

Model construction and validation of Dual-Energy CT multi-parameters combined with clinical indicators for predicting lymph node metastasis in pancreatic ductal adenocarcinoma

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Abstract

Background and purpose Lymph node metastasis (LNM) is a critical prognostic factor in pancreatic ductal adenocarcinoma (PDAC), but preoperative prediction remains challenging. This study aimed to evaluate the predictive value of combining dual-energy CT (DECT) multiparameters with clinical indicators for LNM in PDAC, and to develop a preoperative model to support clinical decision-making.

Methods A total of 126 pathologically confirmed PDAC patients were retrospectively enrolled and divided into training (n=87) and test (n=39) cohorts. Univariate and multivariate Logistic regression were used to identify independent predictors of LNM and construct a combined model. Model performance was

assessed using the area under the receiver operating characteristic curve (AUC), calibration curves, and decision curve analysis (DCA).

Results Multivariate Logistic regression identified CA19-9, intratumoral necrosis, and the slope of the energy attenuation curve (λ) in venous phase (λ_{VP}) as independent predictors of LNM. The combined model yielded an AUC of 0.816 (95% CI: 0.730–0.874) in the training cohort and 0.761 (95% CI: 0.613–0.909) in the test cohort, with satisfactory calibration (Hosmer-Lemeshow test: $P=0.722$ and $P=0.604$, respectively). DCA confirmed superior net benefit within threshold probabilities of 0–0.65 (training cohort) and 0–0.8 (test cohort).

Conclusion The combined model integrating DECT multiparameters and clinical indicators effectively predicts LNM in PDAC, demonstrating favorable diagnostic efficacy and clinical application value.

Introduction

Pancreatic ductal adenocarcinoma (PDAC) is a highly malignant tumor characterized by insidious onset, rapid progression and extremely poor prognosis. It has become the fourth leading cause of cancer-related death worldwide, with a 5-year survival rate of only approximately 10% [1]. Lymph node metastasis (LNM) serves as a key indicator of disease progression in PDAC, which directly determines the clinical staging, treatment selection and long-term survival prognosis of patients [2, 3]. Clinically, radical surgical resection is the first-line treatment for PDAC patients without LNM, whereas those with LNM require combination with preoperative neoadjuvant therapy or extended lymph node dissection. Moreover, some patients with extensive metastasis may even lose the opportunity for surgery. Therefore, accurate and noninvasive preoperative evaluation of LNM status in PDAC patients is a critical prerequisite for achieving individualized diagnosis and treatment and improving patient survival prognosis.

Histopathological examination remains the gold standard for the diagnosis of LNM. However, as an invasive procedure with sampling bias, it can hardly meet the requirements of clinical preoperative evaluation. Conventional CT and MRI mainly rely on morphological features such as lymph node size and

shape to assess the risk of metastasis, whereas early metastatic lymph nodes often exhibit no obvious morphological abnormalities [4, 5]. In addition, lymph node enlargement can also be caused by non-neoplastic factors including inflammatory reactive hyperplasia, leading to a high rate of missed diagnosis and misdiagnosis. Thus, the clinical value of evaluating LNM solely based on morphological indicators is limited [6].

Dual-energy CT (DECT) overcomes the limitations of conventional CT with mixed-energy imaging. By acquiring tissue attenuation data at different X-ray energy levels through multi-energy scanning, it can reconstruct various quantitative parameters, including monoenergetic CT value, iodine concentration (IC), normalized iodine concentration (NIC), slope of the energy attenuation curve (λ), and effective atomic number (Z_{eff}). These parameters can precisely reflect biological characteristics such as tumor tissue composition and microcirculatory perfusion, thereby providing functional evidence for the assessment of tumor invasion and metastasis risk [7–10]. Meanwhile, serum tumor markers, intratumoral necrosis, as well as other clinical and imaging morphological indicators, have also been verified as important influencing factors for LNM in PDAC [11–13]. Therefore, constructing a predictive model by combining DECT quantitative parameters with the aforementioned clinical and imaging morphological indicators is expected to compensate for the limitations of single-indicator evaluation and further improve the accuracy of preoperative prediction of LNM in PDAC.

Methods

Patient selection

This retrospective study was approved by Institutional Review Board of the First Affiliated Hospital of USTC. Individual informed consent was waived due to the retrospective study design. A primary cohort of patients who underwent surgical resection for PDAC at the First Affiliated Hospital of USTC between January 2023 and October 2025 was enrolled in this study. Patient flowchart, inclusion, and exclusion criteria are shown in Fig. 1. All patients were assigned to training cohort and test cohort at a ratio of 7:3 using stratified random sampling (stratified by LNM status) with training cohort used for model construction and test cohort for model validation (Comparisons of baseline patient characteristics and DECT quantitative parameters between the training and test cohorts are detailed in Supplementary Tables E1 and E2).

Clinicopathological data

Baseline clinical data were collected, including age, Gender, and laboratory examination indicators such as CA19-9, CA125, CEA, and neutrophil-to-lymphocyte ratio (NLR). Pathological data on LNM were retrieved from the clinical case system. LNM was defined as the presence of tumor cells in lymph node sections [14]. Patients were categorized into LNM-positive ($n = 77$) and LNM-negative ($n = 49$) groups based on pathological findings.

DECT scanning protocols

All patients underwent scanning using a 256-slice CT scanner (Revolution Apex, GE Healthcare). The scanning parameters were set as follows: tube voltage with rapid switching between high and low energy levels (80/140 kVp); automatic tube current modulation ranging from 200 to 300 mA; detector collimation of 256×0.625 mm; gantry rotation time of 0.5 s per rotation; image matrix of 512×512; and scan pitch of 0.992. Unenhanced scanning was performed first, followed by an intravenous bolus injection of contrast medium (Iohexol, 300 mgI/mL, GE Healthcare, Milwaukee, WI, USA) at a flow rate of 3.0–4.0 mL/s, with a dose of 1.5 mL/kg calculated according to patient body weight. The timing of each phase in the enhanced scan was controlled by aortic bolus tracking: when the contrast concentration in the abdominal aorta reached a threshold of 100HU, the late arterial phase, portal venous phase, and delayed phase sequences were initiated after delays of 25s, 60s, and 180s, respectively. All acquired image data were transferred to an advanced postprocessing workstation (Advanced Workstation 4.7, GE Healthcare) and the picture archiving and communication system. The reconstructed section thickness and interval were both set at 1.25 mm.

