

Prognostic Stratification According to Size and Dominance of Radiologic Solid Component in Clinical Stage IA Lung Adenocarcinoma



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ABSTRACT

Introduction: Although several studies have investigated the prognostic significance of the radiographic appearance of stage IA lung adenocarcinoma, the prognostic impact of solid component size or consolidation-to-tumor ratio (CTR) of part-solid nodules (PSNs) still remains controversial. This study aimed to clarify the combined prognostic impact of the mentioned radiographic features of PSNs and compare it with that of pure solid nodules in the current TNM classification.

Methods: We retrospectively investigated 1014 patients with clinical stage IA (TNM eighth edition) adenocarcinoma who underwent curative resection. Overall survival (OS) and pathologic characteristics of pure solid nodules, solid-dominant PSNs (CTR > 0.5), and ground-glass opacity (GGO)-dominant PSNs (CTR ≤ 0.5) were compared according to T category.

Results: Patients with pure solid nodules (297 cases) had significantly shorter OS compared with those with PSNs (717 cases) ($p < 0.001$) but a marginal difference compared with those with solid-dominant PSNs (286 cases) ($p = 0.051$). No significant difference in OS was found according to T category in those with GGO-dominant PSNs (431 cases). Patients with cT1b and T1c solid-dominant PSNs had significantly worse prognosis compared with those with other PSNs and had comparable prognosis with those with cT1b pure solid nodules ($p = 0.892$). Higher frequency of nodal and lymphovascular involvement and pathologic upstaging was observed with T category progression in solid-dominant PSNs.

Conclusions: An hierarchy of prognosis and pathologic malignant characteristics was observed according to T category in patients with solid-dominant PSNs but not in those with GGO-dominant PSNs, suggesting the importance of classifying PSNs on the basis of solid component size and CTR for accurate prognostic comparison with pure solid nodules.

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Keywords: Lung adenocarcinoma; Prognosis; Part-solid nodule; Ground-glass opacity; High-resolution computed tomography

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Introduction

Since the adaptation of the current eighth edition of TNM classification for lung cancer staging,¹ several retrospective studies have investigated the prognostic significance of solid component size and the presence of ground-glass opacity (GGO) component on high-resolution computed tomography (CT) for early stage adenocarcinomas.²⁻¹⁴ Among these studies, those conducted in Japan and other Asian countries revealed that patients with pure solid nodules had distinctive malignant behavior and worse prognosis after curative resection compared with patients with part-solid nodules (PSNs).²⁻⁸ Consequently, applying the same classification to pure solid nodules and PSNs remains controversial, despite both nodules having a similar solid component size. Moreover, evidence has also suggested that all PSNs should be separately classified into a category with good prognosis regardless of the total tumor size, solid component size, and consolidation-to-tumor ratio (CTR).^{5,9}

In contrast, CTR is a proven prognostic predictor for early stage adenocarcinoma presenting as PSNs.¹⁴⁻²⁰ Unexpected pathologic nodal involvement, upstaging, and disease recurrence after curative resection of PSNs are not uncommon in our clinical practice, especially when they present with a solid component-dominant shadow. There is expected to be some hierarchy of malignancy and prognosis in PSNs. Nevertheless, the prognostic impact of CTR and clinical T category of PSNs compared with pure solid nodules in the current TNM classification has yet to be fully elucidated. To improve the accuracy of subsequent revisions of the TNM classification, detailed validation analyses and accumulation of knowledge on the basis of various large-scale data sets are required.

This study therefore aimed to investigate and clarify the prognostic impact of the radiographic appearance of pure solid nodules and PSNs among patients with clinical stage IA adenocarcinoma on the basis of large-scale data from a single Japanese institute.

Materials and Methods

Study Population

This study retrospectively reviewed the clinicopathologic features of 1188 consecutive patients with clinical stage IA adenocarcinoma who underwent curative resection at our institution between 2010 and 2017. Those who underwent wedge resection (116 cases), had synchronous or metachronous multiple lung cancer (48 cases), and had insufficient data (10 cases) were excluded. Ultimately, 1014 patients with available data were enrolled. The medical records of all patients were then reviewed for the following clinicopathologic factors:

age, sex, pack-year smoking, preoperative serum carcinoembryonic antigen level, tumor size, surgical procedure, adjuvant chemotherapy, pathologic invasion size, nodal involvement, lymphovascular involvement (LVI), visceral pleural invasion, pulmonary metastasis, and predominant subtype. Clinical and pathologic stages were determined according to the eighth edition of the TNM classification. Lymph nodes that had swollen to greater than or equal to 10 mm in the short axis on CT or had abnormal accumulation on positron emission tomography (PET)-CT as indicated by a standardized uptake value greater than or equal to 2.5 were pathologically evaluated by means of endobronchial ultrasound-guided transbronchial needle aspiration.

