



Analysis of risk factors and management of unexpected intraoperative bleeding during video-assisted thoracic surgery for non-small cell lung cancer: a case-control study

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Background: Intraoperative bleeding is one of the most dangerous complications of thoracoscopic surgery and seriously endangers the life of patients. How to prevent and manage intraoperative bleeding is a core concern for every thoracic surgeon. The aim of our study was to analyze the related risk factors of unexpected intraoperative bleeding during video-assisted thoracoscopic surgery (VATS) and the strategies for managing bleeding.

Methods: A total of 1,064 patients who underwent anatomical pulmonary resection were analyzed retrospectively. According to the presence or absence of intraoperative bleeding, all cases were divided into an intraoperative bleeding group (IBG) and a reference group (RG). Clinicopathological characteristics and perioperative outcomes were compared in both groups. In addition, the sites, reasons, and coping strategies of intraoperative bleeding were summarized and analyzed.

Results: After rigorous screening, 67 patients with intraoperative bleeding and 997 patients without intraoperative bleeding were included in our study. Compared with the RG, among patients in the IBG, there was a higher incidence of history of chest surgery ($P < 0.001$), higher incidence of pleural adhesion ($P = 0.015$), higher incidence of squamous cell carcinoma ($P = 0.034$), and the fewer early T-stage cases ($P = 0.003$). In the multivariate analyses, a history of chest surgery ($P = 0.001$) and T stage ($P = 0.010$) were independent risk factors of intraoperative bleeding. The IBG was associated with the longer operative time, the more blood loss, the higher rates of intraoperative blood transfusion and conversion, the longer hospital stay and the more complications. There were no significant differences in the duration of chest drainage ($P = 0.066$) between IBG and RG. The most common injury site of intraoperative bleeding was the pulmonary artery (72%). The commonest cause of intraoperative bleeding was the accidental injury of energy device (37%). The most frequently used method for managing intraoperative bleeding was suturing of the bleeding site (64%).

Conclusions: Although unexpected intraoperative bleeding during VATS is unavoidable, it can be controlled provided that positive and effective hemostasis are achieved. However, prevention is the priority.

Keywords: Intraoperative bleeding; lung cancer; vascular injury

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Introduction

The emergence of video-assisted thoracoscopic surgery (VATS) has been perceived as a major breakthrough in the field of thoracic surgery, and it is a representative operation of minimally invasive thoracic surgery. Thoracoscopic lobectomy was first reported in the literature in the early 1990s (1). Since then, thoracoscopic surgery has been widely recognized and developed rapidly all over the world. Compared with the traditional thoracotomy approach, VATS has various advantages including shorter hospitalization, faster postoperative recovery, lower incidence of postoperative pulmonary complications, less postoperative pain, better quality of life, and similar long-term outcomes (2-5). In addition, our previous study showed that the total non-surgery costs of VATS lobectomy were significantly lower than those of the traditional method (6). However, thoracoscopic surgery can still involve intraoperative and postoperative complications (7-11), the most dangerous and troublesome complication which is intraoperative bleeding caused by inadvertent vascular injury. We conducted a case-control study to retrospectively summarize and analyze the unexpected intraoperative bleeding caused by pulmonary vessel injury during thoracic

surgery, and explored the related factors of intraoperative bleeding and the strategies for controlling bleeding. We present this article in accordance with the STROBE reporting checklist (available at <https://jtd.amegroups.com/article/view/10.21037/jtd-23-305/rc>).

