Clinical Trial/Experimental Study

Medicine®

OPEN

CO_2 artificial pneumothorax on coagulation and fibrinolysis during thoracoscopic esophagectomy

Yunqin Ren, MD, Hong Yan, PhD*, Hengjiang Ge, PhD, Ji Peng, MD, Han Zheng, MD, Peng Zhang, MD

Abstract

Background: CO_2 artificial pneumothorax creates a sufficient operative field for thoracoscopic esophagectomy. However, it has potential complications and continuous CO_2 insufflation may impede coagulation and fibrinolysis. We sought to compare the effects of CO_2 artificial pneumothorax on perioperative coagulation and fibrinolysis during thoracoscopic esophagectomy.

Methods: We investigated patients who underwent thoracoscopic esophagectomy with (group P, n = 24) or without CO_2 artificial pneumothorax (group N, n = 24). The following parameters of coagulation–fibrinolysis function: intraoperative bleeding volume; serum levels of tissue plasminogen activator (t-PA), plasminogen activator inhibitor (PAI-1), thromboelastogram (TEG), D-Dimer; and arterial blood gas levels were compared with two groups.

Results: Group P showed higher levels of $PaCO_2$, reaction time (R) value and kinetics (K) value, but significantly lower pH value, alpha (α) angle and Maximum Amplitude (MA) value at 60 minutes after the initiation of CO_2 artificial pneumothorax than group N ($P < .05$, all). The t-PA level after CO_2 insufflation for 60 minutes was significantly higher in group P than in group N ($P < .05$), but preoperative levels were gradually restored on cessation of CO_2 insufflation for 30 min ($P > .05$). There was no significant difference in D-dimer.

Conclusion: CO_2 artificial pneumothorax during thoracoscopic esophagectomy had a substantial impact on coagulation and fibrinolysis, inducing significant derangements in pH and $PaCO_2$.

Trial registration: The study was registered at the Chinese clinical trial registry (ChiCTR1800019004)

Abbreviations: ABP = arterial blood pressure, ASA = American society of anesthesiology, α angle = alpha angle, MA = maximum amplitude, t-PA = tissue plasminogen activator, BP = non-invasive cuff blood pressure, ECG = electrocardiogram, HR = heart rate, I/E = inspiration-expiration ratio, K = kinetics, PAI-1 = plasminogen activator inhibitor, R = reaction time, SD = standard deviation, SpO_2 = pulse oxygen saturation, TEG = thromboelastogram, TNM = tumor node metastasis.

Keywords: thoracoscopic esophagectomy, artificial capnothorax, coagulation and fibrinolysis, acidosis

1. Introduction

Thoracoscopic esophagectomy is the mainstay in the treatment of esophageal cancer.[1] However, this procedure requires complete lung collapse and a broad surgical field. In the past, the main ventilation mode for collapsed lung was intubation of double-lumen bronchial catheter and one-lung ventilation, but this method had many drawbacks. The establishment of CO_2 artificial pneumothorax has been shown to provide better surgical field.[2] The current method of choice for lung ventilation during thoracoscopic esophagectomy is single-lumen endotracheal tube intubation with the establishment of a CO_2 artificial pneumothorax and bilateral lung ventilation. In 2006, Palanivelu et al introduced CO_2 artificial pneumothorax, which is an approach of anesthesia intubation in thoracoscopic esophagectomy with the two-lung ventilation approach.[3] Since then, there has been growing interest in CO_2 artificial pneumothorax. In 2011, Ninomiya et al[4] reported the use of intrathoracic CO_2 insufflation for thoracoscopic esophagectomy in the left lateral position. Studies have shown that artificial pneumothorax is beneficial for maintaining stable hemodynamics and oxygenation.[5,6] However, the technique is not widely applied because it can lead to complications such as arterial hypercapnia, CO_2 embolism, and hypotension, resulting from impaired venous return,[7] as well as derangements in the coagulation and fibrinolysis system due to continuous CO_2 insufflation. Data on the latter are scarce. On the basis of experimental data, some researchers have concluded that as long as the intrathoracic pressure is controlled to no more than 10 mmHg, artificial pneumothorax will not have any significant impact on the body.[8,9] According to our clinical observation and review of relevant literature, we found that as long as the flow rate and pressure of

Editor: Somchai Amornyotin.

This study was approved by the ethics committee of Daping Hospital [ethics batch: (2017) No. 67], and all the subjects signed informed consent.

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Department of Anesthesiology, Daping Hospital, Army Medical University, Chongqing, China.

* Correspondence: Hong Yan, Department of Anesthesiology, Daping Hospital, Army Medical University, 10 Changjiang Zhilu, Daping, Chongqing City 400042, PR China. (e-mail: cqyanhong@163.com).

How to cite this article: Ren Y, Yan H, Ge H, Peng J, Zheng H, Zhang P. CO_2 artificial pneumothorax on coagulation and fibrinolysis during thoracoscopic esophagectomy. Medicine 2021;100:2(e23784).

