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Correlation between clinicopathological characteristics of lung adenocarcinoma and the risk of venous thromboembolism

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Abstract

Background: Patients with primary lung adenocarcinoma are at increased risk of venous thromboembolism (VTE). However, lung adenocarcinoma characteristics differ across histological subtypes. Therefore, we performed comprehensive analyses on the clinicopathological characteristics of lung adenocarcinoma and risk of VTE.

Methods: A total of 952 surgically resected lung adenocarcinoma cases were reviewed and classified according to criteria of the International Association for the Study of Lung Cancer (IASLC)/American Thoracic Society (ATS) /European Respiratory Society (ERS). The correlation between this classification and VTE risk was retrospectively analyzed. The risks of other clinicopathological features including pleural invasion, vascular invasion and associated surgical intervention risks were also assessed.

Results: Of the 952 patients, 100 (10.4%) cases experienced VTE events during the follow-up period. Among those with VTE, 28 (28%) were found before surgery, 47 (47%) were found within 1 month after surgery, and 91 (91%) were found in hospital. Univariate analysis revealed that ages, extent of resection and presence of micropapillary features were predictive of VTE risk. Furthermore, multivariable analysis demonstrated that the presence of micropapillary features (subdistribution hazard ratio [SHR] 1.560, 95% CI: 1.043–2.330) and age >60 (SHR: 2.270, 95% CI:1.491–3.470) were associated with increased risk of VTE. After one year, the probability of developing VTE was 13.1% and 8.3% in patients with micropapillary features and those without, respectively.

Conclusions: VTE is a common complication for lung adenocarcinoma patients who undergo surgery, especially during the perioperative process and hospitalization. Presence of micropapillary subtype and age are positively associated with VTE risk.

KEYWORDS
adenocarcinoma, histological classification, lung cancer, micropapillary subtype, venous thromboembolism

INTRODUCTION

Lung cancer accounts for more than one-quarter of cancer-related deaths worldwide, and for all the different stages combined, the 5-year survival rate is currently less than 20%.[1] Venous thromboembolism (VTE) is a frequent complication in patients with non-small cell lung cancer (NSCLC).[2–4] VTE is significantly associated with the histological types of NSCLC.[5,6] Patients with adenocarcinoma are reported to be at a higher VTE risk than those with squamous cell carcinoma.[7] However, no large studies have further investigated the risk of VTE associated with the different adenocarcinoma subtypes.

In 2011, the International Association for the Study of Lung Cancer (IASLC), American Thoracic Society (ATS), and European Respiratory Society (ERS) proposed a new international multidisciplinary lung adenocarcinoma

classification system,[8] which was subsequently adopted by the World Health Organization in 2015.[9] According to this system, tumors are classified into different subtypes. Semi-quantitative recording of the subtypes in 5% increments encourages the observers to identify all subtypes that may be present rather than focusing on a single predominant subtype.[8–11] Many studies show that adenocarcinoma histological subtypes are associated with prognosis, driver gene alterations, and radiomic features.[12–15] Here, we performed a retrospective observational cohort study to investigate the risk of VTE associated with the different lung adenocarcinoma subtypes in consecutive patients treated in our center. Additionally, the risks of other pathological features including pleural invasion, vascular invasion and association with surgical interventions risks were also assessed.

METHODS

Study population

Consecutive patients with newly diagnosed lung adenocarcinoma treated with surgical resection between May 2010 and August 2018 were included in this study. The inclusion criterion was histological confirmation of lung adenocarcinoma. The exclusion criteria were as follows: VTE diagnosis at least 3 months before the surgery, continuous anticoagulation treatment with vitamin K antagonists or low-molecular-weight heparins, and insufficient data. Eligible patients were selected from the electronic medical record system. Tissue specimens were obtained from the department of pathology in our medical center.

This study was approved by the ethics committees of the Beijing Chao-Yang Hospital, Capital Medical University (No. 2016-79). All procedures were performed in accordance with the Helsinki Declaration.