Methods

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Liaoning Cancer Hospital & Institute (No. 20230421). Between 1 January 2017 to 31 December 2019, a total of 1,263 patients underwent pulmonary resection for lung cancer in the Department of Thoracic Surgery, Liaoning Cancer Hospital & Institute (Cancer Hospital of Dalian University of Technology). The sample size was determined by the number of surgical cases in our center during the study period. The patient data including sex, age, smoking history [the never-smokers were defined as those who either have never smoked or have smoked less than 100 cigarettes in their lifetime by the World Health Organization (WHO) (12)], history of chest disease, history of chest surgery, neoadjuvant therapy, anticoagulant therapy, position of tumor (central type or peripheral type), location of tumor (left or right), pleural adhesion, pathological type, and tumor (T) and node (N) descriptor, were retrospectively collected from the hospital database. The pathological categorizations were performed according to the 2015 WHO classification of lung tumors (13). All tumors included in our study were classified according to the latest edition of tumor-node-metastasis (TNM) classification for lung cancer (14). Due to the anonymized nature of this study, the requirement for the informed consent of the patients was waived. Nonetheless, all the patients signed informed consent for surgery, and they were aware of that the relevant clinicopathological data would be used anonymously for scientific research.

Inclusion and exclusion criteria

Inclusion criteria

(I) Primary lung cancer; (II) non-small cell lung cancer; (III) segmentectomy, lobectomy, sleeve lobectomy or

Highlight box

Key findings

- A history of chest surgery and T stage were related to intraoperative bleeding.
- The most common bleeding site was the pulmonary arteries, the main cause was the accidental injury of energy device, and the most common coping strategies was suture.
- For the management of intraoperative bleeding, effective hemostasis and prevention strategy are both important.

What is known and what is new?

- Intraoperative bleeding is unavoidable and may lead to catastrophic consequences.
- The injury of bronchial artery cannot be ignored.
- Prevention strategies are helpful to reduce the incidence of intraoperative bleeding.

What is the implication, and what should change now?

- Prevention is more important than emergency measures.

pneumonectomy; (IV) complete systematic lymph node dissection (the number of removed lymph node stations in both N1 and N2 groups, including the subcarinal station, was greater than or equal to three); (V) a complete record of the clinical data.

Exclusion criteria

(I) Pulmonary metastasis of other tumors; (II) small cell lung cancer; (III) wedge resection; (IV) distant metastasis of primary lung cancer; (V) only thoracotomy biopsy without lung cancer resection; (VI) incomplete systematic lymph node dissection; (VII) incomplete clinical data.

The definition of intraoperative bleeding

During anatomical lung resection, due to various reasons (such as the lesion itself, patient factors, and surgical operation), the blood vessels are prone to unexpected injured and bleeding. Such bleeding cannot be completely stopped by conventional gauze compression. Further hemostasis and even emergency measures such as extending surgical incision and intraoperative blood transfusion may be required. In our study, the identification of intraoperative vascular injury only included the injury of major blood vessels and their branches in the thoracic cavity; the injury of small blood vessels that were difficult to distinguish with the naked eye, such as wound oozing caused by the release of pleural adhesions and dissection of lymph nodes, was not considered as intraoperative bleeding. By reviewing the surgical record or video, whether the patient had intraoperative bleeding was judged by two authors (Hongxu Liu and Wei Chen).

Surgery

According to each patient's lung lesion and individual condition, the appropriate procedure, including wedge resection, segmentectomy, lobectomy, sleeve lobectomy or pneumonectomy, was decided after internal discussion of the department. All video-assisted thoracic surgeries were performed under single-lung anesthesia. In the middle axillary line, a 4–5 centimetres utility incision was made through the fourth or fifth intercostal space according to the location of tumor, with or without additional ports. In our center, the uniportal VATS approach has become the mainstream and was applied to the majority of patients, and only a few patients were treated by multiportal approach.

For some complicated cases, hybrid VATS was applied, and its incision length ranged from 5–10 centimetres without rib spreading. The stapler commonly used during the operation was ETHICON device or easyEndo.

Statistical analysis

The categorical data were presented as counts and proportions, and the abnormally distributed continuous data were expressed as medians and quartiles. For two groups, the dichotomous or categorical variables were compared by the chi-square test, and the discrete or continuous variables were compared by Mann-Whitney U test. A logistics regression model was applied to analyze the risk factors associated with intraoperative bleeding. Potentially predictive risk factors were identified using a significance level of $P < 0.05$ by a univariate analysis and were then subjected to multivariable analysis. A P value < 0.05 was considered statistically significant. All analyses were performed using SPSS 22.0 software (IMB Corp., Armonk, NY, USA).