Lobectomy and lobe-specific or systematic nodal dissection were the basic operative procedures received by the patients. Some patients with GGO-dominant lesions in whom segmentectomy was intentionally performed or mediastinal node dissection was omitted were included. The surgical approach included thoracoscopic or open thoracotomy, determined on the basis of the time period and surgeon's preference. Postoperative surveillance was performed using chest and abdominal CT and laboratory data every 6 to 12 months.

Radiographic Evaluation

All patients underwent contrast-enhanced CT imaging with a 64-channel multidetector CT (Revolution HD, GE Medical Systems, Milwaukee, WI) set at the following parameters: gantry rotation speed of 0.5 seconds per rotation, collimation of 0.625 mm, table incrementation speed of 39.37 mm/s with a helical pitch of 0.984, and tube voltage of 120 kV. CT images were reconstructed with a section thickness of 1.25 mm and viewed on standard lung windows (level -600 Hounsfield Unit [HU]; width 1500 HU) and mediastinal windows (level 30 HU; width 400 HU).

A PSN was defined as a tumor consisting of both GGO and solid components, whereas a pure solid nodule was defined as a tumor consisting of only solid component. CTR was defined as the ratio of the maximum size of consolidation to the maximum tumor size. PSNs were divided into two subtypes, GGO-dominant and solid-dominant PSNs using a CTR cutoff value of 0.5 (Fig. 1A). Our findings revealed that some nodules with a CTR of 1.0 were PSNs, which contained GGO component only in part of their periphery. These nodules were mostly composed of a solid component, and GGO component was not included in the measurement axis of the maximum diameter of the entire nodules. Pure GGOs without solid component (i.e., clinical stage 0 diseases) were excluded from this study. Radiographic evaluations were performed by three investigators, including two experienced thoracic radiologists (KO and YS) and one

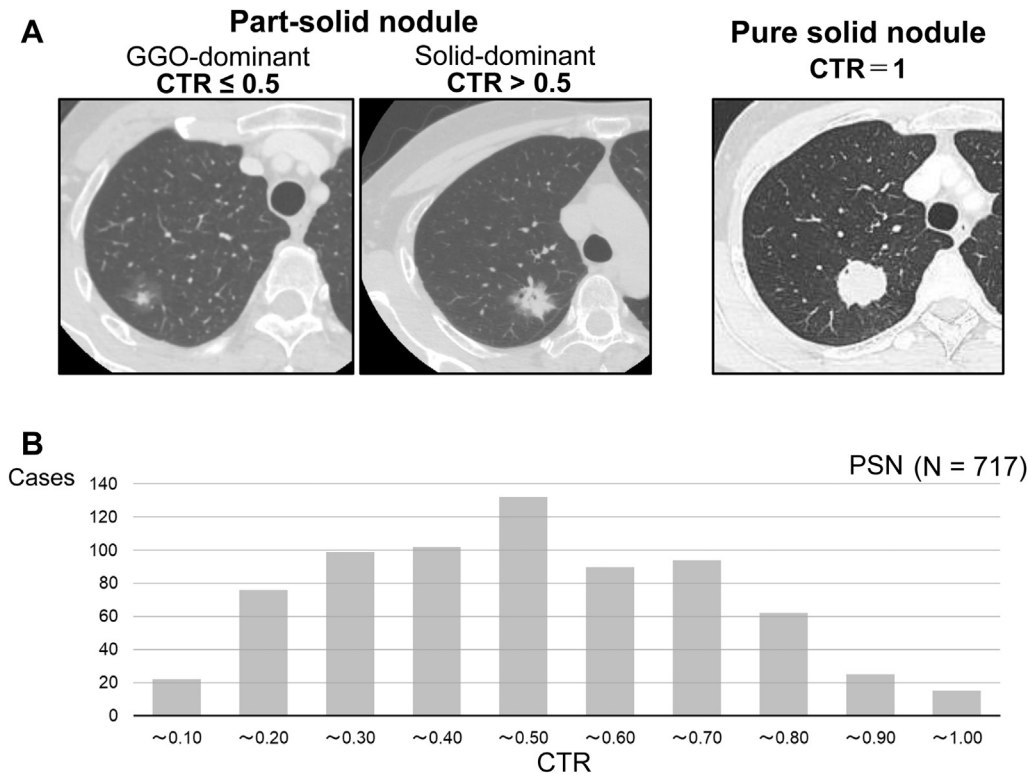


Figure 1. (A) Representative computed tomography images of pure solid nodules, solid-dominant PSNs, and GGO-dominant PSNs. (B) Histogram of the distribution of CTR of PSNs. CTR, consolidation-to-tumor ratio; GGO, ground-glass opacity; PSN, part-solid nodule.

experienced thoracic surgeon (MN). Disagreements among the investigators were resolved through discussion and consensus.

