ARCHIVES OF THE TURKISH SOCIETY OF CARDIOLOGY

Official journal of the TURKISH SOCIETY OF CARDIOLOGY

Incremental Diagnostic Value of Computed Tomography Attenuation in Differentiating Malignant Pericardial Effusion: A Retrospective Observational Study

Bilgisayarlı Tomografi Attenüasyonunun Malign Perikardiyal Efüzyonun Ayırıcı Tanısındaki Artımlı Tanısal Değeri: Retrospektif Gözlemsel Bir Çalışma

ABSTRACT

Objective: Malignant pericardial effusion (MPE) is associated with poor prognosis and frequently presents as cardiac tamponade. While cytology is the diagnostic gold standard, its sensitivity is limited. Computed tomography (CT) attenuation, measured in Hounsfield Units (HU), may reflect fluid composition and assist in the non-invasive differentiation of MPE.

Method: This retrospective, single-center study included 102 patients who underwent percutaneous pericardiocentesis and thoracic CT. Patients were classified as having malignant or non-malignant effusion based on pathological findings. CT attenuation was measured at three standardized axial levels. Diagnostic performance was assessed using multivariate logistic regression and receiver operating characteristic (ROC) analysis. Two predictive models were compared: Model 1 (clinical and laboratory variables) and Model 2 (Model 1 + CT attenuation).

Results: MPE was diagnosed in 44 patients (43.1%). CT attenuation values were significantly higher in the MPE group (median 24.4 HU vs. 9.3 HU, P < 0.001). On multivariate analysis, male sex, elevated pericardial fluid protein, low glucose, and high lactate dehydrogenase were independent predictors of MPE. CT attenuation also emerged as an independent predictor when added to the model (Model 2) (odds ratio [OR] = 1.076, 95% confidence interval [CI]: 1.026–1.128, P = 0.003). The inclusion of CT attenuation improved the model's diagnostic performance (area under the curve [AUC]: 0.893 for Model 2 vs. 0.860 for Model 1). Model 2 demonstrated superior diagnostic performance (AUC = 0.893), with a CT attenuation cut-off of 16.45 HU yielding a sensitivity of 88.2% and a specificity of 78.3%.

Conclusion: CT attenuation provides incremental diagnostic value in identifying MPE when combined with conventional clinical and biochemical parameters. In settings where rapid diagnosis is critical, its non-invasive and reproducible nature may support early detection of malignant conditions.

Keywords: Hounsfield units, malignant pericardial effusion, pericardiocentesis

ÖZET

Amaç: Malign perikardiyal efüzyon (MPE), kötü prognoz ile ilişkilidir ve sıklıkla kardiyak tamponad olarak ortaya çıkar. Sitoloji tanıda altın standart olsa da, duyarlılığı sınırlıdır. Bilgisayarlı tomografi (BT) ile Hounsfield Ünitesi (HU) cinsinden ölçülen attenüasyon, sıvı kompozisyonunu yansıtabilir ve MPE'nin invaziv olmayan şekilde ayırıcı tanısında yardımcı olabilir.

Yöntem: Bu retrospektif, tek merkezli çalışmada, perkütan perikardiyosentez ve toraks BT'si yapılan 102 hasta analiz edildi. Hastalar patolojik bulgulara göre malign veya malign olmayan olarak sınıflandırıldı. BT attenüasyonu, üç standart aksiyel düzeyde ölçüldü ve tanısal değeri çok değişkenli lojistik regresyon ve ROC eğrisi analizi ile değerlendirildi. İki prediktif model karşılaştırıldı: Model 1 (klinik ve laboratuvar değişkenleri) ve Model 2 (Model 1 + BT attenüasyonu).

Bulgular: MPE, 44 (%43.1) hastada saptandı. BT attenüasyon değerleri MPE grubunda anlamlı derecede daha yüksekti (medyan 24.4 HU vs. 9.3 HU, P < 0.001). Çok değişkenli analizde, erkek cinsiyet, yüksek perikardiyal sıvı proteini, düşük glukoz ve yüksek laktat dehidrogenaz düzeyleri MPE için bağımsız prediktörler olarak belirlendi. BT attenüasyonu modele (Model 2) eklendiğinde, bağımsız bir prediktör olarak da anlamlı tespit edildi (OR = 1.076, %95 GA: 1.026–1.128, P = 0.003). BT attenüasyonunun dahil edilmesi modelin tanısal performansını artırdı (Model 2 için AUC: 0.893 vs. Model 1 için 0.860). Model 2, 16.45 HU BT attenüasyon kesim değeri ile %88.2 duyarlılık ve %78.3 özgüllük sağladı.

ORIGINAL ARTICLE
KLİNİK ÇALIŞMA

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Received: April 09, 2025
Accepted: April 18, 2025

Cite this article as: İnan D, Demirtola Mammadli Aİ, Gençol Akçay G, Tekin AF, Mammadli A. Incremental Diagnostic Value of Computed Tomography Attenuation in Differentiating Malignant Pericardial Effusion: A Retrospective Observational Study. *Turk Kardiyol Dern Ars.* 2025;53(5):304–311.

