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Original Article

Subcutaneous Adipose Tissue Attenuation Change on Chest CT Is Associated with Overall Survival After Allogeneic Hematopoietic Stem Cell Transplantation

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ABSTRACT

OBJECTIVE: Early chest computed tomography (CT) examinations are frequently performed after allogeneic hematopoietic stem cell transplantation (allo-HSCT) due to respiratory symptoms or clinical deterioration. Subcutaneous adipose tissue attenuation (SATA) has recently been proposed as a quantitative imaging marker of systemic tissue alterations related to fluid redistribution and inflammatory processes. This study aimed to evaluate interval changes in SATA after allo-HSCT and to investigate their association with overall survival.

MATERIAL AND METHODS: In this retrospective single-center study, adult allo-HSCT recipients who underwent non-contrast chest CT both before transplantation and within 30 days after transplantation were included. SATA was measured in Hounsfield units (HU) using standardized circular regions of interest placed in the anterior chest wall. The interval change in attenuation Hounsfield units (ΔHU) was calculated as post-transplant minus pre-transplant values. Cox proportional hazards regression was used to assess the association between ΔHU and survival. Kaplan–Meier analysis was performed after dichotomization according to the median ΔHU value.

RESULTS: A total of 104 patients were included. SATA increased on early post-transplant CT compared with baseline ($P < 0.001$). Higher ΔHU values were associated with worse overall survival (hazard ratio per 5-HU increase: 1.18; 95% confidence interval: 1.03–1.35; $P = 0.016$). Patients with ΔHU above the median (16-HU) demonstrated significantly poorer survival compared with those below the median (log-rank $P = 0.0003$).

CONCLUSION: SATA increases after allo-HSCT, and greater interval increases are associated with worse survival outcomes. Quantitative assessment of SATA may provide a simple, non-invasive imaging biomarker for early risk stratification in allo-HSCT recipients.

KEYWORDS: Allogeneic hematopoietic stem cell transplantation, chest CT, subcutaneous adipose tissue attenuation, imaging biomarker, overall survival

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INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains a potentially curative treatment for a wide range of hematologic malignancies and bone marrow failure syndromes. Despite advances in conditioning regimens, donor selection, and supportive care, allo-HSCT continues to be associated with substantial early morbidity and mortality related to treatment toxicity, immune activation, endothelial injury, and systemic inflammatory responses.[1-3] Early identification of patients at increased risk of adverse outcomes remains an important clinical challenge in the post-transplant period.

Chest computed tomography (CT) is frequently performed in allo-HSCT recipients during the early post-transplant phase because of respiratory symptoms, fever, or non-specific clinical deterioration.[4-6] In addition to detecting pulmonary complications such as infection, drug-related lung injury, or graft-related inflammatory processes, CT examinations also provide quantitative information regarding extrapulmonary tissues. Increasingly, CT-derived body composition and tissue attenuation parameters have been recognized as potential imaging biomarkers reflecting systemic physiological or pathological states.[7]

Adipose tissue is no longer considered a passive energy storage compartment but rather a metabolically active tissue with important structural and endocrine functions.[8,9] In recent years, CT-based measurements of adipose tissue quality—commonly assessed through attenuation values in Hounsfield units (HU)—have been associated with cardiometabolic risk and other adverse clinical outcomes.[10-12]

In particular, increased attenuation of subcutaneous adipose tissue on CT may reflect changes in tissue composition and fluid content. In a recent chest CT study, subcutaneous fat tissue density was markedly higher in patients with pulmonary edema than in patients with viral or Pneumocystis jirovecii pneumonia and healthy controls.[11] Histologic data from other clinical settings also suggest that higher subcutaneous adipose tissue radiodensity can be accompanied by smaller adipocytes and expansion of the interstitial compartment.[12] Because CT examinations are commonly performed in transplant recipients, quantitative assessment of subcutaneous adipose tissue attenuation (SATA) may provide additional information beyond conventional radiologic findings.

However, the potential clinical relevance of SATA in allo-HSCT recipients has not been systematically investigated. In particular, it remains unclear whether interval changes in SATA following transplantation may be associated with clinical outcomes such as overall survival.