DECT image analysis

Morphological analysis

Conventional morphological parameters were measured and evaluated on reconstructed 70keV images, including tumor location (pancreatic head and neck vs. body and tail), maximum cross-sectional diameter, preoperative radiological vascular invasion (involving the superior mesenteric artery, celiac trunk, common hepatic artery, superior mesenteric vein, and splenic vein), as well as intratumoral necrosis (defined as non-enhancing areas within the tumor on contrast-enhanced images). The final diagnosis of vascular invasion and intratumoral necrosis was based on postoperative pathological findings as the gold standard.

Quantitative parameter measurement

Virtual monochromatic images at 40keV and 70keV were reconstructed, and IC maps as well as Zeff images were generated simultaneously. Two radiologists independently manually delineated regions of interest (ROIs) on the 70keV virtual monochromatic images at the largest cross-section of the solid component of pancreatic ductal adenocarcinoma lesions. Calcifications, intratumoral necrosis, and vascular structures were strictly avoided during ROI delineation to ensure the accuracy and homogeneity of the measured regions.

Subsequently, the delineated ROIs were copied synchronously to the registered 40keV virtual monochromatic images and iodine concentration maps for quantitative parameter extraction. The parameters included 40keV attenuation values in the arterial phase ($HU_{40keV-A}$), venous phase ($HU_{40keV-V}$), and delayed phase ($HU_{40keV-D}$), as well as 70keV attenuation values in the arterial phase ($HU_{70keV-A}$),

venous phase ($HU_{70keV-V}$), and delayed phase ($HU_{70keV-D}$). The slope of the energy attenuation curve (λ) was calculated as follows: $\lambda = (HU_{40keV} - HU_{70keV}) / 30$, where HU_{70keV} and HU_{40keV} referred to the attenuation values (Hounsfield units, HU) at 70keV and 40keV, respectively.

For calibration and standardization of the measured values, the iodine concentration of the abdominal aorta (AA) at the same level as the lesion was measured simultaneously on iodine maps as a reference standard, yielding normalized iodine concentration in the arterial phase (NIC-A), venous phase (NIC-V), and delayed phase (NIC-D). The formula was as follows: $NIC = IC_{lesion} / IC_{AA}$. Meanwhile, iodine concentration ratios $IC(A/V)$, $IC(A/D)$, and $IC(V/D)$ were calculated based on the IC values obtained at each phase. In addition, the effective atomic number values in the arterial phase (Zeff-A), venous phase (Zeff-V), and delayed phase (Zeff-D) were measured on effective atomic number images, respectively. The mean values of each parameter from the three ROIs measured by each radiologist were calculated separately, and these mean values were used as the final valid data for subsequent statistical analysis.

Observer and consistency testing

All morphological analyses and DECT quantitative parameter measurements of CT images in this study were independently performed in a blinded manner by two radiologists with more than 5 years of experience in abdominal CT diagnosis. Both radiologists were unaware of the patients's clinical data, pathological results and LNM status to avoid bias. Interobserver measurement consistency was tested using intraclass correlation coefficient (ICC), with $ICC > 0.75$ considered good agreement. The mean values of the measurements from the two radiologists were finally adopted as the study data for subsequent statistical analysis.

Statistical Analysis

Continuous variables were presented as mean $\pm$ standard deviation. Categorical variables were presented as cases (percentage), including Gender, tumor location, serum tumor markers, vascular invasion, and intratumoral necrosis. Independent samples t-test was used for between-group comparisons of normally distributed continuous variables, while Mann-Whitney U test was applied for non-normally distributed variables.

Univariate Logistic regression analysis was performed for all clinical features, dual-energy CT morphological features and quantitative parameters to preliminarily screen variables associated with LNM in PDAC. Variables with $P < 0.05$ in univariate analysis were included in the multivariate logistic regression model. Independent predictors were selected using the forward stepwise method, and odds ratios with 95% CI were calculated. A combined clinical-radiological predictive model was constructed based on the results of multivariate regression.

Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic performance of each independent predictor and the combined model, with the calculation of the area under the curve

(AUC) and 95% CI. The Delong test was used to compare differences in AUC among different models to verify the diagnostic advantage of the combined model. The calibration of the model was assessed by the Hosmer-Lemeshow test, and the clinical net benefit of the model was evaluated by decision curve analysis (DCA).

All statistical analyses were performed using SPSS 27.0.1 (IBM Corp., Armonk, NY, USA) and MedCalc version 23 (MedCalc Software, Ostend, Belgium). Statistical significance was set at $p < 0.05$.

Results

Demographic, Clinical and Imaging Characteristics of Patients

A total of 126 pathologically confirmed PDAC patients were enrolled in this study, including 80 males and 46 females. According to postoperative pathological findings, 77 patients were assigned to the LNM-positive group and 49 to the LNM-negative group. The age of patients in the LNM-positive group was 62.55 ± 1.27 years, which was significantly lower than 66.39 ± 1.20 years in the LNM-negative group, with a statistically significant difference ($P < 0.05$). There were no significant differences in Gender, tumor location, and tumor size between the two groups (all $P > 0.05$).

The levels of CA19-9, NLR, and the incidences of vascular invasion and intratumoral necrosis in the LNM-positive group were significantly higher than those in the LNM-negative group, with all differences statistically significant (all $P < 0.05$). However, there were no significant differences in CA125 and CEA levels between the two groups (all $P > 0.05$). Detailed characteristics of the two groups are summarized in **Table 1**.

Table 1 Baseline characteristics of patients.

Characteristic	LNM-positive n=77	LNM-negative n=49	P-value
Age (mean $\pm$ SD)	62.55 $\pm$ 11.38	66.39 $\pm$ 9.08	0.048
Gender (n, %)			0.273
Male	46 (59.7%)	34 (69.4%)	
Female	31 (40.3%)	15 (30.6%)	
CA19-9, n (%)			0.009
0-37 U/mL	15 (19.5%)	20 (40.8%)	
$\geq$ 37 U/mL	62 (80.5%)	29 (59.2%)	
CA125, n (%)			0.316
0 $\leq$ 35 U/mL	50 (64.9%)	36 (73.5%)	
$\geq$ 35 U/mL	27 (35.1%)	13 (26.5%)	
CEA, n (%)			0.460
0-5 ng/mL	42 (54.5%)	30 (61.2%)	
$\geq$ 5 ng/mL	35 (45.5%)	19 (38.8%)	
NLR	3.77 $\pm$ 0.22	2.95 $\pm$ 0.55	$\leq$ 0.001
Tumor size(mm)	36.87 $\pm$ 13.29	37.51 $\pm$ 13.92	0.655
Tumor location, n(%)			0.861
Head and neck	53 (68.8%)	33 (67.3%)	
Body and tail	24 (31.2%)	16 (32.7%)	
Vascular invasion, n (%)			0.024
negative	36 (46.8%)	35 (71.4%)	
positive	41 (53.2%)	14 (28.6%)	
Intratumoral necrosis, n (%)			$\leq$ 0.001
negative	19 (24.7%)	29 (59.2%)	
positive	58 (75.3%)	20 (40.8%)	

Abbreviations: LNM, lymph node metastasis; NLR, neutrophil-to-lymphocyte ratio.