DOI: 10.5543/tkda.2025.70300

Sonuç: BT attenüasyonu, konvansiyonel klinik ve biyokimyasal parametrelerle birlikte kullanıldığında MPE ayırt etmede ilave tanısal katkı sağlamıştır. Hızlı, tekrarlanabilir ve non-invaziv bir arac olarak, hızlı tanı gerektiren bu vakalarda, malignitenin erken tespitini destekleyebilir.

Anahtar Kelimeler: Hounsfield ünitesi, malign perikardiyal efüzyon, perikardiyosentez

Pericardial effusion (PE) refers to the abnormal accumulation of fluid in the pericardial sac and can result from a wide range of etiologies, including benign inflammatory conditions and malignancies.[1,2] Among these, malignant pericardial effusion (MPE) is of particular concern due to its association with advanced-stage cancers and poor prognosis.[3,4] Rapid and accurate identification of MPE is essential for guiding timely oncologic and palliative interventions.

Cytological evaluation remains the gold standard for determining the etiology of PE; however, its sensitivity is often suboptimal, particularly in early or inactive stages of the disease.[1,5] Additional limitations include inadequate sample acquisition, insufficient aspirated fluid, and the time-consuming nature of cytological analysis.[1] In this context, adjunctive diagnostic tools, such as biochemical fluid analysis and imaging modalities, have gained increasing clinical relevance. The clinical course of the disease may also aid in differentiating the underlying cause of PE.[1]

While biochemical analysis is well established in differentiating pleural effusions (PLE) and ascites, its application to PE is often extrapolated from those criteria.[6,7] Studies using Light's criteria and serum-effusion albumin gradients have shown that most PEs are exudative in nature.[8-10] Among biochemical parameters, low glucose levels, elevated lactate dehydrogenase (LDH), and low albumin concentrations have been reported to be more suggestive of MPE.[10-11]

Recent advances in computed tomography (CT) have enhanced its ability to characterize tissue based on attenuation values, expressed in Hounsfield Units (HU), thereby contributing significantly to both diagnostic and therapeutic strategies in various cardiac conditions.[12] For example, CT attenuation plays a key role in differentiating thrombus from pannus in prosthetic valve dysfunction and is used for calcium scoring in aortic stenosis to guide treatment decisions.[12,13] In patients with PLE, prior studies have shown that attenuation values significantly differ between exudates and transudates.[14,15] These findings support the idea that CT attenuation may also offer deeper insight into the characteristics of PE by reflecting features such as protein content, cellularity, or hemorrhagic components—traits more commonly observed in MPE.[11,16,17]

This study aims to evaluate the incremental diagnostic contribution of CT attenuation in distinguishing malignant from non-malignant PE. By comparing two diagnostic models—one based on conventional clinical and biochemical data, and the other incorporating radiologic attenuation values—we seek to determine whether CT-based metrics can enhance diagnostic accuracy in routine clinical practice.

ABBREVIATIONS

AUC	Area under the curve
CRP	C-reactive protein
CT	Computed tomography
HU	Hounsfield units
LDH	Lactate dehydrogenase
MPE	Malignant pericardial effusion
NT-proBNP	N-terminal pro-B-type natriuretic peptide
OR	Odds ratio
PC	Pericardiocentesis
PE	Pericardial effusion
PLE	Pleural effusion
ROC	Receiver operating characteristic
ROI	Region of interest

Materials and Methods

Study Design and Population

This retrospective, single-center observational study included 128 consecutive patients who underwent percutaneous pericardiocentesis (PC) for cardiac tamponade or severe PE between May 2020 and January 2024. Patients were excluded if they lacked PE sampling or CT data, had PE secondary to aortic dissection, or developed PE as a complication of structural and/or coronary procedures. Additionally, patients with marked pericardial calcification, significant CT artifacts, or non-diagnostic PE pathology reports were excluded. The study population was divided into two groups based on the final pathological diagnosis of the effusion: malignant and non-malignant. This study was approved by the Basaksehir Cam & Sakura City Hospital Ethics Committee (Approval Number: E-96317027-514.10-234532847, Date: 17.01.2024). Informed consent was waived due to the retrospective nature of the study. All procedures were conducted in accordance with ethical standards and the principles of the Declaration of Helsinki.

