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Clinical T categorization in stage IA lung adenocarcinomas: prognostic implications of CT display window settings for solid portion measurement

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Abstract

Objectives Our study aimed at evaluating the prognostic implications of lung and mediastinal CT display window settings for solid portion measurements on the eighth-edition lung cancer staging system's clinical T (cT) categorization.

Methods We retrospectively analyzed 691 surgically treated patients from 2009 to 2015 for clinical stage IA lung adenocarcinomas. Solid portions were measured at the lung and mediastinal window settings, respectively, and cT categories were determined for each measurement (cT_{lung} and $cT_{mediastinum}$). The prognostic power of the two cT factors for disease-free survival (DFS) was assessed using Cox regression, and concordance indices (C-indices) were compared using the Student *t* test. Subsequently, the patients were split into training and validation cohorts to calculate optimal cutoffs for the cT categorization of mediastinal window–based solid portions ($cT_{optimal}$) and validate its prognostic performance.

Results Both cT_{lung} ((cT1b: adjusted HR, 3.547; $p = 0.017$), (cT1c: adjusted HR, 9.439; $p < 0.001$)) and $cT_{mediastinum}$ ((cT1b: adjusted HR, 4.635; $p < 0.001$), (cT1c: adjusted HR, 11.235; $p < 0.001$)) were significantly associated with DFS for each multivariable Cox model. The C-indices were 0.772 (95% CI, 0.702–0.842) for cT_{lung} and 0.787 (95% CI, 0.726–0.848) for $cT_{mediastinum}$ ($p = 0.789$). The optimal cutoffs for cT categorization of the mediastinal window–based solid portions were 0.9 cm and 1.8 cm. However, there were no significant differences in the C-indices among cT_{lung}, $cT_{mediastinum}$, and $cT_{optimal}$ ($p > 0.05$).

Conclusions The prognostic performances of the cT categorizations at the lung and mediastinal windows were not significantly different. The current cT categorization based on the lung window measurement is appropriate as it stands.

Key Points

- *Discriminatory power of the eighth-edition clinical T category was not significantly affected by the CT display window settings.*
- *Given the facts that the lung window setting enables more sensitive detection of the solid portions and higher correlation with the pathological invasive components, our findings may support adherence to the usage of the lung window setting for the solid portion measurement per the current recommendations.*

Keywords Non–small cell lung carcinoma · Adenocarcinoma · Multidetector computed tomography · Neoplasm staging · Disease-free survival

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Abbreviations

AIC	Akaike's information criterion
C-index	Concordance index
cT_{lung}	Clinical T categorization based on solid portion measurement with the lung window setting using the eighth-edition T coding system
$cT_{mediastinum}$	Clinical T categorization based on solid portion measurement with the mediastinal window setting using the eighth-edition T coding system
$cT_{optimal}$	Clinical T categorization for the mediastinal window–based solid portion using optimal cutoffs
DFS	Disease-free survival
EMR	Electronic medical record
IQR	Interquartile range
TDR	Tumor disappearance ratio

Introduction

Pulmonary adenocarcinoma is the most common histological subtype of non–small cell lung cancer, and its incidence continues to increase in females globally [1]. On chest CT, the mainstay modality for the evaluation of lung cancer, adenocarcinoma, and its preinvasive precursors manifests as pure ground-glass, part-solid, or solid nodules [2].

Recent studies have revealed that solid portions in part-solid nodules are reflective of the invasive adenocarcinoma component pathologically [3], and the solid portion size is more closely associated with patients' prognosis than the total tumor size covering the ground-glass opacity [4–7]. These findings led to the revision in the eighth-edition TNM staging for lung cancer, and thus, the clinical T (cT) categorization is now determined based on the solid portion measurement on CT scans [8]. Importantly, the current cT categorization system proposed by the International Association for the Study of Lung Cancer (IASLC) and radiological lung nodule measurement guideline by the Fleischner Society recommend that the solid portion be measured using the lung window setting of CT scans [8, 9], which employs a wide window width to display the lung parenchyma and its abnormal pathologies.

There is still controversy, however, on the merits and demerits of the lung and mediastinal window settings. The advantage of the mediastinal window is its potential to promote inter-reader agreement in lung nodule classification and measurements [10–12], while the lung window setting enables more sensitive detection of the solid portions and higher correlation with the pathological invasive components [3, 12, 13]. To date, studies have focused on the radiological–pathological correlation for assessing the appropriateness of each window setting for the diagnosis of invasive adenocarcinomas [3, 12, 13]. However, the prognostic implication of CT display window settings on the cT categorization, especially for the eighth-edition T coding system, has not yet been investigated. A scrupulous analysis from various angles in terms of diagnosis, prognostication, and practicality should be considered comprehensively to decide on the most felicitous CT window setting to be used for lung cancer staging, as well as for routine clinical practice. Therefore, the purpose of our study was to evaluate and compare the prognostic performance of cT categories determined using the solid portion measurements with the lung and mediastinal window settings for disease-free survival (DFS) in patients with clinical T1N0M0 (stage IA) lung adenocarcinomas.

Materials and methods

This retrospective analysis was approved by the Institutional Review Board of Seoul National University Hospital. The requirement for written informed consent was waived. Our study population (691/691) was reported previously [14]. In the prior study, we aimed to compare the prognostic performances of cT categorization between the longest and average diameter measurements on CT scans. The current study deals with the prognostic implication of CT display window settings on the cT categorization.