Interobserver Concordance

Two blinded experienced radiologists independently measured all DECT quantitative parameters, with interobserver agreement assessed by ICC. All parameters showed excellent consistency (ICC: 0.84–0.97, all 95% CIs >0.78), and λ_{VP} had a good ICC of 0.93 (95% CI: 0.89–0.96). Mean duplicate measurements were used for subsequent analyses.

DECT quantitative parameters

The comparison of DECT quantitative parameters between the LNM-positive and LNM-negative groups is presented in **Table 2**. HU40kev-A, HU40kev-V, HU70kev-V, λ_{AP} , λ_{VP} , NIC-V, Zeff-A, Zeff-V, Zeff-D, and IC(V/D) in the LNM-positive group were significantly higher than those in the LNM-negative group (all $P<0.05$), among which λ_{VP} showed the most significant difference ($P<0.001$). No statistically significant differences were found in the other DECT quantitative parameters between the two groups (all $P>0.05$). Representative cases of PDAC patients with and without LNM, showing the characteristic differences in DECT quantitative parameters, imaging features and corresponding pathological findings, are presented in **Fig. 2** and **Fig. 3**, respectively.

Table 2 Comparison of DECT quantitative parameters.

Characteristic	LNM-positive n=77	LNM-negative n=49	P-value
HU _{40keV} -A	124.66 ± 3.18	114.83±3.58	0.047
HU _{40keV} -V	186.88 ± 4.74	163.06 ± 5.53	0.002
HU _{40keV} -D	195.03 ± 4.54	182.30 ± 6.22	0.120
HU _{70keV} -A	55.90 ± 1.32	52.64 ± 1.21	0.087
HU _{70keV} -V	75.17 ± 1.84	68.15 ± 2.27	0.018
HU _{70keV} -D	78.37 ± 1.61	74.87 ± 2.16	0.189
λ _{AP}	2.31 ± 0.07	2.07± 0.13	0.030
λ _{VP}	3.74 ± 0.93	3.16 ± 0.91	0.001
λ _{DP}	3.89 ± 0.10	3.64 ± 0.12	0.107
NIC-A	0.10 ± 0.00	0.09 ± 0.01	0.132
NIC-V	0.42 ± 0.01	0.36 ± 0.01	0.006
NIC-D	0.68 ± 0.01	0.64 ± 0.02	0.150
Zeff-A	8.31 ± 0.17	8.24 ± 0.17	0.016
Zeff-V	8.67 ± 0.03	8.59 ± 0.04	0.023
Zeff-D	8.78 ± 0.24	8.69 ± 0.24	0.033
IC(A/V)	0.62 ± 0.02	0.66 ± 0.03	0.258
IC(A/D)	0.60 ± 0.02	0.58 ± 0.03	0.652
IC(V/D)	0.96 ± 0.20	0.88 ± 0.20	0.044

Abbreviations: DECT, Dual-energy computed tomography; HU, Hounsfield unit; λ, Slope of the energy attenuation curve; NIC, Normalized iodine concentration; Zeff, Effective atomic number; IC, iodine concentration.

Univariate and Multivariate Logistic Regression Analysis of Risk Factors for LNM in PDAC

Univariate Logistic regression analysis was conducted for all clinical characteristics, DECT morphological features and quantitative parameters in the training cohort (n=87) to screen variables associated with LNM in PDAC. The results showed that CA19-9, intratumoral necrosis, HU40keV-V, HU70keV-V, λ_{VP} and NIC-V were significantly correlated with LNM in PDAC (all P<0.05).

All variables with statistical significance in the univariate analysis were further included in the multivariate Logistic regression model with the forward stepwise method. The results revealed that CA19-9 (OR=4.787, 95%CI:1.476–15.526, P=0.009), intratumoral necrosis (OR=6.865, 95%CI:2.249–20.957, P<0.001), and λ _VP (OR=2.302, 95%CI:1.295–4.090, P=0.004) were independent predictive factors for LNM in PDAC. Detailed results of univariate and multivariate Logistic regression analyses are shown in **Table 3**.

Table 3 Univariate and multivariate logistic regression analysis of predictive factors for LNM in the training cohort of PDAC patients.

Variables	Univariate logistic regression			Multivariate logistic regression		
	OR	95%CI	P-value	OR	95%CI	P-value
CA19-9 (>37 U/mL)	4.441	1. 614-12.215	0.004	4.787	1.476-15.526	0.009
Intratumoral necrosis	3.980	1.592-9.948	0.003	6.865	2.249-20.957	<0.001
HU _{40keV} -V	1.015	1.004-1.027	0.008			
HU _{70keV} -V	1.029	1.001-1.058	0.040			
λ _VP	2.000	1.223-3.270	0.006	2.302	1.295-4.090	0.004
NIC-V	2.650	1.157-3.390	0.045			

Abbreviations: λ _VP—Slope of the energy attenuation curve in the venous phase—NIC-V—Normalized iodine concentration in the venous phase.

Diagnostic Performance Evaluation of the Predictive Model

ROC curve analysis was performed to evaluate the diagnostic performance of CA19-9, intratumoral necrosis, λ _VP, and the combined model for LNM in PDAC. The differences in the area under the curve (AUC) among different models were compared using the Delong test. In the training cohort, the AUC values (95%CI) of CA19-9, intratumoral necrosis, and λ _VP for predicting LNM were 0.645 (0.535–0.745), 0.662 (0.553–0.760), and 0.675 (0.566–0.771), respectively. The combined model achieved an AUC of 0.816 (95%CI:0.730–0.874) in the training cohort and 0.761 (95%CI:0.613–0.909) in the test cohort (n=39). The AUC of the combined model was significantly higher than that of any single predictor in both cohorts (all P<0.001). The ROC curves of the single predictors and the combined model are shown in **Fig. 4**.

