

Peer review file

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Reviewer A

Comment 1: Usually variables with $p < 0.2$ are included in the regression instead of $p < 0.05$.

Reply 1: Thanks for your professional and rigorous advice. We have corrected it and re-conducted a statistical analysis.

Changes in the text: Any variable with a p-value of 0.2 in the univariate analysis was included in multivariate analysis. (Page 7, line 156)

Table 4 Multivariate analysis of the risk of the VTE in patients received lung resection using continuous variables (include surgical approach)

Parameter	Odds ratio	95% Confidence interval	P value
Age(y)	1.08	1.03-1.12	0.001
Surgical approach	1.64	0.70-3.81	0.255
Diabetes mellitus	1.43	1.17-1.74	0.522
Lymphocyte count $\times 10^9$ (/L)	0.26	0.10-0.72	0.009
D-dimer($\mu\text{g/mL}$)	1.43	1.17-1.74	< 0.001

(Page 31, line 514-516)

Comment 2: Please clarify what is a modified Caprini score and how it is different than Caprini score, especially in laparoscopic surgery.

Reply 2: We're so sorry for confusing you on this issue. We showed modified Caprini score in Table 3, but the title was not accurate enough. 'Laparoscopic surgery' is not included in this model, and adding this one will make the score more effective.

Changes in the text: Table 3 Prevalence of modified Caprini risk factors by VTE status. (Page 29, line 504)

Comment 3: Please emphasis this information that Caprini score did not stratify VTE risk in this population.

Reply 3: We did another analysis to illustrate the issue (Table 7). In the analysis of each group, the incidence of VTE did not increase with the increase of score.

Changes in the text: According to the modified Caprini score, there were fewer

patients in the high-risk group, and the incidence of VTE not increased with the increase of risk.(Page 3, line 45-46)

In this study, there were only 4 patients in high-risk group, and the incidence of VTE in low-risk group (0-4), moderate-risk group (5-8) and high-risk group (≥ 9) was 12.3% (37/300), 7.5% (10/133) and 0% (0/4), respectively ($P > 0.05$). In the subgroup analysis, the results were similar. And the AUC of the modified Caprini score is 0.474 ($P=0.558$). These results suggest that the modified Caprini score is not effective enough for VTE risk stratification in patients after lung surgery. (Page 14, line 290-296)

Table 7 Incidence of VTE in subgroups with different risk stratification

Group	0-4	5-8	≥ 9
All	12.3%(37/300)	7.5%(10/133)	0(0/4)
Non-small cell lung cancer	18.5%(25/135)	7.9%(10/126)	0(0/4)
Benign	7.3%(12/165)	0(0/7)	0(0/0)

(Page 32, line 523-524)

Comment 4: Previous studies have demonstrated Caprini scores can risk stratify patients for VTE. Only 4 patients were in the high risk group, which may limit the ability of the scoring system to discriminate VTE risk. (*Hachey KJ. Caprini venous thromboembolism risk assessment permits selection for postdischarge prophylactic anticoagulation in patients with resectable lung cancer. J Thorac Cardiovasc Surg 2016;151:37-44.e1*)

Reply 4: That's a really good question. When we got results from our study, we were also surprised, because they're different with Hachey's study and others. Then, we compared the tables carefully, and found several difference in the patients. Patients in our study more less received open surgery(79/437 vs 162/232) and central venous access(7/437 vs 68/232) than Hachey's study. These factors lead to the tendency of our patients to the low-risk group and the moderate-risk group. As a result, there were only four people in the high-risk group. This may be the bias of a single-center sample, which still needs to be verified by multicenter studies.

Changes in the text: Hachey et al. retrospectively assigned modified Caprini score to 232 patients undergoing pneumonectomy and proved that modified Caprini score can stratify the risk of VTE.(2) By comparing patients information, patients in our study were less likely to undergo open surgery (79/437 vs 162/232) and central venous access (7/437 vs 68/232), which may be the reason for the small number of high-risk group and the inefficiency of the modified Caprini score in our study. (Page 14, line 296-302)

Comment 5: Please describe statistical methods for calculating AUC.