Received: 22 July 2019 / Received in final form: 6 February 2020 / Accepted: 12 November 2020

http://dx.doi.org/10.1097/MD.0000000000023784

artificial pneumothorax are well controlled, artificial pneumothorax will not significantly affect the patient's respiratory and circulatory systems, nor cause serious complications, which indicates that it can be safely applied in clinical practice.[5,10]

Therefore, in this study, we compared the perioperative levels of various parameters associated with coagulation and fibrinolysis in esophageal cancer patients undergoing thoracoscopic esophagectomy with and without CO_2 artificial pneumothorax. With these data, we sought to evaluate the risk of bleeding or thrombosis during the perioperative period and accordingly develop a theoretical basis for whether interventional measures are necessary.

2. Material and methods

2.1. Study design

We enrolled 48 patients who underwent thoracoscopic esophagectomy for esophageal cancer, at our center between November 2017 and March 2018. This study was approved by the ethics committee of Daping Hospital [ethics batch: (2017) No. 67], and all the subjects signed informed consent.

2.2. Patients

Of these 48 patients, 35 were men and 13 were women, with their ages ranging from 53 to 67 years [mean ± standard deviation, (SD) = 60.06 ± 7.13 years]. The criteria for inclusion in this study were as follows: preoperative gastroscopy confirmed a pathological diagnosis of esophageal squamous cell carcinoma; TNM stage was below T3a; no significant abnormality detected in cardiopulmonary function, liver and kidney function, or coagulation function; no history of the use of drugs affecting coagulation function within two weeks before the operation; no acute or chronic infection, no metabolic or endocrine diseases; American Society of Anesthesiologists (ASA) grade II-III.

By using the random number table method, the 48 enrolled patients were classified into two equal groups with (group P) or without (group N) the establishment of CO_2 artificial pneumothorax. All patients underwent surgery under general anesthesia.

2.3. Surgical procedures

2.3.1. Anesthesia. Once the patients were placed in the appropriate position on the operating table, their vital monitors were continuously monitored: electrocardiogram (ECG), heart rate (HR), non-invasive cuff blood pressure (BP), pulse oxygen saturation (SpO_2), body temperature (T). After administration of local anesthesia, catheters were inserted into the right internal jugular vein and left radial artery. Thereafter, invasive arterial blood pressure (ABP) was continuously monitored. For all patients, general anesthesia was induced and intubation was performed. For patients in group P, a single-lumen endotracheal tube (diameter: 7 mm, females; 7.5 mm, males) was inserted under the guidance of a video laryngoscope. For patients in group N, the left double-lumen endobronchial tube (size: 35F, female; 37F, male) was inserted into the left side under the guidance of a fiberoptic bronchoscope. After successful intubation, the connections of the anesthesia machine were established, and the respiratory parameters were adjusted as appropriate. In group P, bilateral lung ventilation was initiated, with tidal volume of 8 mL/kg, respiratory rate, 12 times/min, and inspiration-expiration ratio (I/E) of 1/2. In group N, one-lung ventilation was established, with tidal volume of 6 mL/kg, respiratory rate of 15 times/min, I/E of 1/2 These values were maintained both before and after the operation. The volume of fluid infusion and the depth of anesthesia were adjusted according to the hemodynamic status during the operation, and care was taken to ensure that the blood pressure fluctuation was not more than 20% before the operation.

2.4. CO_2 insufflation

The patient was positioned and covered with towels; the operative area was sterilized. After inserting trocars the patient was connected with a CO_2 pneumoperitoneum machine to inflate the peritoneum at a speed of 12 L/min, while maintaining the intrathoracic pressure at 6 to 8 mmHg; this resulted in lung collapse on the affected side. Thoracoscopic and laparoscopic esophagectomy was performed after the establishment of the CO_2 artificial pneumothorax.

2.5. Monitoring indicators

Blood samples were collected at different time points: 60 minutes before induction of anesthesia (T1), 60 minutes after the initiation of CO_2 artificial pneumothorax establishment or 60 minutes after one-lung ventilation (T2), 30 minutes after the termination of CO_2 artificial pneumothorax or 30 minutes after bilateral pulmonary ventilation (T3), and the first and the third postoperative days (T4,T5). The major parameters measured during the perioperative period were as follows: arterial blood gas analysis; thromboelastogram (TEG) parameters, including reaction time (R value), which represents the time from the beginning of measurement until blot formation, and is related to the change of coagulation factor function, clot formation rate (K value and α Angle), which represents the speed and clot formation and are closely related to fibrinogen level, and maximum amplitude (MA), which represents the clot strength and is related to the function of platelet aggregation; serum levels of tissue plasminogen activator (t-PA), which catalyzes the conversion of plasminogen to plasmin to degrade fibrin(ogen) and some coagulation factors and is the key substance of the fibrinolytic system; plasminogen activator inhibitor (PAI-1), which is also known as endothelial plasminogen activator inhibitor and is the key protein regulating fibrinolytic activity; D-dimer; and intraoperative bleeding volume (using the weighing method). The rate of postoperative complications, including anastomotic fistula, pulmonary infection, arrhythmia, incision infection, and chylothorax, were also recorded.