Calibration and Clinical Utility Evaluation of the Combined Predictive Model

The Hosmer-Lemeshow (H-L) goodness-of-fit test was performed to assess the calibration performance of the combined predictive model in the training and test cohorts, respectively. The results demonstrated that the model had favorable goodness-of-fit in both the training cohort (χ^2 =5.329, df=8, P=0.722) and

the test cohort ($\chi^2=6.384$, $df=8$, $P=0.604$), indicating that the predicted probabilities of LNM by the model were highly consistent with the actual pathological results. The calibration curves of the combined model in the two cohorts are presented in **Fig. 5**.

Performance Evaluation and Clinical Applicability of the Combined Predictive Model

DCA was used to evaluate the clinical net benefit of the combined model for LNM prediction, with the treat-all and treat-none strategies as references. The results showed that within the clinically relevant risk threshold probability range of 0-0.65 in the training cohort and 0-0.8 in the test cohort, the combined model achieved a significantly greater net benefit in clinical decision-making for LNM in PDAC compared with the two reference strategies. This indicated that the model could effectively balance the clinical risks of missed diagnosis and overtreatment in clinical practice. The DCA curves of the combined model are shown in **Fig. 6**.

Discussion

In this study, we identified λ_VP , intratumoral necrosis, and CA19-9 as independent predictors of LNM in PDAC. The combined model incorporating these factors achieved optimal diagnostic performance, with AUC values of 0.816 in the training cohort and 0.761 in the test cohort, which were significantly higher than those of any single parameter. This non-invasive tool addresses critical limitations of conventional CT-based nodal staging, providing reliable preoperative LNM assessment to guide clinical decision-making.

As established in prior work, accurate LNM staging is a cornerstone of treatment planning and prognostic stratification in PDAC [16,17]. While the 8th edition of the AJCC lymph node staging system provides a standardized framework [18], conventional CT assessment of nodal status remains limited by suboptimal accuracy and poor interobserver reproducibility [19-21]. These challenges arise because CT cannot reliably distinguish metastatic nodes from inflammatory hyperplasia, nor detect small, non-enlarged metastases. Thus, our study addresses an unmet clinical need by leveraging quantitative imaging and serological markers to refine LNM risk stratification.

In the present study, patients in the LNM-positive group had a significantly lower mean age than those in the LNM-negative group, suggesting that younger patients with PDAC may be more prone to LNM. Another retrospective study including 414 patients with surgically resected PDAC also demonstrated that elderly patients had significantly poorer prognosis, with overall survival and recurrence-free survival decreasing significantly with advancing age. This finding further supports the association between age and prognosis in PDAC [22].

CA19-9 is the most widely used and representative tumor marker in the clinical diagnosis and treatment of PDAC, and its expression level is closely associated with tumor invasion, metastasis, and prognosis. Multiple studies have confirmed that it can serve as an important reference for evaluating disease status in PDAC [23-25]. One multi-institutional retrospective study enrolling 2,034 patients who underwent

pancreaticoduodenectomy investigated the role of preoperative CA19-9 in predicting lymph node involvement in resectable PDAC. It confirmed that CA19-9 exhibited sufficient ability to predict the risk of lymph node positivity (AUC = 0.60, 95% CI = 0.57–0.63; $P < 0.001$). When different thresholds were tested, a cutoff of 37 U/ml yielded a sensitivity of 74.4% and specificity of 42.1%, with the optimal diagnostic odds ratio among all thresholds [24]. In the present study, the proportion of patients with CA19-9 > 37 U/mL was significantly higher in the LNM-positive group than in the LNM-negative group ($P = 0.009$). Multivariate regression analysis showed that CA19-9 > 37 U/mL was an independent risk factor for LNM in PDAC, with a regression coefficient of 1.57, odds ratio of 4.787 (95%CI: 1.476–15.526), and $P = 0.009$. These findings clearly indicate that elevated CA19-9 can independently predict the risk of LNM in PDAC patients, further supporting the close relationship between CA19-9 and LNM. Regarding diagnostic performance, ROC curve analysis in our study demonstrated an AUC of 0.645 (95% CI: 0.535–0.745) for CA19-9 in predicting LNM of PDAC, suggesting moderate predictive efficacy. Although it does not reach ideal diagnostic accuracy, its advantages of convenience, non-invasiveness, and repeatability still endow it with important clinical practical value.

Notably, NLR is an easily accessible hematological parameter that reflects systemic inflammation and immune status. It is convenient to measure and cost-effective, and its value in tumor prognostic evaluation has been well established in numerous studies. An elevated NLR promotes a pro-tumor inflammatory microenvironment, suppresses anti-tumor immunity, and facilitates tumor proliferation, invasion, and metastasis. It has been independently associated with poor prognosis in various malignancies, including PDAC. Previous studies have confirmed that a high preoperative NLR is an important prognostic indicator in early-stage PDAC, and its combination with CA19-9 can significantly improve the prediction accuracy of early recurrence, suggesting substantial clinical potential for NLR in the assessment and prognosis of PDAC [26, 27]. In the present study, NLR levels were significantly higher in the LNM-positive group than in the LNM-negative group ($P < 0.001$), which is consistent with findings reported in the literature.

Similarly, Vascular invasion represents an important route for tumor cells to breach tissue barriers and develop distant metastasis, and its presence directly reflects the invasive and metastatic potential of malignant cells. Multiple studies have confirmed its close association with tumor progression, metastasis, and poor prognosis in PDAC [28, 29]. The present study demonstrated that the proportion of patients with vascular invasion was significantly higher in the LNM-positive group than in the LNM-negative group ($P = 0.024$). These findings clearly indicate a strong correlation between vascular invasion and LNM in PDAC, suggesting that vascular invasion may serve as an important pathological factor promoting LNM in PDAC.

Comparison of DECT quantitative parameters between groups showed that several parameters, including HU40keV-V, λ_{VP} , NIC-V, and Zeff-V, were significantly higher in the LNM-positive group than in the LNM-negative group ($P < 0.05$). Among these parameters, λ_{VP} exhibited the most significant intergroup difference ($P < 0.001$). These parametric differences reflect biological heterogeneity in blood supply characteristics, iodine uptake capacity, and atomic composition between metastatic and non-

metastatic lesions. PDAC tumor cells with LNM demonstrate more active proliferation and higher microvascular density, leading to increased retention of iodine contrast agent in the venous phase, thereby elevating the slope of the energy attenuation curve and normalized iodine concentration [30]. Multivariate Logistic regression analysis confirmed that λ_{VP} , CA19-9, and intratumoral necrosis were independent predictive factors for LNM in PDAC. These results not only verify the core value of multi-parametric DECT in predicting LNM but also demonstrate the complementary role of combining quantitative imaging parameters with clinical and pathological indicators, providing more objective evidence for the non-invasive preoperative evaluation of LNM in PDAC.

