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*Original Article*

# The impact of laparoscopic versus open surgeries on the incidence of postoperative deep vein thrombosis in patients with gastrointestinal malignancy-a cohort study

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**Abstract:** Objectives: This study aims to comparison the incidence of laparoscopic and open procedures on venous thromboembolism in patients receiving gastrointestinal malignancy surgery. Methods: In consecutive patients who underwent laparoscopic or open surgery between December 2014 and November 2015 with a new diagnosis of gastrointestinal malignancy were included in this observational study. Data on patient demographics, characteristics, and perioperative outcomes, with particular emphasis on thromboembolism and coagulation function, were evaluated comparing laparoscopic and open gastrointestinal malignancy surgery. Results: A total of 148 patients completed the protocol and were included into outcomes analysis, 75 (50.7%) cases in LS group and 73 (49.3%) cases in OS group. Patients' clinical features were close between the two groups. The total DVT incidence was 26.4% (laparoscopic 32.0% vs open 20.6%, $P$=0.043), and the symptomatic DVT incidence was 4.7% (5.3% vs 4.1%, $P$=1.0). The intraoperative arterial blood gas analysis ($PaCO_2$ and pH value) had significant statistical differences in two groups ($P$<0.001 and $P$<0.001, resp). Laparoscopic and open cases had comparable operating time and blood loss ($P$=0.012 and $P$=0.023, resp). The rates of postoperative complications were similar between the two groups. The prothrombin time (PT) and activated partial thromboplastin time (APTT) were only decreased in LS group at the early postoperative period. After the surgery, the D-dimer levels were increased in both groups with the changes were more pronounced in the LS group, and the similar trend was found in TEG parameters, including alpha angle and MA. Conclusions: The gastrointestinal malignancy patients who received laparoscopic surgery had higher incidence of DVT by vascular Doppler ultrasound. Therefore, more attention should be paid to these patients in order to prevent the occurrence of fatal thrombotic events.

**Keywords:** Laparoscopic surgery, deep vein thrombosis, gastrointestinal malignancy surgery, D-dimer, thromboelastography

## Introduction

Deep vein thrombosis (DVT) is a potentially fatal complication after major surgery [1]. Patients diagnosed with DVT have increased risk of forming pulmonary embolism (PE), which can strike suddenly, sometimes with deadly consequences. According to previous reports, the average incidence of DVT following general surgery is as high as 25%, and ranges from 2% in low-risk patients to 80% in the highest-risk patients without prophylaxis [2, 3]. However, the incidence of postoperative DVT has long been presumed to be lower in China and other Asian countries than in Western countries [4]. Meanwhile, for the consideration of the high incidence of postoperative bleeding with anticoagulation therapy, the pharmacological prophylaxis was not widely administered in patients undergoing general surgery. A previous study from Japan revealed that venous thromboembolism (VTE), manifesting as DVT or PE, occurred in 24.3% of patients undergoing abdominal surgery [5]. Yet, the epidemiological data in Chinese population is insufficient. Considering the potential fatal consequences, additional investigations for the prevalence of DVT in patients after malignancy surgery are warranted.

Venous stasis, abnormal activation of blood coagulation, and endothelial damage (Virchow's triad) influence the development of DVT [6]. The stress response, pain and inflammation

induced by the surgery lead to hypercoagulability and promote the postoperative DVT [7, 8]. Besides, the surgical position and postoperative immobilization also promote the DVT via resulting in venous stasis [9, 10]. In addition, patients with malignant tumor are notably at higher risk for postoperative VTE indicated by studies that patients undergoing surgical treatment of cancer have a twofold higher risk of postoperative DVT and a more than threefold higher risk of fatal PE than patients do undergoing similar operations without cancer [3, 11].