2.6. Statistical analysis

The sample size was determined as follows: The primary outcome was R value of the coagulation factor in the TEG. According to our preliminary experiment, the R value was 7.1 minutes in the experimental group and 6.2 minutes in the control group, with SD of 1.1. We set $\alpha = 0.05$ and $\beta = 0.8$. The sample size was 42, with 21 in each group. Considering a 10% drop-off rate, we finally enrolled 24 patients in each group.

The SPSS 19 software was used for data analysis. Countable data were analyzed using the χ^2 test, and all measurements were expressed as $x \pm s$. Intra-group comparisons were made by repeated-measurement analysis of variance. The Bonferroni method was used for comparisons at each time point, and

inter-group comparisons were made using multivariate analysis of variance. $P < .05$ was considered to indicate statistical significance.

3. Results

3.1. Demographics and clinicopathologic factors

The study population comprised of 48 patients equally divided into two groups. The duration of operation in group P was significantly less than that in group N ($P < .05$). There were no significant intergroup differences in the age, sex, weight, intraoperative bleeding volume, and pathological stage ($P > .05$). (Table 1).

3.2. Perioperative morbidity and mortality

Postoperative complications were observed in 2 cases (8.33%) in group N and in 3 cases (12.5%) in group P two weeks after thoracoscopic esophagectomy. There was no death in either group. No significant intergroup difference was observed in terms of complications and mortality ($P > .05$). Intervention did not increase morbidity or mortality (Table 2).

3.3. Blood gas analysis

In group P, the pH value decreased significantly 60 minutes after the initiation of CO_2 artificial pneumothorax ($P < .05$) while the $PaCO_2$ increased significantly ($P < .05$). These findings suggest that the blood H^+ level increased significantly after the beginning of CO_2 artificial pneumothorax. However, 30 minutes after the termination of CO_2 artificial pneumothorax, the pH value and $PaCO_2$ were restored quickly to the preoperative level ($P > .05$) (Fig. 1).

3.4. TEG comparison

Group P showed significantly longer R value 60 minutes after the start of CO_2 artificial pneumothorax ($P < .05$), thereby suggesting that time of initiation of coagulation was prolonged. The K value was significantly prolonged and the alpha angle was significantly decreased ($P < .05$). This suggested that the rate of blood clot formation was decreased. Further, the MA value was significantly decreased ($P < .05$), suggesting that the strength of blood clotting was decreased. The changes in the R, K, α angle, and MA values were the same even 30 minutes after the termination of artificial pneumothorax; the levels were still different from that the pre-anesthesia values ($P < .05$), and were restored to preoperative levels only on postoperative days 1 and 3. In addition, there were significant difference in R value, K value, α angle and MA between group P and group N at T2 and T3. There were no significant differences in the TEG levels at different time points in group N (Fig. 2).

3.5. Changes in t-PA and PAI-1

The t-PA in group P at 60 minutes after the initiation of CO_2 pneumothorax was higher than in group N ($P < .05$) and gradually returned to the preoperative level at 30 minutes after the cessation of CO_2 pneumothorax. No significant intergroup difference was noted in terms of the PAI-1 (Fig. 3).

3.6. D-Dimer

The levels of D-dimer in both group P and group N were increased on the 1st and 3rd postoperative days ($P < .05$), but there were no significant differences between the values in the 2 groups (Fig. 4).

4. Discussion

Our results indicated that during the establishment of CO_2 artificial pneumothorax, obvious changes occurred in the arterial blood gas levels, the pH value decreased, and $PaCO_2$ increased. Together, these changes manifested as respiratory acidosis and hypercapnia. The proportion of patients with moderate or high degree of hypercapnia ($PaCO_2 > 50$ mmHg) accounted for 70% of the total study population. Studies such as those by Brock et al.[11] investigating the effects of different CO_2 artificial pneumothorax pressures on hemodynamics have revealed that although CO_2 artificial pneumothorax has some effects on circulation, it does not induce any significant changes in the $PaCO_2$. Similarly, Sancheti et al[12] showed that no significant change occurred in the $PaCO_2$ in patients who underwent thoracoscopic pulmonary wedge resection with single-lumen

Table 1

Demographic and clinicopathologic factors of patients.

Project	Group P (n = 24)	Group N (n = 24)	P^*
Age (yr)	62 ± 7.31	58.13 ± 6.54	.059
Gender (m/f)	17:7	18:6	.745
Weight (kg)	62.04 ± 9.51	61.00 ± 4.73	.633
Pathological staging (T1:T2:T3)	5:14:5	6:15:3	.731
Operative blood loss (mL)	127.08 ± 48.85	125.42 ± 32.30	.890
Operation time (min)	239.33 ± 35.69	271.88 ± 31.31	.002

Table 2

Perioperative morbidity and mortality (n/%).

