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Prognostic role of standard uptake value according to pathologic features of lung adenocarcinoma

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Abstract

Objective: To evaluate the influence of lung adenocarcinoma second predominant pattern on the maximal standard uptake value (SUVmax) and its prognostic effect in different histologic groups.

Methods: We retrospectively collected surgically resected pathologic stage I and II lung adenocarcinoma from nine European institutions. Only patients who underwent preoperative PET-CT and with available information regarding SUVmax of T (SUVmaxT) and N1 (SUVmaxN1) component were included.

Results: We enrolled 344 patients with lung adenocarcinoma. SUVmaxT did not show any significant relation according to the second predominant pattern ($p = 0.139$); this relationship remained nonsignificant in patients with similar predominant pattern. SUVmaxT influenced the disease-free survival in the whole cohort ($p = 0.002$) and in low- and intermediate-grade predominant pattern groups ($p = 0.040$ and $p = 0.008$, respectively). In the high-grade predominant pattern cohort and in the pathologic N1 cases, SUVmaxT lost its prognostic power. SUVmaxN1 did not show any significant correlation with predominant and second predominant patterns and did not have any prognostic impact on DFS.

Conclusions: SUVmaxT is influenced only by the adenocarcinoma predominant pattern, but not by second predominant pattern. Concurrently, in high-grade predominant pattern and pN1 group the prognostic power of SUVmaxT becomes nonsignificant.

Keywords

SUV, PET-CT, lung cancer, lung adenocarcinoma

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Introduction

In recent decades, lung adenocarcinoma has become the most frequent histotype of non-small cell lung cancer (NSCLC) worldwide, overcoming squamous cell carcinoma.[1] In 2011, the American Thoracic Society (ATS)/European Respiratory Society (ERS)/International Association for the Study of Lung Cancer (IASLC) issued a classification[2] that introduced new adenocarcinoma subtypes; each subtype has unique pathologic features and results in different clinical manifestations. High-grade patterns, solid and micropapillary, show worse disease-free survival (DFS) and overall survival (OS), while the low-grade (lepidic) subtype has better long-term outcomes.[3,4] Adenocarcinomas are often composed of two or more subtypes mixed together in different proportions so that a predominant and a second predominant pattern can be found according to their presence inside the same tumor.[2]

Positron emission tomography (PET)/computed tomography (CT) is routinely used in the preoperative workup and clinical staging of lung cancer due to its high sensitivity power, despite suboptimal specificity.[5] Maximum standard uptake value (SUVmax) is the most used parameter to quantify the metabolism of a lung lesion; previous experiences have identified significant differences in SUVmax according to the predominant pattern in lung adenocarcinoma and a concurrent significant correlation with OS and DFS.[6–8] Nevertheless, to date, the possible effect of second predominant pattern has not been fully studied.

The aim of this study was to verify a possible preoperative patient stratification by analyzing the influence of second predominant pattern on SUVmax and validate the prognostic impact of SUVmax related to the primary tumor and to ipsilateral hilar lymph nodes in a multicentric cohort of early-stage resected lung adenocarcinomas.

Methods

This study was approved by the ethical committee of Verona and Rovigo, Italy, on 13 February 2019 (protocol number 8543).

Patients

All consecutive pathologic stage I and II adenocarcinomas operated on between January 2014 and December 2017 in nine European thoracic surgery departments were retrospectively collected. Seven Italian institutions (IRCCS Sacro Cuore don Calabria Hospital in Negrar di Valpolicella, Verona; University Hospital of Parma; University Hospital of Pisa; University Hospital of Varese; University of Sacred Heart, IRCCS Fondazione Policlinico Agostino Gemelli in Rome; IRCCS Arcispedale Santa Maria Nuova, Reggio Emilia; University Hospital of Turin), one Spanish (Clinica Universidad de Navarra), and one Swiss (Cantonal Hospital Lucerne) participated in this study.

We included in this study only patients with complete information regarding preoperative PET/CT and SUVmax. Patients with pure adenocarcinoma (composed of a single pattern), invasive mucinous subtype (both as predominant and second predominant pattern), with the same percentage of predominant and second predominant pattern, and those with parietal pleural invasion (PL3) were excluded.