Gastrointestinal surgery for malignant tumor is a growing body of abdominal operations all over the world. Both the open surgery (OS) and the laparoscopic surgery (LS) are commonly used procedures for the tumor resection. Compared with OS, the LS causes mild invasion, decreased bleeding, attenuated pain, reduced rate of wound infection, shortened in bed time, and probably accelerated activity rehabilitation. According to the aforementioned DVT pathogenesis, it was postulated that, for those benefits, the incidence of DVT after LS should be reduced compared with OS [12]. However, some pathophysiological changes of promoting DVT are aroused including the pneumoperitoneum and the patient's position caused venous blood flow stasis in lower limb and the hypercapnia induced hypercoagulability, *etc* [13]. Therefore, it remains controversial whether the LS is the preferable procedure for patients with malignant tumor for the sake of reducing the DVT incidence. In addition, an important limitation that for previous reported rates of the DVT, as far as we know, is that in most studies the DVT was not the primary study outcomes and the incidence was recorded after clinical significant manifestation developed, which might cause the underestimation of the incidence of DVT after OS or LS for gastrointestinal tumor resection. The present study was aimed to evaluate the impact of laparoscopic surgery and open surgery on the incidence of postoperative DVT and the coagulation-fibrinolysis functions so as to explore the pathogenesis of postoperative DVT in patients undergoing resection surgery for gastrointestinal malignant tumors.

## Methods

### *Patients*

This study was approved by the Institutional Ethics Review Boards of the First Affiliated Hospital of Chongqing Medical University (No. 2014-82) and registered in ClinicalTrials.gov (NCT02297269). The study recruited patients admitted in this institution between December 2014 and November 2015 with a new diagnosis of gastrointestinal malignancy, who were scheduled to receive surgeries to remove the tumors.

Before surgery, the verbal and written informed consents were obtained from all patients. The patients meeting the following inclusion criteria were enrolled in this study: diagnosis with gastrointestinal malignancy and scheduled to undergoing OS or LS for definitive primary treatment, minimum of 7 days of postoperative follow-up. Patients were excluded in case of age less than 18 years, body mass index less than 18 or over 30, anticipated duration of surgery shorter than 45 minutes, conversion from laparoscopic to open surgery, tumor distant metastasis, peritonitis or uncontrolled general infection, palliative surgery, diagnosed with DVT or coagulation dysfunction before surgery, major postoperative complications leading to reoperation or bleeding, renal or hepatic failure (creatinine clearance less than 30 mL/min or a transaminase increase over 3 times upper limit normal), bleeding disorders, mental disorder, intracranial hemorrhage or neurosurgery within the previous 6 months, pregnancy or lactation, or refusal to participate.

### *Procedure of anesthesia and surgery*

All patients were administered general anesthesia with propofol and sevoflurane by a specified anesthesia group. The electrocardiogram (ECG), heart rate (HR), $SpO_2$, arterial blood pressure, and body temperature were continuously monitored. HR was maintained at 60-100 beats/minute, $SpO_2$ at 98-100%, mean arterial pressure (MAP) at 65-80 mmHg, and body temperature was maintained at 37±1°C, and corresponding treatments would be administered at the discretion of anesthesiologist when those signs out of expected levels. All operations were performed by the same surgical team, which have had experience in open and laparoscopic gastrointestinal malignancy surgery. The patients in OS group were placed in the supine position and incision of 15 cm length was made in the middle of the abdomen. Abdominal exploration was performed, and the position of gastrointestinal malignancy was identified. Differently from the open surgery,