Pathologic Evaluation

Histologic classification of the resected specimens was determined according to the WHO International Histologic Classification of Tumors. Adenocarcinomas

were classified into adenocarcinoma in situ, minimally invasive adenocarcinoma, and invasive adenocarcinoma on the basis of the pathologic invasion size. Invasive adenocarcinoma was subclassified on the basis of the predominant subtype. This study defined adenocarcinoma in situ, minimally invasive adenocarcinoma, and lepidic predominant adenocarcinoma as a low-grade subtype; papillary predominant, acinar predominant,

Table 1. Comparison of Characteristics Between Patients With Part-Solid Nodules and Pure Solid Nodules

Variables	Part-Solid Nodules			Pure Solid Nodules	p Value ^a
	All n = 717	GGO-dominant (CTR ≤ 0.5) n = 431	Solid-dominant (CTR > 0.5) n = 286	(CTR = 1) n = 297	
Age (y)	67 (61-73)	68 (61-73)	67 (62-73)	66 (59-72)	0.111
Sex, man	286 (40%)	164 (38%)	122 (43%)	159 (54%)	<0.001
Pack-year smoking, >10	231 (32%)	129 (30%)	102 (36%)	154 (52%)	<0.001
Serum CEA level, ≥ 5 ng/mL	76 (11%)	33 (8%)	42 (15%)	63 (21%)	<0.001
Total tumor size (mm)	21 (16-27)	20 (15-26)	22 (17-28)	19 (15-25)	<0.001
Solid component size (mm)	9 (5-14)	6 (4-9)	15 (11-19)	19 (15-25)	<0.001
CTR	0.45 (0.29-0.63)	0.32 (0.22-0.42)	0.67 (0.59-0.75)	1.00	<0.001
Procedure, lobectomy	590 (82%)	325 (75%)	265 (93%)	289 (97%)	<0.001
Approach, thoracoscopic	646 (90%)	398 (92%)	248 (88%)	221 (74%)	<0.001
Adjuvant chemotherapy, yes	32 (4%)	10 (2%)	22 (8%)	41 (14%)	<0.001

Note: Values are presented as n (%) or median (IQR).

^ap value for the comparison between all part-solid nodules and pure solid nodules using the chi-square test or Mann-Whitney U test. CEA, Carcinoembryonic antigen; CTR, consolidation-to-tumor ratio; GGO, ground-glass opacity; IQR, interquartile range.