Results

Patient characteristics

The detailed procedure of patient selection is shown in *Figure 1*. After rigorous screening, 1,064 patients were included in our study, of whom, 67 (6.30%) patients comprised the intraoperative bleeding group (IBG) and 997 (93.70%) patients comprised the reference group (RG) without intraoperative bleeding. The overwhelming majority of patients completed the operation under the uniportal VATS, and only 22 patients completed the operation under multiportal VATS (1 case in IBG and 21 cases in RG). The patients' clinicopathological characteristics are summarized in *Table 1*. Compared with RG, the IBG group had higher incidence of history of chest surgery ($P < 0.001$), higher incidence of pleural adhesion ($P = 0.015$), higher incidence of squamous cell carcinoma ($P = 0.034$), and fewer early T-stage cases ($P = 0.003$). In the univariate and multivariate analyses, history of chest surgery [odds ratio (OR) 4.941; 95% confidence interval (CI): 2.038–11.975; $P < 0.001$ and OR 5.130; 95% CI: 2.047–12.853; $P = 0.001$, respectively] and T stage (OR 2.124; 95% CI: 1.291–3.496; $P = 0.003$ and OR 2.014; 95% CI: 1.182–3.429; $P = 0.010$, respectively) were independent risk factors of intraoperative bleeding (*Table 2*).

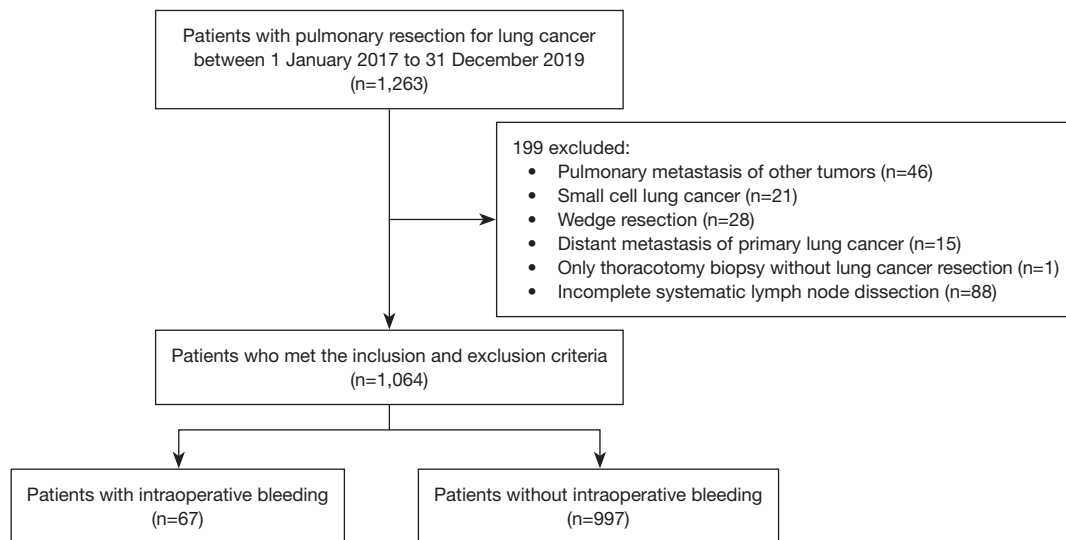


Figure 1 Flow chart of the patient selection.