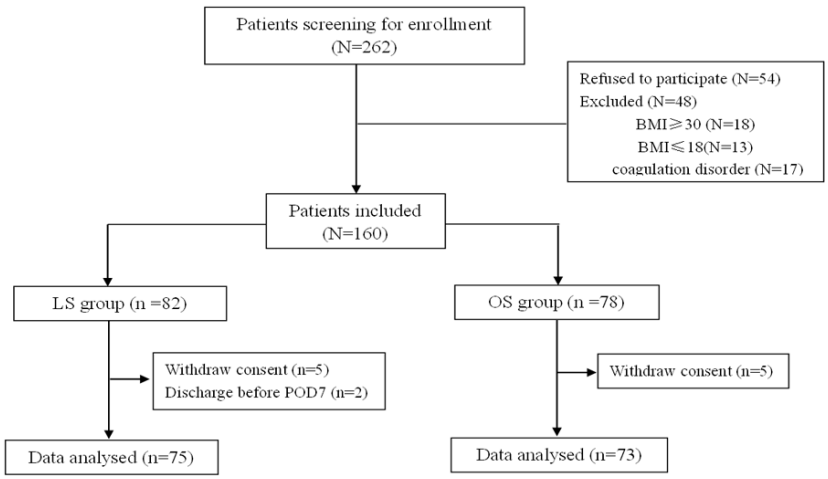


**Figure 1.** Flowchart of the study. BMI indicates body mass index; OS, open surgery; LS, laparoscopic surgery; POD, postoperative day.

the patient in LS group were placed in trendelenburg's position or reverse trendelenburg's position, and administered a vertical incision of 3 cm length above the umbilicus. Then, a pneumoperitoneum needle was used to puncture theperitoneum, and carbon dioxide gas was infused to create pneumoperitoneum with a pressure of 10 to 12 mmHg. Another two to three work ports (12 mm length) were made at sites chosen according to the tumor location. The surgical approach and the resection extent in each group were determined by the surgeons' discretion according to the location, the volume, and the stages of the tumor.

*Outcomes*

The primary outcome of this study is the incidence of DVT diagnosed by Doppler ultrasound after laparoscopic and open gastrointestinal malignancy surgery within 7 days postoperatively. Vascular Doppler ultrasound was carried out daily by the same experienced operator to detect DVT in the lower limbs (calf veins, popliteal veins, superficial femoral and profund femoral veins and iliac veins) until the 7th day after surgery. Patients with at least two following signs in the Doppler ultrasound examination would be diagnosed with DVT: no Doppler signal, echogenic filled lumen, and inability to compress the vein not due to extravascular causes. Notably, once the patients were diagnosed with DVT, the antithrombotic measures including the enhancing the lower limbs activity and anticoagulant would be applied if necessary. For all patients, the following baseline characteristics were collected: age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) class, Type of cancer, smoking habit, and medical comorbidities (hypertension, ischemic heart disease, diabetes, chronic obstructive pulmonary disease, etc). Perioperative data were collected including estimated blood loss, total operative time, postoperative hospital stay, postoperative complications (surgical-site infection, anastomotic leak, pneumonia, etc). Arterial blood gas analysis including partial pressure of carbon dioxide ($PaCO_2$) and pH value were measured at the time of 5 minutes preoperatively (T1), 30 minutes after starting surgery (T2) and 10 minutes postoperatively (T3). Hematological examinations (prothrombin time, PT; activated partial thromboplastin time, APTT; thrombin time, TT and D-dimer levels) and Thromboelastography (TEG) analysis (reaction time, R value; K value; alpha angel; and maximum amplitude, MA) were conducted 1 d before surgery and on postoperative days (PODs) 1, 3, 5 and 7.

*Statistical analysis*

Based on the study outcomes in our pilot study, a 25% difference between the OS group and LS group in the incidence of DVT with in the seven days after the surgery was used to estimate the sample size required in this study. Statistical power of 80% at the 0.05 significance level required 64 subjects in each group. Assuming a 20% dropout rate, a total of 160 patients were scheduled to recruit and with a 1:1 ratio to each group.