Data Collection and Variables

Demographic data, comorbidities (e.g., diabetes mellitus, hypertension, coronary artery disease), and clinical history (e.g., history of pericarditis, tuberculosis, or coronavirus disease 2019) were recorded. Peripheral blood samples obtained within approximately 6-12 hours after PC, as well as PE samples, were reviewed from hospital records. Laboratory parameters included serum levels of C-reactive protein (CRP), procalcitonin, albumin, creatinine, liver enzymes, N-terminal pro-B-type natriuretic peptide (NT-proBNP), and uric acid, along with lactate dehydrogenase and pH values. All PE samples were evaluated through cytological examination, microbiological analysis, and

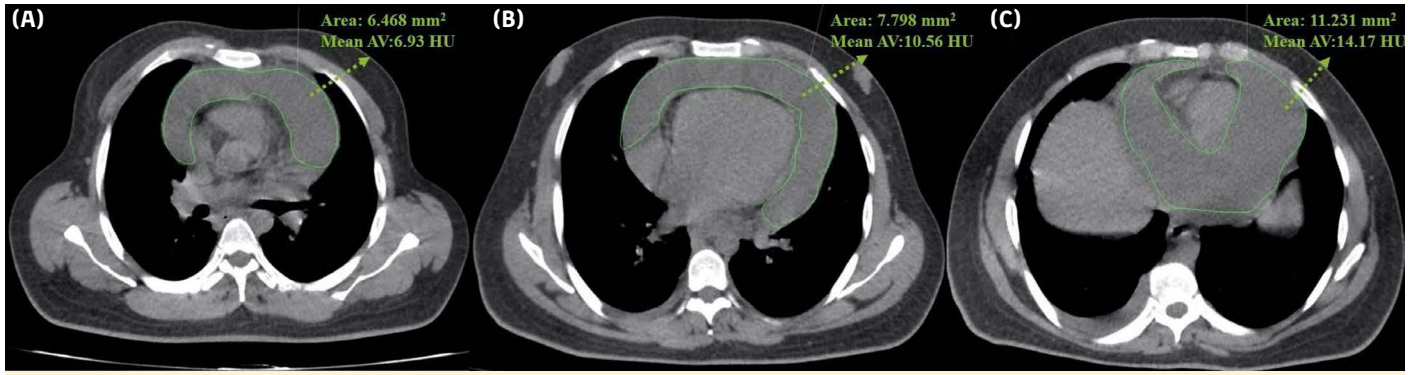

Figure 1. Measurement of the area and attenuation value of PE by CT in the upper (A), middle (B) and lower (C) regions during diastole.

CT; computed tomography, HU; hounsfield unit, PE; pericardial effusion.

biochemical testing, including total protein, albumin, glucose, pH, LDH, and adenosine deaminase. The diagnosis of exudative PE was supported by Light's criteria (PE-to-serum LDH ratio > 0.6 or PE LDH > two-thirds of the upper normal limit of serum LDH; PE-to-serum total protein ratio > 0.5), and by a serum-to-effusion albumin gradient of < 1.1 g/dL.[8]

Imaging Protocol

All patients underwent transthoracic echocardiography performed by a trained cardiologist using a Philips cardiovascular ultrasound system (Epic CVx, USA) with an X51 transducer. Echocardiographic findings considered significant for tamponade included a plethoric inferior vena cava, early diastolic collapse of the right ventricular free wall, late diastolic compression of the right atrium, cardiac swinging within the pericardial sac, and a relative inspiratory increase of > 60% in tricuspid inflow or a relative inspiratory decrease of > 30% in mitral inflow velocity.[18] Additionally, all patients underwent non-contrast thoracic CT. CT attenuation values of the PE were assessed in all patients using post-processed images obtained approximately 24-48 hours prior to PC. Imaging was performed with a 320-multidetector CT scanner (Aquilion One, GENESIS Edition; Canon Medical Systems, Otawara, Japan) following the institutional thoracic CT protocol, which included the following parameters: reconstructed slice thickness of 5 mm, gantry rotation time of 350 ms, tube voltage of 120 kV, and effective tube current of 325-750 mA. Images were acquired using 320 × 0.5 mm collimation. Axial CT images were transferred to a dedicated workstation and analyzed using Philips IntelliSpace Portal 12.0 (Philips HealthCare®). Based on previous studies,[11,16,17] attenuation values (measured in Hounsfield Units, HU) were determined by placing circular regions of interest (ROIs) in three predefined axial slices representative of the PE collection:

- Level 1: Pulmonary artery bifurcation
- Level 2: Mid-ventricular level (four-chamber view)
- Level 3: Sub-diaphragmatic level.

The average HU value calculated from these three levels was used for statistical analysis. In addition to attenuation, the two-dimensional area of the PE at each level was measured to support visual and volumetric correlation, as illustrated in Figure 1A-C.