Groups	Anastomotic fistula	Pulmonary infection	Arrhythmia	Incision infection	Chylothorax	Overall complication rate	Death
Group N (n = 24)	1 (4.16%)	1 (4.16%)	0	0	0	2 (8.33%)	0
Group P (n = 24)	1 (4.16%)	1 (4.16%)	1 (4.16%)	0	0	3 (12.5%)	0
P value	1.000	1.000	0.312	1.000	1.000	0.637	1.000

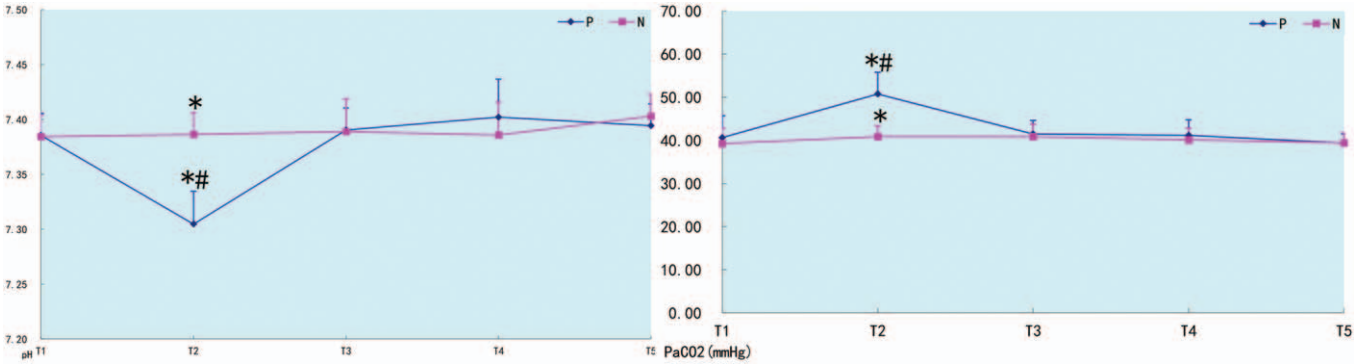

Figure 1. Changes in blood gas analysis in the two groups (P and N) (n = 24). pH and $PaCO_2$. T1: 60 minutes before induction of anesthesia, T2: 60 minutes after the initiation of CO_2 artificial pneumothorax establishment or 60 minutes after one-lung ventilation, T3: 30 minutes after the termination of CO_2 artificial pneumothorax or 30 minutes after bilateral pulmonary ventilation, T4: The 1st-day postoperative day, T5: The 3rd-day postoperative day. $^{*}P < .05$ vs. group N, $^{\#}P < .05$ vs. T1.

endotracheal intubation or double-lumen bronchial intubation with establishment of CO_2 artificial pneumothorax. On the other hand, the results reported by Tran et al[13] are similar to those reported in the current study. The possible discrepancy between the results of the abovementioned studies may be attributed to the following factors: The dispersion rate of CO_2 in human body is 25 times that of O_2, whereas the absorption rate is faster. For the resection of esophageal cancer, a large surgical wound is required and the pressure of CO_2 in the thoracic cavity becomes positive during CO_2 artificial pneumothorax, which in turn increases the rate of CO_2 absorption in the blood. Only a few respiratory parameters were assessed in this experiment, those assessed were within the acceptable permissible hypercapnia range and indicated a protective pulmonary ventilation strategy.

Acidosis is known to be an important cause of coagulation dysfunction, but the specific underlying mechanism is still unclear.[14–16] Coagulation is initiated by the activation of coagulation factors, which can transform prothrombin into thrombin and fibrinogen into fibrin, in the presence of thrombin; this is accompanied by platelet activation and the formation of