Statistical analysis was performed with Statistical Package for the Social Sciences (SPSS) software (version 17.0; SPSS Inc., Chicago, Ill). Data follow normal distribution is presented as mean ± standard deviation. Continuous variables were analyzed with *t*-test or ANOVA of repeated measure. Categorical variables were compared by the chi-square test or Fisher's exact test. When $p$ value <0.05

**Table 1.** Characteristics of the eligible patients

| Parameters | LS group (n=75) | OS group (n=73) | *P* value |
|---|---|---|---|
| Age (years) | 60.75±6.30 | 61.03±5.97 | 0.782 |
| Gender (male/female) | 36/39 | 32/41 | 0.611 |
| BMI (kg/m$^2$) | 24.95±3.08 | 25.42±3.18 | 0.361 |
| ASA Grading | | | 0.627 |
| I or II | 60 | 56 | |
| III | 15 | 17 | |
| Cancer type | | | 0.339 |
| Gastric cancer | 17 | 20 | |
| Colon cancer | 30 | 31 | |
| Rectal cancer | 28 | 22 | |
| Hypertension | 22 | 25 | 0.521 |
| Coronary artery disease | 11 | 9 | 0.677 |
| COPD | 6 | 10 | 0.264 |
| Diabetes | 25 | 31 | 0.252 |
| Current smoker | 27 | 22 | 0.449 |

BMI, body mass index; COPD, chronic obstructive pulmonary disease; ASA, American Society of Anesthesiologists.

**Table 2.** Comparison of $PaCO_2$, $PaO_2$ and pH between the LS and OS groups

| Parameters | Time | LS group (n=75) | OS group (n=73) | *P* value |
|---|---|---|---|---|
| $PaCO_2$ (mmHg) | T1 | 40.7±1.9 | 40.9±3.2 | 0.197 |
| | T2 | 49.1±3.8 | 41.2±3.8 | 0.001 |
| | T3 | 41.4±2.8 | 40.7±3.1 | 0.119 |
| pH | T1 | 7.33±0.06 | 7.35±0.04 | 0.167 |
| | T2 | 7.22±0.06 | 7.35±0.05 | 0.001 |
| | T3 | 7.32±0.05 | 7.32±0.12 | 0.844 |

Data are presented as mean ± SD. $PaCO_2$, arterial partial pressure of carbon dioxide; $PaO_2$, arterial partial pressure of oxygen; pH, hydrogen ion concentration.

(2-sided), difference was considered to be statistically significant.

## Results

A total of 160 patients were enrolled in this study with 78 in OS group and 82 in LS group. There were 148 patients completed the protocol and were included into outcomes analysis, 75 cases in LS group and 73 cases in OS group (**Figure 1**). Causes for exclusion and dropout are listed in **Figure 1**. The demographics and preoperative variables of these two groups were summarized in **Table 1**. The baseline characteristics and preoperative comorbidities (including hypertension, coronary artery disease, chronic obstructive pulmonary disease, and diabetes) and current smokers were comparable between the two groups.

Overall in 148 patients, DVT developed in 39 patients (26.4%), diagnosed by lower limbs vascular Doppler ultrasound, with 24 cases (32.0%) in LS group and 15 cases (20.6%) in OS group, respectively (*P*=0.043). Of these patients, 35 cases were detected in calf veins, 3 cases occurred in popliteal veins and 1 case occurred in superficial femoral vein. Symptomatic DVT was confirmed in 4 patients (5.3%) in LS group and 3 patients (4.1%) in OS group in terms of presenting with signs and symptoms during the postoperative follow-up period. No difference of symptomatic DVT incidence was found between these two groups (5.3% vs 4.1%, *P*=1.0) and no episode of PE was observed. Comparison of the two approaches showed that the patients who underwent LS had a significantly longer total operating time and lower blood loss than those in OS group ( *P*=0.012 and *P*=0.023, resp) (**Table 2**). No difference in the intraoperative fluid infusion volume were found between these two groups (*P*=0.201). As expected, both the anal aeroflux-us time (2.8±0.6 days vs 3.1±0.8 days, *P*=0.016) and the off-bed ambulation time (2.8±0.5 days vs 3.2±1.0 days, *P*=0.004) were earlier in LS group than that in OS group. And the hospitalization time of patients in LS group was reduced compared with that in OS group (7.2±1.3 days vs 7.8±1.8 days, *P*=0.024). The perioperative complications including surgical-site infection, anastomotic leak, pneumonia and urinary infection were comparable between the two groups (*P*>0.05).