ROC curve analysis further validated the diagnostic value of single parameter and the combined model for LNM in PDAC. Single parameter analysis showed that λ_{VP} (AUC = 0.675) and intratumoral necrosis (AUC = 0.662) yielded slightly better diagnostic performance than CA19-9 (AUC = 0.645), suggesting that imaging and pathological features may be superior to individual serum markers in reflecting tumor invasiveness. As a direct pathological sign of active tumor proliferation and insufficient blood supply, intratumoral necrosis showed a high AUC value, indicating its close association with LNM. As a quantitative DECT parameter, λ_{VP} reflects differences in tumor microcirculatory perfusion and indirectly indicates the invasive potential of tumor cells, which accounts for its favorable predictive efficacy. Furthermore, when λ_{VP} , CA19-9, and intratumoral necrosis were incorporated into the combined predictive model, the AUC reached 0.816 in the training cohort and 0.761 in the test cohort, both of which were significantly higher than any single parameter. The combined model comprehensively evaluates the risk of LNM by integrating serological, imaging, and pathological morphological information, effectively compensating for the limitations of single parameter. This is consistent with recent research trends in the non-invasive prediction of PDAC [31-33] and can provide a more reliable reference for accurate preoperative clinical evaluation.

In the present study, the calibration and clinical decision-making value of the combined predictive model were systematically evaluated. The Hosmer–Lemeshow test and calibration curves revealed that the combined model exhibited favorable goodness of fit in both the training and test cohorts, indicating high consistency between the predicted probabilities and the actual observed probabilities. These results demonstrate excellent calibration performance, allowing the model to reliably reflect the true risk of LNM in patients with PDAC.

DCA further confirmed that within the clinically relevant risk threshold ranges of 0-0.65 in the training cohort and 0-0.8 in the test cohort, the combined model achieved significantly higher net benefit than both the treat-all and treat-none strategies. This suggests that in clinical practice, the model can effectively balance the clinical risks of missed diagnosis and overtreatment, providing practical decision support for the non-invasive preoperative evaluation of LNM in PDAC patients.

This study has several limitations. First, as a single-center retrospective study, selection bias was inevitable. Second, only internal test cohort validation was performed, and external multicenter validation was lacking; therefore, the generalizability of our findings requires further investigation. In addition,

variations in DECT scanning parameters and postprocessing protocols across different institutions may affect the stability of the model in cross-center applications.

Conclusion

λ_{VP} , CA19-9, and intratumoral necrosis were independent predictive factors for LNM in PDAC. The combined model integrating these three factors showed significantly superior diagnostic performance for LNM compared with any single parameter, providing a reliable multi-dimensional tool for noninvasive preoperative clinical assessment of LNM risk in PDAC.

Abbreviations

AUC	Area under the curve
CI	Confidence interval
DCA	Decision curve analysis
DECT	Dual-energy computed tomography
HU	Hounsfield unit
ICC	Intraclass correlation coefficient
IC	Iodine concentration
LNM	Lymph node metastasis
NLR	Neutrophil-to-lymphocyte ratio
NIC	Normalized iodine concentration
OR	Odds ratio
PDAC	Pancreatic ductal adenocarcinoma
ROI	Region of interest
ROC	Receiver operating characteristic
Z _{eff}	Effective atomic number
λ	slope of the energy attenuation curve

Declarations

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Not applicable.

Author contributions

H. Z., S.M., P.C. were involved in the literature search, figures, study design, data analysis, and writing. H.Z., W.Z., J.L, B.W. and M.J. were involved in data collection, Quality control of data and algorithms. C.Z., A.S. and W.W. were involved in study design and article review. All authors read and approved the final manuscript.

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Data availability

The dataset used or analyzed during the current study is available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

The study was approved by Institutional Review Board of the First Affiliated Hospital of USTC (Approval No.: 2026-RE-113). Individual informed consent was waived due to the retrospective study design. All procedures performed in this study involving human participants were in accordance with the Declaration of Helsinki.

Consent for publication

All authors have read and approved the final manuscript.

Competing interests

The authors declare no competing interests.

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Figures

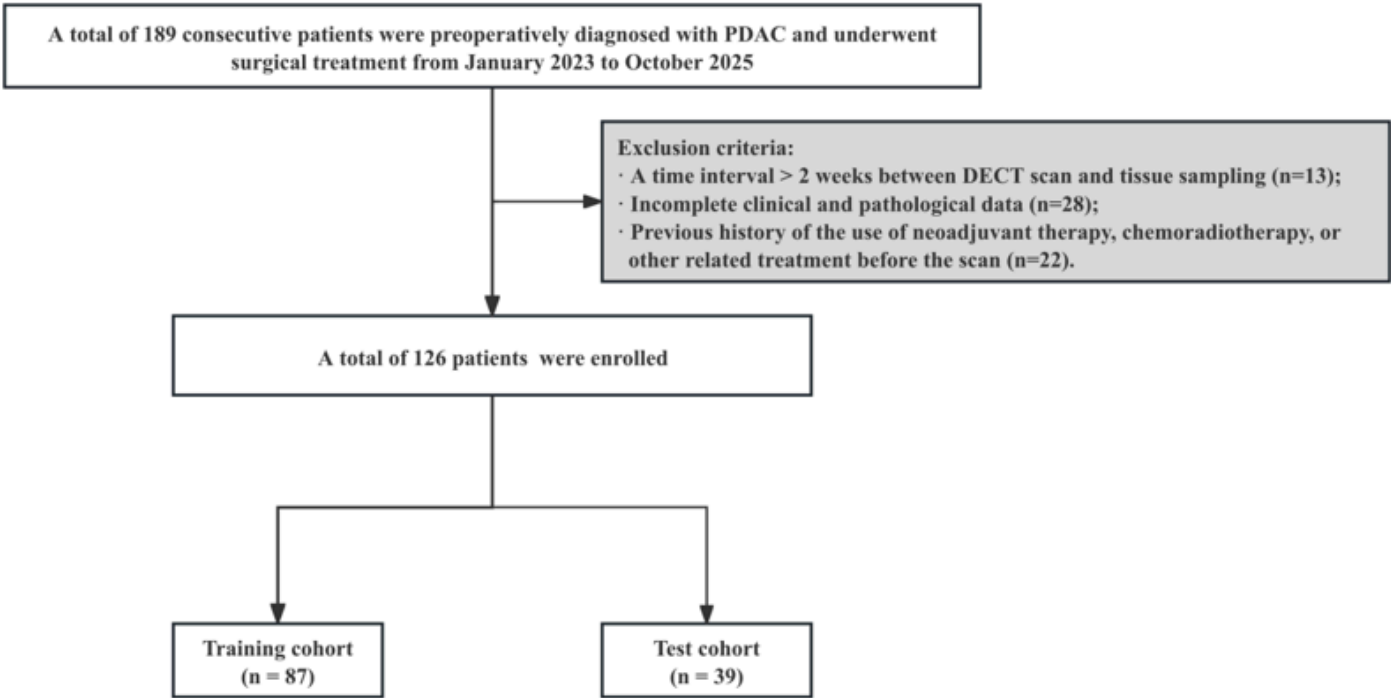


Figure 1

Flow diagram.