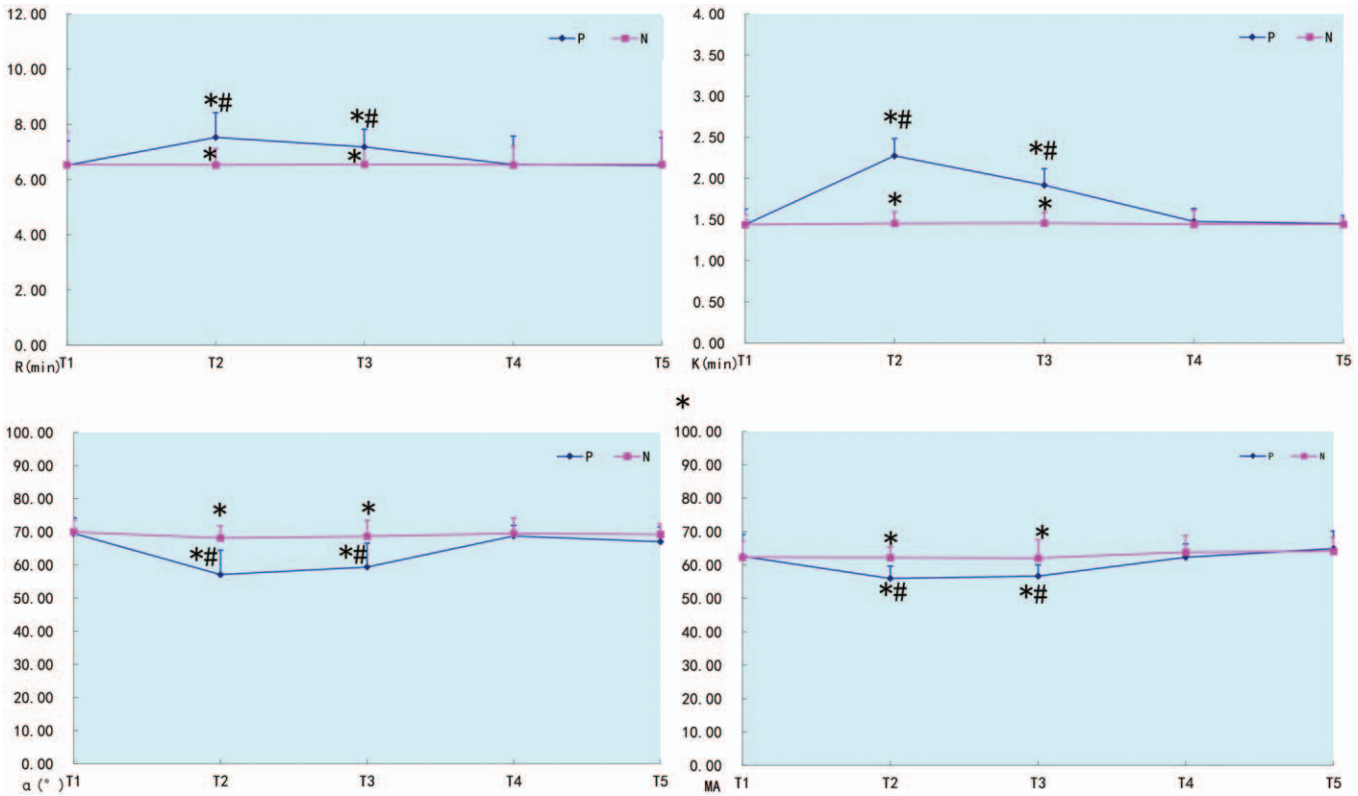

Figure 2. TEG changes in the two groups (P and N) (n = 24). R, K, Alpha angle and MA. T1: 60 minutes before induction of anesthesia, T2: 60 minutes after the initiation of CO_2 artificial pneumothorax establishment or 60 minutes after one-lung ventilation, T3: 30 minutes after the termination of CO_2 artificial pneumothorax or 30 minutes after bilateral pulmonary ventilation, T4: The 1st-day postoperative day, T5: The 3rd-day postoperative day. $^{*}P < .05$ vs. group N, $^{\#}P < .05$ vs. T1.

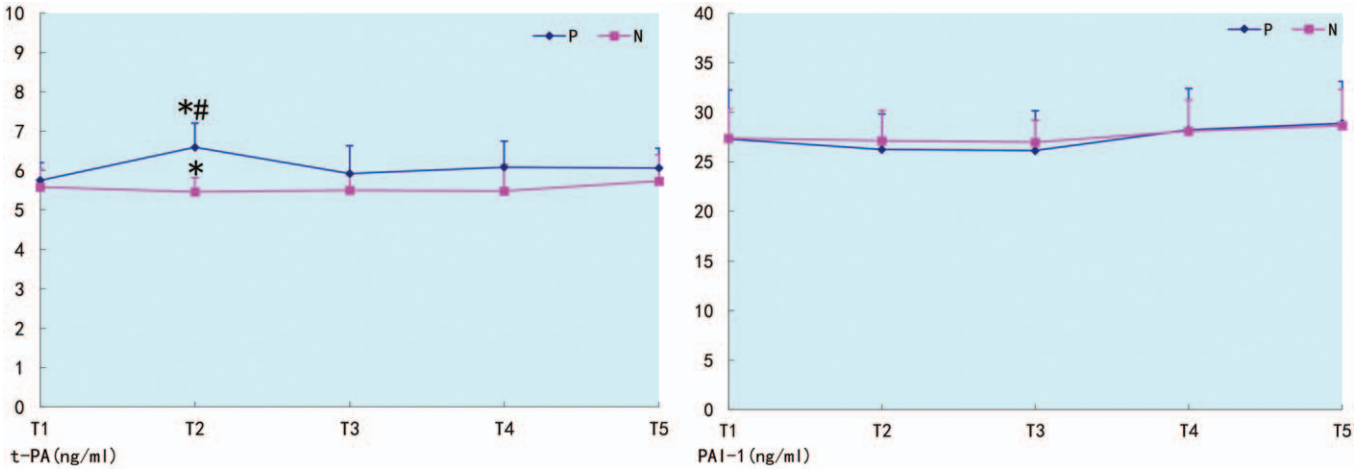

Figure 3. t-PA and PAI-1 Changes in the two groups (P and N) (n = 24). t-PA and PAI-1. T1: 60 minutes before induction of anesthesia, T2: 60 minutes after the initiation of CO_2 artificial pneumothorax establishment or 60 minutes after one-lung ventilation, T3: 30 minutes after the termination of CO_2 artificial pneumothorax or 30 minutes after bilateral pulmonary ventilation, T4: The 1st-day postoperative day, T5: The 3rd-day postoperative day. $^{*}P < .05$ vs. group N, $^{\#}P < .05$ vs. T1.