Prior to and instantly after the surgery, arterial blood gas analysis, including $PaCO_2$ and pH values, were comparable between the two groups (**Table 3**). Although all the indexes of arterial blood gas analysis in OS group were not changed during the surgery, the intraoperative $PaCO_2$ and pH values in LS group were remarkable elevated. Compared with T1 time point, the $PaCO_2$ increased and the pH values decreased in LS group at T2 time point (*P*<0.001 and *P*<0.001, resp). After the surgery,

**Table 3.** Details of surgeries and postoperative outcomes

| Parameters | LS group (n=75) n, (%) | OS group (n=73) n, (%) | *P* value |
|---|---|---|---|
| Intraoperative parameters | | | |
| Operating time (min) | 206.0±49.0 | 186.0±43.0 | 0.012 |
| Blood loss (ml) | 299±55 | 317±39 | 0.023 |
| Fluid infusion (ml) | 2201±268 | 2260±288 | 0.201 |
| Postoperative parameters | | | |
| Total DVT incidence | 24 (32.0%) | 15 (20.6%) | 0.043 |
| Symptomatic DVT incidence | 4 (5.3%) | 3 (4.1%) | 1.0 |
| Anal aerofluxus time (days) | 2.8±0.6 | 3.1±0.8 | 0.016 |
| Ambulation time (days) | 2.8±0.5 | 3.2±1.0 | 0.004 |
| Hospital stay (days) | 7.2±1.3 | 7.8±1.8 | 0.024 |
| Surgical-site infection | 3 (4.0%) | 5 (6.8%) | 0.491 |
| Anastomotic leak | 3 (4.0%) | 4 (5.5%) | 0.717 |
| Pneumonia | 2 (2.7%) | 2 (2.7%) | 1.0 |
| Urinary infection | 1 (1.33%) | 2 (2.7%) | 0.617 |

DVT, deep vein thrombosis.

**Table 4.** Comparison of coagulation parameters between the LS and OS groups

| Time | PT (s) | APTT (s) | TT (s) | DD (mg/L) |
|---|---|---|---|---|
| LS group (n=75) | | | | |
| Preoperative | 11.62±1.52 | 30.24±2.76 | 17.21±1.57 | 1.32±0.53 |
| POD1 | 12.77±0.98$^{*}$ | 26.62±3.29$^{*,\#}$ | 17.13±1.93 | 1.72±0.70$^{*,\#}$ |
| POD3 | 11.56±1.09 | 27.18±3.08$^{*,\#}$ | 17.04±1.61 | 2.22±1.07$^{*,\#}$ |
| POD5 | 11.68±1.02 | 29.66±3.70 | 16.98±1.37 | 2.20±1.11$^{*,\#}$ |
| POD7 | 11.48±0.60 | 30.61±2.56 | 17.06±1.42 | 2.15±0.75$^{*,\#}$ |
| OS group (n=73) | | | | |
| Preoperative | 11.52±1.27 | 30.97±2.85 | 17.32±2.19 | 1.30±0.44 |
| POD1 | 11.76±1.00 | 30.12±3.57 | 17.23±1.97 | 1.50±0.60$^{\#}$ |
| POD3 | 11.60±1.85 | 31.04±3.63 | 17.19±1.46 | 1.70±0.63$^{\#}$ |
| POD5 | 11.45±1.16 | 29.80±4.29 | 17.43±1.86 | 1.73±0.54$^{\#}$ |
| POD7 | 11.79±1.37 | 30.36±3.50 | 17.20±1.69 | 1.63±0.71$^{\#}$ |

PT, prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin time; DD, D-dimer. $^{*}$*P*<0.05 compared with OS group at the same time point; $^{\#}$*P*<0.05 compared with preoperative time point in the same group.

these two indexes had no statistical differences with T1 time point (*P*=0.083 and *P*=0.107, resp).