Reply 5: Thanks for your this coment, which we have added.

Changes in the text: We used the area under the receiver operating characteristic (ROC) curve to discriminate patients between the patients with VTE and those without VTE. (Page 8, line 158-160)

Comment 6: What VTE prophylaxis regimen was used for these patients?

Reply 6: Thanks for your this coment. In this study, all patients received physical prophylaxis. Some patients received non-standard perioperative anticoagulant therapy. Different drugs and doses made it difficult to accurately assess their effects on thrombosis, so they were not included in this study.

Changes in the text: Patients will be excluded from the study if they have one of following conditions: current VTE, perioperative prophylactic anticoagulation and insufficient clinical data. All patients received physical prophylaxis, including ankle pump exercise, graduated compress stocking (GCS), also went to the ground as early as possible after operation. (Page 5, line 95-102)

Comment 7: Please clarify in the methods section that patient with both benign and malignant disease were included in the analysis. Please also provide some description of what benign cases were included.

Reply 7: We have made a supplement to this problem.

Changes in the text: Malignant tumors and benign diseases were included, among which benign diseases mainly included presumed malignant nodules, pulmonary vesicles, bronchiectasis and so on. (Page 5, line 93-95)

Comment 8: They should add to this discussion that approximately 40% of VTE occur post discharge, according to a NSQIP analysis.

Reply 8: This is a very helpful suggestion. In this retrospective study, it is very difficult to follow up patients all over the country for a long time. Short follow-up time may lead to a low incidence of VTE, which will affect the results of the analysis to a certain extent. Thanks for your literature for our study and reference. In this regard, we had a further discussion.

Changes in the text: In this retrospective study, the follow-up period ended when the patients were discharged from the hospital. And the median days of receiving ultrasound and hospitalization after operation were 5 days and 7 days, respectively. Thomas et al reported that about 40% of VTE occurred after discharge (43). Overall, the incidence of postoperative VTE in our study may be underestimated, which may also lead to deviations in the results of the analysis. Therefore, this is only the result of our single-center study, and the results still need to be verified by a large sample of multicenter studies. (Page 14, line 303-315)

Comment 9: They are several typos, for example Caprini is misspelled in the abstract and there are punctuation errors.

Reply 9: We apologize for the mistakes in language expression, and we have asked assisting language checkers to help us solve these problems.

Changes in the text: Capriin Caprini (Page 2, line 25), 1.15x10⁹/L (Page 2, line 39),

therapeutic therapeutic (Page 3, line 53) and so on.

Reviewer B

Major issues:

Comment 1: What was the median hospital length of stay for the cohort? Given the fact that patients were only followed during their hospital length of stay, the incidence of VTE presented in the study may be underestimated.

Reply 1: Thanks for your helpful and rigorous advice. The median hospital length of stay in this study was 12 days. And the median days of receiving ultrasound and hospitalization after operation were 5 days and 7 days, respectively. Moghadamyeghaneh et al reported that the first week after operation was the most common time for postoperative VTE (Moghadamyeghaneh Z, Hanna MH, Carmichael JC, Nguyen NT, Stamos MJ. A nationwide analysis of postoperative deep vein thrombosis and pulmonary embolism in colon and rectal surgery. *J Gastrointest Surg.* 2014;18(12):2169-2177. doi:10.1007/s11605-014-2647-5). Of course, Thomas et al also reported that about 40% of VTE occurred after discharge. Whatever, the incidence of postoperative VTE in our study may be underestimated (Thomas DC, Arnold BN, Hoag JR, et al. Timing and Risk Factors Associated With Venous Thromboembolism After Lung Cancer Resection. *Ann Thorac Surg.* 2018;105(5):1469-1475. doi:10.1016/j.athoracsur.2018.01.072). In this retrospective study, it is difficult to follow up patients from all over the country for a long time, so we can not get enough satisfactory follow-up data. It is also a great pity for us. In the future, we will do a prospective study to verify these results.