Table 1 Clinicopathological characteristics of patients

Characteristics	IBG (N=67)	RG (N=997)	P value
Gender			0.995
Female	37 (55.22)	551 (55.27)	
Male	30 (44.78)	446 (44.73)	
Age			0.126
<60 years	25 (37.31)	468 (46.94)	
≥60 years	42 (62.69)	529 (53.06)	
Smoke			0.428
No	38 (56.72)	614 (61.58)	
Yes	29 (43.28)	383 (38.42)	
History of chest disease			0.348
No	60 (89.55)	924 (92.68)	
Yes	7 (10.45)	73 (7.32)	
History of chest surgery			<0.001*
No	60 (89.55)	974 (97.69)	
Yes	7 (10.45)	23 (2.31)	
Neoadjuvant therapy			0.366
No	60 (89.55)	923 (92.58)	
Yes	7 (10.45)	74 (9.42)	
Anticoagulant therapy			0.109
No	63 (94.03)	976 (97.89)	
Yes	4 (5.97)	21 (2.11)	

Table 1 (continued)

Table 1 (continued)

Characteristics	IBG (N=67)	RG (N=997)	P value
Position of tumor			0.105
Central type	13 (19.40)	125 (12.84)	
Peripheral type	54 (80.60)	872 (87.46)	
Location of tumor			0.094
Left	33 (49.25)	388 (38.92)	
Right	34 (50.75)	609 (61.08)	
Pleural adhesion			0.015*
No	44 (65.67)	782 (78.43)	
Yes	23 (34.33)	215 (21.56)	
Pathological type			0.034*
Squamous	16 (23.88)	143 (14.34)	
Non-squamous	51 (76.12)	854 (85.66)	
T stage			0.003*
Tis–T1	35 (52.24)	697 (69.91)	
T2–4	32 (47.76)	300 (30.09)	
N stage			0.187
N0	48 (71.64)	783 (78.54)	
N1–2	19 (28.36)	214 (21.46)	

Data are expressed as n (%). *, $P < 0.05$. IBG, intraoperative bleeding group; RG, reference group.

Table 2 Discriminant factors for distinguishing the intraoperative bleeding group from reference group

Characteristics	Univariable logistics regression		Multivariable logistics regression	
	OR (95% CI)	P value	OR (95% CI)	P value
Gender				
Female	Reference			
Male	1.002 (0.609–1.647)	0.995		
Age				
<60 years	Reference			
≥60 years	1.486 (0.892–2.476)	0.128		
Smoking history				
No	Reference			
Yes	1.223 (0.742–2.017)	0.429		
History of chest disease				
No	Reference			
Yes	1.477 (0.652–3.347)	0.350		
History of chest surgery				
No	Reference		Reference	
Yes	4.941 (2.038–11.975)	<0.001*	5.130 (2.047–12.853)	0.001*
Neoadjuvant therapy				
No	Reference			
Yes	1.455 (0.642–3.297)	0.369		
Anticoagulant therapy				
No	Reference			
Yes	2.951 (0.983–8.858)	0.054		
Position of tumor				
Central type	Reference			
Peripheral type	0.595 (0.316–1.122)	0.109		
Location of tumor				
Left	Reference			
Right	0.656 (0.400–1.077)	0.096		
Pleural adhesion				
No	Reference			
Yes	1.901 (1.123–3.219)	0.017*	1.553 (0.898–2.685)	0.115
Pathological type				
Squamous	Reference		Reference	
Non-squamous	0.534 (0.296–0.962)	0.037*	0.707 (0.375–1.335)	0.285

Table 2 (continued)

Table 2 (continued)

Characteristics	Univariable logistics regression		Multivariable logistics regression	
	OR (95% CI)	P value	OR (95% CI)	P value
T stage				
Tis–T1	Reference		Reference	
T2–4	2.124 (1.291–3.496)	0.003*	2.014 (1.182–3.429)	0.010*
N stage				
N0	Reference			
N1–2	1.448 (0.834–2.516)	0.189		

*, P<0.05. OR, odds ratio; CI, confidence interval; T, tumor; N, node.