Study population

The electronic medical records (EMRs) of all patients who underwent surgical resection for lung cancer between January 2009 and December 2015 at our hospital were retrospectively searched. Among 2360 patients, 900 with clinical stage IA non–small cell lung cancers, who underwent standard lobectomy and did not have synchronous or metachronous lung cancers, were identified. Of these, patients with pure ground-glass nodules were excluded ($n = 77$). In addition, patients with lung cancers other than the adenocarcinoma spectrum were also excluded ($n = 132$). Consequently, the final study population consisted of 691 patients (281 males and 410 females; Fig. 1). The median age was 64 years (interquartile range (IQR), 57–70 years) for males and 62 years (IQR, 55–70 years) for females ($p = 0.021$). Detailed patient and nodule characteristics are described in Table 1.

Data collection

Patient characteristics and clinical information, including age, sex, past history of malignancy other than lung cancer, family history of lung cancer, smoking history, date of the preoperative chest CT scan, surgery date, and pathological diagnosis, were recorded from the EMRs. Interval between the CT scan and surgery was calculated. For the nodule characteristics at the preoperative chest CT scans, nodule type (part-solid or solid) and location were obtained from the radiology reports.

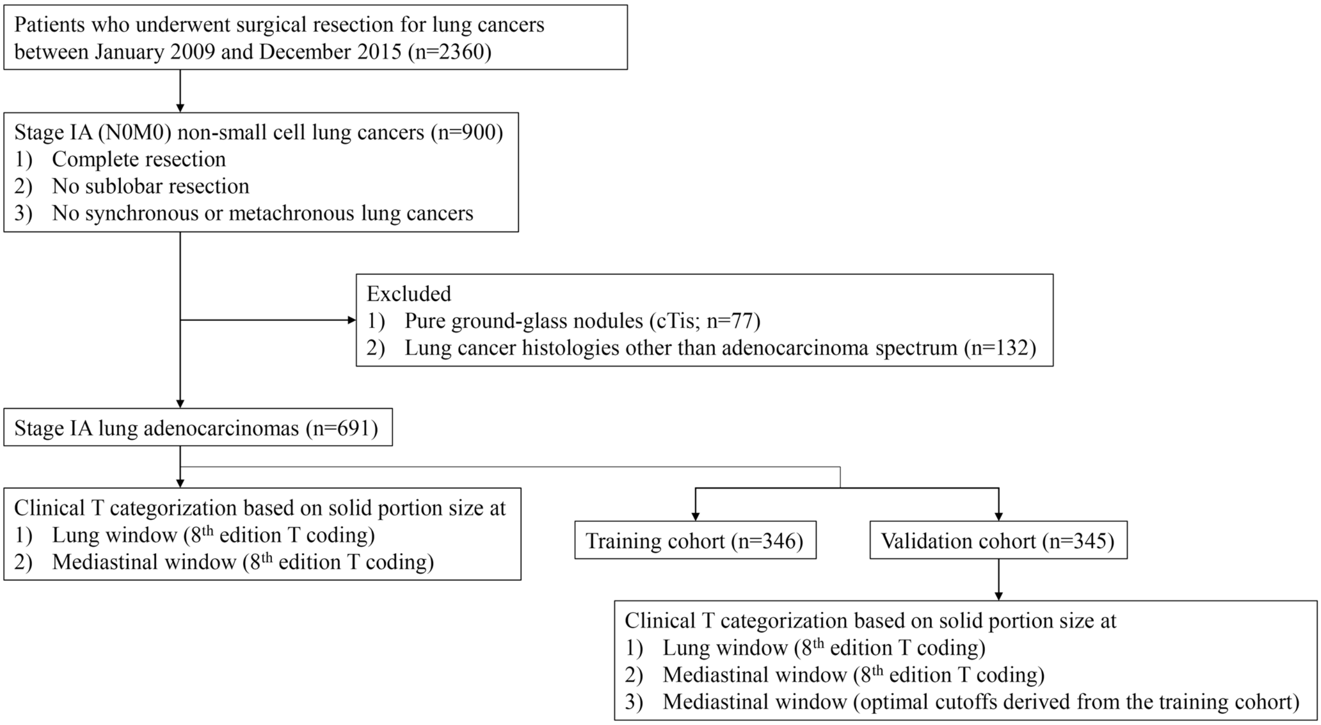


Fig. 1 Flow diagram of patient inclusion and schematic representation of the study workflow

Solid portion size (longest diameter) was measured on axial CT images of the lung window (window width, 1500 Hounsfield units (HU); level, − 700 HU) and mediastinal window settings (window width, 400 HU; level, 30 HU), respectively, by one of two trained radiology technicians (either M.L. or J.Y.J., both of whom have experience of approximately 5000 lung nodule measurements) under the supervision of a board-certified thoracic radiologist (H.K. with 8 years of CT experience). All the CT image reviewers were blinded to the patients' outcomes. Then, the cT category was determined based on the eighth edition of the American Joint Commission on Cancer TNM staging system for lung cancer [8]. Therefore, the cT category (cT1mi/cT1a, cT1b, and cT1c) was coded twice for each nodule using the solid portion size measured at the two different window settings (hereafter, cT_{lung} for cT based on the lung window measurement and $cT_{mediastinum}$ for cT based on the mediastinal window measurement). Detailed CT scanning protocols are described in Electronic Supplementary Material (online).

DFS was measured from the date of surgery to the date of first evidence of recorded clinical (local/regional) recurrence and/or distant metastasis confirmed by imaging or histological evidence or death from any cause [15]. The times of censoring were determined as the date of the last chest CT scans.