Changes in the text: In this retrospective study, the follow-up period ended when the patients were discharged from the hospital. And the median days of receiving ultrasound and hospitalization after operation were 5 days and 7 days, respectively. The length of follow-up is closely related to the diagnosis of VTE. On the one hand, Moghadamyeghaneh et al reported that the first week after operation was the most common time for postoperative VTE (42). On the other hand, Thomas et al reported that about 40% of VTE occurred after discharge (43). Besides, The missed diagnosis of ultrasound examinations may also underestimate the incidence of VTE. Overall, the incidence of postoperative VTE in our study may be underestimated, which may also lead to deviations in the results of the analysis. Therefore, this is only the result of our single-center study, and the results still need to be verified by a large sample of multicenter studies. (Page 14, line 303-315)

Comment 2: Did all patients receive VTE prophylaxis? What was the prophylaxis protocol (mechanical vs chemical or both)? Was it a standardized method for all patients?

Reply 2: In this study, all patients received physical prophylaxis. Some patients received non-standard perioperative anticoagulant therapy. Different drugs and doses

made it difficult to accurately assess their effects on thrombosis, so they were not included in this study.

Changes in the text: Patients will be excluded from the study if they have one of following conditions: current VTE, perioperative prophylactic anticoagulation and insufficient clinical data. All patients received physical prophylaxis, including ankle pump exercise, graduated compress stocking (GCS), also went to the ground as early as possible after operation. (Page 5, line 95-102)

Comment 3: How many patients were found to have DVT with duplex ultrasound and how many with CT? Please define the criteria to choose one method over the other?

It is well known that ultrasound examinations significantly underestimate the incidence of venous thrombosis.

Reply 3: I'm sorry we haven't stated this criteria clearly. In this study, all patients were screened for DVT by duplex ultrasonography of both lower extremities before and after operation. If the patient has typical PE symptoms, high Caprini score (≥ 9) or newly diagnosed DVT after operation, CTPA would be performed. The missed diagnosis of ultrasound is indeed a key problem for the diagnosis of VTE, which may underestimate the incidence of VTE. Thanks for your suggestion, which we have added in the discussion.

Changes in the text: In this study, DVT events were confirmed by duplex ultrasonography, and PE events were confirmed by computed tomography pulmonary angiography (CTPA). All patients were screened for DVT by duplex ultrasonography of both lower extremities before and after operation. If the patient has typical PE symptoms (chest pain, haemoptysis, dyspnoea or persistent hypoxaemia), high Caprini score (≥ 9) or newly diagnosed DVT after operation, CTPA would be performed.

(Page 6, line 116-124)

The missed diagnosis of ultrasound examinations may also underestimate the incidence of VTE. Overall, the incidence of postoperative VTE in our study may be underestimated, which may also lead to deviations in the results of the analysis. Therefore, this is only the result of our single-center study, and the results still need to be verified by a large sample of multicenter studies. (Page 15, line 310-315)

Comment 4: What was the time from preoperative ultrasound to surgery?

Reply 4: Ultrasound is one of the routine examinations of patients on admission. The median time from ultrasound to operation is 3 days.

Changes in the text: The median time from ultrasound to operation is 3 days, and the median days of receiving ultrasound, CTPA and hospitalization after operation were 5 days, 7 days and 7 days, respectively. (Page 14, line 304-306)

Comment 5: How many ultrasounds did each patient get? What was the median time from surgery to diagnosis of VTE?

Reply 5: In this study, all patients were screened by ultrasonography once before and after operation. The median days of receiving ultrasound after operation were 5 days.

Changes in the text: All patients were screened for DVT by duplex ultrasonography of both lower extremities once before and after operation. (Page 6, line 119-120)
The median time from ultrasound to operation is 3 days, and the median days of receiving ultrasound, CTPA and hospitalization after operation were 5 days, 7 days and 7 days, respectively. (Page 14, line 304-306)

Comment 6: Several studies have shown that open procedures have been associated with an increased risk of VTE. The authors should include the variable that are used in the score.