Statistical Analysis

Continuous variables were assessed for normality using the Shapiro-Wilk test. As most variables were not normally distributed, results are presented as medians and interquartile ranges (IQR) for continuous variables, and as frequencies and percentages for categorical variables. Group comparisons were conducted using the Mann-Whitney U test for continuous variables and the chi-square test for categorical variables. To identify potential predictors of MPE, univariate logistic regression was performed for selected demographic, clinical, and PE-related variables. Parameters with a P-value < 0.05 and/or deemed clinically relevant were included in the multivariate analysis. In Model 1, conventional variables such as sex, inflammatory markers, and PE characteristics were included. In Model 2, CT attenuation values (measured in HU) were added to assess their incremental diagnostic value. The performance of both models was compared using several metrics, including the area under the curve (AUC), Nagelkerke R^2, -2 Log Likelihood, and Brier Score. Optimal cut-off values for continuous predictors were determined by receiver operating characteristic (ROC) analysis using the maximum Youden's index, and the corresponding sensitivity and specificity were reported. All statistical analyses were performed using IBM SPSS Statistics version 30 (IBM Corp., Armonk, NY, USA) and R software (version 4.4.1; R foundation for Statistical Computing, Vienna, Austria). A two-tailed p-value < 0.05 was considered statistically significant.

Results

A total of 128 patients who underwent PC were evaluated, of whom 102 met the inclusion criteria and were included in the final analysis. MPE was identified in 44 patients (43.1%). The remaining etiological causes of PE in the study population are summarized in Table 1. Baseline demographic and clinical characteristics of patients with malignant and non-malignant effusions are presented in Table 2. Patients with MPE were more frequently male (75% vs. 47%, P = 0.005) and had significantly lower rates of diabetes mellitus (P = 0.017) and prior history of pericarditis (P = 0.002). Exudative effusion was more common in patients with MPE (P < 0.001). Among laboratory findings, patients with MPE exhibited significantly higher levels of procalcitonin (P = 0.022), NT-proBNP (P = 0.001), aspartate aminotransferase (P = 0.001), alanine aminotransferase

Table 1. Etiological Causes Underlying Pericardial Effusion in the Study Population

	n	%
Etiological Causes of PE		
Malignancy	44	43
Pneumonia	3	3
Pericarditis	13	13
Uremia	5	5
Heart failure	4	4
Multisystem autoimmune disease	9	9
Idiopathic	14	14
Tuberculosis	3	3
Hypothyroidism	2	2
Other	5	5
Malignant Causes of PE		
Lung cancer	17	39
Leukemia/Lymphoma	6	14
Breast cancer	4	9
Gastrointestinal cancers	11	25
Gynecological cancers	2	4
Head and neck cancers	2	4
Other	2	4

PE, Pericardial effusion.

(P = 0.011), triglycerides (P = 0.018), D-dimer (P = 0.040), and fibrinogen (P < 0.001). In contrast, serum albumin and glucose levels did not differ significantly between the groups. PE analysis revealed that MPE patients had higher levels of total protein (P < 0.001), albumin (P < 0.001), and LDH (P < 0.001), along with lower pH values (P < 0.001). CT attenuation values were significantly elevated in the MPE group, with a median of 24.4 HU compared to 9.3 HU in the non-MPE group (P < 0.001). Short-term (in-hospital) mortality was significantly higher among MPE patients (39% vs. 17%, P = 0.023), as was long-term mortality (82% vs. 34%, P < 0.001).

Univariate logistic regression analysis identified several demographic, clinical, and PE-related variables as potential predictors of MPE (Table 3). Multivariate logistic regression was performed using two models, with the results summarized in Table 4. Model 1 included demographic, clinical, and PE-related variables. In this model, male sex (odds ratio [OR] = 0.189, 95% confidence interval [CI]: 0.064–0.554, P = 0.002), higher PE protein levels (OR = 1.099, 95% CI: 1.036–1.166, P = 0.022), and lower PE glucose levels (OR = 0.971, 95% CI: 0.948–0.995, P = 0.017) emerged as independent predictors of MPE. In Model 2, CT attenuation values were added to the variables in Model 1. With this addition, CT attenuation became a significant independent predictor (OR = 1.076, 95% CI: 1.026–1.128, P = 0.003).

To further evaluate the diagnostic performance of these models, ROC curve analyses were conducted. The results are illustrated in

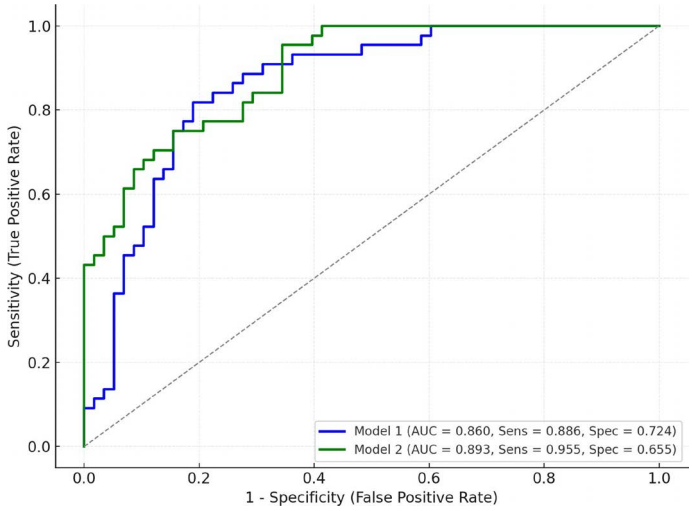

Figure 2. ROC curve analyses comparing the diagnostic performance of different models for malignant PE.