Therefore, the aim of the present study was to evaluate changes in SATA on chest CT before and after allo-HSCT and to investigate whether the interval change in attenuation Hounsfield units (ΔHU) is associated with overall survival. We hypothesized that early changes in SATA may reflect systemic tissue alterations detectable on CT and may be associated with prognosis in allo-HSCT recipients.

MATERIAL AND METHODS

Study Design and Population

This retrospective single-center study was approved by the Koç University Biomedical and Retrospective Research Ethics Committee (approval number: 2026.077.IRB2.039; February 11, 2026). The requirement for informed consent was waived by the Ethics Committee because of the retrospective design of the study. Patient anonymity was preserved, and all data were handled in accordance with institutional and international ethical standards.

Chest CT examinations of patients who underwent allo-HSCT between December 4, 2017, and June 13, 2025, were retrospectively reviewed. As shown in Figure 1, patients with radiological or clinical evidence of infection, those diagnosed with pulmonary edema, those with non-120 kVp CT acquisition, and patients with insufficient CT image quality were excluded from the analysis. Among the remaining patients, adult recipients (≥18 years) who had both pre-transplant and early post-transplant non-contrast chest CT examinations were included.

Early post-transplant CT examinations were defined as CT scans obtained within the first 30 days after transplantation. After applying the inclusion and exclusion criteria, the final study population consisted of patients with available paired pre- and post-transplant CT examinations suitable for quantitative analysis. The interval between the baseline CT examination and allogeneic HSCT was recorded and summarized as the median and interquartile range (IQR).

Clinical information including age, sex, underlying hematologic diagnosis, transplantation date, mortality status, and follow-up duration was obtained from institutional electronic medical records. In addition, the hematopoietic cell transplantation-comorbidity index (HCT-CI) and the occurrence of clinically significant graft-versus-host disease (GVHD) were recorded. GVHD was analyzed as a binary variable and defined as the presence of grade III–IV acute GVHD (yes/no).

Computed Tomography Acquisition Protocol

All chest CT examinations were performed using 64–detector row CT systems (Somatom® Definition AS and Somatom® Definition Flash; Siemens Healthineers, Forchheim, Germany). Scans were obtained without intravenous contrast administration with patients in the supine position during end-inspiratory breath-hold and with the arms positioned above the head.

The scan range extended from the lung apices to the costophrenic angles. Tube voltage was standardized at 120 kVp, and tube current was adjusted using automatic exposure modulation. Images were acquired with a 512 × 512 matrix and a patient-adapted reconstruction field of view. Images were reconstructed using a medium soft-tissue convolution kernel with slice thicknesses ranging from 1 to 3 mm. For each patient, pre- and post-transplant CT examinations were evaluated using image series reconstructed with the same slice thickness.

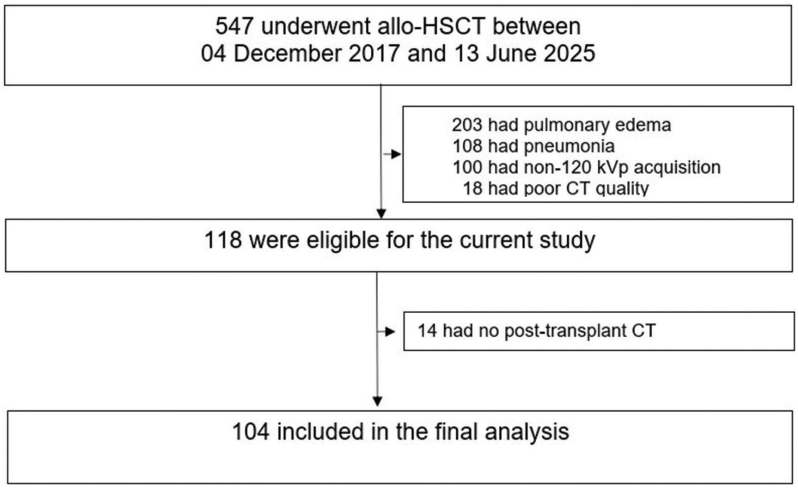

Figure 1. Flowchart of the study population

HSCT: hematopoietic stem cell transplantation, CT: computed tomography

Measurement of Subcutaneous Adipose Tissue Attenuation

SATA was measured on axial CT images. Mediastinal window settings (window width: 350 HU; window level: 50 HU) were used only to facilitate consistent anatomical localization and region of interest (ROI) placement.