Histological evaluation

Subtype analysis was conducted according to the IASLC/ATS/ERS classification and performed independently by two pathologists blinded to the clinical data. Tumors with the morphological subtype that existed in the greatest proportion were classified as the predominant subtype groups.[8,9,16] The presence of a specific histological pattern was defined when the component was present in at least 5% of the sample.[17] For all tumors, we assessed pleural and vascular invasion. Tumor stages were assigned according to the eighth edition of the IASLC TNM classification.[18]

Diagnosis and classification of venous thromboembolism

All VTE events including deep venous thromboembolism (DVT) and pulmonary thromboembolism (PE) were objectively diagnosed. The DVT events were confirmed via venous ultrasound or a computed tomography venous angiogram, while PE was diagnosed via computed tomography or ventilation-perfusion scanning. Additionally, for all included patients, we investigated and recorded whether mobilization, and VTE prophylaxis were performed before or after surgery. All incidentally detected VTE cases were included.

Screening and follow-up strategies

All patient information was extracted from electronic medical records and our databases. Any suspected thrombosis or cancer status during routine post-surgical follow-up was recorded. After resection, the patients were followed up with history and physical (H&P) and chest computed tomography (CT) ± contrast every 6 months for 2–3 years, then H&P and a low-dose noncontrast-enhanced chest CT annually. All medical records, focusing on VTE, were reviewed from the date of the first objective diagnosis of lung adenocarcinoma either to the date of death or to the last medical follow-up record, whichever occurred earlier. Follow-up was carried out to the end of January 2020.