AUC, Area under the curve; PE, Pericardial effusion; ROC, Receiver operating characteristic.

Figure 2, which compares the performance of Model 1 and Model 2. Model 1 demonstrated an AUC of 0.860, with a sensitivity of 88.6% and a specificity of 72.4%. Model 2, which incorporated CT attenuation, showed slightly superior performance, with an AUC of 0.893, a sensitivity of 95.5%, and a specificity of 65.5%. In addition to ROC analysis, overall model performance was assessed using complementary metrics, including Nagelkerke R^2, -2 log-likelihood, and Brier score. As illustrated in Figure 3, Model 2 outperformed Model 1 across all evaluation indices, supporting the incremental value of CT-based radiological assessment.

Lastly, to determine optimal diagnostic thresholds, cut-off values were calculated for CT attenuation, PE protein, and PE glucose. The optimal cut-off value for CT attenuation was 16.45 HU, which yielded a sensitivity of 88.2% and a specificity of 78.3%. For PE protein, the best cut-off was 30.5 g/L, providing a sensitivity of 94.1% and a specificity of 62.2%. For PE glucose, the optimal cut-off was 58 mg/dL, with a sensitivity of 66% and a specificity of 80%.

Discussion

In this study, male sex, elevated PE protein, low PE glucose, and high serum CRP levels emerged as independent clinical and laboratory predictors of MPE. Notably, the integration of CT attenuation values—expressed in HU—into the diagnostic model added significant discriminatory power. These findings highlight the potential role of CT attenuation as a valuable, non-invasive imaging biomarker that can complement traditional fluid analysis in the etiological assessment of pericardial effusion.

Studies investigating the relationship between visceral effusions and CT attenuation have initially and extensively focused on PLE. Early studies in this area found that CT attenuation alone had limited accuracy in distinguishing exudates from transudates.[19,20] These studies noted overlapping attenuation values and emphasized the importance of interpreting CT findings in conjunction with clinical data to improve diagnostic sensitivity.[19,20] In a recent large cohort

Table 2. Baseline Characteristics of the Study Population

Variables	Malignant (n = 44)	Non-Malignant (n = 58)	P
Age, years	55.5 (41.5-64.0)	63.0 (47.0-74.0)	0.098
Male, n (%)	33 (75%)	27 (47%)	0.005
DM, n (%)	5 (11%)	19 (33%)	0.017
HT, n (%)	14 (32%)	30 (52%)	0.069
CAD, n (%)	3 (7%)	10 (17%)	0.143
HF, n (%)	2 (5%)	8 (14%)	0.181
AF, n (%)	6 (14%)	14 (25%)	0.203
TB, n (%)	1 (2%)	3 (5%)	0.632
COVID-19, n (%)	12 (27%)	8 (14%)	0.133
Smoking, n (%)	9 (20%)	7 (12%)	0.062
CFR, n (%)	3 (7%)	10 (17%)	0.143
Hepatic cirrhosis, n (%)	0 (0%)	1 (2%)	0.569
History of pericarditis, n (%)	1 (2%)	16 (27%)	0.002
Tamponade on TTE, n (%)	33 (75%)	36 (62%)	0.203
Exudative PE, n (%)	43 (97%)	12 (21%)	<0.001
Serous PE, n (%)	4 (9%)	27 (46%)	<0.001
Drained PE, mL	800 (500-1000)	670 (400-1000)	0.163
BMI, kg/m^2	24.11 (21.47-26.02)	26.82 (22.59-31.47)	0.016
HGB, g/dL	11 (9.9-12.2)	11.7 (9.5-13)	0.183
WBC, 10^9/L	11.1 (6.1-15.6)	8.4 (6.0-11.5)	0.064
PLT, 10^9/L	270.5 (183.7-392.5)	251.5 (187.5-308.5)	0.501
Procalcitonin, ng/mL	0.25 (0.10-0.71)	0.08 (0.05-0.33)	0.022
CRP, mg/dL	64.1 (34.2-138.2)	22.9 (6.5-104.4)	0.367
NT-proBNP, pg/mL	926 (561-1250)	895 (389-2262)	0.001
Uric acid, mg/dL	5.50 (3.22-6.85)	4.3 (4.45-6.35)	0.44
Creatinine, mg/dL	0.84 (0.63-1.33)	0.89 (0.65-1.40)	0.102
BUN, mg/dL	71.5 (42.2-107.0)	35.8 (25.2-57.9)	0.403
AST, U/L	36 (22-93)	21 (16-31)	0.772
ALT, U/L	31.0 (18.0-127.0)	18.5 (12.0-41.0)	0.001
ALP, U/L	137.0 (88.0-201.5)	106.0 (75.0-146.2)	0.011
Total cholesterol	139.5 (119.7-166.5)	149 (119.7-193.5)	0.140
Triglyceride, mg/dL	115 (91-133)	87 (73-121)	0.018
D-dimer, ng/mL	6.12 (1.83-8.70)	1.09 (0.26-1.90)	0.040
Fibrinogen, mg/dL	461 (302-512)	365 (293-742)	<0.001
TSH, mlU/L	1.44 (1.10-2.37)	1.77 (0.81-3.10)	0.057
Serum glucose, mg/dL	110.5 (93.5-139.0)	116 (101.5-149.2)	0.735
Serum total protein, g/L	59.5 (54.2-66.0)	64.0 (59.0-68.2)	0.029
Serum albumin, g/L	34.0 (29.0-38.0)	36.0 (33.7-40.2)	0.482
Serum LDH, U/L	329.5 (224.0-519.2)	249.0 (194.5-322.5)	0.245
Serum pH	7.39 (7.36-7.42)	7.41 (7.37-7.44)	0.035
PE glucose, mg/dL	50.5 (34.0-68.0)	72.9 (60.7-8.22)	0.622
PE total protein, g/L	38.5 (35.0-46.0)	27 (22.7-38.0)	<0.001
PE albumin, g/L	28.4 (22.5-32.4)	21.0 (16.5-26.4)	<0.001
PE LDH, U/L	1131.5 (375-2329.7)	422 (164.7-909.2)	<0.001
PE, pH	7.33 (7.30-7.36)	7.39 (7.37-7.40)	<0.001
Attenuation value in CT, HU	24.4 (16.8-33.5)	9.32 (5.99-17.6)	<0.001
Recurrent PE, n (%)	10 (23%)	11 (19%)	0.895
In-hospital mortality, n (%)	17 (39%)	10 (17%)	0.023
Long-term mortality, n (%)	36 (%82)	20 (34%)	<0.001