The hematological examinations showed that the perioperative TT value had no significant changes in these two groups (*P*>0.05) (**Table 4**). The PT value was decreased in LS group at the POD1 (*P*<0.001). The APTT value was decreased in LS group at the POD1 (*P*<0.001) and POD3 (*P*<0.001). Besides, compared with preoperative outcomes, the D-dimer levels in both groups were remarkable increased at the POD1, POD3, POD5 and POD7. Meanwhile, the levels of D-dimer in LS group were higher than those in OS group at the postoperative 7 days follow-up period. No significant differences were found in APTT value of OS group among perioperative period (*P*>0.05).

All the included patients were also assessed with TEG analysis and found that the R and K values showed no statistically significant postoperative variation in these two groups (*P*>0.05) (**Table 5**). Compared with preoperatively, the alpha angel was significantly increased in both groups (*P*<0.05). And the alpha angel was higher in LS group than that in OS group at each postoperative time point, respectively (*P*<0.05), the same trend was observed for MA.

## Discussion

This study demonstrated that, without thromboprophylaxis, laparoscopic surgery had higher incidence of DVT in comparison with open surgery in patients for gastrointestinal malignancy resection. Additionally, we also observed postoperative coagulation dysfunction in both groups. Nevertheless, the more significant induced hypercoagulability in patients received LS after the surgery was also revealed in this study. Arterial blood gas analysis indicated that $PaCO_2$ increased and pH decreased during pneumoperitoneum in LS group compared with OS group. Hematological examinations revealed that only the laparoscopic procedure had a slight effect on PT value. The APTT value was remarkable decreased in LS group at the early postoperative period and the D-dimer levels

**Table 5.** Comparison of TEG parameters between the LS and OS groups

| Time | R (min) | K (min) | α (degree) | MA (mm) |
|---|---|---|---|---|
| LS group (n=75) | | | | |
| Preoperative | 6.04±1.16 | 1.69±0.61 | 60.19±4.31 | 63.79±6.78 |
| POD1 | 5.75±1.55 | 1.79±0.71 | 69.31±5.42*,# | 69.62±5.91*,# |
| POD3 | 5.86±1.17 | 1.71±0.84 | 70.66±5.20*,# | 70.45±6.08*,# |
| POD5 | 6.00±1.17 | 1.72±0.74 | 73.11±3.40*,# | 71.93±7.69*,# |
| POD7 | 5.85±1.24 | 1.88±0.89 | 73.65±5.13*,# | 74.33±8.37*,# |
| OS group (n=73) | | | | |
| Preoperative | 6.23±1.20 | 1.82±0.72 | 61.11±5.83 | 64.53±3.71 |
| POD1 | 6.13±1.33 | 1.83±0.71 | 65.77±3.81# | 66.01±4.60# |
| POD3 | 6.03±1.16 | 1.84±0.73 | 67.52±5.65# | 67.08±5.71# |
| POD5 | 6.10±1.50 | 1.71±0.70 | 69.03±6.03# | 69.59±6.55# |
| POD7 | 6.00±1.26 | 1.70±0.67 | 69.18±3.73# | 68.42±6.17# |

TEG, thrombelastography; R, reaction time; K, kinetic time; α, alpha angel; CI, coagulation index; MA, maximum amplitude; POD, postoperative day. *$P$<0.05 compared with OS group at the same time point; #$P$<0.05 compared with preoperative time point in the same group.

were sharply increased in both groups after the surgery. Further analysis showed that the level of D-dimer in LS group was higher than that in OS group. In addition, the TEG analysis showed the signs of hypercoagulable state in these groups, more dramatic in LS group. These findings suggest that compared with the open surgery, the laparoscopic procedure may further promote the developing of DVT in patients undergoing gastrointestinal malignancy resection.