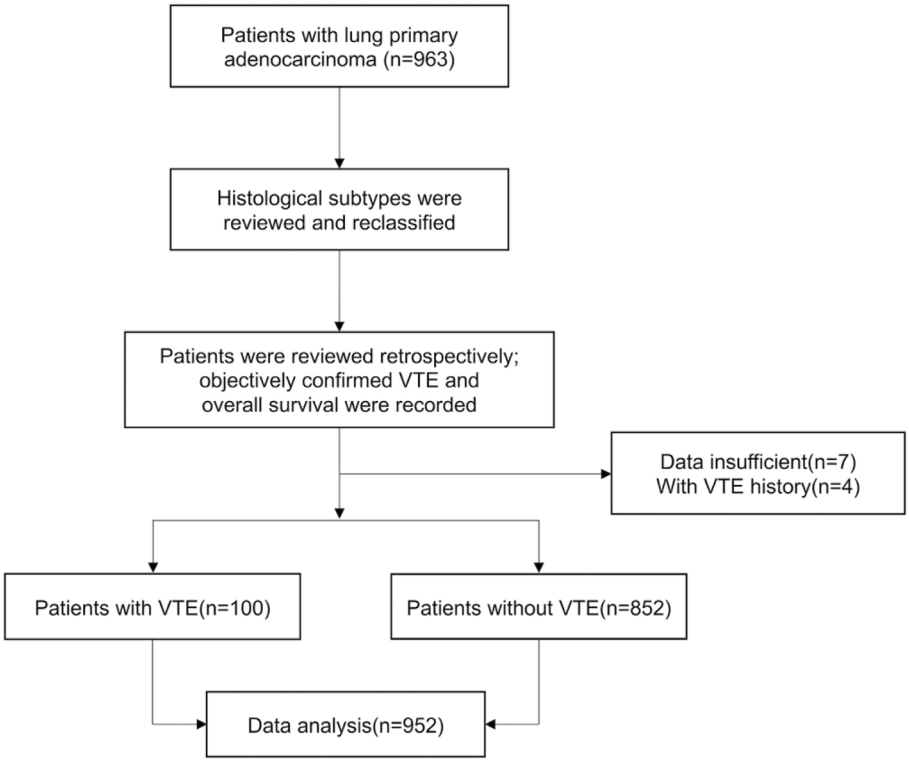
Statistical analysis

Continuous variables were compared using medians and interquartile ranges. For categorical variables, the percentage of patients in each category was calculated. A competing risk analysis was performed to determine the overall cumulative incidence of VTE, with death considered a competing event. Clinical characteristics were compared between the subgroups of patients with and without VTE using the Gray's test. The Fine-Gray regression analysis was used to calculate the risk factors of VTE, modeled as a dependent variable in multivariable analysis. There were two components in the multivariable analysis: (1) the independent variable that was significant in the univariable analysis, and (2) the recognised basic independent variables related to the occurrence of VTE; specifically, age, sex, body mass index (BMI), and clinical TNM (cTNM) stage. All statistical tests were two-sided, and p-values <0.05 were considered statistically significant. NCSS statistical software (Version 12.0; NCSS) and R (Version 3.4.4; R Foundation) were used to conduct the Gray's test and Fine-Gray regression analysis. SPSS (Version 25.0; IBM) was used for all other analyses. The study was reviewed by a professional epidemiologist.

RESULTS

A total of 963 consecutive patients with newly diagnosed lung adenocarcinoma were identified. Four patients were excluded due to the occurrence of DVT or

FIGURE 1 Study flow diagram



PE more than three months before recruitment, and seven patients were excluded due to incomplete baseline data. In total, 952 eligible patients were included (Figure 1).

Patient characteristics

A total of 952 patients had a median age of 61 years, and 418 (43.9%) patients were male. There were 458 (48.15%) patients with a BMI of less than 23.9 with

718 (75.4%) stage I patients in all patients, 122 (12.9%) stage II patients, 86 (9.0%) stage III patients and 26 (2.7%) stage IV patients. Stratified by surgery performed, 84 (8.8%) patients had undergone thoracotomy, and 868 (91.2%) had undergone video-assisted thoracoscopic surgery (VATS). Additionally, 852 (89.5%) had undergone radical surgery, and 100 (10.5%) had undergone palliative surgery, including segmentectomy and wedge resection to obtain pathological specimens or relieve symptoms. Out of all patients, 572 (60.1%) had a hospital stay lasting ≤13 days, 477 (50.1%) had an operation lasting ≤150 min, 558 (58.6%) had an intraoperative blood loss of ≤100 ml, and 13 received intraoperative blood transfusions. No one received induction therapy prior to surgery. Following lung surgery, 318 (33.4%) patients were administered adjuvant systemic therapy, including chemotherapy, radiotherapy, and molecular targeted therapy (Table 1). All patients had their clotting profiles (including prothrombin time, activated partial thromboplastin time, and international normalized ratio, platelet levels) measured before surgery, and all were within a normal range.

Histological parameters

According to the IASLC/ATS/ERS 2011 criteria, this lung adenocarcinoma cohort of 952 cases included adenocarcinoma in situ (AIS) (11.1%; $n = 106$), minimally invasive adenocarcinoma (MIA) (1.8%; $n = 17$), lepidic predominant (13.1%; $n = 125$), acinar predominant (43.6%; $n = 415$), papillary predominant (12.2%; $n = 116$), micropapillary predominant (5.3%; $n = 50$), solid predominant (9.1%; $n = 87$), and mucinous adenocarcinoma (3.8%; $n = 36$).

Most adenocarcinomas showed histological heterogeneity, comprising a mixture of two or more subtypes. Out of all patients, 433 (45.5%) presented with lepidic pattern, 708 (74.4%) with acinar pattern, 361 (37.9%) with papillary pattern, 262 (27.5%) with micropapillary pattern, 206 (21.6%) with solid pattern, and 57 (6.0%) with mucinous pattern. Vascular invasion was present in 194 (20.4%) and pleural invasion in 224 (23.5%) of all patients (Table 2).