AF, Atrial Fibrillation; ALP, Alkaline Phosphatase; ALT, Alanine Aminotransferase; AST, Aspartate Aminotransferase; BMI, Body Mass Index; BUN, Blood Urea Nitrogen; CAD, Coronary Artery Disease; CFR, Chronic Renal Failure; COVID-19, Coronavirus Disease 2019; CRP, C-Reactive Protein; CT, Computed Tomography; DM, Diabetes Mellitus; HF, Heart Failure; HGB, Hemoglobin; HT, Hypertension; HU, Hounsfield Unit; LDH, Lactate Dehydrogenase; NT-proBNP, N-Terminal Pro-B-Type Natriuretic Peptide; PC, Pericardiocentesis; PE, Pericardial Effusion; PLE, Pleural Effusion; PLT, Platelet Count; TB, Tuberculosis; TSH, Thyroid-Stimulating Hormone; TTE, Transthoracic Echocardiography; WBC, White Blood Cell Count.

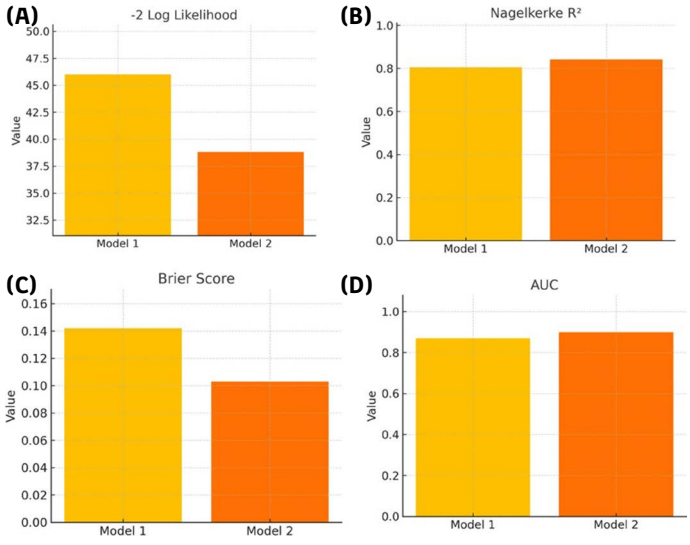

Figure 3. Model performance comparison between Model 1 and Model 2. (A) Model Fit: -2 Log Likelihood, (B) Explained Variance: Nagelkerke R², (C) Calibration: Brier Score, (D) Discrimination: AUC.