A circular ROI with a diameter of approximately 1 cm was placed within the subcutaneous adipose tissue of the anterior chest wall at a standardized anatomical location defined by the intersection of the midclavicular line and the level of the xiphoid tip. At the predefined anatomical level, three separate circular ROI measurements were obtained from the subcutaneous adipose tissue while avoiding skin, breast tissue, muscle, vessels, fibrous septa, and imaging artifacts. The mean of these three measurements was used as the final SATA value for each CT examination. Care was taken to avoid inclusion of skin, breast tissue, muscle, vessels, fibrous septa, or imaging artifacts.

Mean attenuation values were recorded in HU. Measurements were performed on both pre-transplant and post-transplant CT scans. The ΔHU was calculated as: ΔHU = Post-transplant SATA − Pre-transplant SATA. To assess measurement reproducibility, all CT examinations were re-measured by the same thoracic radiologist after a 4-week interval while blinded to the initial measurements. For the primary analyses, the initial measurements were used. Repeat measurements were performed solely for intraobserver reproducibility assessment and were not averaged with the initial measurements. Intraobserver agreement was assessed using the intraclass correlation coefficient (ICC).

Representative pre- and early post-transplant CT images demonstrating ROI placement are shown in Figure 2.

Assessment of Pleural and Pericardial Effusions

Pleural and pericardial effusions were evaluated on early post-transplant CT examinations. Effusion thickness was measured on axial images at the point of maximal fluid accumulation perpendicular to the adjacent pleural or pericardial surface. Measurements were recorded in millimeters.

These findings were evaluated as contextual imaging parameters reflecting possible fluid redistribution in the early post-transplant period.

Outcome Definition

The primary outcome of the study was overall survival. Survival time was calculated from the date of allo-HSCT to the date of death or last clinical follow-up. Patients who were alive at the last follow-up were censored at that date.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation or median (IQR), as appropriate. Categorical variables were presented as counts and percentages.

Pre- and post-transplant SATA measurements were compared using the paired-samples t-test.

Overall survival was calculated from the date of allo-HSCT to death from any cause or last clinical follow-up. The association between the ΔHU and overall survival was first evaluated using univariable Cox proportional hazards regression with ΔHU analyzed as a continuous variable (per 5 HU increase). Multivariable Cox regression analysis was then performed to adjust for clinically relevant covariates including age, sex, underlying hematologic diagnosis, the HCT-CI, and GVHD. Because pleural and pericardial effusions may represent downstream manifestations of the same biological pathway reflected by ΔHU, these variables were evaluated in separate sensitivity analyses rather than included in the primary multivariable model. Owing to missing values for HCT-CI and GVHD, analyses including these variables were performed using complete-case data. As an additional sensitivity analysis, the interval between the baseline CT examination and transplantation was included in the multivariable model to assess whether variability in baseline CT timing influenced the observed association between ΔHU and survival.

To facilitate visualization of survival patterns, patients were additionally dichotomized according to the cohort median