Occurrence and management of venous thromboembolism

Venous ultrasound of the lower extremities for DVT screening was performed before or after surgery in 680 (71.4%)

TABLE 1 Baseline demographic and clinical characteristics of the study population

Characteristic	All patients ($n = 952$) (%[a])	Patients with VTE ($n = 100$) (%[b])	$\chi 2$	p-value
Age (years)			15.474	<0.001
≤60	470 (49.4)	31 (6.6)		
>60	482 (50.6)	69 (14.3)		
Gender			1.598	0.206
Male	418 (43.9)	38 (9.1)		
Female	534 (56.1)	62 (11.6)		
BMI (kg/m^2)			2.882	0.090
<23.9	458 (48.1)	40 (8.7)		
≥ 23.9	494 (51.9)	60 (12.1)		
Smoking history			3.695	0.055
Current and former	287 (30.3)	22 (7.7)		
Never	665 (69.7)	78 (11.7)		
COPD			0.249	0.618
Yes	173 (18.1)	20 (11.6)		
No	779 (81.9)	80 (10.3)		
Surgical approach			0.173	0.677
VATS	868 (91.2)	92 (10.6)		
Thoracotomy	84 (8.8)	8 (9.5)		
Extent of resection			8.959	0.030
Segmentectomy	16 (1.7)	2 (12.5)		
Wedge	84 (8.8)	8 (9.5)		
Lobectomy	842 (88.4)	86 (10.2)		
Pneumonectomy	10 (1.1)	4 (40.0)		
Hospitalization time (days)			1.452	0.228
≤13	572 (60.1)	54 (9.4)		
>13	380 (39.9)	46 (12.1)		
Duration of operation (min)			2.231	0.135
≤150	477 (50.1)	43 (9.01)		
>150	475 (49.9)	57 (12.0)		
Intraoperative blood loss (ml)			1.727	0.189
≤100	558 (58.6)	52 (9.3)		
>100	394 (41.4)	48 (12.2)		
Blood transfusion			2.243	0.134
Yes	13 (1.4)	3 (23.1)		
No	939 (98.6)	97 (10.3)		
Tumor stage			1.711	0.635
pT1	725 (76.2)	72 (9.9)		
pT2	183 (19.2)	24 (13.2)		
pT3	27 (2.8)	2 (7.4)		
pT4	17 (1.8)	2 (11.8)		
Nodal status			4.945	0.176
pN0	753(79.1)	73 (9.7)		
pN1	102 (10.7)	16 (15.7)		
pN2	86 (9.0)	11 (12.8)		
N3	11 (1.2)	0 (0.0)		
Metastases			1.290	0.256
M0	926 (97.3)	99 (10.7)		
M1	26 (2.7)	1 (3.8)		
cTNM stage			5.131	0.164
I	718 (75.4)	69 (9.6)		
II	122 (12.9)	17 (13.9)		
III	86 (9.0)	13 (15.1)		

(Continues)

TABLE 1 (Continued)

Characteristic	All patients ($n = 952$) (%[a])	Patients with VTE ($n = 100$) (%[b])	$\chi 2$	p-value
IV	26 (2.7)	1 (3.8)		
Adjuvant therapy			2.850	0.091
Yes	318 (33.4)	42 (13.2)		
No	634 (66.6)	58 (9.1)		

Abbreviations: BMI, body-mass index; COPD, chronic obstructive pulmonary disease; VATS, video-assisted thoracic surgery; VTE, venous thromboembolism.
[a]Proportion of subgroups in the total population.
[b]Proportion of VTE patients in the subgroup population.