Pathologic diagnosis

Pathological diagnoses in 74% (508/691) of the study population were established by the attending pathologists of our hospital according to the 2011 lung adenocarcinoma classification described by the IASLC/American Thoracic Society/European Respiratory Society [16]. As the pathological diagnoses were determined as a part of routine clinical practice, and the specimens were not reviewed specifically for this study, 26% (183/691) of the patients were diagnosed before implementation of the 2011 adenocarcinoma classification.

Statistical analysis

Patients' age was compared between men and women using the Mann–Whitney *U* test. The number of patients in each cT category was calculated and compared between cT_{lung} and $cT_{mediastinum}$ using the McNemar–Bowker test. The prognostic implications of the clinico-radiological variables on DFS were analyzed using the Cox proportional hazard model. Univariable Cox analysis was initially performed, and variables with *p* values of less than 0.10 were used as candidates for multivariable Cox regression analysis. Backward stepwise elimination was used as the model selection procedure based on Akaike's information criterion (AIC) [17, 18]. Then, the final prediction models, including the independent predictors for DFS, were identified. Two separate multivariable analyses were performed using cT_{lung} and $cT_{mediastinum}$ as T factors. That is, the two multivariable Cox models included the same candidate variables except for the T factor. The proportional hazard assumption was evaluated by the scaled Schoenfeld residuals using the cox.zph function in R package survival.

Table 1 Patient and nodule characteristics

Variable	No. of patients ($n = 691$)
Age (years)[a]	63 (55, 70)
Sex	
Male	281 (40.7)
Female	410 (59.3)
Past history of malignancy other than lung cancer[b]	
Yes	116 (16.8)
No	552 (79.9)
Family history of lung cancer[c]	
Yes	42 (6.1)
No	629 (91.0)
Smoking history	
Never smoker	446 (64.5)
Ex- or current smoker	245 (35.5)
Nodule location	
Upper lobes	382 (55.3)
Other lobes	309 (44.7)
Nodule type	
Part-solid	353 (51.1)
Solid	338 (48.9)
Clinical T category[d]	
cT1mi	32 (4.6)
cT1a	110 (15.9)
cT1b	323 (46.7)
cT1c	226 (32.7)
Pathology	
Adenocarcinoma in situ	17 (2.5)
Minimally invasive adenocarcinoma	19 (2.7)
Invasive adenocarcinoma	655 (94.8)
Cancer recurrence or deaths	96 (13.9)
Disease-free survival (days)[a]	1170 (748, 1791)
CT-surgery interval (days)[a]	19 (2, 30)

Unless otherwise specified, numbers in parentheses are percentages

[a] Data are median with interquartile range in parentheses

[b] Data were not available in 23 patients (3.3%)

[c] Data were not available in 20 patients (2.9%)

[d] Clinical T categorization based on the eighth-edition TNM classification for lung cancer [8]

The discriminatory performances of cT_{lung} and $cT_{mediastinum}$ in prognostication were investigated using the concordance index (C-index) from a univariable model. A higher C-index indicates a better predictive performance. The C-indices were compared between cT_{lung} and $cT_{mediastinum}$ using the Student t test for dependent samples [18]. The AIC was used to compare the model fits [19]. A lower AIC represented a better model fit.

To guarantee a fair comparison for the prognostic performance of cT between the solid portion measurements in the lung and mediastinal window settings, a secondary analysis was conducted. First, patients were partitioned into a training cohort ($n = 346$) and a validation cohort ($n = 345$) using stratified random sampling. Then, for the training cohort, the optimal number of cT categories for the solid portion size measured at the mediastinal window, which could minimize the AIC values, was calculated [20]. In the next step, the optimal cutoffs for cT categorization were defined with the most significant split (likelihood ratio test and log-rank test) [20]. This novel cT categorization system ($cT_{optimal}$) was applied to the validation cohort. Therefore, for the validation cohort, three cT categorization systems were acquired, as follows: cT_{lung}, $cT_{mediastinum}$, and $cT_{optimal}$. The C-indices for the prognostic discrimination and AIC for the model fit were evaluated as described above.

Survival curve for each cT categorization system was computed using the Kaplan–Meier method. All the statistical analyses were performed using the SPSS Statistics version 25 (IBM Corp.) and R software, version 3.5.1 (http://www.R-project.org; package: caret, survcomp, and survival). Open-source R function codes (findcutnum and findcut) were used to find the optimal number of risk groups and optimal cutoffs [20]. A p value < 0.05 was considered to indicate statistical significance. Data imputation was not performed for the missing values.

Results

In our study population, 51.1% (353/691) were part-solid nodules and 48.9% (338/691) were solid nodules. The median solid portion size was 1.7 cm (IQR, 1.1–2.2 cm) at the lung window and 1.5 cm (IQR, 0.9–2.0 cm) at the mediastinal window (Fig. 2). The solid portion measured at the mediastinal window setting led to significant down staging of the cT categories ($p < 0.001$; Table 2). Specifically, 19.5% (63/323) of cT1b cases were down staged to cT1a, while 0.6% (2/323) were up staged to cT1c. In these two up staged tumors, the solid portions measured at the mediastinal window were not regarded as being solid at the lung window due to more highly attenuated inner solid components. In cT1c cases, 26.5% (60/226) were shifted to cT1b and 0.9% (2/226) were staged down to cT1a.