All patients underwent pulmonary resection (either anatomical or nonanatomical) with radical intent (R0 resection) and lymph node dissection, but surgical technique (either open or minimally invasive) depended on each institution's preferences.

PET/CT features

PET/CT was performed in each institution within a maximum of 20 days before surgery. Data regarding the SUVmax of the T factor (SUVmaxT) and of ipsilateral hilar lymph nodes (SUVmaxN1) were retrieved by patients' records. Images were interpreted by nuclear radiologists of the same institutions, blinded to patients' outcomes. SUVmax was calculated as the highest tumor voxel value for the primary lung tumor and homolateral hilar lymph nodes (when present) in each patient; SUV was finally normalized by body weight in all centers.

Histologic classification

All cases were diagnosed according to the ATS/ERS/IASLC classification and all adenocarcinoma subtypes were recorded semiquantitatively in 5% increments by pathologists in each institution. Diagnoses were reached by consensus among pathologists of the same institution who were blinded to patients' outcomes. All cases were staged according to the eighth edition International Union Against Cancer/American Joint Committee on Cancer TNM classification.

Endpoints

The primary endpoint of this study was to evaluate the association between the SUVmaxT and the second predominant pattern. Secondly, we investigated the influence of SUVmaxT and SUVmaxN1 on DFS.

Statistical analysis

Data were analyzed using SPSS version 26.0 for IOS. Continuous variables were expressed in terms of mean with standard deviation (SD) or median with range; categorical variables were expressed in terms of frequency. Two-tailed Pearson chi-square test and analysis of variance test were used for intergroup comparison of

categorical variables while the Student *t* test was used for continuous variables. DFS was defined as the time from the day of surgery until the first evidence of relapse or last follow-up and OS as the time from the day of surgery until death from any cause or the last follow-up. Recurrence was classified as local (along surgical suture line), regional (ipsilateral lung, ipsilateral chest wall, or ipsilateral hilar or mediastinal lymph node involvement), or distant.[9] Survival and time to relapse were estimated with Kaplan-Meier and differences in survival were determined by log-rank analysis. Preoperative and postoperative prognostic factors were investigated using Cox proportional hazards regression model; multivariate analysis was performed only with variables that were statistically significant at the univariate analysis. The hazard ratio (HR) and 95% confidence intervals (CIs) were reported for covariates.

Results

In total, 344 patients met all the inclusion criteria and had full information regarding preoperative PET/CT and SUVmax. Table 1 shows the preoperative, intraoperative, and postoperative features of patients. A total of 185 (53.8%) were male and mean age was 68.9 years; all patients received a radical (R0) resection. The majority of patients (248 [72.1%]) had pathologic stage I (148 stage IA and 100 stage IB), while the remaining 96 patients (27.9%) had pathologic stage II (14 stage IIA, 82 stage IIB). Mean SUVmaxT was 7.16 (±SD 6.03), while the median value was 5; SUVmaxN1 was 1.43 (±SD 3.46) in all the cohorts and 3.61 (±SD 3.98) in the pN1 patients.

According to the adenocarcinoma predominant pattern, mean SUVmaxT was present as follows: lepidic, 4.35; acinar, 7.35; and papillary, 6.84 (intermediate-grade group, 7.20); solid, 10.78; and micropapillary, 7.75 (high-grade group, 10.25); the difference between predominant patterns SUVmaxT was statistically significant ($p < 0.001$) and maintained the statistical significance when calculated as grade group ($p < 0.001$). Conversely, according to the second predominant pattern, mean SUVmaxT was present as follows: lepidic, 6.20; acinar, 7.39; papillary, 8.01; solid, 8.66; micropapillary, 6.13. We did not observe any significant difference between SUVmaxT when divided based on second predominant patterns ($p = 0.139$) or their grade group ($p = 0.769$).

Mean OS of the cohort was 57.3 months (95% CI 55.1–59.4). Predominant pattern significantly influenced OS ($p = 0.001$). Concurrently, SUVmaxT had a significant impact on OS both when considered as a continuous variable ($p = 0.001$) and when dichotomized according to the median value ($p = 0.002$).