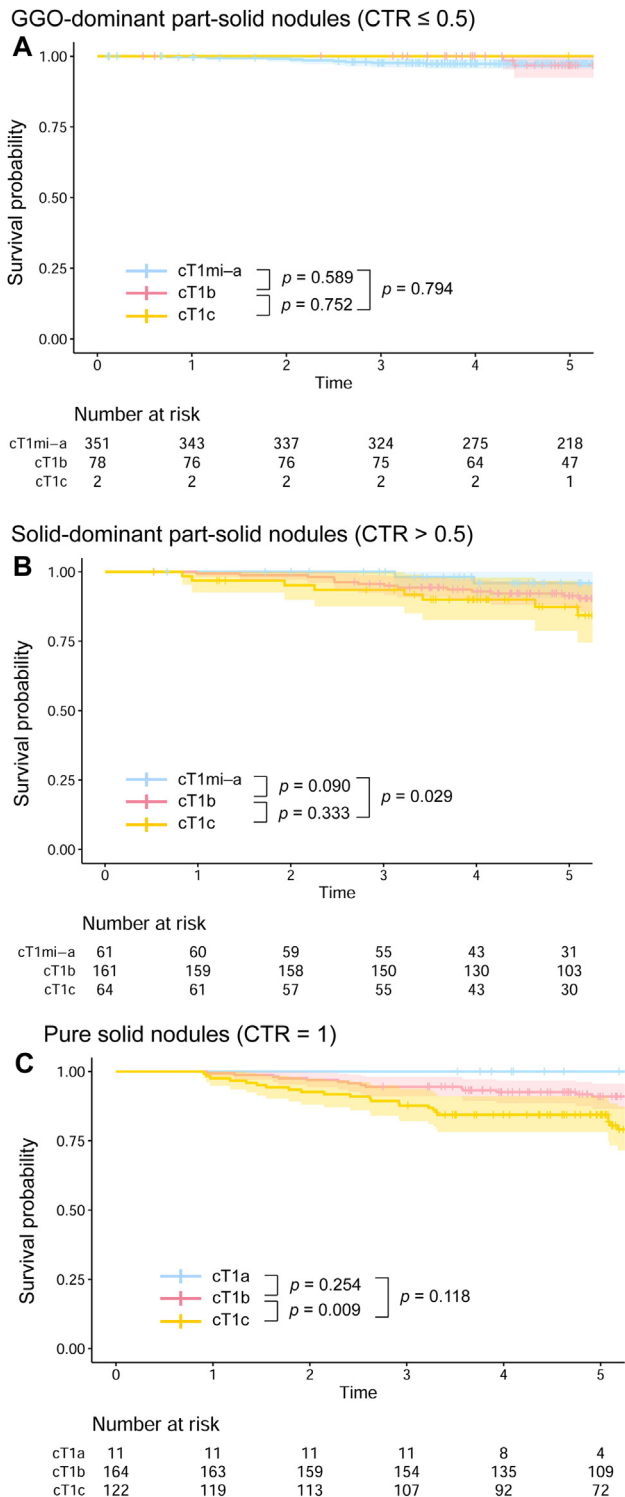


Figure 3. Overall survival curves according to T category in each radiographic appearance. (A) The 5-year overall survival rates of cT1mi-a, T1b, and T1c GGO-dominant PSNs were 97.3% (95% CI: 94.9-98.6), 96.7% (95% CI: 87.6-99.2), and 100%, respectively. (B) The 5-year overall survival rates of cT1mi-a, T1b, and T1c solid-dominant PSNs were 95.9% (95% CI: 84.5-99.0), 91.3% (95% CI: 85.5-94.9), and 87.3% (95% CI: 74.9-93.9), respectively. (C) The 5-year overall survival rates of cT1a, T1b, and T1c pure solid nodules were 100%, 91.0% (95% CI: 85.2-94.6), and 84.4% (95% CI:

Results

The median follow-up duration after surgery was 61 months (range: 1-136), and 5-year OS rate was 93.0% for the entire cohort. OS curves according to clinical T category of the eighth edition of the TNM classification are presented in [Supplementary Figure 1](#). A clear stratification of prognosis was identified between cT1mi (238 cases), cT1a (403 cases), cT1b (188 cases), and cT1c (185 cases).

Among the 1014 patients, 297 (29%) had pure solid nodules and 717 (71%) had PSNs, including 431 GGO-dominant PSNs and 286 solid-dominant PSNs. [Figure 1B](#) illustrates a histogram of the CTR distribution of the 717 PSNs. Patients with PSNs comprised more women and light smokers compared with those with pure solid nodules. Moreover, patients with PSNs exhibited less frequent preoperative carcinoembryonic antigen elevations, larger total tumor sizes, and smaller solid component sizes compared with those with pure solid nodules. Lobectomy, thoracotomy, and adjuvant chemotherapy were more frequently indicated in patients with pure solid nodules ([Table 1](#)).

Patients with PSNs had a significantly longer OS compared with those with pure solid nodules ($p < 0.001$) ([Fig. 2A](#)), although the difference in OS between solid-dominant PSNs and pure solid nodules was marginally significant ($p = 0.051$) ([Fig. 2B](#)). Multivariate analysis identified CTR (hazard ratio [HR] = 2.991, 95% confidence interval [CI]: 1.059-8.448), age (HR = 1.047, 95% CI: 1.022-1.072), and solid component size (HR = 1.058, 95% CI: 1.019-1.100) as independent prognostic factors for OS ([Table 2](#)).

Differences in OS according to clinical T category on each radiographic appearance were then analyzed ([Fig. 3A-C](#)). Among GGO-dominant PSNs, no significant difference in OS was observed between cT1mi-a, cT1b, and cT1c, with high 5-year OS rates (96.7%-100%). Among solid-dominant PSNs, cT1b and cT1c had comparable OS ($p = 0.333$), which was marginally lower than that of cT1mi-a ($p = 0.090$ and $p = 0.029$). cT1b and cT1c had 5-year OS rates of 91.3% and 87.3%, respectively. Among pure solid nodules, however, cT1b had a significantly higher OS compared with cT1c ($p = 0.009$). The 5-year OS rate of cT1b (91.0%) was equivalent to that of cT1b solid-dominant PSNs.