TABLE 2 Histological characteristics of the study population

Characteristic	All patients ($n = 952$) (%[a])	Patients with VTE ($n = 100$) (%[b])	$\chi 2$	p-value
AIS	106 (11.1)	8 (7.5)	0.880	0.348
MIA	17 (1.8)	1 (5.9)	0.310	0.577
Predominant subtype[c]				
Lepidic	125 (13.1)	13 (10.4)	0.010	0.920
Acinar	415 (43.6)	47 (11.3)	0.379	0.538
Papillary	116 (12.2)	8 (6.9)	2.022	0.155
Micropapillary	50 (5.3)	7 (14.0)	0.561	0.454
Solid	87 (9.1)	9 (10.3)	0.004	0.952
Mucinous	36 (3.8)	7 (19.4)	3.071	0.080
Lepidic pattern			1.257	0.262
Absent	519 (54.5)	50 (9.6)		
Present	433 (45.5)	50 (11.5)		
Acinar pattern			1.121	0.290
Absent	244 (25.6)	21 (8.6)		
Present	708 (74.4)	79 (11.2)		
Papillary pattern			0.676	0.411
Absent	591 (62.1)	58 (9.8)		
Present	361 (37.9)	42 (11.6)		
Micropapillary pattern			6.127	0.047
Absent	690 (72.5)	62 (9.0)		
Present	262 (27.5)	38 (14.5)		
Solid pattern			0.110	0.740
Absent	746 (78.4)	77 (10.3)		
Present	206 (21.6)	23 (11.2)		
Mucinous pattern			0.773	0.379
Absent	895 (94.0)	92 (10.9)		
Present	57 (6.0)	8 (14.0)		
Vascular invasion			0.179	0.673
Absent	758 (79.6)	81 (10.7)		
Present	194 (20.4)	19 (9.8)		
Pleural invasion			0.892	0.345
Absent	728 (76.5)	80 (11.0)		
Present	224 (23.5)	20 (8.9)		

Abbreviations: AIS, adenocarcinoma in situ; MIA, minimal invasive adenocarcinoma; VTE, venous thromboembolism.
[a]Proportion of subgroups in the total population.
[b]Proportion of VTE patients in the subgroup population.
[c]The subtype that occupied most of the tumor was defined as the predominant subtype. The presence of a specific histological pattern is defined as the percentage of the specific histologic component ≥5%.

TABLE 3 Characteristics of venous thromboembolism

Characteristic	No. of patients (%)
Total episodes	100 (10.4)
Location of VTE	
DVT alone	86 (9.0)
Lower extremity and pelvis	85 (8.9)
Upper extremity and neck	1 (0.1)
PE alone	7 (0.7)
Segmental/subsegmental	6 (0.6)
Above segmental	1 (0.1)
DVT and PE combined	7 (0.7)
Lower extremity DVT and segmental PE	4 (0.4)
Lower extremity DVT and above segmental PE	3 (0.3)
Clinical presentation	
Incidental/screened	89 (9.3)
Symptomatic	11 (1.1)
Patient situation	
Ambulatory	9 (0.9)
Hospitalized	91 (9.5)
Time of occurrence	
Before surgery	28 (2.9)
Within one month after operation	47 (4.9)
One month after operation	25 (2.6)

Abbreviations: DVT, deep venous thromboembolism; PE, pulmonary embolism; VTE, venous thromboembolism.

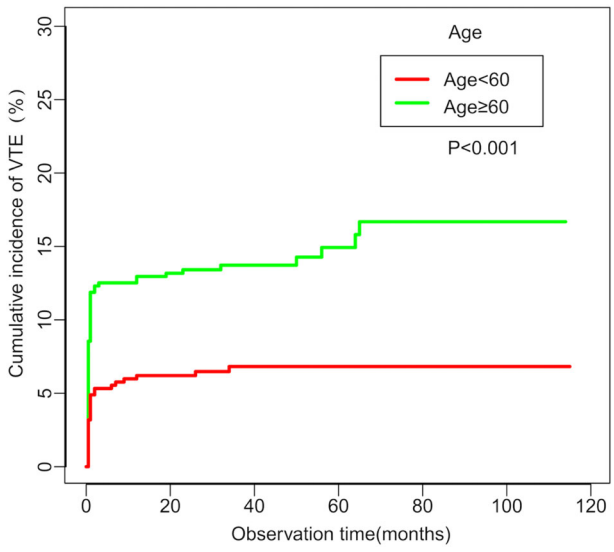


FIGURE 2 Cumulative incidence of venous thromboembolism in patients with lung adenocarcinoma by age ($p < 0.001$)

patients. The median follow-up period was 41 months (27–63 months). Overall, 100 (10.4%) patients experienced VTE events during the follow-up period. Of those, DVT alone (including lower extremity, upper extremity, neck, or pelvis DVT) developed in 86 (9.0%) patients, PE alone developed