Reply 6: Thanks for your detailed and professional advice. Based on this, we re-analyzed the data. Firstly, we included the surgical approach into the multivariate analysis, and the results showed that it was not an independent risk factor for VTE. After that, we included the duration of operation into multivariate analysis, and the results showed that it was an independent risk factor for VTE.

Changes in the text: Considering the multicollinearity, NSCLC, squamous cell carcinoma and FDP were excluded. Surgical approach and the duration of operation were separately included in multivariate analysis.. (Page 10, line 205-207)

Firstly, we included the surgical approach into the multivariate analysis, and the results showed that it was not an independent risk factor for VTE (Table 4). After that, we included the duration of operation into multivariate analysis to identify the independent risk factors for VTE (Table 5). (Page 10, line 208-213)

Table 4 Multivariate analysis of the risk of the VTE in patients received lung resection using continuous variables (include surgical approach)

Parameter	Odds ratio	95%	P value
		Confidence interval	
Age(y)	1.08	1.03-1.12	0.001
Surgical approach	1.64	0.70-3.81	0.255
Diabetes mellitus	1.43	1.17-1.74	0.522
Lymphocyte countx10 ⁹ (/L)	0.26	0.10-0.72	0.009
D-dimer(μg/mL)	1.43	1.17-1.74	<0.001

Table 5 Multivariate analysis of the risk of the VTE in patients received lung resection using continuous variables (include duration of operation)

Parameter	Odds ratio	95%	P value
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		Confidence interval	
Age(y)	1.08	1.03-1.12	0.001
Duration of operation(min)	1.01	1.00-1.01	0.031
Diabetes mellitus	0.54	0.12-2.45	0.423
Lymphocyte countx10 ⁹ (/L)	0.31	0.12-0.84	0.021
D-dimer(μg/mL)	1.42	1.18-1.70	<0.001

(Page 31, line 514-519)

Comment 7: There is not enough evidence in the paper to reach the conclusion that the Caprini score can't assess the risk of VTE (Line 249). The variables used in the current analysis were different than the one's the Caprini score uses. The cohort only includes 4 patients in the high-risk group, which is clearly a selection bias.

Reply 7: We do need more data analysis to support this conclusion. In this regard, we have conducted further analysis and discussion. We listed the variables contained in the modified Caprini score in Table 3 (*Hachey KJ. Caprini venous thromboembolism risk assessment permits selection for postdischarge prophylactic anticoagulation in patients with resectable lung cancer. J Thorac Cardiovasc Surg 2016;151:37-44.e1*). The purpose of the analysis of other factors is to identify independent risk factors that are not included in the score. We were also surprised with these results, so we compared the results with Hachey's study. The results showed that patients in our study were less likely to undergo open surgery (79/437 vs 162/232) and central venous access (7/437 vs 68/232), which may be the reason for the small number of high-risk group and the inefficiency of the modified Caprini score in our study.

Changes in the text: In this study, there were only 4 patients in high-risk group, and the incidence of VTE in low-risk group (0-4), moderate-risk group (5-8) and high-risk group (≥ 9) was 12.3% (37/300), 7.5% (10/133) and 0% (0/4), respectively ($P > 0.05$). In the subgroup analysis, the results were similar. And the AUC of the modified Caprini score is 0.474 ($P = 0.558$). These results suggest that the modified Caprini score is not effective enough for VTE risk stratification in patients after lung surgery. Hachey et al. retrospectively assigned modified Caprini score to 232 patients undergoing pneumonectomy and proved that modified Caprini score can stratify the risk of VTE (2). By comparing patients information, patients in our study were less likely to undergo open surgery (79/437 vs 162/232) and central venous access (7/437 vs 68/232), which may be the reason for the small number of high-risk group and the

inefficiency of the modified Caprini score in our study. (Page 14, line 293-302)
 Therefore, this is only the result of our single-center study, and the results still need to be verified by a large sample of multicenter studies. (Page 15, line 313-315)
 The results suggested that the modified Caprini score may not accurately assess the risk of VTE after pulmonary surgery. (Page 10, line 208-213)

Table 7 Incidence of VTE in subgroups with different risk stratification

Group	0-4	5-8	≥9
All	12.3%(37/300)	7.5%(10/133)	0(0/4)
Non-small cell lung cancer	18.5%(25/135)	7.9%(10/126)	0(0/4)
Benign	7.3%(12/165)	0(0/7)	0(0/0)

(Page 32, line 523-524)

Minor Issues

Comment 1: Line 6 - There is a typing mistake on Caprini

Reply 1: We have made a correction to this.