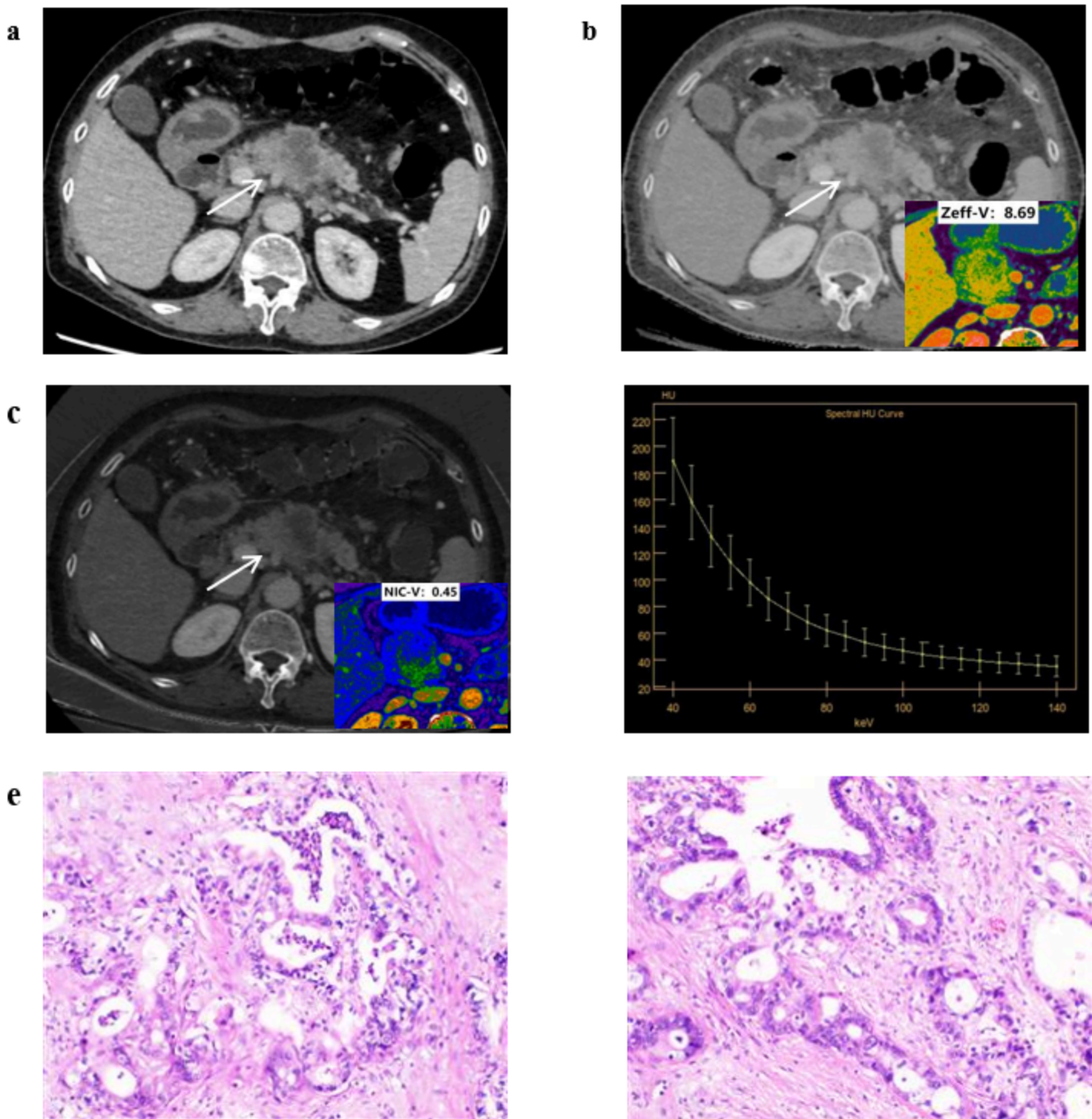


Figure 2

A 64-year-old male patient with poorly differentiated pancreatic ductal adenocarcinoma (PDAC) and peripancreatic lymph node metastasis (LNM). **a** Venous-phase 40-keV monoenergetic image (HU40keV-V: 189.76). **b** Venous-phase effective atomic number map (Zeff-V: 8.69). **c** Venous-phase iodine concentration map (NIC-V: 0.45). **d** Venous-phase energy attenuation curve (λ_{VP} : 3.68). **e** Hematoxylin and eosin (HE) staining ($\times 200$), tumor tissue shows glandular and cribriform arrangement with invasive

growth and necrosis. **f** Hematoxylin and eosin (HE) staining ($\times 400$), tumor cells exhibit marked atypia with disorganized glandular architecture.