blood clots through adhesion and aggregation with fibrin. Thus, the formation rate and stability of blood clots, which are the final products of the coagulation process, are important factors influencing coagulation. The levels of TEG can provide a fair assessment of the entire process of coagulation–fibrinolysis and affords a rapid and comprehensive evaluation of coagulation factors, platelet energy, fibrinogen, and fibrinolysis. Further, the R value reflects the time required for the initial blood clot formation in the presence of coagulation factors, while the K value and α angle reflect the process of coagulation under the combined action of fibrinogen and platelets. The rate and value of MA reflect the maximum strength of blood clots, which is mainly influenced by the number and function of platelets (20%) and fibrin (80%). In the present study, the R value in group P was significantly increased at 60 minutes after the imitation of CO_2 artificial pneumothorax ($P < .05$), and the time of initiation of coagulation was also prolonged. These findings suggest that the coagulation function was decreased. On the other hand, the significant increase in the K value, significant decrease in the angle of alpha ($P < .05$), and decrease in the rate of blood clot formation indicate that the function of fibrinogen was decreased and the synthesis of blood clot was inhibited in group P. This may be because thrombin, which promotes the formation of blood clots, is affected by the acidic environment in the body. Meng et al[17] showed that at a pH value of 7.0, the rate of prothrombin activation is decreased by 55% to 70%. Martini et al[18] measured the changes in the plasma thrombin–antithrombin III complex content at different time points and showed a significant decrease in the rate of thrombin generation during acidosis. This suggests that acidosis causes a decrease in the rate of thrombin generation, thereby leading to a decrease in coagulation function. In addition, the significant decrease in the MA value in group P at 60 minutes after the initiation of CO_2 artificial pneumothorax ($P < .05$) and the consequent decrease in the strength and stability of blood clot together suggest a decrease in the functions of fibrinogen and platelet aggregation. This may be explained by the fact that abnormal platelet function in an acidic environment leads to a decrease in the cross-linking strength between platelet and fibrins, which in turn weakens the strength of the blood clot. Studies[19] have shown that in the presence of acidosis, the internal structure and shape of platelets undergo certain changes such as loss of pseudopodia, change of shape to globular, which results in a decrease in their hemostatic function. In this experiment, at the end of 30 minutes after the termination of artificial pneumothorax, the corresponding values of R, K, α angle and MA also were restored to some extent with the return of the $PaCO_2$ and pH values to the pre-anesthesia levels; however, the levels of the former group of parameters were still different from those recorded before the operation ($P < .05$) and only normalized on postoperative day 1. These findings suggest that with the correction of acidic environment in vivo, there is a gradual improvement in the coagulation function, but the effect of acid environment on coagulation function persists for a certain period of time. Studies have shown that correcting the pH value once acidosis has occurred does not completely reverse the acidosis-induced damage to coagulation function.[20,21]

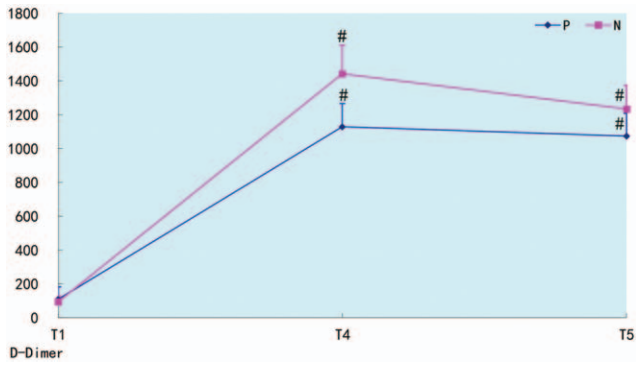

Figure 4. D-Dimer Changes in the 2 groups (P and N) (n = 24). D-Dimer. T1: 60 minutes before induction of anesthesia, T2: 60 minutes after the initiation of CO_2 artificial pneumothorax establishment or 60 minutes after one-lung ventilation, T3: 30 minutes after the termination of CO_2 artificial pneumothorax or 30 minutes after bilateral pulmonary ventilation, T4: The 1st-day post-operative day, T5: The 3rd-day postoperative day. $^{*}P < .05$ versus group N, $^{\#}P < .05$ vs. T1.