Changes in the text: It is also important to evaluate whether the modified Caprini score can accurately assess the risk of VTE in patients after lung resection. (Page 2, line 25)

Comment 2: Line 31 – There is typing mistake on therapeutic.

Reply 2: We have made a correction to this.

Changes in the text: Surgical resection is a very important therapeutic modality for some lung diseases. (Page 3, line 53)

Comment 3: How many of the sublobar resections were segmentectomies, and how many wedge resections?

Reply 3: Thanks for your comment. We have made a supplement to this.

Changes in the text: In sublobectomy, 47 cases were segmental lobectomy and 86 cases were wedge resection. (Page 8, line 174-175)

Comment 4: This whole first section of the results (Lines 134 – 149) is basically a repeat of Table 1. Given that there are so many variables and values, it is difficult to read.

Reply 4: Thanks for your meaningful advice. We have cut down the tedious parts.

Changes in the text: The mean BMI, duration of operation, WBC count, lymphocyte count, PLT count, MPV, LDL, bloodglucose, D-dimer, AT, FDP, PT, APTT, FBG, TT were 23.9±3.4kg/m², 158.9±60.7mins, 12.8±3.3x10⁹/L, 1.1±0.5x10⁹/L, 219.5±66.3x10⁹/L, 10.5±0.9fl, 2.5±0.8mmol/L, 6.6±1.8mmol/L, 1.7±1.6μg/mL, 85.8±11.8%, 5.7±5.2mg/L, 12.4±1.1s, 29.5±4.9s, 313.5±76.3mg/dL, 17.3±1.4, respectively.

(Page 9, line 183-187)

Comment 5: Line 191 – “risk factor” may be a better word choice than “impact factor”.

Reply 5: We have made a correction to this.

Changes in the text: We identified four independent risk factors associated with VTE. (Page 11, line 240)

Reviewer C

Comment 1: The authors need to outline the specific time points for screening DVT exams pre and post op and for CTPA when symptomatic.

Reply 1: Thanks for your helpful advice. We have made a correction to this.

Changes in the text: In this retrospective study, the follow-up period ended when the patients were discharged from the hospital. The median time from ultrasound to operation is 3 days, and the median days of receiving ultrasound, CTPA and hospitalization after operation were 5 days, 7 days and 7 days, respectively. (Page 14, line 304-306)

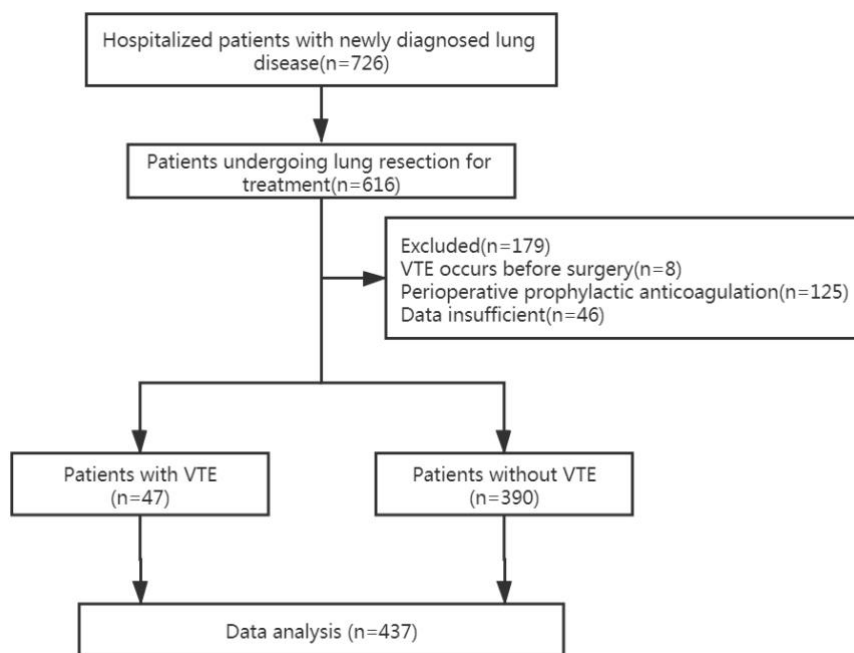
Comment 2: Why were the 125 patients on prophylactic anticoagulation excluded? Were these patients on therapeutic anticoagulation preoperatively or was this for prophylactic anticoagulation at the time of surgery?