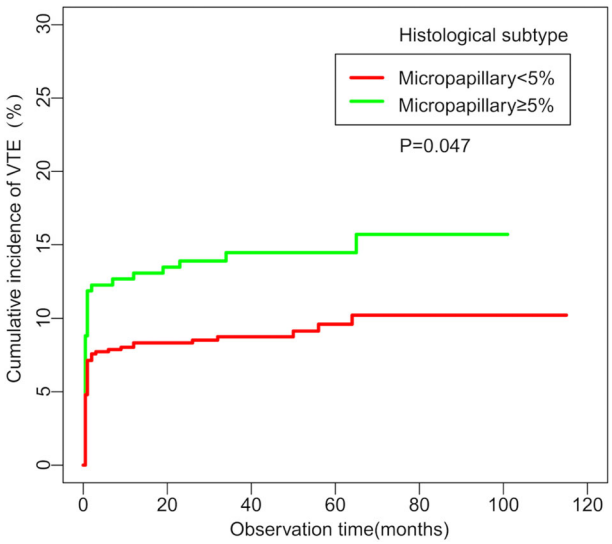


FIGURE 3 Cumulative incidence of venous thromboembolism in patients with lung adenocarcinoma by micropapillary subtype ($p = 0.047$)

in seven (0.7%) patients, and both DVT and PE developed in seven (0.7%) patients. For the DVT cases, 89.2% (83 of 93, including 80 lower extremity and three DVTs with PEs) were asymptomatic. 64.3% of the PE cases (9 of 14) remained asymptomatic that were incidentally found. Among those with VTE, 28 (28%) were found before surgery, 47 (47%) were found within 1 month after surgery, and 91 (91%) were found in hospital (Table 3).

All patients were encouraged to ambulate on the first day after operation for VTE prophylaxis and other comorbidities. Once VTE was discovered to require treatment, anticoagulation therapy was provided. Additionally, 14 patients required intensive care unit (ICU) admission due to postoperation comorbidities, and only these patients had received VTE anticoagulation prophylaxis. Death was documented in 98 (10.3%) patients at the time of the final analysis.

Factors associated with venous thromboembolism

In the univariate analysis, the presence of VTE was more prevalent in patients above 60 years old than in patients below or equal to 60 years old (Gray's test $p < 0.001$). Of the 482 patients above 60 years old, VTE developed in 69 patients (14.3%), whereas VTE developed in only 31 out of 470 patients (6.6%) who were aged 60 years or younger. The probability of developing VTE in patients above 60 and those younger or equal to 60 was 13.0% and 6.2%, respectively, in the first year, and 13.4% and 6.2%, respectively, in the second year (Figure 2). Finally, the extent of resection had a significant relationship with VTE (Gray's test, $p = 0.030$). There was no significant association between other demographic or clinical features with VTE risk (Table 1).

TABLE 4 Factors associated with an increased venous thromboembolism risk in patients with lung adenocarcinoma

Parameter	SHR	95%CI	*p*-value
Age[a]	2.270	1.491–3.470	<0.001
Gender[b]	1.410	0.944-2.100	0.094
BMI[c]	1.420	0.960-2.100	0.079
Extent of resection[d]	1.250	0.598–2.260	0.550
cTNM stage[e]	1.090	0.870–1.370	0.450
Micropapillary[f]	1.560	1.043-2.330	0.030

Abbreviations: BMI, body mass index; CI, confidence interval; SHR, subdistribution hazard ratio.
[a]Age: ≤60 versus >60.
[b]Gender: Male versus female.
[c]BMI: <23.9 versus ≥ 23.9.
[d]Extent of resection: Segmentectomy versus wedge versus lobectomy versus pneumonectomy.
[e]cTNM stage:I versus II versus III versus IV.
[f]Micropapillary: absent versus present.