Table 3 Perioperative outcomes of patients

Outcomes	IBG (N=67)	RG (N=997)	P value
Operative time (min)	235 (195, 265)	180 (150, 220)	<0.001*
Blood loss (mL)	150 (100, 300)	50 (50, 100)	<0.001*
Transfusion			<0.001*
No	59 (88.06)	991 (99.40)	
Yes	8 (11.94)	6 (0.60)	
Conversion			<0.001*
No	38 (56.72)	921 (92.38)	
Yes	29 (43.28)	76 (7.62)	
Duration of chest drainage (days)	4 (3, 6)	4 (3, 6)	0.066
Postoperative hospital stay (days)	8 (7, 10)	7 (6, 9)	0.002*
Postoperative complication (Clavien-Dindo grade)			0.017*
No	47 (70.15)	828 (83.05)	
1–2	13 (19.40)	94 (9.43)	
3–5	7 (10.45)	75 (7.52)	
30-day mortality			1
No	67 (100.00)	996 (99.90)	
Yes	0 (0.00)	1 (0.10)	

Data are expressed as n (%) or median (interquartile range). *, P<0.05. IBG, intraoperative bleeding group; RG, reference group.

Perioperative outcomes

The perioperative outcomes are listed in Table 3. The median operative time was longer, the blood loss was more, the rate of intraoperative blood transfusion was higher, the rate of conversion was higher, the postoperative hospital stay was longer, and the rate of postoperative complication

was higher for patients with intraoperative bleeding. The median blood loss of patients in IBG was 150 mL (range, 30–2,500 mL). There were no significant differences in the duration of chest drainage (P=0.066), between IBG and RG. In terms of 30-day mortality, only 1 patient in RG died as a result of acute respiratory distress syndrome.

Table 4 The sites, reasons, and coping strategies of intraoperative bleeding

Items	n [%]
Sites	
Pulmonary artery	48 [72]
Pulmonary vein	7 [10]
Bronchial artery	10 [15]
Azygos vein	2 [3]
Reasons	
Stapler	6 [9]
Energy device	25 [37]
Dissection	16 [24]
Other*	20 [30]
Coping strategy	
Suture	43 [64]
Silk ligation	4 [6]
Hemostatic clip	3 [4]
Stapler	4 [6]
Energy device	6 [9]
Absorbable hemostat	11 [16]
Simultaneous application of various methods	4 [6]

*, other reasons included excessive stretching of lung tissue, incomplete clamping of clip, unknown reasons, etc.

Table 5 Pulmonary artery injury sites

Sites	n
Right	
Upper lobe	9
Middle lobe	3
Lower lobe	7
Left	
Upper lobe	18
Lower lobe	11

Sites, reasons, and coping strategies of intraoperative bleeding

As shown in *Table 4*, the predominant injury site of intraoperative bleeding was the pulmonary artery (72%). Commonly, the pulmonary artery injury mainly occurred in

the upper lobe (*Table 5*). The immediate reasons of vascular injury could be classified into four categories: stapler (9%), energy device (37%), dissection (24%) and other reasons (30%). Stapler related problems included stapling failure, laceration of the vessel, etc. The problems related to energy device were damage to vessels caused by using ultrasonic scalpel and electric hook, including false fire, sticking, oozing of vascular stump, etc. Dissection-related problems referred to the laceration of vessels caused by the inaccurate grasp of the force in the process of dissection. Other reasons included excessive stretching of lung tissue, incomplete clamping of clip, unknown reasons, etc. The most common method for managing intraoperative bleeding was suturing the bleeding site (64%). Other methods included silk ligation and the application of hemostatic clips, stapler, energy device, and absorbable hemostat. A total of 4 cases (6%) were treated by 2 or more of these hemostasis methods.