Reply 2: We are sorry to have confused you on this issue. In this study, some patients received non-standard perioperative anticoagulant therapy. Different drugs and doses made it difficult to accurately assess their effects on thrombosis, so they were not included in this study.

Patients who received prophylactic anticoagulation during the perioperative period were excluded.

Changes in the text: Patients will be excluded from the study if they have one of following conditions: current VTE, perioperative prophylactic anticoagulation and insufficient clinical data. The application of perioperative prophylactic anticoagulation was not standard, which made it difficult to accurately evaluate its effect on VTE, so these patients were not included in this study. (Page 5, line 95-100)

Fig. 1. Selection of the study cohort



(Page 22, line 482-483)

Comment 3: Did the 437 patients enrolled in this study receive either postoperative prophylactic dose heparin or low-molecular weight heparin? The authors must clarify if the patients in this study routinely received prophylactic anticoagulation intraoperatively and postoperatively?

Reply 3: We're sorry to bother you again on the issue of anticoagulation. All the 437 patients received prophylactic anticoagulation.

Changes in the text: Patients will be excluded from the study if they have one of following conditions: current VTE, perioperative prophylactic anticoagulation and insufficient clinical data. (Page 5, line 95-97)

Comment 4: Can the authors provide additional details of their analysis on which factors in the Caprini score had an inverse association with VTE? You should also analyze the Caprini score of the subgroups with and without cancer to see if it functions better in those subgroups.

Reply 4: We have analyzed the factors in the modified Caprini score (Table 3). The results showed that in the modified Caprini RAM, advanced age, major open surgery (≥ 45 min) and present cancer were positively correlated with VTE. But none of the factors was negatively related to VTE. Multivariate analysis showed that age, duration of operation and D-dimer level were independent risk factors for VTE. The inclusion of D-dimer and better stratification of the duration of surgery may help the modified Caprini score to better stratify VTE risk. We also expressed it in the discussion section before. The incidence of VTE in the low risk group was higher than that in the moderate risk group, which indicated that the modified Caprini score could not well stratify risk of the population.

According to your suggestion, we have conducted a subgroup analysis, but the results showed that the score was still not a good assessment of VTE risk in each subgroup.

Changes in the text: In order to further evaluate the effectiveness of the modified Caprini score, we conducted a subgroup analysis (Table 7). Among all patients, the incidence of VTE in low-risk group (0-4), moderate-risk group (5-8) and high-risk group (≥ 9) was 12.3% (37/300), 7.5% (10/133) and 0% (0/4), respectively. In addition, similar results were obtained in NSCLC and benign disease groups.

(Page 11, line 232-236)

Table 7 Incidence of VTE in subgroups with different risk stratification

Group	0-4	5-8	≥ 9
All	12.3%(37/300)	7.5%(10/133)	0(0/4)
Non-small cell lung cancer	18.5%(25/135)	7.9%(10/126)	0(0/4)
Benign	7.3%(12/165)	0(0/7)	0(0/0)

(Page 32, line 523-524)

Comment 5: Were the D-dimer levels obtained pre-op or post-op? The D-dimer levels can be affected by the postoperative state, and this should be included in the discussion. Were the D-dimer levels associated with the presence of cancer? Was their association with VTE independent of the presence of cancer?