Recurrence was seen in 88 patients (25.6%); in 31 cases, recurrence was local or regional; in 18 cases, patients had a distant metastasis, while in 25 cases, disease recurrence was both loco-regional and distant. No detailed information on the site of recurrence was available for 14 patients. Mean DFS of the whole cohort was 49.3 months (95% CI 46.5–52.0). Predominant patterns significantly influenced DFS ($p = 0.01$) and maintained statistical significance when calculated as grade ($p = 0.016$; Figure 1). SUVmaxT significantly influenced the DFS ($p < 0.001$); when divided according to the median value, SUVmaxT maintained its high significance ($p < 0.001$; Figure 2). At univariable analysis, grade of predominant pattern, tumor size, male sex, and SUVmaxT were significantly related to the DFS; tumor size and SUVmaxT were confirmed to be highly significant also at multivariable analysis ($p = 0.0014$, HR 1.040, 95% CI 1.008–1.073; and $p = 0.002$, HR 1.046, 95% CI 1.016–1.077, respectively; Table 2).

In order to evaluate the impact of second predominant pattern on SUVmaxT in more homogeneous subgroups, we analyzed different cohorts of patients with similar predominant pattern.

Low-grade predominant pattern

Sixty-five patients had a lepidic predominant pattern. Second predominant pattern was present as follows: 58 (89.2%) with an intermediate-grade pattern (acinar, 49 [75.4%]; papillary, 9 [13.8%]) and 7 (10.8% with a high-grade pattern; solid, 4 [6.2%]; micropapillary, 3 [4.6%]).

The second predominant pattern did not have a significant influence on SUVmaxT when calculated according to the single pattern ($p = 0.097$) or according to the grade group ($p = 0.176$). At univariable analysis, SUVmaxT was the only factor significantly influencing DFS ($p = 0.040$; HR 1.169, 95% CI 1.007–1.356; Table 2).

Intermediate-grade predominant pattern

This group accounted for 222 patients. A total of 157 (70.7%) had an acinar predominant pattern and 65 (29.3%) a papillary predominant pattern. Second predominant pattern was present as follows: 90 lepidic (40.5%), 72 (32.4%) intermediate-grade (acinar, 32 [14.4%]; papillary, 40 [18.0%]), and 60 (27%) high-grade (30 solid and 30 micropapillary, 13.5%, respectively).

The SUVmaxT did not have a significant difference between the two predominant patterns ($p = 0.547$). According to the second predominant pattern, no significant difference was found according to different subtypes ($p = 0.128$) and grade ($p = 0.150$).

As reported in Table 2, at univariable and multivariable analysis tumor size and SUVmaxT were independent prognostic factors for DFS ($p < 0.001$; HR 1.036, 95% CI 1.018–1.055; and $p = 0.008$; HR 1.051, 95% CI 1.013–1.091, respectively).

Table 1. Preoperative, intraoperative, and postoperative features of patients and tumors.

Patient characteristics	Values
Male	185 (53.8)
Age, y	68.9 ± 8.6
Smoking history	
Never	88 (25.6)
Active	88 (25.6)
Former	155 (45.1)
BMI	25.5 ± 4.7
Previous cancer	137 (39.8)
Cardiovascular disease	216 (62.8)
Diabetes	53 (15.4)
Respiratory disease	93 (27.0)
ASA	
1	47 (13.7)
2	180 (52.3)
3	101 (29.4)
4	12 (3.5)
SUVmaxT	5.2 (0-38)
Right side	194 (56.4)
Site	
Upper lobe	203 (59)
Middle lobe	28 (8.1)
Lower lobe	100 (29.1)
Type of resection	
Wedge resection	26 (7.6)
Segmentectomy	24 (7.0)
Lobectomy	288 (83.7)
Bilobectomy/pneumonectomy	3 (0.9)
Other	3 (0.9)
Type of lymphadenectomy	
Sampling	130 (37.8)
Lobe specific/systematic	214 (62.2)
Surgical technique	
Open	170 (49.4)
Minimally invasive	174 (51.6)
Predominant pattern	
Lepidic	65 (18.9)
Acinar	157 (45.6)
Papillary	65 (18.9)
Solid	47 (13.7
Micropapillary	10 (2.9)
Second predominant pattern	
Lepidic	95 (27.6)
Acinar	118 (34.3)
Papillary	59 (17.2)
Solid	35 (10.2)
Micropapillary	37 (10.8)
Pathologic stage	
I (IA1, IA2, IA3, IB)	148 (72.1%)
II (IIA, IIB)	96 (27.9%)
Size of the tumor, mm	24.8 (±12.6)