The percentages of recurrences were 2.8% in cT1mi and cT1a, 10.8% in cT1b, and 25.2% in cT1c for cT_{lung} (Table 3). For $cT_{mediastinum}$, the percentages of recurrences were 2.9% in cT1mi and cT1a, 13.5% in cT1b, and 28.3% in cT1c. Median follow-up interval was 1170 days (IQR, 748–1791 days).

Cox regression analysis for DFS in patients with stage IA lung adenocarcinomas

On univariable analyses, age (hazard ratio (HR), 1.036; 95% confidence interval (CI), 1.013–1.060; $p = 0.002$), sex

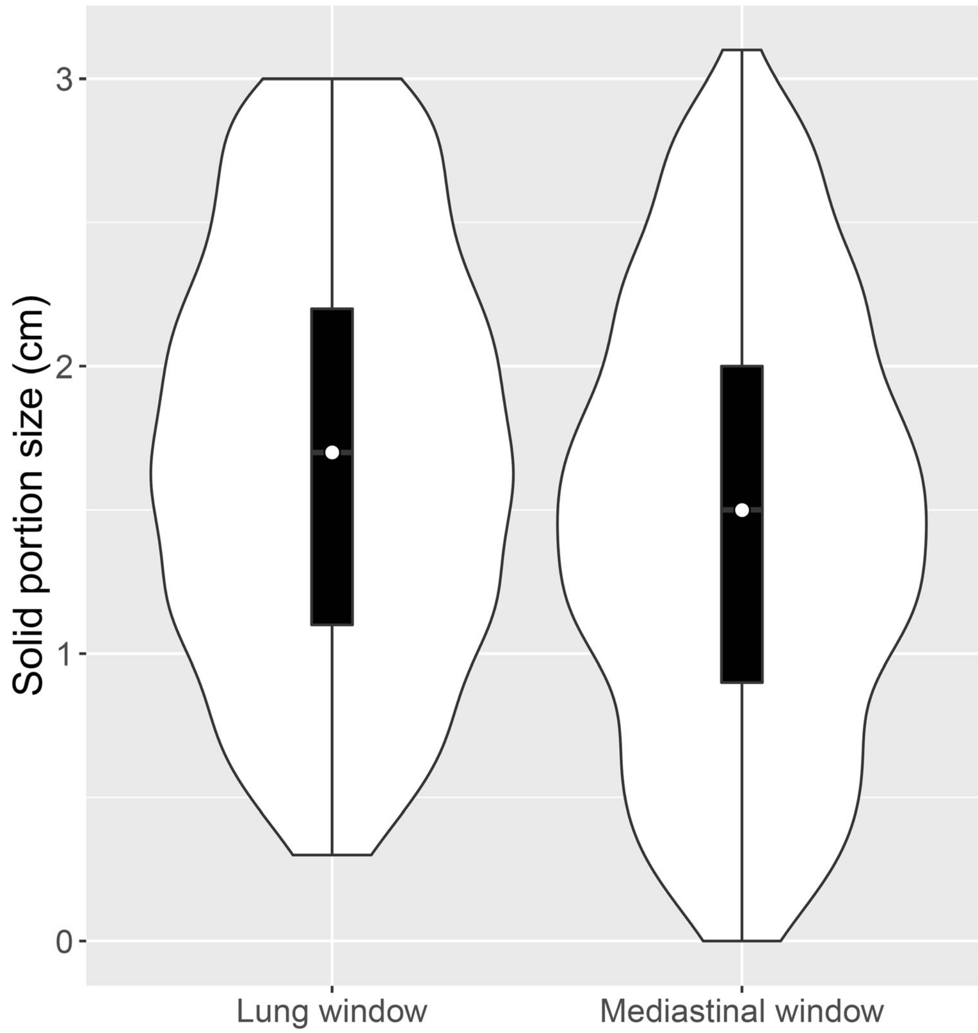


Fig. 2 Violin plots for solid portion measurements in stage IA lung adenocarcinomas with the lung and mediastinal window settings. The usage of the mediastinal window resulted in a slight decrease in the longest diameter of the solid portions

(female; HR, 0.713; 95% CI, 0.478–1.065; $p = 0.098$), nodule type (solid nodule; HR, 1.611; 95% CI, 1.070–2.426; $p = 0.022$), cT_{lung} ((cT1b: HR, 3.833; 95% CI, 1.362–10.785; $p = 0.011$), (cT1c: HR, 10.400; 95% CI, 3.772–28.670; $p < 0.001$)), and $cT_{mediastinum}$ ((cT1b: HR, 4.912; 95% CI, 2.090–11.540; $p < 0.001$), (cT1c: HR, 12.369; 95% CI, 5.283–28.960; $p < 0.001$)) had p values of less than 0.10. Other variables, including past history of malignancy, family history of lung cancer, smoking status, and nodule location, were not significantly associated with disease recurrence. Detailed results are listed in Table 4.