Reply 5: We're sorry that we have not made this question clear. We collected the laboratory data before operation, the first day, the third day and the fifth day after operation. Because surgery has a great impact on these factors, we included the data of the first day after operation into the analysis. We have also revised and supplemented this.

D-dimer is a very sensitive index for monitoring the changes of blood coagulation, even if it is also affected by many factors, such as age, tumor, surgery, chemotherapy and so on. Therefore, D-dimer is included in VTE risk prediction models such as Vienna score (*Eichinger S, Heinze G, Jandeck LM, Kyrle PA. Risk assessment of recurrence in patients with unprovoked deep vein thrombosis or pulmonary embolism: the Vienna prediction model. Circulation. 2010;121(14):1630-1636. doi:10.1161/CIRCULATIONAHA.109.925214*), and has been widely used. We have also done a study on the dynamic changes and correlation of D-dimer in the perioperative period of lung cancer (accepted, unpublished). If you are interested, you can pay attention to it.

Changes in the text: The VTE risk of patients varies dynamically with treatment, so we collected the laboratory data before operation, the first day, the third day and the fifth day after operation. At the same time, surgery has a great impact on these factors, so we included the data from the first day after operation in the analysis. (Page 7, line 148-151)

In this study, we tried to evaluate the risk of postoperative VTE, and the change of

D-dimer was clearly correlated with surgery. So we analyzed the level of D-dimer on the first day after operation, and the results showed that it was an independent risk factor for postoperative VTE. (Page 13, line 276-279)

Comment 6: Almost 40% of the patients had benign disease. What were the specific benign diagnoses being treated?

Reply 6: Benign diseases mainly included presumed malignant nodules, pulmonary vesicles, bronchiectasis and so on.

Changes in the text: Malignant tumors and benign diseases were included, among which benign diseases mainly included presumed malignant nodules, pulmonary vesicles, bronchiectasis and so on. (Page 5, line 93-95)

Comment 7: How were the variables chosen for the multivariable analysis?

Reply 7: Thanks for your question. We have explained this problem in detail.

Changes in the text: Any variable with a p-value of 0.2 in the univariate analysis was included in multivariate analysis. (Page 8, line 156)

Considering the multicollinearity, NSCLC, squamous cell carcinoma and FDP were excluded. Surgical approach and the duration of operation were separately included in multivariate analysis. (Page 10, line 205-207)

Minor points:

Comment 1: The labs values on lines 146-149 should be listed after right after the lab name to make It easier to read.

Reply 1: Because this part was expressed in Table 1, in order to avoid the article being too tedious, we have deleted it.

Changes in the text: The mean BMI, duration of operation, WBC count, lymphocyte count, PLT count, MPV, LDL, bloodglucose, D-dimer, AT, FDP, PT, APTT, FBG, TT were $23.9 \pm 3.4 \text{ kg/m}^2$, $158.9 \pm 60.7 \text{ mins}$, $12.8 \pm 3.3 \times 10^9/\text{L}$, $1.1 \pm 0.5 \times 10^9/\text{L}$, $219.5 \pm 66.3 \times 10^9/\text{L}$, $10.5 \pm 0.9 \text{ fl}$, $2.5 \pm 0.8 \text{ mmol/L}$, $6.6 \pm 1.8 \text{ mmol/L}$, $1.7 \pm 1.6 \mu\text{g/mL}$, $85.8 \pm 11.8\%$, $5.7 \pm 5.2 \text{ mg/L}$, $12.4 \pm 1.1 \text{ s}$, $29.5 \pm 4.9 \text{ s}$, $313.5 \pm 76.3 \text{ mg/dL}$, 17.3 ± 1.4 , respectively. (Page 9, line 183-187)

Comment 2: On line 151 “an no case” should be “and no case.”

Reply 2: We have made corrections to this.

Changes in the text: and no case developed PE alone. (Page 9, line 189)