The laparoscopic procedure has been widely applied in major cancer surgery. Compared with OS, LS has several indisputable physiological benefits and allows for more rapidly recovery after the surgery. Nonetheless, the need for pneumoperitoneum and special position during laparoscopic surgery could lead to an increased risk of DVT [1, 9]. Meanwhile, some studies reported that malignancy is an independent and major risk factor for DVT [14-16]. Therefore, doubts have been raised regarding the suitability of LS for cancer patients without prophylaxis [17-19]. Interestingly, data from the previous literature showed the opposite results about the incidence of DVT in patients received abdominal malignant tumor surgery without prophylaxis. Bouchard-Fortier et al reported that the rate of DVT was low in patients undergoing minimally invasive surgery for a gynecologic malignancy despite no prophylaxis [20]. Shapiro et al also found that laparoscopic colorectal surgery was associated with a lower DVT incidence than open approach [21]. On the contrary, Cheung et al showed that the incidence of DVT was relatively high after laparoscopic resection for rectosigmoid cancers, and Lee et al reported the similar outcome (41.7%) [22, 23]. Our study supports the latter outcomes and found that the postoperative DVT occurred in 24 (32.0%) patients of LS group, which was higher than that in OS group. The possible explanation is that the majority of low-incidence studies were based on symptomatic DVT prior to objective verification. This brings into question the possibility of a potential selection bias, because many patients with DVT are either asymptomatic or manifest only minimal symptoms in clinical practice. Actually, in our study, the patients need to be treated with anticoagulation therapy were also rare.

Historically, the Virchow's triad of blood stasis, changes in vessel wall, and hypercoagulability remain the major factors associated with DVT, all these factors are present to varying degrees when a patient undergoes laparoscopic surgery [6]. During a laparoscopic procedure, the intra-abdominal pressure is raised to 10 to 12 mmHg, which causes venous stasis in the lower extremities by compressing the vena cava and iliac veins. According to the Pouisselles' Law, the flow in a vessel lumen is proportional to the fourth power of the lumen radius. Therefore, the small changes after compression can lead to a large reduction in blood flow [24]. Besides, Jorgensen' research also found that the special position used by laparoscopic procedure leads to a further decrease in venous flow and velocity with a significant increase in the femoral vein diameter and subsequent venous stasis [24]. Subsequently, venous distension causes endothelial damage and activation of the coagulation cascade [6]. In addition, a previous study in animal model found that hemodynamic alterations associated with carbon dioxide-based laparoscopy are more related to gas absorption than to the increase in intra-abdom-

inal pressure [25]. Hypercapnea has been shown to increase venous pressure either directly or via other humoral mechanisms [26]. Similarly, our results showed that $PaCO_2$ increased and pH decreased during pneumoperitoneum compared with open procedure. Hence, speed up the discharge of $CO_2$ by increasing the frequency of mechanical ventilation properly may be a better way for the patients during laparoscopic surgery.