[Tables 3-5](#) reveals the difference in pathologic findings of PSNs and pure solid nodules according to clinical T category. Among GGO-dominant PSNs, cT1b and T1c

76.6-89.7), respectively. CI, confidence interval; CTR, consolidation-to-tumor ratio; GGO, ground-glass opacity; PSN, part-solid nodule.

Table 3. Comparison of Pathologic Findings According to Clinical T Category, GGO-Dominant Part-Solid Nodules (CTR ≤ 0.5)

Variables	cT1mi and T1a (n = 351)	cT1b and T1c (n = 80)	p Value ^a
Pathologic invasion size (mm)	5 (3-7)	12 (11-18)	<0.001
Pathologic nodal involvement, present	1 (0.2%)	0	1.000
Lymphovascular involvement, present	21 (6%)	15 (19%)	0.001
Visceral pleural invasion, present	5 (1%)	4 (5%)	0.066
Pulmonary metastasis, present	2 (0.6%)	1 (1%)	0.815
Predominant subtype			<0.001
Low-grade (AIS, MIA, lepidic)	263 (75%)	42 (53%)	
Moderate-grade (papillary, acinar, invasive mucinous)	88 (25%)	37 (46%)	
High-grade (solid, micropapillary)	0	1 (1%)	
Pathologic upstaging	8 (2%)	5 (6%)	0.073
pStage IB	5	4	
pStage IIA-IIIB	2	1	
pStage IIIA-IIIB	1	0	
EGFR mutation status, mutant ^b	150 (57%)	39 (55%)	0.788

Note: Values are presented as n (%) or median (IQR).

^ap value for the chi-square test or Mann-Whitney *U* test.

^bCases with unknown EGFR mutation status were excluded.

AIS, adenocarcinoma in situ; CTR, consolidation-to-tumor ratio; GGO, ground-glass opacity; IQR, interquartile range; MIA, minimally invasive adenocarcinoma; pStage, pathologic stage.

had larger invasion sizes ($p < 0.001$) and more frequent LVI ($p = 0.001$) and moderate-grade subtypes ($p < 0.001$) than cT1mi and T1a (Table 3). Among solid-dominant PSNs, cT1b had larger invasion sizes ($p < 0.001$) and more frequent LVI ($p = 0.002$) and moderate-grade subtypes ($p < 0.001$) compared with cT1mi and T1a. cT1c had larger invasion sizes ($p < 0.001$) and more frequent nodal involvement ($p = 0.009$) and pathologic upstaging ($p = 0.009$) than cT1b (Table 4). Among pure solid nodules, cT1c had larger invasion size ($p < 0.001$) and more frequent LVI ($p =$

0.039), pulmonary metastasis ($p = 0.005$), and pathologic upstaging compared with cT1a and T1b (Table 5).

Figure 4A reveals the results of integrated prognostic analysis for each group according to radiographic appearance and clinical T category. All GGO-dominant PSNs had an OS comparable with that of cT1mi—a solid-dominant PSNs ($p = 0.861$) or cT1a pure solid nodules ($p = 0.542$), with the highest OS rates. cT1b to cT1c solid-dominant PSNs had an OS equivalent to that of cT1b pure solid nodules ($p = 0.892$). Patients with cT1c pure solid nodules were distinctively found to have

Table 4. Comparison of Pathologic Findings According to Clinical T Category, Solid-Dominant Part-Solid Nodules (CTR > 0.5)

Variables	cT1mi and T1a (n = 61)	cT1b (n = 161)	p Value ^a	cT1c (n = 64)	p Value ^b
Pathologic invasion size (mm)	9 (7-9)	15 (13-17)	<0.001	24 (22-26)	<0.001
Pathologic nodal involvement, present	2 (3%)	9 (6%)	0.376	11 (17%)	0.009
Lymphovascular involvement, present	8 (13%)	54 (34%)	0.002	25 (39%)	0.443
Visceral pleural invasion, present	3 (5%)	14 (9%)	0.412	8 (13%)	0.456
Pulmonary metastasis, present	0	4 (2%)	0.280	5 (8%)	0.123
Predominant subtype			<0.001		1.000
Low-grade (AIS, MIA, lepidic)	37 (61%)	44 (27%)		17 (27%)	
Moderate-grade (papillary, acinar, invasive mucinous)	23 (38%)	115 (72%)		47 (73%)	
High-grade (solid, micropapillary)	1 (1%)	2 (1%)		0	
Pathologic upstaging	5 (8%)	24 (15%)	0.264	20 (31%)	0.009
pStage IB	3	11		6	
pStage IIA-IIIB	2	9		7	
pStage IIIA-IIIB	0	4		7	
EGFR mutation status, mutant ^c	23 (51%)	70 (54%)	0.863	38 (63%)	0.270

Note: Values are presented as n (%) or median (IQR).