Table 2 Clinical T category shifts in lung adenocarcinomas according to the CT window settings for solid portion measurement

		$cT_{mediastinum}$		
		cT1mi and cT1a	cT1b	cT1c
cT_{lung}	cT1mi and cT1a	142 (100)	0	0
	cT1b	63 (19.5)	258 (79.9)	2 (0.6)
	cT1c	2 (0.9)	60 (26.5)	164 (72.6)

Numbers in parentheses are percentages. Percentages were calculated as a proportion of each cT_{lung} category

cT_{lung}, clinical T categorization based on the solid portion measurement with the lung window setting; *$cT_{mediastinum}$*, clinical T categorization based on the solid portion measurement with the mediastinal window setting

The multivariable Cox regression model, which included cT_{lung} as a T classifier, showed that age (adjusted HR, 1.028; 95% CI, 1.005–1.051; $p = 0.016$) and cT_{lung} ((cT1b: adjusted HR, 3.547; 95% CI, 1.258–10.001; $p = 0.017$), (cT1c: adjusted HR, 9.439; 95% CI, 3.413–26.105; $p < 0.001$)) were independent risk factors for DFS. When $cT_{mediastinum}$ was utilized as a T classifier, the final Cox model included age (adjusted HR, 1.023; 95% CI, 1.000–1.046; $p = 0.049$) and $cT_{mediastinum}$ ((cT1b: adjusted HR, 4.635; 95% CI, 1.969–10.912; $p < 0.001$), (cT1c: adjusted HR, 11.235; 95% CI, 4.773–26.447; $p < 0.001$)) as independent risk factors. The proportional hazard assumption was not violated for any of the included variables ($p > 0.05$).

Table 3 Clinical T categorization and number of recurrences

Lung window			Mediastinal window		
Clinical T category[a]	No. of patients ($n = 691$)	No. of recurrences or deaths ($n = 96$)	Clinical T category[a]	No. of patients ($n = 691$)	No. of recurrences or deaths ($n = 96$)
cT1mi and cT1a	142 (20.5)	4 (2.8)	cT1mi and cT1a	207 (30.0)	6 (2.9)
cT1b	323 (46.7)	35 (10.8)	cT1b	318 (46.0)	43 (13.5)
cT1c	226 (32.7)	57 (25.2)	cT1c	166 (24.0)	47 (28.3)

Numbers in parentheses are percentages. For the number of recurrences, percentages were calculated as a proportion of each cT category

[a] Clinical T categorization based on the cutoffs from the eighth-edition TNM classification for lung cancer [8]

Comparison of the C-indices between cT_{lung} and $cT_{mediastinum}$

The C-indices were 0.772 (95% CI, 0.702–0.842) for cT_{lung} and 0.787 (95% CI, 0.726–0.848) for $cT_{mediastinum}$. There were no significant differences between cT_{lung} and $cT_{mediastinum}$ ($p = 0.789$). The AICs were 1145.6 for cT_{lung} and 1134.1 for $cT_{mediastinum}$. The Kaplan–Meier survival curves according to cT_{lung} and $cT_{mediastinum}$ are visualized in Fig. 3.

Optimal cutoffs for cT categorization based on the solid portion measurement with the mediastinal window setting

The optimal number of cT categories for stratifying the solid portion measurements with the mediastinal window setting was three, and the optimal cutoffs, calculated from the training cohort, were 0.9 cm and 1.8 cm (i.e., the three categories were ≤ 0.9 cm, > 0.9 cm and ≤ 1.8 cm, and > 1.8 cm). In the validation cohort, the C-indices for predicting DFS were 0.783 (95% CI, 0.695–0.870) for cT_{lung}, 0.810 (95% CI, 0.738–0.883) for $cT_{mediastinum}$, and 0.793 (95% CI, 0.712–0.874) for $cT_{optimal}$. Mediastinal window–based solid portion measurement combined with the eighth-edition T coding system showed the highest discriminatory power, but there were no significant differences among the three cT categorization systems ($cT_{optimal}$ vs. cT_{lung}, $p = 0.310$; $cT_{optimal}$ vs. $cT_{mediastinum}$, $p = 0.872$; cT_{lung} vs. $cT_{mediastinum}$, $p = 0.888$; Fig. 4). The AICs were 519.2 for cT_{lung}, 511.3 for $cT_{mediastinum}$, and 516.6 for $cT_{optimal}$.

Discussion

In this study, we demonstrated that cT_{lung} and $cT_{mediastinum}$ had comparable prognostic performances for DFS prediction in stage IA lung adenocarcinomas, and they did not exhibit significant differences. Solid portion measurement at the mediastinal window yielded a slightly better model fit; however, the difference in AIC between cT_{lung} and $cT_{mediastinum}$ was minimal. Notably, $cT_{optimal}$ based on the optimal cutoffs was not superior to cT_{lung} or $cT_{mediastinum}$, which implied that the eighth-edition T coding system is appropriate as it stands, and it would be a good prognostic factor even when applied to the mediastinal window–based solid portion measurement.

Table 4 Univariable Cox regression analysis for disease-free survival in stage IA lung adenocarcinomas

Variable	Subcategory	HR	95% CI of HR	p value
Age (year)		1.036	1.013, 1.060	0.002
Female sex		0.713	0.478, 1.065	0.098
Past history of cancer		1.376	0.836, 2.266	0.209
Family history of lung cancer		1.494	0.690, 3.232	0.308
Ex- or current smoker (reference: never smoker)		1.294	0.862, 1.942	0.213
Location at upper lobes (reference: other lung lobes)		0.844	0.565, 1.259	0.405
Solid nodule (reference: part-solid nodule)		1.611	1.070, 2.426	0.022
cT_{lung} (reference: cT1mi and cT1a)	cT1b	3.833	1.362, 10.785	0.011
	cT1c	10.400	3.772, 28.670	< 0.001
$cT_{mediastinum}$ (reference: cT1mi and cT1a)	cT1b	4.912	2.090, 11.540	< 0.001
	cT1c	12.369	5.283, 28.960	< 0.001