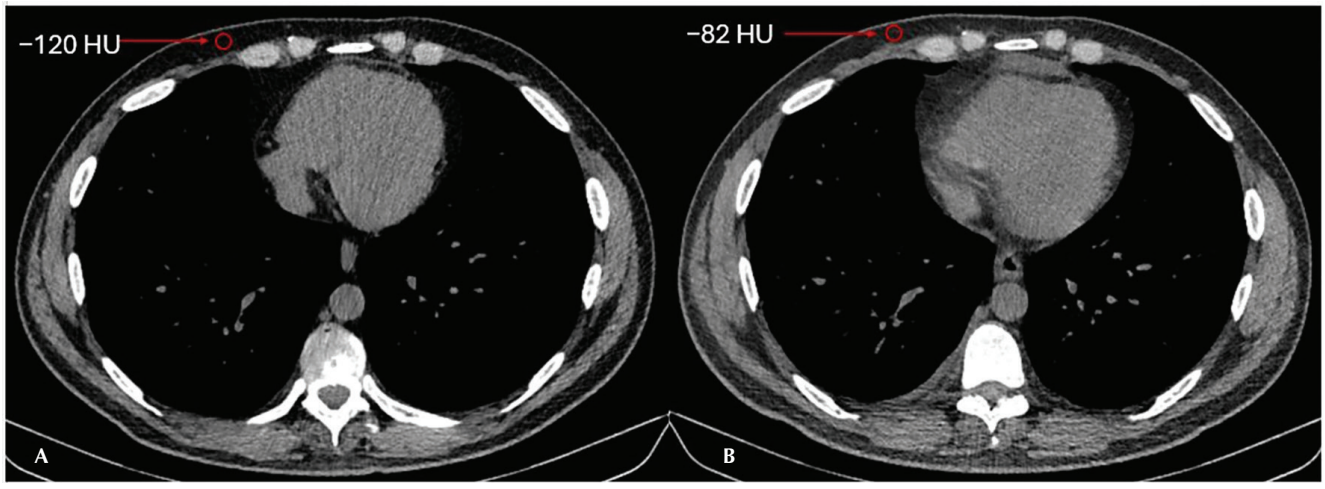

Figure 2. Representative axial non-contrast chest CT images demonstrating subcutaneous adipose tissue attenuation measurements before (A) and after (B) allogeneic hematopoietic stem cell transplantation. A circular region of interest (ROI) was placed within the anterior chest wall subcutaneous adipose tissue at the level of the xiphoid tip while avoiding skin, muscle, vessels, fibrous septa, and imaging artifacts. The displayed attenuation values represent the mean ROI attenuation (HU)

CT: computed tomography, HU: Hounsfield units

ΔHU value, and Kaplan–Meier survival curves were compared using the log-rank test. Because the median represented a data-derived cutpoint, this analysis was considered descriptive and intended for visualization rather than confirmatory inference. Univariable Cox regression was also performed using the dichotomized ΔHU variable.

The proportional hazards assumption was evaluated for the Cox regression models, and the linearity of the continuous ΔHU term was assessed before final model interpretation. All statistical tests were two-sided, and a *P* value <0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 28.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Patient Characteristics

As illustrated in Figure 1, a total of 104 patients were included in the final analysis. As summarized in Table 1, the baseline CT examination was performed a median of 10 days before transplantation (IQR: 9–16 days). The mean age of the study population was 51.5±14.5 years, and 63 patients (60.6%) were male. The most common indications for allo-HSCT were acute myeloid leukemia, acute lymphoblastic leukemia, and non-Hodgkin lymphoma. During the follow-up period, 54 deaths (51.9%) were observed. The median follow-up duration was 15.2 months (IQR: 3.9–40.1 months).

Changes in Subcutaneous Adipose Tissue Attenuation

SATA increased significantly on early post-transplant CT compared with pre-transplant baseline measurements. The mean pre-transplant SATA value was −113.0±8.4 HU, whereas the mean post-transplant SATA value was −96.5±9.6 HU. The mean ΔHU was 16.5±10.8 HU, indicating a substantial increase in adipose tissue attenuation after transplantation (Table 2). Intraobserver reproducibility was good for both pre-transplant and early post-transplant SATA measurements, with ICC values of 0.789 [95% confidence interval (CI), 0.705–0.845] and 0.879 (95% CI, 0.825–0.911), respectively.

Association Between ΔHU and Survival

Overall survival was calculated from the date of transplantation. In univariable Cox regression, increasing ΔHU values were

Table 1. Baseline characteristics of the study population

Variable	Value
Number of patients	**104**
Age (mean ± SD), years	51.5±14.5
Male sex	63 (60.6%)
Female sex	41 (39.4%)
Underlying hematologic diagnosis	
• Acute myeloid leukemia	37 (35.6%)
• Acute lymphoblastic leukemia	16 (15.4%)
• Non-Hodgkin lymphoma*	20 (19.2%)
• Myelodysplastic syndrome	8 (7.7%)
• Myelofibrosis	5 (4.8%)
• Hodgkin lymphoma	4 (3.8%)
• Other diagnoses	14 (13.5%)
GVHD > grade II†	11/54 (20.4%)
HCT-CI‡	Median 2 (IQR 0–3)
Deaths	54 (51.9%)
Median follow-up (IQR), months	15.2 (3.9–40.1)

Data are presented as mean ± standard deviation (SD), number (percentage), or median [interquartile range (IQR)] as appropriate. Follow-up time was calculated from the date of allogeneic hematopoietic stem cell transplantation to the date of death or last clinical follow-up

*Includes diffuse large B-cell lymphoma, follicular lymphoma, peripheral T-cell lymphoma, and other non-Hodgkin lymphoma subtypes.