T-PA is mainly synthesized and released by endothelial cells and is widely expressed by various tissues of the body. T-PA is an important index of the fibrinolytic activity in the fibrinolytic

system. T-PA activates plasminogen and transforms it into active plasminogen, which dissolves the thrombus, thus preventing thrombosis in vivo and results in an increase in t-PA, which is common in primary hyperfibrinolysis. D-Dimer originates from the cross-linked fibrinolytic clots dissolved by the fibrinolytic enzymes and mainly reflects the fibrinolytic function. The change in the content of D-Dimer is a marker of hypercoagulability and hyperfibrinolysis in vivo. An elevation in serum D-Dimer levels is common in secondary hyperfibrinolysis. In the current study, group P showed a significant increase in t-PA at 60 minutes after the initiation of CO_2 artificial pneumothorax ($P < .05$), thereby suggesting that acidosis and compression of intrathoracic blood vessels and lung tissue resulted in endothelial cell injury, which triggered the release of t-PA, leading to primary hyperfibrinolysis. Ayman et al[22] compared laparoscopic surgery with open surgery and demonstrated that CO_2 pneumoperitoneum can lead to injury of the vascular wall, release of coagulation and fibrinolysis factors by vascular endothelial cells, and change in the body's coagulation system. We also found that the value of t-PA gradually decreased at 30 minutes after the termination of CO_2 artificial pneumothorax and returned to the preoperative level on the first postoperative day. This finding may be attributed to the reduction of t-PA release after the termination of CO_2 artificial pneumothorax due to the correction of hypercapnia and release of intrathoracic positive pressure. Both groups showed a postoperative increase in the levels of D-dimer, without any significant intergroup difference in the increments ($P > .05$). This increase may be attributed to the long operation time, large extent of trauma, microthrombosis of the surgical wound, inflammatory reaction after operation, influence of tumor cells on the coagulation system, and the long duration of postoperative bed rest.[23,24]

The intraoperative bleeding volume in group N was 125.64 $\pm$ 29.51, group P was 127.08 $\pm$ 48.85. The bleeding volume in group N was similar with group P. The intraoperative bleeding volume in group P was not increased with the decrease of coagulation function. We thought the diameter of double-lumen bronchial catheter in group N was thicker, and the left main bronchial catheter sac expanded after inflation, which affected the operative field of vision, especially the dissection of upper mediastinal lymph nodes. In group P, the diameter of single-lumen endotracheal tube inserted into artificial pneumothorax was relatively small, and bronchus was not inserted, to avoid injuring blood vessels and shorten the operation time.

Artificial pneumothorax shortens the operation time, however, the establishment of artificial pneumothorax may lead to respiratory and hemodynamic changes. The gas insufflation in artificial pneumothorax can lead to increased airway pressure and mediastinal displacement, along with hemodynamic instability and decreased blood pressure. Insufflation of air injection during endoscopic surgery can lead to serious complications, which may sometimes even be fatal. Therefore, it is important to carefully monitor the hemodynamic status of the patient. Further, additional care must be taken during the establishment of CO_2 artificial pneumothorax for patients with hypovolemia and left ventricular dysfunction.[25]

Our study does have a few limitations. In this study, we did not compare the amount of postoperative bleeding and peritoneal drainage. In our experiment, $PaCO_2$ was maintained in a permissive hypercapnia range (45–55 mmHg) during the establishment of artificial pneumothorax. This range in group P was significantly higher than that in group N. This increased the risk of bleeding group P. However, it remains to be determined whether this increase can be prevented or optimized by adjusting the respiratory parameters, such as tidal volume or respiratory frequency.

To summarize, our findings revealed that the establishment of CO_2 artificial pneumothorax during thoracoscopic esophagectomy had a significant impact on coagulation and fibrinolysis. CO_2 artificial pneumothorax may result in significant derangements in pH and $PaCO_2$, and the resultant respiratory acidosis and hypercapnia may increase the risk of intraoperative bleeding.

Author contributions

Conceptualization: Hengjiang Ge.
Data curation: Ji Peng.
Investigation: Han Zheng.
Methodology: Hong Yan.
Project administration: Yunqin Ren.
Software: Peng Zhang.
Writing – original draft: Yunqin Ren.
Writing – review & editing: Hong Yan.