Discussion

Although the complication rate of thoracoscopic surgery is relatively low, it is an inevitable aspect of all surgeries, and its occurrence is independent of the learning curve (15). Compared with traditional thoracotomy, the operation space and visual field of thoracoscopic surgery are limited to a certain extent. Therefore, once intraoperative bleeding occurs, it will greatly test the aptitude and surgical technique of the surgeon and the cooperative ability of the entire team. Subsequently, intraoperative massive bleeding during thoracoscopic anatomical lung resection is undoubtedly a serious challenge and has always been the concern for every thoracic surgeon. In this study, the incidence of intraoperative bleeding was 6.30%, in line with the articles in the recent decade which reported ranges of 4.11% to 10.83% (16-22). Most of the patients in this study lived in the northeastern region of China. This area has been the center of heavy industry for many years, and the air pollution is high. Polluted air may lead to a significantly higher incidence of lung-related diseases (23-25). Therefore, the incidences of dense adhesions or calcified lymph nodes around the pulmonary arteries without a loose dissection plane may be increased in this population. Combining our own experience with existing literature (26,27), the occurrence of the above unfavorable surgical anatomies may increase the risk of unexpected bleeding issues. Our study showed that the presence or absence of pleural adhesion was associated with intraoperative bleeding. From the analysis of the clinicopathological characteristics of patients

in our study, it could be seen that history of chest surgery and T stage were associated with intraoperative bleeding. History of chest surgery may result in dense perivascular adhesions, which would be a potential risk factor for intraoperative vascular bleeding. The later T stages meant that the size of tumor was larger or the tumor directly invaded the surrounding tissues, making vascular damage more likely to occur in the process of tumor dissociation. At the same time, the limited exposure of the surgical field that resulted from the later T stages also increased the risk of intraoperative bleeding.

Complication

Intraoperative bleeding was found to result in operation-related complications, such as longer operative time, more blood loss, higher transfusion rate, higher conversion rate, longer hospital stay and the more complications. There were no statistical differences in the duration of chest drainage and 30-day mortality. Yamashita *et al.* (17) found that there were parallel perioperative outcomes in patients with and without vessel injury, including duration of chest tube drainage, length of hospital stay, and morbidity rate, despite longer operative time and more blood loss in the vessel injury group. In the study by Miyazaki *et al.* (18), no significant differences in perioperative morbidities, the duration of chest tube insertion and postoperative hospital stay were observed. Igai *et al.* (19) found that compared with the no vessel injury group, 26 patients with vessel injury had same length postoperative hospitalization and morbidity rate. Wu *et al.* (20) asserted that there were no differences in drainage day and 30- or 90-day mortality rate. According to the experience of ours and other centers, intraoperative hemorrhage did not compromise the prognosis as and when the positive and effective hemostasis were taken promptly during the operation.

Bleeding site

In our study, the most common bleeding site was the pulmonary arteries, accounting for 72%. Due to the relatively fragile nature of the pulmonary artery and very high volume blood flow through it, the bleeding caused by pulmonary artery injury is the most threatening. Severe pulmonary artery injury may require unplanned extensive pulmonary resection, such as pneumonectomy, and severe cases may result in an intraoperative patient death (28). In a Japanese retrospective study, it was reported that

pulmonary artery injury occurred relatively easily during left upper lobectomy (43.8%) (29). We found that the pulmonary artery injury sites were mainly located in upper lobe. Therefore, extra attention should be paid to the left upper lobectomy during VATS. The incidence of bronchial artery injury (15%) was second only to that of the pulmonary artery. According to Igai *et al.*'s research (19), there were only 2 patients (7.4%) with bronchial artery injury during thoracoscopic anatomic pulmonary resection. Similarly, 3 cases (7.5%) with bronchial artery bleeding were reported in another study (21). In some articles (17,18,20,22), no cases of bronchial artery bleeding were recorded. However, a highly vascularized bronchial artery as a risk factor for intraoperative bleeding should not be ignored (30). These cases with bronchial artery injury were often related to complete systematic lymph node dissection. Although bleeding from the bronchial artery is common in thoracoscopic surgery, it can be controlled successfully by compression, electrocautery, ultrasonic energy device, or a hemostatic clip (26).

