipose tissue index (ATI) and skeletal muscle index (SMI) can be measured non-invasively using routine abdominal computed tomography (CT). We investigated ATI as a prognostic predictor in angiosarcoma, a representative malignant tumour in the elderly.

Thirty six patients were extracted based on the Japanese Diagnosis Procedure Combination database of our hospital from January 2011 to December 2023. The primary composite end-point was event-free survival (EFS): the time from CT at the initial visit to death/transfer to best supportive care. Areas of adipose tissue (AT) and skeletal muscle were measured using AI-assisted SYNAPSE VINCENT software (FUJIFILM Corporation, Tokyo, Japan) (Appendix S1). Values were normalized for height (cm^2/m^2) (See Appendix S2 for detailed materials and methods).

The baseline characteristics are shown in Table SI. Twenty-seven events had occurred at the time of data analysis. The univariate and multivariate analyses are shown in **Table I**. Among the previously defined factors, ATI [hazard ratio (HR)=0.9830, 95% confidence interval (95% CI)=0.9686–0.9966, p=0.0187], subcutaneous ATI (HR=0.9735, 95% CI=0.9502–0.9954, p=0.0228), BMI (HR=0.8155, 95% CI=0.6647–0.9861, p=0.0429), stage (HR=4.604, 95% CI=1.590–13.33, p=0.0049), and radiation therapy (RT) status (HR=0.1578, 95% CI=0.04317–0.5765, p=0.0052) were significantly associated with EFS in univariate analysis (Table I). Visceral ATI and SMI were not significantly associated with EFS. In the multivariate analysis of subcutaneous ATI, BMI, stage and RT, subcutaneous ATI was significantly associated with EFS (HR=0.9696, 95% CI=0.9423–0.9943, p=0.0230) (Table I). BMI was not significantly associated with EFS (HR=0.8596, 95% CI=0.6935–1.053, p=0.1524). Stratification by subcutaneous ATI found a poorer prognosis for subcutaneous ATI<35 cm^2/m^2 than for subcutaneous ATI>35 cm^2/m^2 (p=0.0313) (**Fig. 1**).

ATI and subcutaneous ATI predicted the prognosis more accurately than BMI or even performance status. Within the BMI range of 20–25, subcutaneous ATI values span 23–84. It is difficult to directly estimate subcutaneous ATI from BMI. Generally, people with pear-shaped bodies are likely to have more subcutaneous AT. Abdominal skinfold is known to correlate with subcutaneous AT measured by CT (2). Using these body features may help in estimating subcutaneous AT volume easily, although there is a limitation in accuracy. Ebadi et al. reported that low subcutaneous ATI is associated with shorter survival in gastrointestinal and respiratory cancers

Table I. Univariate and multivariate analyses

	Univariate analyses			Multivariate analyses		
	HR	95% CI	*p*	HR	95% CI	*p*
Age	1.019	0.9722–1.072	0.4413			
Sex (female, ref=male)	0.8466	0.3599–1.991	0.7028			
ECOG PS (1–2, ref=0)	1.153	0.4590–2.897	0.7617			
Stage (3–4, ref=1–2)	4.604	1.590–13.33	**0.0049**	6.257	1.839–21.29	**0.0033**
Chemotherapy (paclitaxel, ref=other)	0.7198	0.3120–1.661	0.4409			
Radiation therapy (yes, ref=no)	0.1578	0.04317–0.5765	**0.0052**	0.2067	0.05240–0.8154	**0.0244**
BMI (kg/m^2)	0.8155	0.6647–0.9861	**0.0429**	0.8593	0.6935–1.053	0.1524
SMI (cm^2/m^2)	0.9871	0.9401–1.036	0.5950			
ATI (cm^2/m^2)	0.9830	0.9686–0.9966	**0.0187**			
Subcutaneous ATI (cm^2/m^2)	0.9735	0.9502–0.9954	**0.0228**	0.9696	0.9423–0.9943	**0.0230**
Visceral ATI (cm^2/m^2)	0.9860	0.9632–1.005	0.1883			

ATI:adipose tissue index; BMI:body mass index; CI:confidence interval; ECOG PS:Eastern Cooperative Oncology Group Performance Status; HR:hazard ratio; SMI:skeletal muscle index.

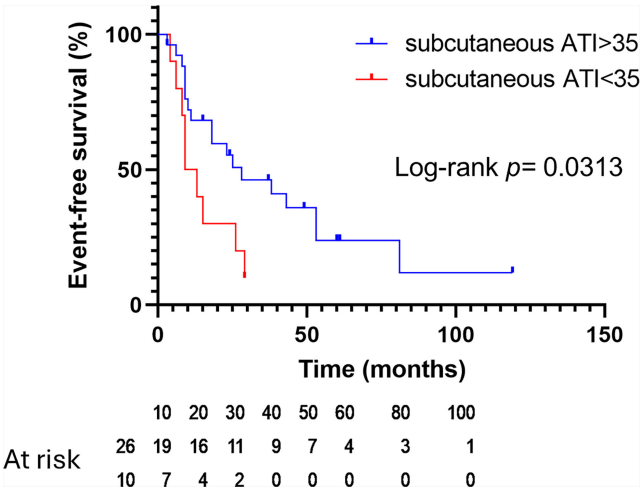

Fig. 1. Kaplan–Meier estimates of event-free survival (EFS) stratified on subcutaneous adipose tissue index (ATI). Red line, subcutaneous ATI<35; blue line, subcutaneous ATI>35. Censored data points are marked with crosses.

and in metastatic renal cell carcinoma in Canada (3. Mengoni et al. reported that abundant subcutaneous AT is associated with enhanced objective response rate to immune checkpoint inhibitors and prolonged progression-free survival in metastatic melanoma (4. Evidence of a link between subcutaneous AT and prognosis has been steadily accumulating. Our study clarifies this association in an elderly Asian cohort with rapidly progressive cutaneous malignancies. ATI primarily reflects a patient's nutritional status. Consistent with our univariate analysis, low BMI is associated with poor prognosis in soft-tissue sarcoma among patients aged ≥60 years (5. However, low body weight might be a consequence rather than a cause of that prognosis. Cancer-related systemic inflammatory response contributes to malnutrition (6. Subcutaneous AT produces the anti-inflammatory cytokine adiponectin, whose expression is higher in subcutaneous AT than in visceral AT in human subjects (7. Serum adiponectin is positively associated with subcutaneous AT volume but inversely associated with visceral AT volume in Japanese men (8. These findings suggest that subcutaneous AT not only reflects nutritional status but also actively participates in the inflammatory response and cancer progression. This condition may be shared among malignant tumours associated with poor prognosis in elderly patients.

ACKNOWLEDGEMENTS

Funding sources: This work was financially supported by JST SPRING under Grant Number JPMJSP2125.

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

The authors have no conflicts of interest to declare.

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