Table 3. Univariate Logistic Regression Analysis of Predictors for Malignant Pericardial Effusion

Variables	OR (95% CI)	P
Age, years	1.002 (0.967–1.038)	0.921
Sex, male	3.444 (1.464–8.103)	0.005
Smoking	1.333 (0.517–3.483)	0.552
CRP, mg/dL	1.010 (1.001–1.019)	0.027
PE glucose, mg/dL	0.962 (0.929–0.997)	0.033
PE total protein, g/L	1.105 (1.006–1.215)	0.038
PE albumin, g/L	1.030 (0.901–1.176)	0.669
PE LDH, U/L	1.000 (1.000–1.001)	0.187
PE pH	1.647 (0.598–4.536)	0.335
WBC, 10^9/L	1.082 (0.955–1.226)	0.217
BMI, kg/m²	0.984 (0.966–1.002)	0.085

BMI, Body Mass Index; CI, Confidence Interval; CRP, C-Reactive Protein; CT, Computed Tomography; HU, Hounsfield Unit; LDH, Lactate Dehydrogenase; OR, Odds Ratio; PE, Pericardial Effusion; WBC, White Blood Cell Count.

study by Gümüş et al.[14] involving 380 patients, exudative PLE demonstrated significantly higher attenuation values compared to transudative PLE (15.1 ± 5.1 HU vs. 5.0 ± 3.4 HU), with a proposed threshold of ≥ 10 HU yielding 89.7% sensitivity and 94.4% specificity. Similarly, Yalçın-Şafak et al.[15] reported higher HU values in exudative PLE (8.82 ± 7.04 HU) compared to transudates (2.91 ± 8.53 HU). In our study, however, no significant overlap in HU values was observed between malignant and non-malignant PE. Despite differences in anatomical compartments and fluid dynamics, these findings support the notion that HU values reliably reflect the biochemical composition of effusion. The median attenuation value observed in our study (24.4 HU in the MPE group vs. 9.3 HU in the non-malignant group, P < 0.001) further reinforces this hypothesis. ROC analysis identified a cut-off value of 16.45 HU, which proved to be discriminatory.

Although PE analysis is routinely performed in all patients undergoing PC, its diagnostic utility remains limited due to low specificity.[6,7] Furthermore, studies comparing pleural and PE compositions have suggested that relying solely on Light's criteria for evaluating PE may be inadequate, highlighting the need for alternative diagnostic approaches.[2,9,10] In this context, Rifkin et al.[16] evaluated the effectiveness of CT attenuation measurements in characterizing PE composition. While they found a correlation between attenuation values and PE hematocrit, no statistically significant correlation was observed with total protein levels.[16] In a subsequent study, Çetin et al.[17] investigated the association between CT attenuation and PE components in distinguishing exudative from transudative PE. Their analysis of 96 patients revealed significantly higher HU values in exudative PE (14.85 ± 10.7 HU) compared to transudates (1.13 ± 4.3 HU, P < 0.001), with strong correlations between attenuation and PE protein, LDH, and albumin. The threshold they proposed—4.7 HU—achieved 80% sensitivity and 87.7% specificity in identifying exudative PE.[17] These findings align with our results and further support the concept that CT attenuation not only reflects the biochemical composition of pericardial fluid but also correlates with the underlying pathophysiological mechanisms associated with malignancy, such as cellular infiltration, hemorrhagic components, and elevated protein content.

Nakamura et al.[11] also evaluated CT attenuation values in 97 patients undergoing PC and examined their correlation with MPE. They found that MPE was associated with lower PE glucose levels and relatively higher attenuation values (median 22.7 HU vs. 17.4 HU, P = 0.08).[11] Compared to their findings, our study

Table 4. Multivariable Logistic Regression Models for Predicting Malignant Pericardial Effusion

Variables	Model 1		Model 2	
	OR (95% CI)	P	OR (95% CI)	P
Sex, male	0.189 (0.064–0.554)	0.002	0.204 (0.065–0.639)	0.006
CRP, mg/dL	1.008 (1.001–1.015)	0.022	1.005 (0.998–1.013)	0.170
PE glucose, mg/dL	0.971 (0.948–0.995)	0.017	0.972 (0.946–0.998)	0.034
PE total protein, g/L	1.099 (1.036–1.166)	0.002	1.094 (1.030–1.162)	0.003
Attenuation value in CT, HU			1.076 (1.026–1.128)	0.003

CI, Confidence Interval; CRP, C-Reactive Protein; CT, Computed Tomography; HU, Hounsfield Unit; OR, Odds Ratio; PE, Pericardial Effusion.

demonstrated a clearer distinction between MPE and non-malignant PE, with a significantly higher median attenuation in the MPE group (24.4 HU vs. 9.3 HU, P < 0.001). Moreover, while Nakamura et al.[11] proposed a threshold of > 20 HU with 89.6% specificity, our multivariate model not only supported this trend but also identified CT attenuation as an independent predictor of malignancy, with an OR of 1.076 per unit HU increase. The broader range of HU values observed in our cohort may be attributed to the inclusion of more advanced-stage malignancies and the standardized placement of ROIs across three anatomical levels. Additionally, differences in the types of malignancies represented in two studies may also explain the variation in attenuation values.

Importantly, our study differs from prior research through its model-based approach, which enables the simultaneous assessment of demographic, clinical, and laboratory variables alongside CT attenuation. The marked improvement in diagnostic performance from Model 1 to Model 2 highlights that HU values provide independent and complementary diagnostic information—potentially capturing aspects of PE composition that may be overlooked by conventional parameters alone.