ASA: American Society of Anesthesiologists; BMI: body mass index; SD: standard deviation; SUVmax: maximum standard uptake value.
Values are n (%), mean ± SD, or median (range).

High-grade predominant pattern

This group accounted for 57 patients. A total of 47 (82.5%) had a solid pattern, while the remaining 10 (17.5%) had a micropapillary pattern. Second predominant pattern was present as follows: 5 lepidic (8.8%); 47 (82.5%) intermediate-grade (37 acinar [64.9%] and 10 papillary [17.5%]), and 5 (8.8%) high-grade (1 solid [1.8%] and 4 micropapillary [7.0%]). There was no difference between the predominant patterns in terms of SUVmaxT ($p = 0.100$). SUVmaxT was not significantly different among second predominant patterns ($p = 0.264$) or among their grades ($p = 0.261$). At univariable analysis, we did not find significant variables influencing DFS; as reported in Table 2, SUVmaxT did not impact on DFS (HR 1.028, 95% CI 0.977–1.081; $p = 0.292$).

pN1 subgroups

Fifty-one patients were pN1. A total of 6 (11.8%) patients had a lepidic predominant pattern, 30 (58.8%) had an intermediate-grade predominant pattern (22 acinar [43.1] and 8 papillary [15.7%]), and 15 (29.4%) had a high-grade predominant pattern (13 solid [25.5%] and 2 micropapillary [3.9%]). In this group of patients, mean SUVmaxT was 5.45 for low-grade group, 10.54 for intermediate group, and 10.67 for high-grade group and was significantly different between groups of predominant pattern ($p = 0.048$); on the other hand, SUVmaxN1 was 1.65 in the low-grade group, 2.76 in the intermediate-grade group, and 5.80 in the high grade group, with no significant differences ($p = 0.111$). When we analyzed the difference of SUVmaxT and SUVmaxN1 according to different subtypes of predominant pattern, we did not find significant differences ($p = 0.176$ and $p = 0.056$, respectively), even if SUVmaxN1 had a clear trend towards statistical significance. Due to the low number of patients in this subgroup, we did not make a subanalysis according to the second predominant pattern.

At univariable analysis neither SUVmaxT (HR 1.041, 95% CI 0.960–1.129; $p = 0.329$) nor SUVmaxN1 (HR 1.128, 95% CI 95% 0.978–1.301; $p = 0.097$) significantly affected DFS.

Discussion

Adenocarcinoma has become the most frequently diagnosed histotype of NSCLC, accounting for roughly 40% of the total.[1] The ATS/ERS/IASLC classification[2] identified different subtypes with different pathologic and clinical peculiarities; moreover, different adenocarcinomas can be composed of one (pure adenocarcinomas) or more than one subtype, which might be present with different proportions. Although the impact of the predominant pattern on long-term outcomes has been proved, the influence of