CI, confidence interval; cT_{lung}, clinical T categorization based on the solid portion measurement with the lung window setting; $cT_{mediastinum}$, clinical T categorization based on the solid portion measurement with the mediastinal window setting; *HR*, hazard ratio

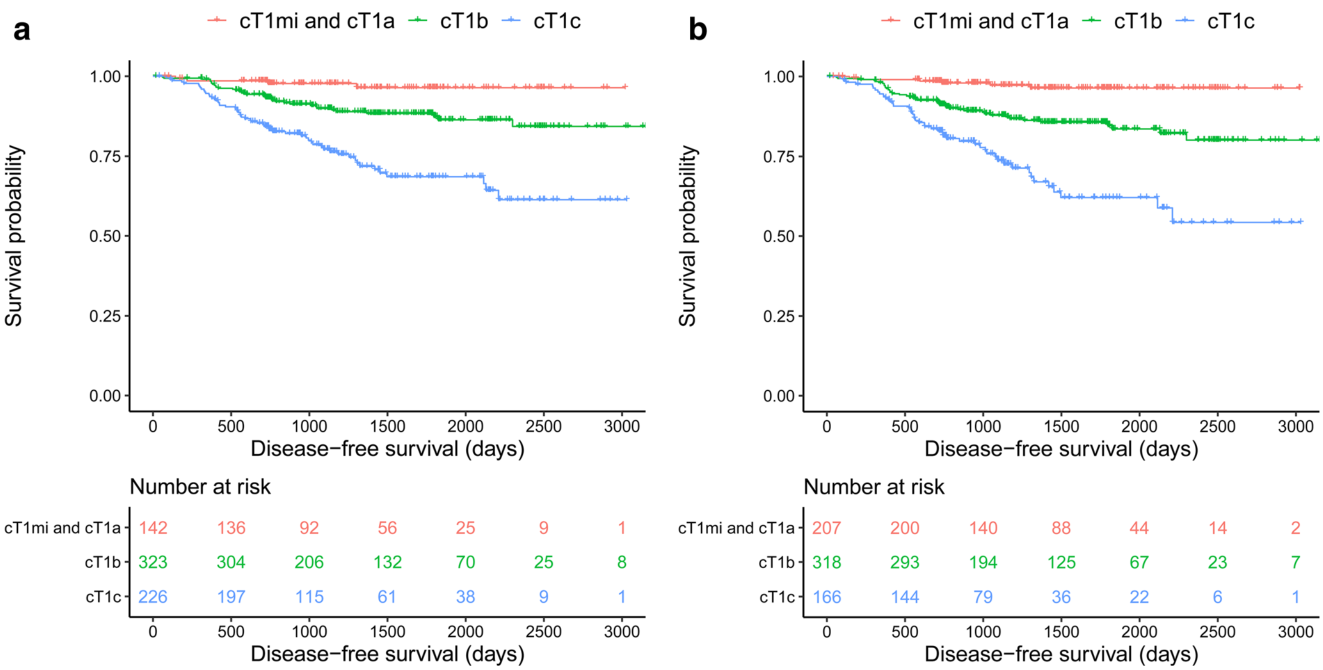


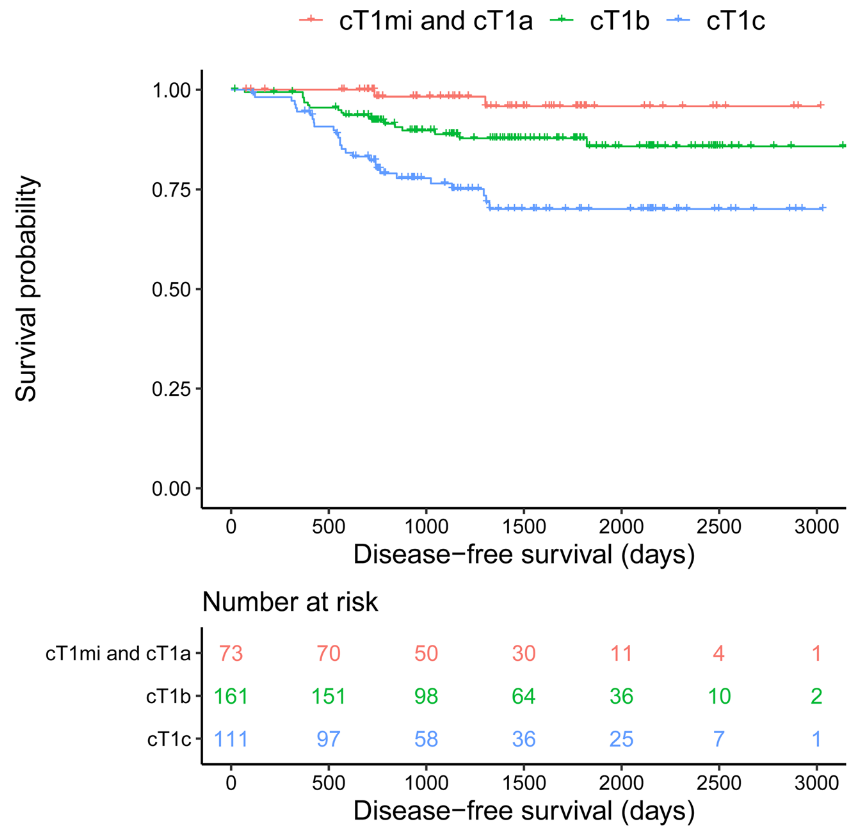
Fig. 3 Kaplan–Meier survival curves for disease-free survival in patients with stage IA lung adenocarcinomas. **a** Clinical T categories based on the solid portion measurements with the lung window setting. **b** Clinical T categories based on the solid portion measurements with the mediastinal window setting. Cutoffs from the eighth-edition T coding system were applied [8]