^ap value for the comparison between cT1mi/T1a and cT1b using the chi-square test or Mann-Whitney *U* test.

^bp value for the comparison between cT1b and cT1c using the chi-square test or Mann-Whitney *U* test.

^cCases with unknown EGFR mutation status were excluded.

AIS, adenocarcinoma in situ; CTR, consolidation-to-tumor ratio; IQR, interquartile range; MIA, minimally invasive adenocarcinoma; pStage, pathologic stage.

Table 5. Comparison of Pathologic Findings According to Clinical T Category, Pure Solid Nodules (CTR = 1)

Variables	cT1a and T1b (n = 175)	cT1c (n = 122)	p Value ^a
Pathologic invasion size (mm)	16 (13-18)	25 (23-27)	<0.001
Pathologic nodal involvement, present	29 (17%)	26 (21%)	0.363
Lymphovascular involvement, present	101 (58%)	85 (70%)	0.039
Visceral pleural invasion, present	40 (23%)	40 (33%)	0.064
Pulmonary metastasis, present	2 (1%)	10 (8%)	0.005
Predominant subtype			0.132
Low-grade (AIS, MIA, lepidic)	10 (6%)	2 (1%)	
Moderate-grade (papillary, acinar, invasive mucinous)	124 (71%)	96 (79%)	
High-grade (solid, micropapillary)	41 (23%)	24 (20%)	
Pathologic upstaging	56 (32%)	63 (52%)	0.008
pStage IB	24	26	
pStage IIA-IIIB	14	19	
pStage IIIA-IIIB	18	18	
EGFR mutation status, mutant ^b	65 (48%)	43 (42%)	0.514

Note: Values are presented as n (%) or median (IQR).

^ap value for the chi-square test or Mann-Whitney *U* test.

^bCases with unknown EGFR mutation status were excluded.

AIS, adenocarcinoma in situ; CTR, consolidation-to-tumor ratio; IQR, interquartile range; MIA, minimally invasive adenocarcinoma; pStage, pathologic stage.

poor prognosis. On the basis of these findings, the proposed modification of the clinical T category after considering the solid component size and CTR revealed a clear prognostic stratification between the groups (Fig. 4B).

Discussion

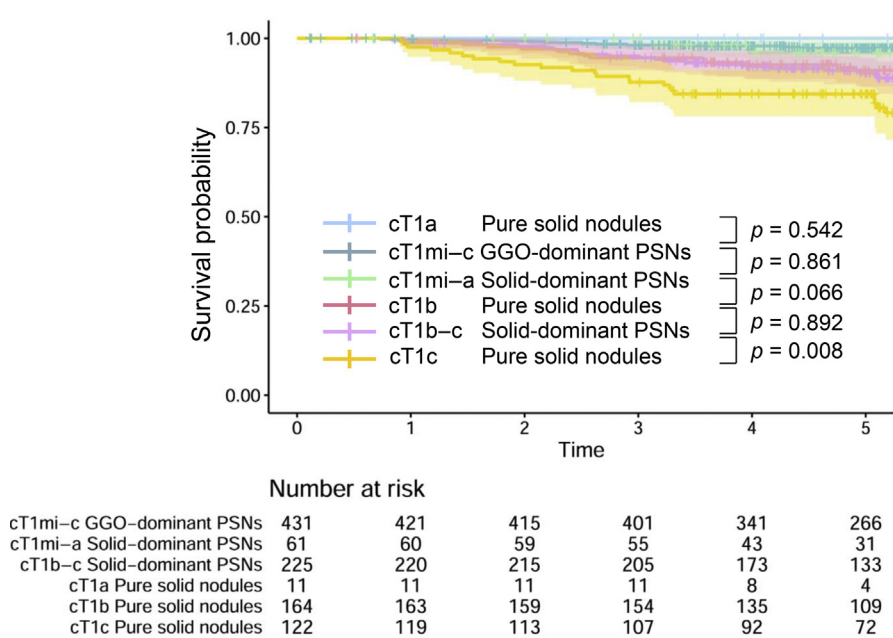
This study investigated the differences in prognosis and malignancy according to the radiographic appearance among 1014 cases with clinical stage IA adenocarcinoma. Notably, differences in OS were observed not only between pure solid nodules and PSNs but also between solid-dominant and GGO-dominant PSNs. In particular, the prognosis of patients with cT1b and T1c solid-dominant PSNs was significantly worse than those with other PSNs and was comparable with that of those with cT1b pure solid nodules. Our findings also revealed differences in pathologic characteristics of each clinical T category, particularly in the frequency of nodal involvement, LVI, and pathologic upstaging among solid-dominant PSNs.