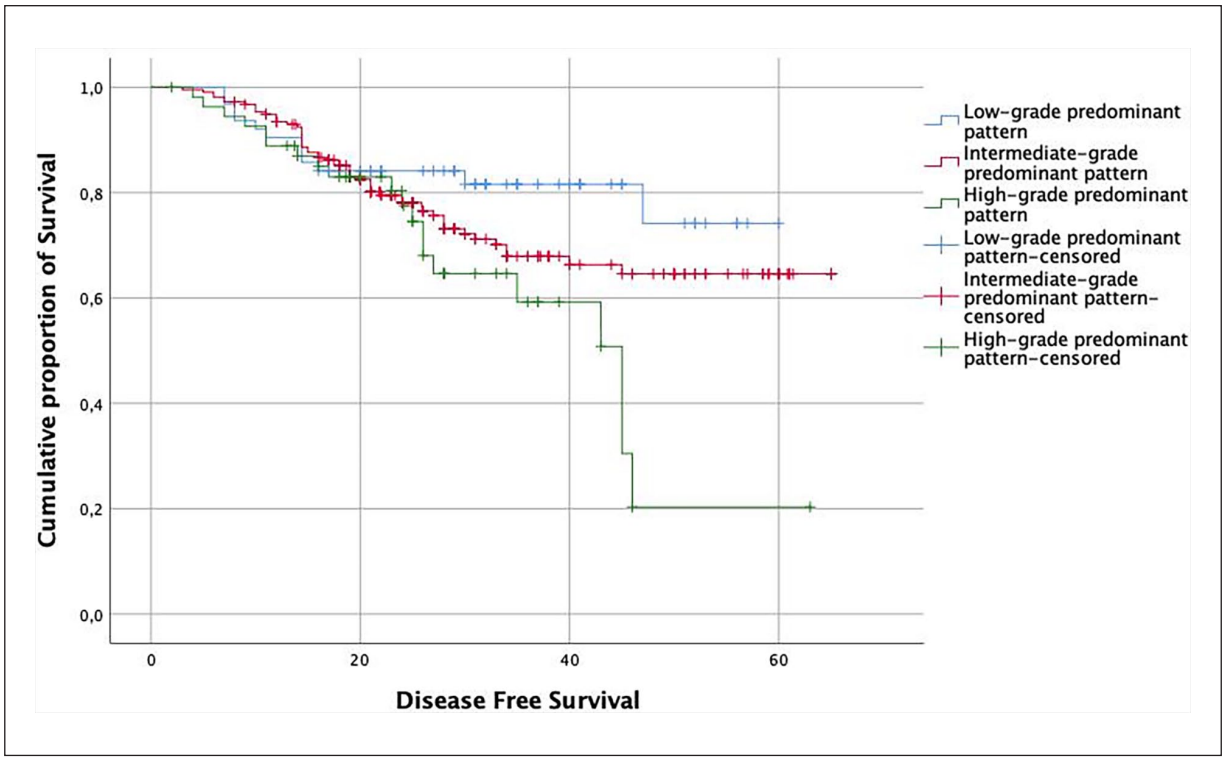

Figure 1. Disease-free survival according to the predominant pattern.