†Available in 54 patients

‡Available in 82 patients

GVHD: graft-versus-host disease, HCT-CI: hematopoietic cell transplantation–comorbidity index

associated with higher mortality risk (HR per 5–HU increase, 1.18; 95% CI: 1.03–1.34; $P = 0.017$). After adjustment for age, sex, and underlying hematologic diagnosis, this association remained significant (HR per 5–HU increase, 1.18; 95% CI: 1.03–1.35; $P = 0.016$) (Table 3). Additional adjustment for HCT-CI and GVHD in complete-case analyses yielded similar results. Sensitivity analyses further showed that additional adjustment for pleural and pericardial effusions, as well as for the interval between the baseline CT examination and transplantation, did not materially alter the observed association between ΔHU and overall survival.

For visualization of survival differences, patients were dichotomized according to the cohort median ΔHU value (16 HU). Patients with ΔHU above the median had a significantly higher mortality risk than those below the median in univariable analysis (HR: 2.61; 95% CI: 1.51–4.51; $P = 0.0006$). As shown in Figure 3, Kaplan–Meier analysis demonstrated significantly poorer survival in patients with ΔHU above the median (log-rank $P = 0.0003$). Because the median represented a data-derived cutpoint, this analysis was performed for visualization of survival patterns rather than confirmatory inference. No evidence of non-linearity was observed for the continuous ΔHU term.

DISCUSSION

In this study, we evaluated interval changes in SATA on chest CT in patients undergoing allo-HSCT and investigated their association with overall survival. Our results demonstrate three principal findings. First, SATA increased significantly on early post-transplant CT compared with pre-transplant baseline values. Second, greater ΔHU were consistently associated with worse overall survival across univariable and multivariable Cox regression models, including sensitivity analyses incorporating clinically relevant transplant-related factors. Third, Kaplan–Meier analysis showed significantly poorer survival in patients with ΔHU values above the cohort median. The stronger separation observed in the median-based Kaplan–Meier analysis compared with the continuous per-5–HU model may partly reflect the limited sample size and the use of a data-derived cutpoint, which can accentuate apparent between-group differences; therefore, the dichotomized analysis should be interpreted as descriptive rather than confirmatory.

Allo-HSCT is associated with profound systemic physiological changes related to conditioning regimens, immune activation, endothelial injury, and inflammatory responses.[1-3] These processes may lead to alterations in vascular permeability, tissue fluid balance, and inflammatory signaling pathways. While CT imaging in this population is primarily performed to evaluate pulmonary complications, the technique also provides quantitative information regarding extrapulmonary tissues.[4-7] Pleural effusion, ascites, and pericardial effusion have also been reported after allo-HSCT and may represent manifestations of systemic fluid imbalance and endothelial dysfunction.[13-15]

To our knowledge, this is the first study to investigate interval changes in SATA on CT in patients undergoing allo-HSCT and to evaluate their association with overall survival. In recent

Table 2. Subcutaneous adipose tissue attenuation measurements

Measurement	Mean (HU)	SD
Pre-transplant SATA	−113.0	8.4
Post-transplant SATA	−96.5	9.6
ΔHU	16.5	10.8

SATA: subcutaneous adipose tissue attenuation, HU: Hounsfield unit, ΔHU: interval change in attenuation Hounsfield units