Additionally, we found that VTE occurred more frequently in the micropapillary present group than in the micropapillary absent group (Gray's test $p = 0.047$). Of the 262 patients in the micropapillary present group, VTE developed in 38 patients (14.5%), whereas VTE developed in 62 out of 690 patients (9.0%) in the micropapillary absent group. The probability of developing VTE in the micropapillary present group and in the micropapillary absent group was 13.1% and 8.3%, respectively, in the first year, and 13.9% and 8.3%, respectively, in the second year (Figure 3). There was no significant association between other histological subtypes and VTE risk, and there was no significant association between other pathological features including pleural and vascular invasion and VTE risk (Table 2).

Subsequently, we performed the Fine-Gray regression analysis including age, sex, BMI, extent of resection, histological subtype, and cTNM stage to identify the risk factors associated with the development of VTE. The classification of age, gender, BMI, surgical resection range, and TNM staging are the same as those in Table 1, and the classification of the presence or absence of micropapillary is the same as in Table 2. Only the micropapillary subtype of ≥5% (SHR 1.560, 95% CI: 1.043–2.330, $p = 0.030$) and age ≥ 60 years (SHR 2.270, 95% CI: 1.491–3.470, $p < 0.001$) were considered independent factors for increased VTE risk. Sex, BMI, the extent of resection, and the cTNM stage were not associated with the development of VTE (Table 4).

DISCUSSION

Previous studies have focused on patients with lung adenocarcinomas that are prone to develop VTE, but these are mainly concentrated in advanced adenocarcinomas. With the development of CT screening, there have been more opportunities for the detection and surgical treatment of adenocarcinoma. Our study showed that even if patients with lung adenocarcinoma were at an early stage, they were still prone to develop VTE, especially those in the micropapillary present group.

High incidence of VTE during the perioperative process and hospitalization

In general, pulmonary ground-glass nodules are primary lung adenocarcinoma.[19] The majority of patients in this study were diagnosed with stage I lung adenocarcinoma. However, the incidence of VTE was similar to the incidence reported for advanced lung adenocarcinoma.[3,5] VTE is a common complication for lung adenocarcinoma patients who undergo surgery, especially during the perioperative process and hospitalization. VTE is a major source of postoperative morbidity and mortality for patients undergoing thoracic surgery.[20,21] VTE events mostly occur during hospitalization, including the perioperative period, and subsequent examinations or treatments, which support that hospitalization is an independent risk factor for VTE.[22–24] In addition, most VTE events in this study were found in the lower extremities which is in agreement with previously reported studies.[25,26] Therefore, we have the same recommendations as previous studies,[25] which is that lower-extremity ultrasonography is probably required for screening post-surgical DVT cases during hospitalization.

Micropapillary subtype and venous thromboembolism

The subtype distribution in our study was similar to that in previously reported studies.[27,28] Interestingly, in our study, we found that there was a significant correlation between the presence of a micropapillary component.

The mechanism underlying the higher risk associated with a micropapillary subtype has not yet been reported. However, previous studies have shown that the micropapillary subtype is associated with larger tumor size, lymph node metastasis, increased rate of recurrence, and patient mortality, indicating the high malignant potential of the micropapillary subtype.[14,15,29,30] This may be a consequence of epithelial-mesenchymal transition. Loss of apical-basal polarity, which causes the micropapillary subtype, has been recognized as an important step in the acquisition of an invasive phenotype.[31] The degree of malignancy was high in the micropapillary present group promoting lung adenocarcinoma growth, invasiveness, and metastasis. Thus, VTE risk may be increased.