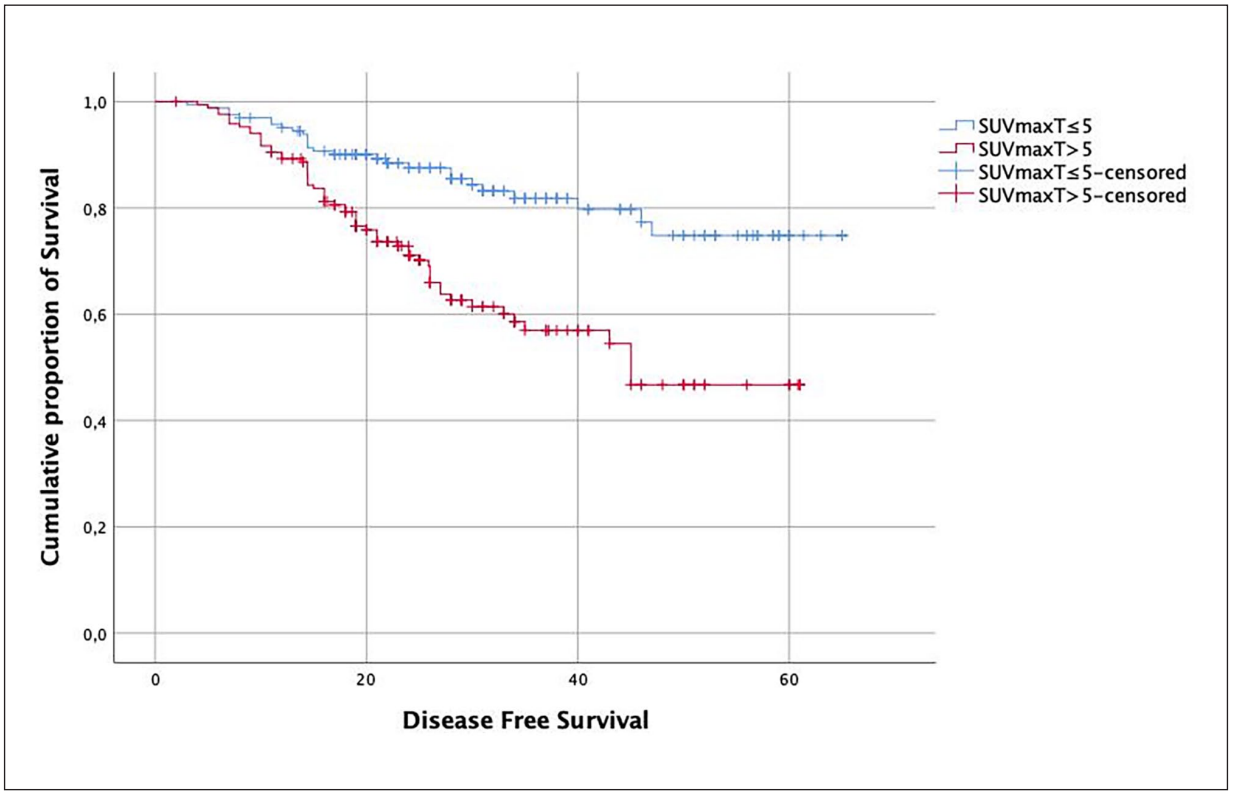

Figure 2. Disease-free survival according to the mean value of SUVmaxT.

Table 2. Univariate and multivariate analysis of the whole cohort and of different subgroups.

Groups	Univariate		Multivariate	
	p	HR (95% CI)	*p*	HR (95% CI)
Entire cohort				
Age	0.076	1.024 (0.998–1.051)		
Smoking history	0.148	1.469 (0.872–2.473)		
Male sex	0.048[a]	1.544 (1.003–2.377)	0.224	1.312 (0.847–2.032)
Lobectomy (vs other resections)	0.940	0.980 (0.577–1.664)		
Size of the tumor	<0.001[a]	1.034 (1.020–1.048)	0.014[a]	1.040 (1.008–1.073)
SUVmaxT	<0.001[a]	1.058 (1.031–1.085)	0.002[a]	1.046 (1.016–1.077)
Lymphovascular invasion	0.113	1.553 (0.900–2.679)		
Pleural invasion	0.315	1.250 (0.809–1.931)		
Grade predominant pattern	0.016[a]	1.548 (1.086–2.205)	0.275	1.227 (0.850–1.773)
Subtype of second predominant pattern	0.610	1.080 (0.803–1.454)		
Low-grade predominant subgroup				
Age	0.809	1.009 (0.937–.087)		
Smoking history	0.120	5.207 (0.652–41.605)		
Male sex	0.543	1.424 (0.547–4.436)		
Lobectomy (vs other resections)	0.146	0.426 (0.135–1.345)		
Size of the tumor	0.083	1.031 (0.996–1.068)		
SUVmaxT	0.040[a]	1.169 (1.007–1.356)	0.040[a]	1.169 (1.007–1.356)
Lymphovascular invasion	0.183	3.173 (0.581–17.333)		
Pleural invasion	0.699	1.250 (0.403–3.877)		
Subtype of second predominant pattern	0.533	0.778 (0.353–1.714)		
Grade second predominant pattern	0.557	0.537 (0.067–4.278)		
Intermediate-grade predominant subgroup				
Age	0.109	1.027 (0.994–1.062)		
Smoking history	0.624	1.164 (0.633–2.140)		
Male sex	0.142	1.469 (0.874–2.562)		
Lobectomy (vs other resections)	0.388	1.390 (0.658–2.940)		
Size of the tumor	<0.001[a]	1.040 (1.022–1.058)	<0.001[a]	1.036 (1.018–1.055)
SUVmaxT	0.001[a]	1.059 (1.024–1.095)	0.008[a]	1.051 (1.013–1.091)
Lymphovascular invasion	0.367	1.352 (0.702–2.603)		
Pleural invasion	0.851	1.056 (0.569–1.873)		
Subtype of second predominant pattern	0.265	1.103 (0.928–1.312)		
Grade second predominant pattern	0.343	1.167 (0.848–1.608)		
High-grade predominant subgroup				
Age	0.248	1.033 (0.978–1.091)		
Smoking history	0.526	1.498 (0.430–5.215)		
Male sex	0.808	1.126 (0.432–2.935)		
Lobectomy (vs other resections)	0.697	0.803 (0.266–2.423)		
Size of the tumor	0.418	1.015 (0.979–1.051)		
SUVmaxT	0.292	1.028 (0.977–1.081)		
Lymphovascular invasion	0.659	1.455 (0.276–7.681)		
Pleural invasion	0.233	1.741 (0.701–4.327)		
Subtype of second predominant pattern	0.284	0.759 (0.459–1.257)		
Grade second predominant pattern	0.413	0.661 (0.245–1.782)		
pN1 subgroup				
Age	0.996	1.000 (0.959–1.043)		
Smoking history	0.618	1.292 (0.473–3.531)		
Male sex	0.591	0.802 (0.358–1.796)		
Lobectomy (vs other resections)	0.706	0.812 (0.276–2.390)		
Size of the tumor	0.848	1.004 (0.963–1.047)		
SUVmaxT	0.329	1.041 (0.960–1.129)		
SUVmaxN1	0.097	1.128 (0.978–1.301)		
Lymphovascular invasion	0.069	0.366 (0.124–1.082)		
Pleural invasion	0.555	1.283 (0.561–2.931)		
Subtype of predominant pattern	0.418	1.158 (0.812–1.652)		
Grade predominant pattern	0.556	1.220 (0.630–2.362)		