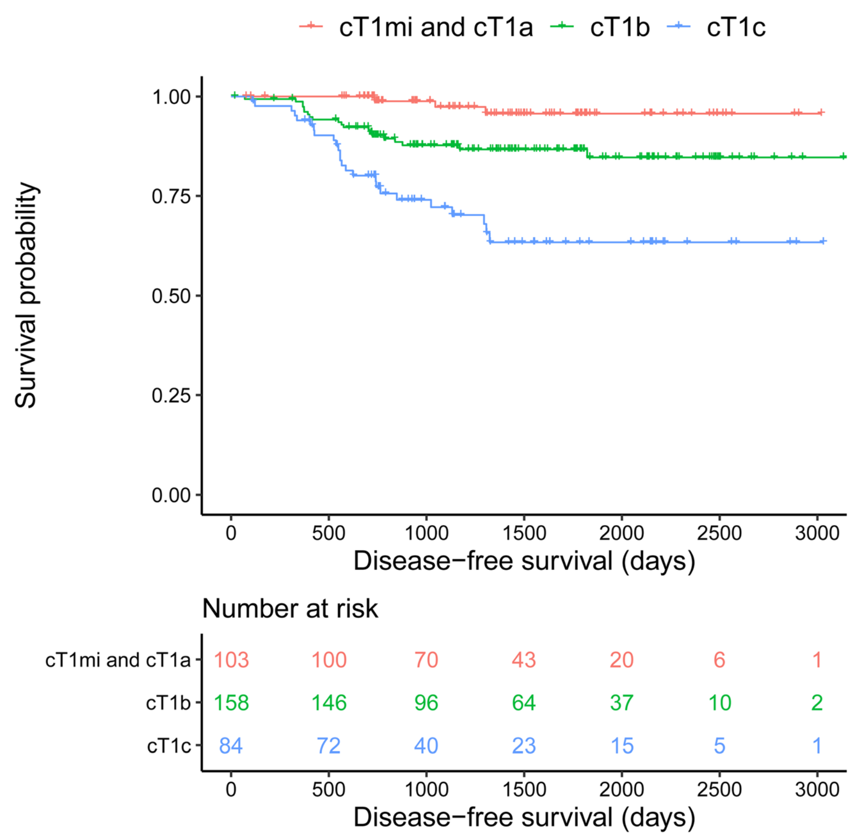
Solid portion measurement at the mediastinal window has been advocated by several researchers [10, 21–25]. A few studies have adopted the concept of the tumor disappearance ratio (TDR) [21–25], defined as (1 − solid portion size at mediastinal window setting / solid portion size at lung window setting). Shimizu et al [24] reported that the stratification of peripheral lung cancers < 20 mm according to the TDR was associated with pathological invasiveness and the patients' prognosis. Other studies reported similar results [22, 23], and Haraguchi et al [21] even stated that the TDR could be applied to advanced-stage (IIIB and IV) lung adenocarcinomas for prognosis prediction. In these circumstances, a prospective clinical trial used TDR as one of the inclusion criteria for selecting candidates for limited resection of peripheral lung cancers [25]. Furthermore, the initial recommendation for the management of subsolid nodules from the Fleischner Society in 2013 explicitly stated that the size of the solid component is best measured with the mediastinal window setting [10], based on the rationale that the mediastinal window setting would enhance inter-reader agreement [11, 26].

The lung window setting, however, provides concrete benefits for solid portion measurements over the mediastinal window setting [3, 13]. First, detection of small solid components can be disregarded with the mediastinal window [27]. The sensitivity of the solid portion detection or radiological diagnosis for minimally invasive adenocarcinomas or invasive adenocarcinomas can be diminished using the mediastinal window. Second, the solid portion measured at the lung window would correspond better to the pathological invasive component than that at the mediastinal window would [3, 12, 13]. Thus, more accurate diagnosis can be established with the lung window–based solid portion, and a higher level of agreement between the clinical and pathological T categorization can be achieved [12]. In addition, Yoo et al [13] even reported that the inter-reader agreement at the lung and mediastinal windows were actually similar for both nodule classification and solid portion measurements. Given these advantages, the Fleischner Society revised its guideline in 2017 to state that lung nodules, including the solid portions of part-solid nodules, should be measured at the lung window [9, 28].

It is apparent that there are advantages and disadvantages for the CT window setting for solid portion measurement. One may suggest that sensitive detection of the solid component and accurate radiological–pathological correlations are the primary concerns, while others would argue that the detection of subtle solid components smaller than 5 mm or differentiation of borderline nodules with solid portions slightly larger or smaller than 5 mm would pose little clinical significance. Thus, a balanced point of view considering various perspectives is required, and a decision can only be reached after considering every aspect of diagnosis and prognostication. Nevertheless, there has been no direct head-to-head comparison between CT window settings for the staging purpose and prognostication. Therefore, we aimed to provide evidence for the optimal CT display window setting for cT categorization by directly comparing cT_{lung} and $cT_{mediastinum}$ in early-stage lung adenocarcinomas. As a result, we revealed that the