References

[1] Mouroux J, Venissac N, Leo F, et al. Surgical treatment of diaphragmatic eventration using video-assisted thoracic surgery: a prospective study. Ann Thorac Surg 2005;79:308–12.
[2] Takemura M, Kaibe N, Takii M, et al. Operative benefits of artificial pneumothorax in thoracoscopic esophagectomy in the left lateral decubitus position for esophageal cancer. Int J Clin Med 2015;06: 967–74.
[3] Palanivelu C, Prakash A, Senthilkumar R, et al. Minimally invasive esophagectomy: thoracoscopic mobilization of the esophagus and mediastinal lymphadenectomy in prone position–experience of 130 patients. J Am Coll Surg 2006;203:7–16.
[4] Ninomiya I, Okamoto K, Fushida S, et al. Efficacy of CO2 insufflation during thoracoscopic esophagectomy in the left lateral position. Gen Thorac Cardiovasc Surg 2017;65:587–93.
[5] Saikawa D, Okushiba S, Kawata M, et al. Efficacy and safety of artificial pneumothorax under two-lung ventilation in thoracoscopic esophagectomy for esophageal cancer in the prone position. Gen Thorac Cardiovasc Surg 2014;62:163–70.
[6] Xu WY, Wang N, Xu HT, et al. Effects of sevoflurane and propofol on right ventricular function and pulmonary circulation in patients undergone esophagectomy. Int J Clin Exp Pathol 2014;7:272–9.
[7] Suarez-Pierre A, Terasaki Y, Magruder JT, et al. Complications of CO2 insufflation during endoscopic vein harvesting. J Card Surg 2017;32: 783–9.
[8] Stolwijk LJ, Tytgat SH, Keunen K, et al. The effects of CO2-insufflation with 5 and 10 mmHg during thoracoscopy on cerebral oxygenation and hemodynamics in piglets: an animal experimental study. Surg Endosc 2015;29:2781–8.
[9] Jones DR, Graeber GM, Tanguilig GG, et al. Effects of insufflation on hemodynamics during thoracoscopy. Ann Thorac Surg 1993;55: 1379–82.
[10] Lin M, Shen Y, Wang H, et al. A comparison between two lung ventilation with CO2 artificial pneumothorax and one lung ventilation during thoracic phase of minimally invasive esophagectomy. J Thorac Dis 2018;10:1912–8.
[11] Brock H, Rieger R, Gabriel C, et al. Haemodynamic changes during thoracoscopic surgery the effects of one-lung ventilation compared with carbon dioxide insufflation. Anaesthesia 2000;55:10–6.
[12] Sancheti MS, Dewan BP, Pickens A, et al. Thoracoscopy without lung isolation utilizing single lumen endotracheal tube intubation and carbon dioxide insufflation. Ann Thorac Surg 2013;96:439–44.
[13] Tran DT, Badner NH, Nicolaou G, et al. Arterial pCO2 changes during thoracoscopic surgery with CO2 insufflation and one lung ventilation. HSR Proc Intensive Care Cardiovasc Anesth 2010;2:191–7.

[14] White H, Bird R, Sosnowski K, et al. An in vitro analysis of the effect of acidosis on coagulation in chronic disease states - a thromboelastograph study. Clin Med (Lond) 2016;16:230–4.
[15] Ranucci M, Baryshnikova E, Simeone F, et al. Moderate-degree acidosis is an independent determinant of postoperative bleeding in cardiac surgery. Minerva Anestesiol 2015;81:885–93.
[16] De Robertis E, Kozek-Langenecker SA, Tufano R, et al. Coagulopathy induced by acidosis, hypothermia and hypocalcaemia in severe bleeding. Minerva Anestesiol 2015;81:65–75.
[17] Meng ZH, Wolberg AS, Monroe DM, et al. The effect of temperature and pH on the activity of factor VIIa: implications for the efficacy of high-dose factor VIIa in hypothermic and acidotic patients. J Trauma 2003;55:886–91.
[18] Martini WZ, Pusateri AE, Uscilowicz JM, et al. Independent contributions of hypothermia and acidosis to coagulopathy in swine. J Trauma 2005;58:1002–9. discussion 1009-1010.
[19] Kashuk JL, Moore EE, Sawyer M, et al. Postinjury coagulopathy management: goal directed resuscitation via POC thrombelastography. Ann Surg 2010;251:604–14.
[20] Martini WZ, Dubick MA, Pusateri AE, et al. Does bicarbonate correct coagulation function impaired by acidosis in swine? J Trauma 2006;61:99–106.
[21] Martini WZ, Dubick MA, Wade CE, et al. Evaluation of tris-hydroxymethylaminomethane on reversing coagulation abnormalities caused by acidosis in pigs. Crit Care Med 2007;35:1568–74.
[22] Abdelrazeq AS, Dwaik MA, Aldoori MI, et al. Laparoscopy-associated portal vein thrombosis: description of an evolving clinical syndrome. J Laparoendosc Adv Surg Tech A 2006;16:9–14.
[23] Mantziari S, Gronnier C, Pasquer A, et al. Incidence and risk factors related to symptomatic venous thromboembolic events after esophagectomy for cancer. Ann Thorac Surg 2016;102:979–84.
[24] Kato F, Takeuchi H, Matsuda S, et al. Incidence of and risk factors for venous thromboembolism during surgical treatment for esophageal cancer: a single-institution study. Surg Today 2016;46:445–52.
[25] Ohtsuka T, Imanaka K, Endoh M, et al. Hemodynamic effects of carbon dioxide insufflation under single-lung ventilation during thoracoscopy. Ann Thorac Surg 1999;68:29–32. discussion 32-23.