CI: confidence interval; HR: hazard ratio; SUVmax: maximum standard uptake value.
[a]Significant.

second predominant pattern has not been fully investigated and results are inconsistent.[3,4,10–12]

In recent decades, 18-fluorodeoxyglucose PET/CT gained increasing importance in the preoperative workup of lung cancer, with a higher sensitivity and specificity compared to CT scan in the clinical staging of NSCLC; PET/CT mix radiologic and metabolic parameters evaluating cellular glucose consumption.[6] Tumor metabolism can be quantified using different parameters, the most commonly used in the clinical setting being the SUVmax.[7] Several authors found significant correlation between the ATS/ERS/IASLC adenocarcinoma classification and the SUVmax, confirming the metabolic difference of each subtype. Kadota et al.[8] reported a significantly higher SUVmax in patients with higher grade predominant pattern adenocarcinoma and in particular the solid subtypes showed the highest SUVmax (6.4 $\pm$ 2.9 SD); similarly, Nakamura and colleagues[13] found significantly different SUVmax values according to the adenocarcinoma subtype. These results are in line with those of other authors[6,14–17] and were confirmed by our study, with a significantly higher SUVmax in the high-grade group compared to the others. The higher SUVmax in this subgroup should be interpreted as an increased local aggressiveness, which is related to a worse prognosis; for instance, Ichikawa et al.[16] found a significant correlation between tumor vascular and pleural invasion and preoperative SUVmax. Nevertheless, no precise cutoffs have been verified to differentiate the predominant pattern with the sole use of PET/CT; in a retrospective study, Sun and coworkers[17] proposed three different cutoffs for each adenocarcinoma grade group that were evaluated in a control cohort with uncertain coincidence rates (88.9% for low-grade, 64.2% for intermediate grade, and 78.6 for high-grade).