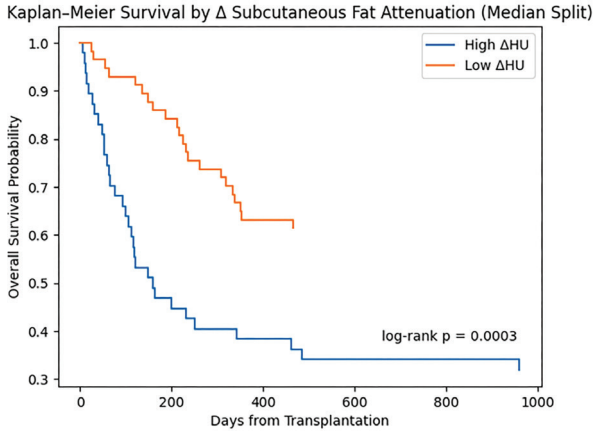

Figure 3. Kaplan–Meier survival curves stratified by the median interval change in attenuation Hounsfield units (ΔHU). Patients with ΔHU above the cohort median (16 HU) showed significantly worse overall survival compared with those below the median (log-rank $P = 0.0003$)

Table 3. Cox regression models for overall survival

Model	Variables included	n/deaths	ΔHU HR per 5 HU	95% CI	*P* value
Univariable	ΔHU	104/54	1.18	1.03–1.34	0.017
Model 1	ΔHU, age, sex, diagnosis	104/54	1.18	1.03–1.35	0.016
Model 2	Model 1 + HCT-CI	82/39	1.24	1.04–1.48	0.016
Model 3	Model 1 + GVHD >2	54/22	1.45	1.13–1.85	0.003
Model 4	Model 1 + HCT-CI + GVHD >2	49/21	1.44	1.09–1.89	0.009
Sensitivity model	Model 4 + any effusion	49/21	1.48	1.12–1.97	0.006

Hazard ratios were estimated using Cox proportional hazards regression. ΔHU represents the interval change in subcutaneous adipose tissue attenuation and is expressed per 5–HU increase. Models including HCT-CI and GVHD were performed as complete-case analyses because of missing data. The sensitivity model additionally included the presence of pleural and/or pericardial effusion

ΔHU: interval change in attenuation Hounsfield units, CI: confidence interval, GVHD: graft-versus-host disease, HCT-CI: hematopoietic cell transplantation–comorbidity index, HR: hazard ratio

years, increasing attention has been directed toward CT-derived tissue attenuation measurements as potential biomarkers of systemic disease states.[7,10-12] Unlike traditional measures of fat quantity, attenuation-based metrics may capture structural or compositional differences within adipose tissue.[10-12]

Subcutaneous adipose tissue is a biologically active tissue whose CT attenuation reflects its composition rather than fat volume alone.[8-10] Higher attenuation values may be associated with lower lipid content and with alterations in the interstitial or cellular components of adipose tissue.[10-12] In the study by Ebadi et al.[12], higher subcutaneous adipose tissue radiodensity was associated with smaller adipocytes, expansion of the interstitial compartment, and increased mortality in patients with cirrhosis.

Previous CT-based studies have shown that adipose tissue attenuation can carry clinically relevant information beyond adipose tissue quantity. Rosenquist et al. demonstrated associations between visceral and subcutaneous fat attenuation and cardiometabolic risk, while Pickhardt et al. showed that automated CT-derived body composition biomarkers can contribute to prediction of future cardiovascular events and mortality.[7,10] In addition, Ebadi et al.[12], reported an association between higher subcutaneous adipose tissue radiodensity and mortality. Together, these findings support the concept that CT-derived adipose tissue attenuation may reflect clinically relevant tissue characteristics.

Our findings extend this concept to the allo-HSCT population. The observed increase in SATA following transplantation suggests that adipose tissue attenuation may be sensitive to early post-transplant systemic changes. Although the precise biological mechanisms underlying these attenuation changes cannot be determined from imaging data alone, several potential explanations may be considered. Conditioning-related endothelial injury, inflammatory activation, and altered vascular permeability are well-described features of the early post-transplant period. These processes may promote interstitial fluid shifts or inflammatory alterations within adipose tissue, potentially leading to measurable changes in CT attenuation.

Importantly, our results demonstrate that the magnitude of attenuation change, rather than the absolute attenuation value at a single time point, was associated with survival. This observation suggests that dynamic changes in adipose tissue attenuation may capture clinically relevant physiological alterations occurring during the early post-transplant phase. In this context, ΔHU may function as a surrogate imaging marker of systemic stress or tissue injury.