Aside from pressure-induced physiologic changes with laparoscopy, concerns have been raised regarding pneumoperitoneum-related alterations in coagulation. However, few evidences were available regarding the alteration in coagulation profile caused by different operative procedures in gastrointestinal malignancy patients. Our study investigated the degree of postoperative changes in coagulation profile and attempted to look for evidences of thrombosis in deep veins of the lower limbs in these patients, who underwent laparoscopic or open surgery. We found that the PT value only changed in LS group at POD1. As the determination of PT is a screening test for assaying extrinsic coagulation function, this result indicated that LS might have exerted certain effects on the extrinsic coagulation path [27]. APTT is a direct measure of coagulation, which mainly reflects the level of intrinsic coagulation function. In the present study, our data showed that the APTT value was remarkable decreased in LS group at the early postoperative period, but it was no statistically significant postoperative decrease in OS group. These results implicated that LS might increase the risk of venous thrombosis by activation of intrinsic coagulation path, which was consistent with the results of some researchers [27, 28]. D-dimer is formed by the sequential action of thrombin, factor XIIIa, and plasmin [29]. In normal conditions, the plasma concentration of D-dimer is less than 0.5 mg/L. In this study, the baseline levels of D-dimer were elevated in both groups, which indicated that the patients might be in a state of pre-thrombosis. Since the relationship between malignant tumor and elevated plasma D-dimer level has been confirmed, these results may be due to the diseases *per se*. Our data also showed that the postoperative D-dimer levels were further elevated in both groups, which suggested that there was activation of the coagulation system and fibrinolytic system postoperatively. Nevertheless, in our research, the postoperative D-dimer levels in LS group were higher than these in OS group. Hence, laparoscopic procedure had a greater promoting influence on coagulation function.

Recent years, some novel blood assays have been rapidly applicated in clinical experiment diagnosis. Of these assays, TEG is a bedside blood test used to assess patients' haemostatic status. The TEG analysis provides a graphic representation of clot formation and lysis with high validity and reliability [30]. The main TEG parameters included: R value, the time elapsed until the onset of clotting; K value, the time from the beginning of a clot formation until the amplitude of TEG reaches 20 mm; alpha angle, the angle formed by the slope of a tangent line traced from the R to the K; MA, measurement of the greatest strength of the clot [31-33]. To the best of our knowledge, there are few published reports regarding the relationship between the TEG parameters and the diagnosis of thrombosis in patients received abdominal malignant tumor surgery. From the TEG analysis, our research showed that both operative procedures (OS and LS) all resulted in increased alpha angle and MA which indicated the enhanced blood coagulation. Similar to the results of above-mentioned coagulation test, the TEG changes were more pronounced in the LS group. These results further suggested that laparoscopic procedure had greater influences on coagulation factors, resulting more severe hypercoagulable state in gastrointestinal malignancy patients.

The length of operation affecting the postoperative DVT incidence had been revealed by a previous study which found that surgical procedures lasting more than 1 hour were associated with an increased risk of DVT [6]. In our study, the average operating time for laparoscopic procedure was 206 minutes (range, 101 to 346 minutes), and that in OS group was 186 minutes (range, 101 to 291 minutes). Despite most surgeons in this research might pass through a learning curve and the time reduces with increasing experience, lymph node dissection for gastrointestinal malignancy patients by laparoscopic procedure was undoubtedly more difficult than open procedure. Therefore, there was also a significant difference in the length of operation between these two groups. Our present analysis also supported the recent concept that the duration of surgery longer than 2 hours

is a high risk factor of developing DVT [34]. However, it is worthy to note that this could be related to the small number of patients recruited into this research and a larger prospective study may be required.

There are some limitations in our study. Firstly, this is a observational study in single center. Therefore, more multi-center, large sample studies need to be conducted to confirm the effects of laparoscopic surgery on the DVT. Secondly, patients assigned to laparoscopic surgery or open surgery were decided by surgeons or themselves, there would be some selective bias to influence the findings. Thirdly, patients in this present study were administered no thromboprophylaxis after surgery. Although no thromboprophylaxis, the postoperative repeated Doppler ultrasound examinations and the consequent antithrombotic measures in positive patients could protect the participants from severe DVT associated morbidity.

In conclusion, the gastrointestinal malignancy patients receiving laparoscopic surgery had higher incidence of DVT than open surgery by vascular Doppler ultrasound. Therefore, more attention should be paid to these patients in order to prevent the occurrence of fatal thrombotic events. In addition, the high incidence of DVT in this present study suggests thromboprophylaxis administration in patient receiving surgery for gastrointestinal malignancy, especially after laparoscopic procedure.

## Disclosure of conflict of interest

None.

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