Previous studies have revealed several results on the prognoses of PSNs and pure solid nodules among those with stage IA adenocarcinoma. Hattori et al.^{3,7} who reported on differences in prognostic stratification according to clinical T category between solid nodules and PSNs, suggested the possibility of classifying all PSNs into the same category. Their innovative idea is reasonable and beneficial given its possibility to solve serious concerns in the current clinical T categorization (i.e., uniform measurement of solid component size in several types of PSNs, which is difficult to measure). The major prognostic difference between pure solid nodules and

PSNs in the aforementioned study was presumably owing to the fact that all PSNs were analyzed together, regardless of CTR.³ Moreover, patients with cT1b and T1c pure solid nodules in the aforementioned study had considerably inferior prognoses (5-y OS rate: 75.2% for cT1b and 62.3% for cT1c) compared with those in our study, although the difference in the frequency of nodal metastasis and pathologic upstaging was minor. This might be partly because the rate of lobectomy for pure solid lesions in their cohort (81%) is lower than that in our cohort (97%). Nonetheless, these prognostic differences led to different conclusions between our study and theirs.³ Their results were supported by other researchers from the People's Republic of China.^{5,6} Ye et al.⁵ revealed that PSNs had a distinctly favorable prognosis regardless of solid component size and prognostic equivalence regardless of CTR in stage IA adenocarcinoma. Characteristically, they evaluated prognosis in terms of lung cancer-specific survival, in which non-cancer deaths or deaths related to other malignancies were censored. Lung cancer-specific survival is considered to be an ideal index to truly evaluate the malignant grade of lung cancer, but it is not a general prognostic indicator and would also make comparisons with other studies difficult.

In contrast, a study from Korea revealed overlapping survival curves of PSNs and pure solid nodules in clinical stage IA adenocarcinoma after adjusting for other clinical factors, such as age, sex, and nodule location.¹² Their results were consistent with ours in terms of 5-year OS rates of each category. They concluded that the clinical T categorization system was valid for PSNs and pure solid nodules. Similar results have been also reported from Japan.¹³ Nevertheless, as indicated by the results of the

A



B

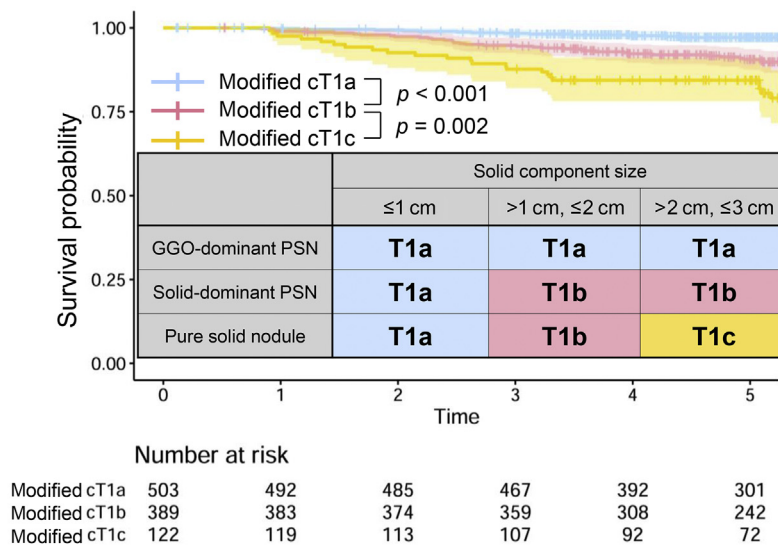


Figure 4. Overall survival curves according to T category and radiographic appearance. (A) The 5-year overall survival rates of cT1a pure solid nodules, T1mi-c GGO-dominant PSNs, T1mi-a solid-dominant PSNs, T1b pure solid nodules, T1b-c solid-dominant PSNs, and T1c pure solid nodules were 100%, 97.2% (95% CI: 95.0-98.5), 95.9% (95% CI: 84.5-99.0), 91.0% (95% CI: 85.2-94.6), 90.3% (95% CI: 85.3-93.6), and 84.4% (95% CI: 76.6-89.7), respectively. (B) The 5-year overall survival rates of modified cT1a, T1b, and T1c were 97.1% (95% CI: 95.1-98.3), 90.6% (95% CI: 87.0-93.2), and 84.4% (95% CI: 76.6-89.7), respectively. CI, confidence interval; GGO, ground-glass opacity; PSN, part-solid nodule.