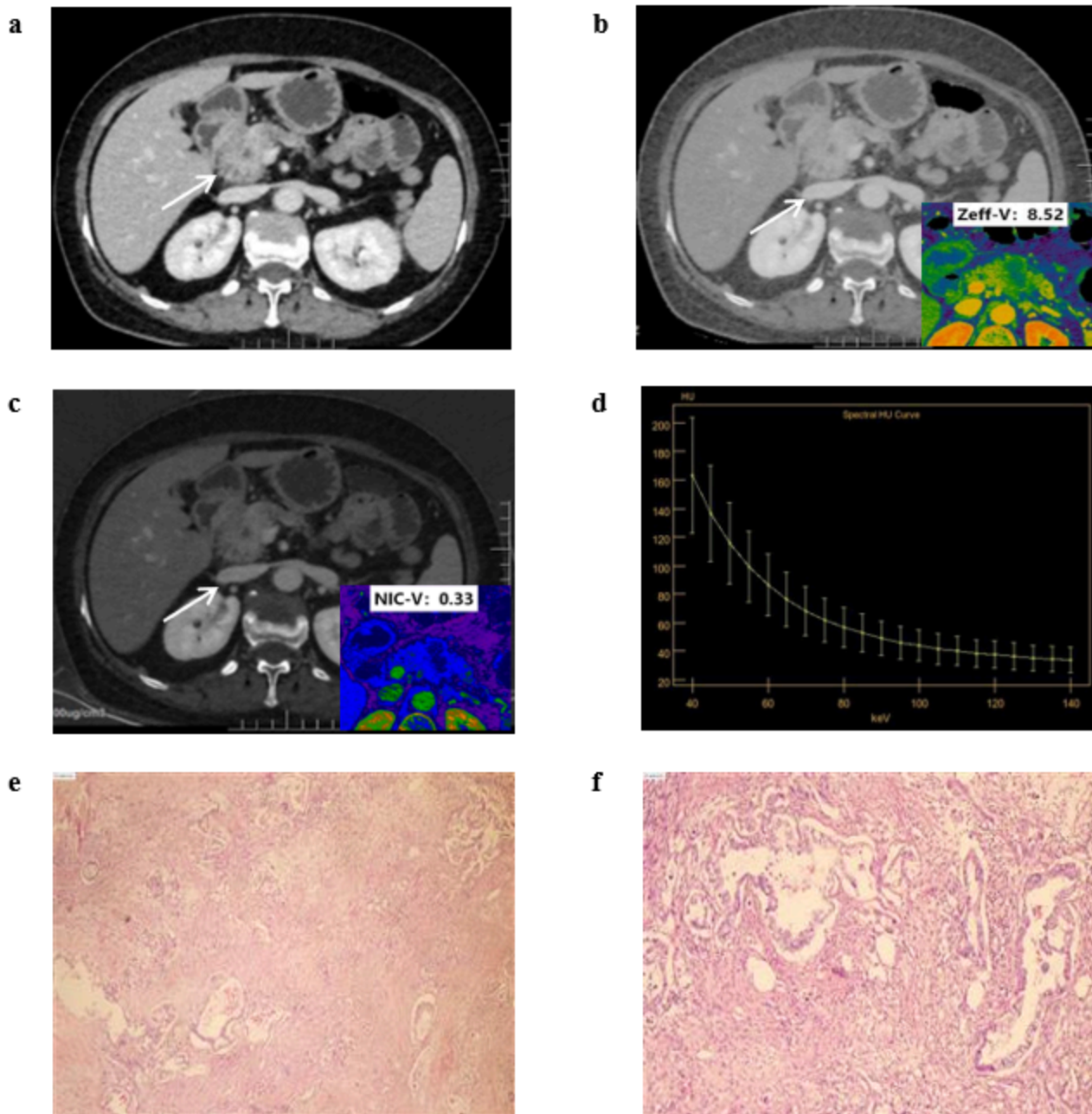


Figure 3

A 68-year-old female patient with moderately differentiated pancreatic ductal adenocarcinoma (PDAC) and no peripancreatic lymph node metastasis (LNM). **a** Venous-phase monoenergetic image at 40 keV (HU40keV-V: 163.06). **b** Venous-phase effective atomic number map (Zeff-V: 8.52). **c** Venous-phase normalized iodine concentration (NIC-V: 0.33). **d** Slope of the venous-phase energy attenuation curve (λ_{VP} : 3.11). **e** Hematoxylin and eosin (HE) staining ($\times 200$), neoplastic glandular nests with surrounding desmoplasia. **f** Hematoxylin and eosin (HE) staining ($\times 400$), tumor cells show marked atypia with disorganized glandular architecture.

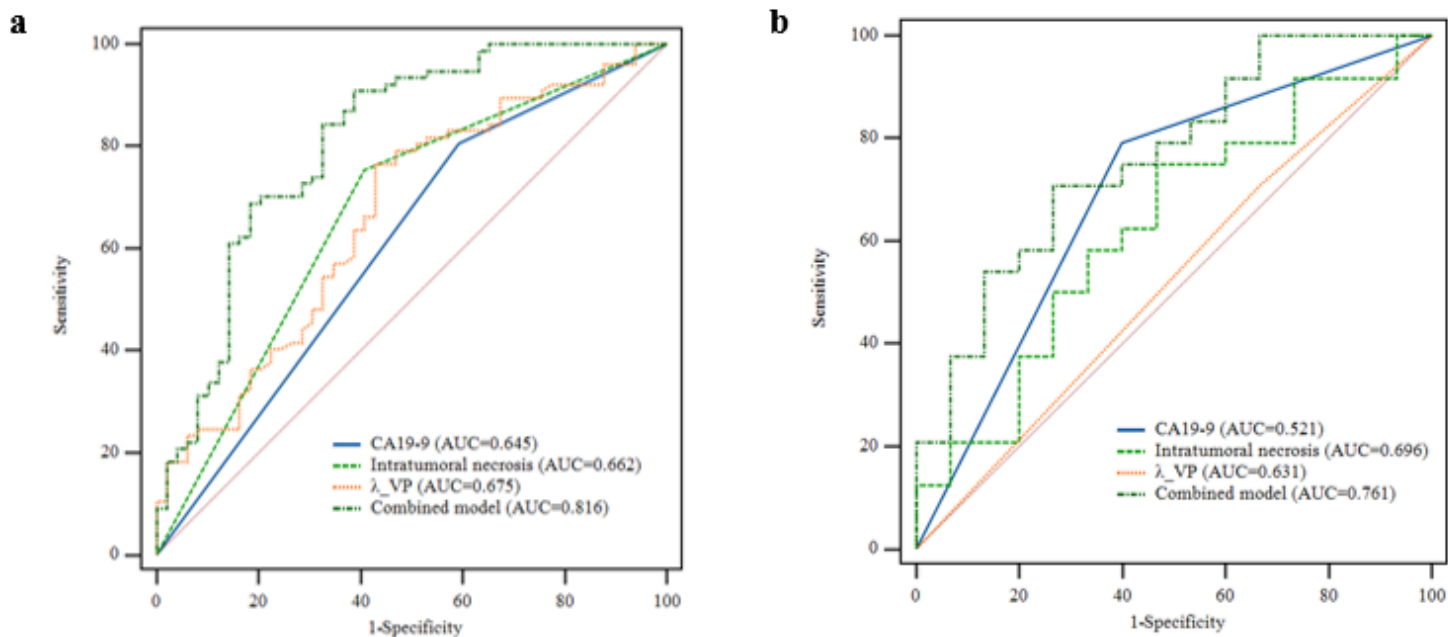


Figure 4

Receiver operating characteristic (ROC) curves showing the diagnostic performance of the combined predictive model for lymph node metastasis (LNM) in patients with pancreatic ductal adenocarcinoma (PDAC). **a** Training cohort; **b** Test cohort. AUC, area under the curve; λ_{VP} , slope of the venous-phase energy attenuation curve.