Fig. 4 Kaplan–Meier survival curves for disease-free survival in the validation cohort according to the three clinical T (cT) categorization systems. **a** cT categories based on the solid portion measurements with the lung window setting. **b** cT categories based on the solid portion measurements with the mediastinal window setting. Cutoffs from the eighth-edition T coding system were applied [8]. **c** Optimal cutoffs (0.9 cm and 1.8 cm; derived from the training cohort) were applied to the solid portion measured at the mediastinal window to classify cT into three groups (optimal number of cT categories)





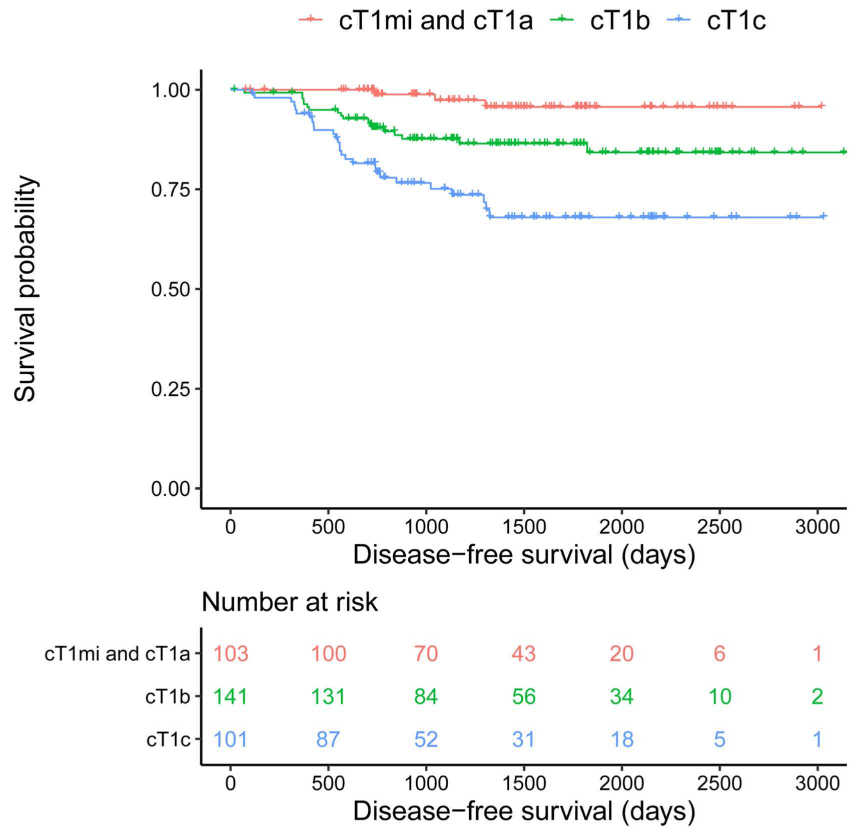


Fig. 4 (continued)

prognostic powers of cT_{lung} and $cT_{mediastinum}$ were comparable and that both were powerful prognostic indicators.

Given that the solid portions in a subset of lung nodules would measure smaller at the mediastinal window, we calculated the optimal cutoffs for cT categorization using mediastinal window–based solid portions, which were 0.9 cm for the differentiation between cT1a and cT1b and 1.8 cm between cT1b and cT1c. Interestingly, the optimal number of risk groups (i.e., cT categories) was three, which was equal to the current eighth-edition T coding system. Nevertheless, in the validation cohort, the prognostic performance of $cT_{optimal}$ was not superior to those based on the current edition (i.e., 1.0 cm and 2.0 cm).

Finally, our study results do not indicate that lung and mediastinal window settings can be used interchangeably for the solid portion measurement in terms of cT categorization. There were significant differences between cT_{lung} and $cT_{mediastinum}$. $cT_{mediastinum}$ led to substantial down staging of cT categories. The current lung nodule management guideline and lung cancer staging system were written based on the solid portion measurement at the lung window [8, 28]. Accordingly, the solid portion measurement should be performed in a consistent manner using the lung window for the present. We assume that our findings may support adherence to the usage of the lung window setting for the solid portion measurement per the current recommendations.

There were several limitations in this study. First, our study was performed retrospectively at a single center. Second, a priori sample size estimation was not carried out. However, we collected and analyzed a large number of stage IA lung adenocarcinomas. Third, pathological information, including the pathological invasive component size or histological subtype, was not analyzed. Nevertheless, the purpose of our study was to investigate the prognostic implications of CT window settings on cT categorization for staging purposes. Assessing the radiological–pathological correlation was not the objective of this study. Fourth, pathological diagnoses were established in 26% of the patients before the implementation of the 2011 lung adenocarcinoma classification [16]. In these patients, bronchioloalveolar carcinomas were regarded as adenocarcinomas in situ, and some of the minimally invasive adenocarcinomas may have been misclassified as invasive adenocarcinomas. However, the pathologic diagnosis was not the outcome variable in our study. Patients' survival (DFS) was the primary endpoint, and thus, the study results were unaffected by the pathological diagnosis. Last, only patients who underwent standard lobectomy were included in our study to reduce bias.

In conclusion, cT categorization with the lung window and mediastinal window settings was not found to be significantly different in terms of the prognostic performances in stage IA lung adenocarcinomas. Thus, the current T coding system based on the solid portion measurement at the lung window is acceptable from the perspective of prognostication.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Chang Min Park.

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Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Study subjects or cohorts overlap Some study subjects or cohorts have been previously reported in a journal article (Kim et al; in press).

Methodology
- retrospective
- diagnostic or prognostic study
- performed at one institution

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