present study and previous studies,^{2-8,11} it is obvious that the prognosis and malignant behavior of PSNs and pure solid nodules are different. It may not be appropriate to apply the same categorization to them unconditionally.

Regardless of the aforementioned concerns, the current study revealed significant prognostic differences

among PSNs according to CTR on the basis of a large-scale data set. Among solid-dominant PSNs, we found prognostic hierarchy according to clinical T category. Differences in the malignant characteristics of each clinical T category, such as the frequency of nodal involvement, LVI, and pathologic upstaging, were consistent with the prognosis. In contrast, although some

differences in the frequency of LVI were found among GGO-dominant PSNs, nodal involvement and pathologic upstaging were rare in all T categories. Therefore, grouping them in the same category would be appropriate from the perspective of pathologic findings and prognosis. Among pure solid nodules, although the *p* values were not below the cutoff given the small number of cT1a cases, prognostic differences according to T category were definitive as previously reported.²⁻⁸ Moreover, we note that pure solid nodules had remarkably higher frequencies of the high-grade subtype and slightly lower EGFR mutation rates than PSNs, which might indicate that they are a biologically distinctive malignant group among adenocarcinomas. Thus, even though clinical stage IA lung adenocarcinoma is a group of diseases with a favorable prognosis, it is important to group them according to their prognosis and malignancy, and our stratification might be applicable, for example, to determine the appropriate indication for intentional sublobar resection.

Some limitations of our study should be considered. First, the solid component size of some PSNs was difficult to measure. In these cases, we found irregularly scattered solid component, borderless solid component that overlapped with the pulmonary vessels, or peripheral GGO that was difficult to distinguish from surrounding secondary shadows. Nonetheless, methods using deep learning algorithms are expected to address problems related to manual measurement in the near future.²¹ Second, we used 0.5 as the cutoff CTR value when dividing PSNs into the two subtypes and omitted the research process of determining the optimal cutoff value. A cutoff of 0.5 has been conventionally used in various studies,¹⁶⁻¹⁸ which made it relatively easy to distinguish subtypes. Nevertheless, we should also be aware that PSNs with a CTR of approximately 0.5, which were at risk of being misclassified, were the most common, as found in [Figure 1B](#). Third, this study included a very small number of cT1c GGO-dominant PSNs and cT1a pure solid nodules. This was unavoidable, similar to that in other large-scale studies.^{3,12} Fourth, PET-CT results were not incorporated into the analysis given that a certain number of cases had not undergone PET-CT preoperatively, mainly in the early part of the study period. It is highly likely that PET-CT can provide more information on tumor malignancy compared with CT.²² In terms of universality and simplicity, however, the use of PET-CT findings for the TNM classification has remained controversial. Finally, this study was a retrospective analysis from a single institute in Japan. Thus, our results may vary depending on the background characteristics of the patients. As the next step, histologic types other than adenocarcinoma should be

incorporated in the analysis. Detailed validations on data sets from various regions, including those outside Asia, are also important and required to improve the accuracy of international classification.

In summary, we performed a large-scale retrospective analysis to compare prognosis and malignancy of PSNs and pure solid nodules among patients with clinical stage IA adenocarcinoma. Our results suggested the importance of discriminating between pure solid nodules and PSNs. Moreover, our findings revealed that classification of PSNs on the basis of solid component size and CTR can more accurately predict the prognosis.

CRediT Authorship Contribution Statement

Masayuki Nakao: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Writing - original draft.

Katsunori Oikado, Yoshinao Sato, Kohei Hashimoto, Junji Ichinose, Yosuke Matsuura, Hironori Ninomiya: Data curation, Writing - review & editing.

Sakae Okumura, Mingyon Mun: Writing - review & editing.

Supplementary Data

Note: To access the supplementary material accompanying this article, visit the online version of the *JTO Clinical and Research Reports* at www.jtocrr.org and at <https://doi.org/10.1016/j.jtocrr.2022.100279>.

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