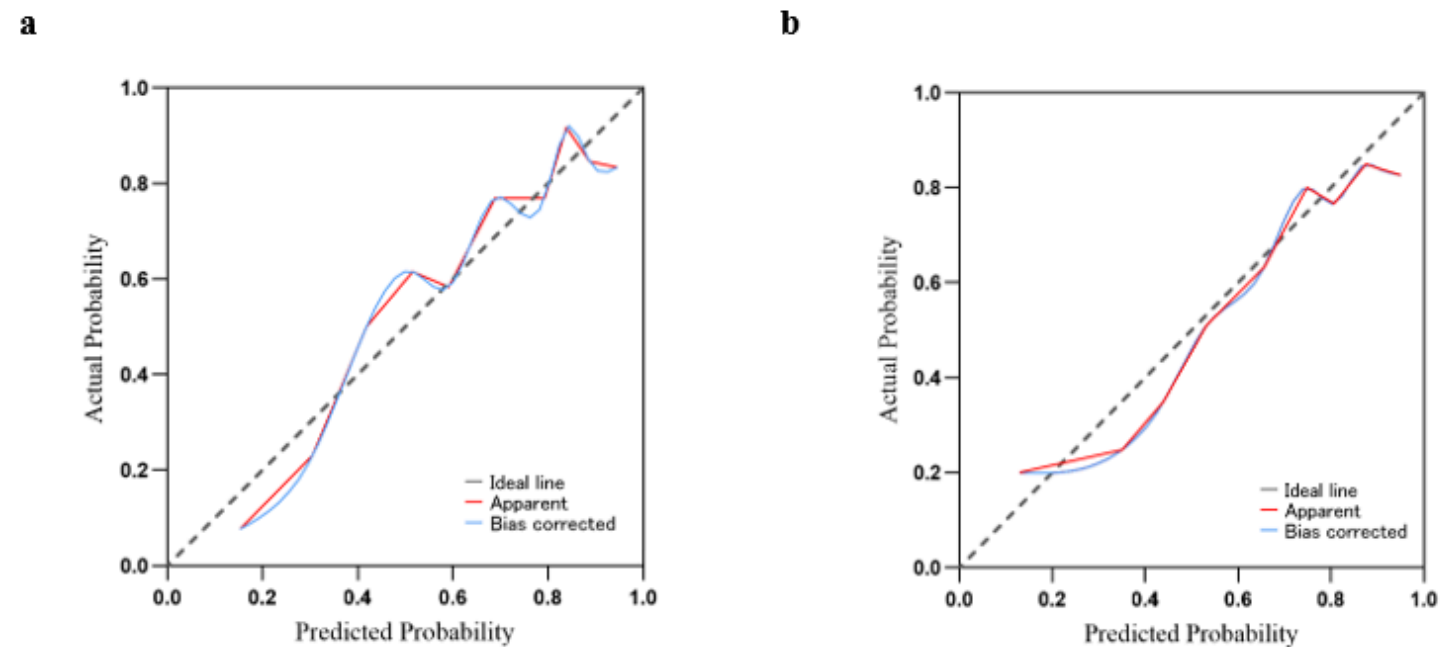


Figure 5

Calibration curves of the combined predictive model for lymph node metastasis (LNM) in patients with pancreatic ductal adenocarcinoma (PDAC). **a** Training cohort; **b** Test cohort

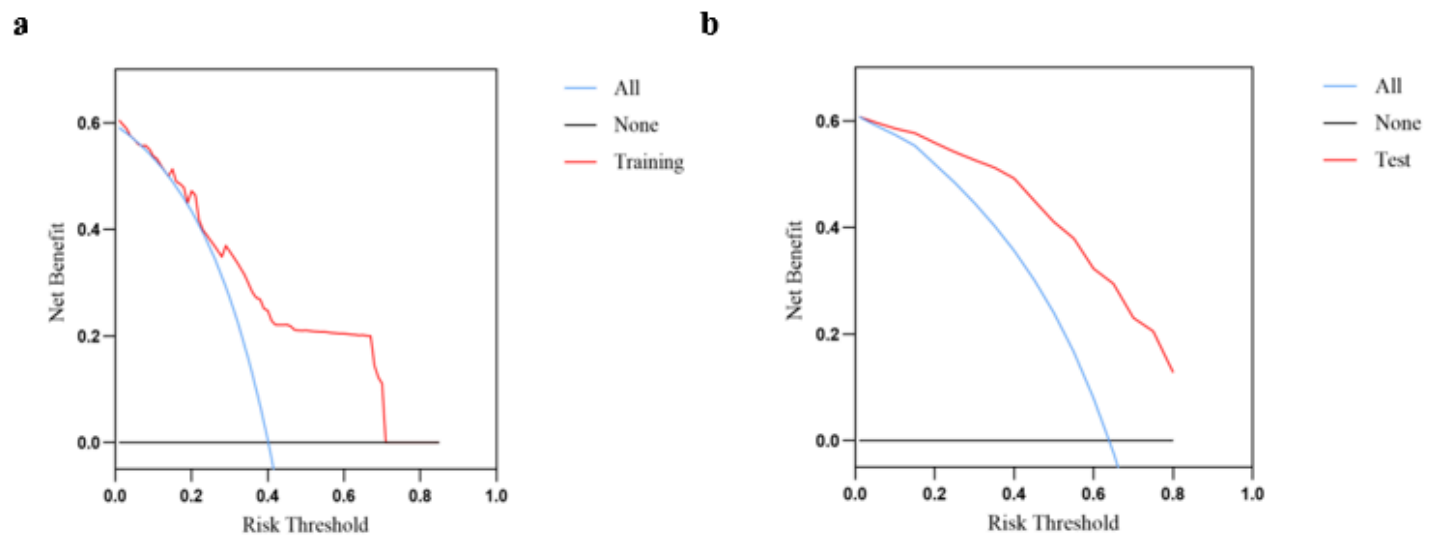


Figure 6

Decision curve analysis (DCA) evaluating the clinical utility of the combined predictive model for lymph node metastasis (LNM) in patients with pancreatic ductal adenocarcinoma (PDAC). **a** Training cohort; **b** Test cohort

Supplementary Files

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