Previous studies have shown that the proportions of different histological subtypes correspond to different survival and recurrence rates.[32–34] Therefore, in future studies, we should not only focus on the presence and predominance of subtypes but also on the influence of the proportion of different subtypes on the occurrence of VTE.

So far, the relationship between vascular and pleural invasion, and the risk of VTE has not yet been reported.

Our study showed there was no significant correlation between vascular and pleural invasion and VTE risk. Possible explanations for these results may be that the impact of local invasion on VTE risk may be relatively limited compared with distant metastasis. The relationship needs to be further demonstrated in prospectively designed large-scale studies.

Age and venous thromboembolism

In this study, we showed that patients older than 60 years were more likely to develop VTE than younger patients. Older patients may experience more complications and are less mobile following surgery resulting in a higher risk of VTE. This finding is supported by previous studies.[35,36]

Surgical interventions and venous thromboembolism

In the univariate analysis, the resection range was significantly correlated with VTE, while the multivariate analysis showed no significant correlation. Most patients received a lobectomy, and there were fewer patients with other resection ranges, and the distribution between the groups was uneven. In future studies, we will expand the sample size balance the gap between groups, and explore whether the extent of resection ultimately affects VTE.

This study found that there was no significant correlation between surgical approach, hospitalization duration, duration of the operation, intraoperative blood loss, or incidence of blood transfusion and the occurrence of VTE, consistent with previous studies.[37–39] However, some previous studies show a relationship between pneumonectomy, VATS and VTE risk.[40,41] We suggest that the increased VTE risk following lung resection is multifactorial. Several factors could increase VTE risk in patients undergoing lung resection, such as the intrinsic procoagulant effect of lung cancer and different surgical techniques, including the manipulation of the pulmonary arteries and ligation of arterial branches. Even limb position in the operating room can potentially play an important role in VTE formation.[37,42]

Other risk factors and venous thromboembolism

Our study showed no significant correlation between sex and VTE risk, consistent with a previous study.[37] However, Young et al. showed that women have a higher risk of VTE.[43] Possible explanations for these discordant findings include differences in study design and patient inclusion criteria.

Our study also reported no significant correlation between tumor stage and VTE risk. However, this is inconsistent with a previous study,[2] which showed that patients at later tumor stages have more metastases, and would consequently be more likely to receive a wider range of surgical resections or receive treatments such as chemotherapy and radiotherapy for longer periods, which ultimately could increase the risk of VTE. This discrepancy between the two studies may be due to the difference in tumor stage distribution. In our study, most patients had early stage tumors and received surgical resection.

Our study also showed no significant correlation between BMI and VTE risk, inconsistent with the significant relationship between BMI and VTE risk reported by Merkow et al. In that study, VTE risk increased as BMI status increased from overweight to morbidly obese.[44] These different findings may be due to differences in study design and patient demographics, including ethnicity and cancer site.

There were several limitations in our study. First, it was a single-center retrospective study. The retrospective design combined with the relatively small sample size raises the possibility of selection and information biases on the part of physicians or patients. Second, although we objectively recorded confirmed VTE with and without symptoms, VTE may have been underdiagnosed because not all patients had undergone VTE screening before and after surgery.

In conclusion, VTE is a common complication in lung adenocarcinoma patients who undergo surgery, especially during the perioperative process and hospitalization. Patients in the micropapillary present group might have a higher risk of VTE. Moreover, patients over 60 years are more likely to develop VTE. Evaluation of adenocarcinoma histological subtypes and age may therefore be helpful for identifying the risk of VTE in patients with lung primary adenocarcinoma. However, these results need to be confirmed in adequately designed prospective studies. In addition, the correlation between the extent of resection and VTE in future studies with larger sample sizes should also be explored.

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CONFLICT OF INTEREST

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