From a clinical perspective, quantitative evaluation of SATA may provide complementary information beyond conventional CT findings. Chest CT examinations are frequently performed in allo-HSCT recipients for various clinical indications, and SATA measurements can be obtained without additional imaging or radiation exposure. Therefore, assessment of adipose tissue attenuation could potentially be incorporated into routine radiologic evaluation as an additional quantitative parameter.

An important methodological consideration is that pleural and pericardial effusions may represent downstream manifestations of the same pathophysiological processes reflected by increasing ΔHU, including endothelial dysfunction, capillary leak, and interstitial fluid redistribution. Therefore, these imaging findings may function as mediators rather than true confounders. For this reason, adjustment for pleural and pericardial effusions was considered a sensitivity analysis rather than the primary multivariable model.

Importantly, patients with clinically or radiologically overt pulmonary edema and pneumonia were excluded from the present study to minimize potential confounding by established pulmonary pathology. Nevertheless, exclusion of overt pulmonary edema does not exclude more subtle systemic endothelial injury, increased vascular permeability, or interstitial fluid redistribution, all of which are recognized features of the early post-transplant period. Accordingly, the observed increase in ΔHU may reflect these subclinical systemic alterations rather than clinically apparent pulmonary edema.

Nevertheless, these findings should be interpreted cautiously. Although increased ΔHU values were associated with worse survival, this observational study cannot establish a causal relationship between adipose tissue attenuation changes and mortality. Rather, ΔHU should be considered a potential imaging biomarker reflecting underlying systemic processes that may influence prognosis. Although these mechanisms are biologically plausible, the present imaging study cannot determine which pathway predominates, and the observed association should not be interpreted as evidence of causality. Future studies integrating imaging biomarkers with circulating markers of endothelial dysfunction and inflammation are warranted to clarify the underlying mechanisms.

Study Limitations

Several limitations should be acknowledged. First, the retrospective design may introduce selection bias related to the clinical indications for CT imaging. Second, measurements were obtained from a single standardized ROI on a single axial CT slice. Although this approach demonstrated good intraobserver reproducibility, future studies should evaluate whether multi-slice or bilateral averaging further improves measurement robustness. Third, biochemical inflammatory markers were not systematically analyzed, limiting the ability to directly correlate imaging findings with laboratory measures of systemic inflammation. Although adjustment for HCT-CI and GVHD yielded similar findings, these analyses were performed on complete-case data because these variables were unavailable for a subset of patients. In addition, several established transplant-related prognostic factors, including conditioning intensity, donor characteristics, HLA matching, remission status at transplantation, and other disease-specific variables, were not available and therefore could not be incorporated into the multivariable analyses. Residual confounding cannot be excluded. Additionally, only overall survival was analyzed. Although the proposed biological mechanisms may be more directly related to non-relapse mortality, reliable cause-of-death classification distinguishing relapse-related from non-relapse mortality was not consistently available. Future studies with adjudicated relapse-related and non-relapse mortality outcomes are needed to clarify whether ΔHU is preferentially

associated with specific causes of death. Finally, external validation in independent cohorts will be necessary to confirm the prognostic value of ΔHU in allo-HSCT recipients.

CONCLUSION

SATA on CT increases following allo-HSCT, and greater interval increases are associated with worse overall survival. These findings suggest that quantitative assessment of adipose tissue attenuation on routine chest CT may serve as a potential imaging biomarker for systemic physiological alterations and risk stratification in allo-HSCT recipients. Prospective studies are warranted to validate these observations and to further investigate the biological mechanisms underlying adipose tissue attenuation changes in this population.

Ethics

Ethics Committee Approval: This retrospective single-center study was approved by the Koç University Biomedical and Retrospective Research Ethics Committee (approval number: 2026.077.IRB2.039; February 11, 2026).

Informed Consent: The requirement for informed consent was waived by the Ethics Committee because of the retrospective design of the study. Patient anonymity was preserved, and all data were handled in accordance with institutional and international ethical standards.

Footnotes

Authorship Contributions

Concept: Z.A., Y.P., Design: Z.A., Y.P., Data Collection or Processing: Z.A., T.T., Analysis or Interpretation: Z.A., T.T., Y.P., Literature Search: Z.A., Writing: Z.A., Y.P.

Conflict of Interest: No conflict of interest was declared by the authors.

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