The detrimental effect of high-grade subtypes, namely solid and micropapillary, on both DFS and OS have been reported in the literature.[9] Cha and coworkers[18] showed that even small percentages of micropapillary pattern might have negatively influenced OS, while both solid and micropapillary patterns were related to worse DFS. Moreover, Sica and colleagues[10] found a prevalence of high-grade component in metastatic tissue, even in patients who had an intermediate-grade predominant pattern adenocarcinoma. Consequently, the possibility to foresee even a small component of a high-grade subtype might allow tailoring the treatment accordingly. Based on these data, we aimed to verify any possible correlation between SUVmaxT and second predominant pattern according to long-term outcomes and, to our knowledge, this is the first large multicentric study focusing on this issue. Our results did not show any significant correlation between SUVmaxT and the second predominant pattern, also when we analyzed patients in subgroups with homogeneous predominant patterns. Kadota and colleagues[8] explored the different impact of SUVmax according to the adenocarcinoma subtypes; in particular, they found that more than half (61%) of those with intermediate-grade predominant pattern and highest SUVmax had a high-grade second predominant pattern and 71% of these cases had a high mitotic count; due to the small number of patients in this subgroup (18), the authors could not make any further conclusions.

As mentioned before, SUVmax has been shown to be significantly related to long-term outcomes. In a retrospective analysis of prospectively collected data, Ventura and colleagues[6] calculated a cutoff value for the SUVmax (3.75), which clearly divided their population in two groups with different mean OS (87.7 and 57.8 months, respectively). Similarly, other studies confirmed the correlation between a higher SUVmax and a worse prognosis (either OS or DFS)[8,16] mostly using median values of SUVmax of their population. In our study, we investigated the impact of SUVmaxT on DFS. Our results showed that this correlation was significant only in the general population and in the subset of patients with a low- or intermediate-grade predominant pattern, but this significance was lost in the high-grade predominant pattern group. Similarly, when we analyzed the subgroup of patients with pathologically verified N1 disease, SUVmaxT was not significantly related to DFS. We can speculate that these results confirm that the metabolic uptake of the tumor has a higher significance in patients with an early-stage limited disease or less aggressive adenocarcinoma subtype, but both a locally advanced status and a more aggressive histologic subtype can have a much stronger and more significant influence on DFS.

In a subgroup of pathologic N1 cases, we explored the correlation of SUVmaxN1 and the grade of predominant pattern and any possible correlation with DFS; correlation with second predominant pattern was not calculated due to the small number of patients in this group. The predictive and prognostic value of SUVmaxN1 has not been fully explored in the literature.[5] Although there was a difference among the three grade groups, the statistical significance was not fully reached, but, again, this might be due to the low number of patients in this subgroup. Concurrently, at univariable analysis, SUVmaxN1 did not show any impact on DFS.

SUVmax is the most used parameter for its high reproducibility and availability, but it is limited as it takes into account only data from a single voxel. Several authors proposed volumetric measures to better define the metabolic features of the whole nodule. Metabolic tumor volume (MTV) and total lesion glycolysis (TLG) have been proposed as potential prognostic factors. Retrospective analysis[6,19–21] suggests a better prognostic potential of both MTV and TLG compared to SUVmax in NSCLC. On the other hand, a recent meta-analysis[22] did not find significant differences in terms of prognostic power among SUVmax, MTV, and TLG. In our study, SUVmax (both

related to the T and to the N) was the only parameter analyzed as it was the most easily retrieved by all the participating institutions.

Almost half of our patients were operated with an open approach. This relatively high rate of open surgery might be explained by the multi-institutional character of this study and by the study period (2014–2017) during which minimally invasive techniques were less commonly used than today.

Although our study is based on a large multicentric database, it presents some limitations. The main limitations regard its retrospective nature, the different systems of acquisition of the PET-CT images, and their observer-dependent results at each independent institution, without external review or concordance analysis.

Conclusions

Our results confirm that SUVmaxT and SUVmaxN1 are strictly correlated to the predominant patterns in a cohort of resected stage I and II lung adenocarcinoma. The influence of second predominant pattern is not significant, also in subgroups with homogeneous predominant patterns. SUVmaxT can therefore scarcely discriminate different patterns in a single lung adenocarcinoma. Moreover, the prognostic potential of SUVmaxT is lost in cohorts with high-grade predominant subtypes and in case of locally advanced disease. Our results therefore suggest that the use of SUVmaxT as a predictive and prognostic factor should be taken into account with extreme caution.

Authors' note

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