The malignancy rate in our cohort was notably high, with 43.1% of patients diagnosed with MPE, approximately 39% of which were attributable to lung cancer. The rate of idiopathic PE in our study was 14%, consistent with rates reported in Western Asia and Africa (10–15%), but significantly lower than those observed in Western Europe and North America (80–90%).[1,20–24] This discrepancy likely reflects regional differences in diagnostic infrastructure and disease prevalence. Another key finding in our study was the strong association between MPE and both short- and long-term mortality. This aligns with earlier reports highlighting the poor prognosis of patients with MPE.[3,5,11] However, the mortality rates observed in our study—39% in-hospital and 82% at long-term follow-up—were markedly higher. Potential explanations include the inclusion of patients with advanced-stage malignancies and the predominance of cases presenting with cardiac tamponade at baseline, indicating more severe disease. These results underscore the urgent need for early, accurate, and non-invasive differentiation of MPE, which may facilitate timely oncologic and palliative management.

This study has several limitations. First, its retrospective, single-center design may introduce selection bias and limit the generalizability of the findings to broader populations. Additionally, no external validation was performed to assess the reproducibility of the results in independent cohorts, which further limits their generalizability. Second, although a standardized ROI placement protocol was applied across three predefined anatomical levels to ensure consistency in attenuation measurements, the lack of inter-observer variability assessment and reliance on a single imaging workstation may reduce reproducibility in other settings. Additionally, variability in CT protocols (e.g., contrast use, slice thickness, scanner type) across centers remains a potential confounder for future clinical adoption. Third, attenuation values can be influenced by several non-malignant factors, such as hemorrhagic effusions, high-protein inflammatory effusions (e.g., tuberculous or purulent), or post-radiation changes. While our exclusion criteria and subgroup analyses aimed to minimize this effect, such overlap cannot be entirely ruled out and may impact specificity. Fourth, although cytological evaluation remains the current reference standard for diagnosing malignancy, it has well-known limitations in sensitivity, particularly in patients with low tumor burden, prior chemotherapy or immunotherapy, and localized effusions. As a result, some cases classified as "non-malignant" may, in fact, represent false negatives. Fifth, while CT attenuation was shown to improve diagnostic accuracy in this study, it is important to acknowledge that routine implementation may introduce additional cost and accessibility challenges, particularly in low-resource settings. This represents a practical limitation in translating clinical benefit into real-world applicability. Lastly, the study did not incorporate advanced imaging features such as radiomic texture analysis, enhancement characteristics, or machine learning-based classification, all of which may further enhance diagnostic performance. Similarly, molecular or immunohistochemical markers in PE were not routinely assessed, limiting pathophysiological correlations. Despite these limitations, this study provides valuable insights into the added diagnostic utility of CT attenuation in pericardial effusion and lays the groundwork for future research that integrates imaging, laboratory, and molecular data into clinical decision-making.

Conclusion

In this retrospective observational study, we demonstrated that CT attenuation values, when integrated with conventional clinical and laboratory parameters, significantly improve diagnostic accuracy in distinguishing malignant pericardial effusion from non-malignant causes. A CT attenuation threshold of > 16.45 HU showed high diagnostic performance, closely correlating with PE characteristics and reflecting underlying malignant pathology. Our model-based approach confirms that CT attenuation is an independent predictor of malignancy and offers incremental value beyond standard biochemical analysis. These findings suggest that CT attenuation may serve as a valuable, non-invasive imaging biomarker and should be considered in the routine evaluation of PE, particularly in patients at risk for malignancy or with inconclusive cytology. Early identification of MPE using attenuation data may facilitate more timely oncologic referral and management, ultimately improving clinical outcomes.

Ethics Committee Approval: Ethics committee approval was obtained from Başakşehir Çam & Sakura City Hospital Ethics Committee (Approval Number: E-96317027-514.10- 234532847, Date: 17.01.2024).

Informed Consent: Informed consent was waived due to the retrospective nature of the study.

Conflict of Interest: The authors have no conflicts of interest to declare.

Funding: The authors declared that this study received no financial support.

Use of AI for Writing Assistance: AI-assisted technologies were not used in this article.

Author Contributions: Concept – D.İ.; Design – D.İ., A.İ.D.M., A.M.; Supervision – A.İ.D.M., A.M.; Resource – D.İ., G.G.A., A.F.T.; Materials – D.İ., A.İ.D.M., A.M.; Data Collection and/or Processing - D.İ., A.İ.D.M., G.G.A., A.F.T.; Analysis and/or Interpretation - D.İ., A.İ.D.M., A.M.; Literature Review – D.İ., G.G.A., A.F.T., A.M.; Writing – D.İ., A.İ.D.M.; Critical Review – A.M.

Peer-review: Externally peer-reviewed.

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