Bleeding reason

Our results demonstrated that the intraoperative vascular injuries were mostly related to the use of energy device (37%) and the violent dissection of vessel structures (24%). In fact, except for stapler-related bleeding, we can find that most bleeding cases were caused by accidents and could be avoided to some extent in clinical practice by recalling and watching surgical videos. In the cases with tight lymph nodes around blood vessels, due to insufficient judgment, in the process of separating blood vessels and lymph nodes through ultrasonic scalpel, electric hook or surgical instruments, accidental damage to blood vessels will inevitably occur. This is something that every surgeon doesn't want to mention and can't avoid. Sometimes, inappropriate manipulation by assistants, such as unclear exposure and excessive stretching of lung tissue, may lead to the vascular injury and bleeding. Although the incidence of surgical stapler-related bleeding (9%) was relatively rare, it was not negligible. According to study of Brown (31), the patient could suffer a massive intraoperative hemorrhage or even death after stapler or device malfunction. They also found that from July 2001 to October 2003, among 5,117 cases with malfunctioning devices, the "staples not forming" was the most commonly reported problem. In our study, 3 of 6 stapler-related bleeding cases involved failure of the staples to form properly. Besides, other adverse events

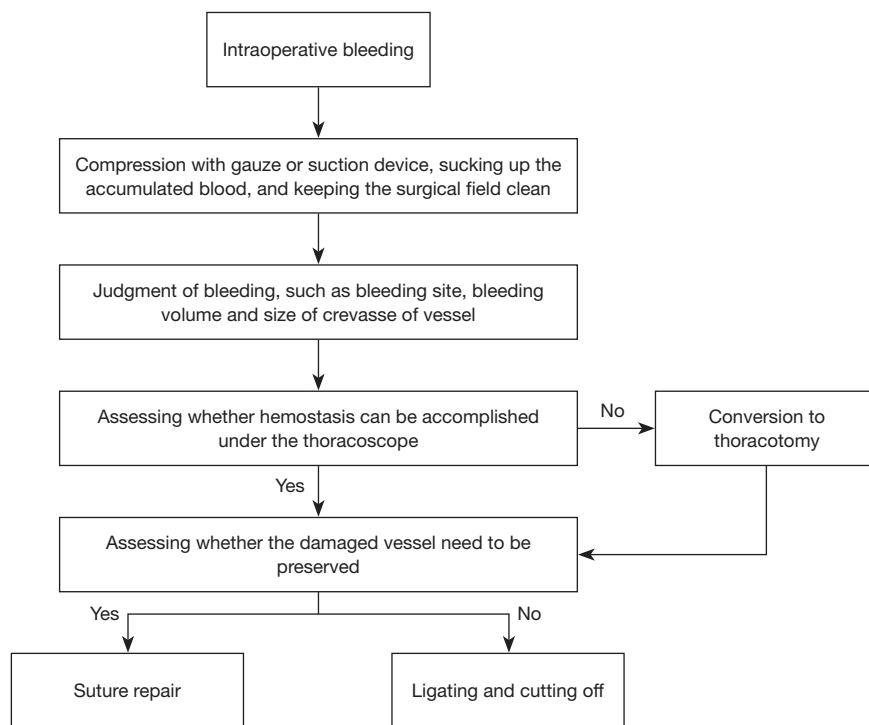


Figure 2 The treatment algorithm for intraoperative bleeding.

of stapling, including oozing, laceration of the adjacent vessels, technical vascular injury at insertion, and rupture of the stamp, have been reported (32). As the consequences of stapling failure are serious and sometimes irreparable, it is necessary to check the stapler before use. At the same time, it is very important to be familiar with device-specific failsafe mechanisms and protocols to deal with these rare occurrences. In fact, in the process of using the stapler, we often found that there was a small amount of bleeding in the stump of the vessel. Although this would not lead to massive bleeding and would slowly coagulate itself, it would affect the clarity of the surgical field. Therefore, for selected vessels, we often ligate the vessels before dividing it with the stapler, to avoid the bleeding from the stump.

Coping strategy

Expedited and effective hemostasis is the key to avoid the further aggravation and poor outcomes of intraoperative bleeding. The treatment algorithm of our institution for intraoperative bleeding is summarized in *Figure 2*. The first step is to control the bleeding immediately, ideally with direct gauze compression, and keep the surgical field clean and visible after suctioning the accumulated blood. Then,

assessing the vascular injury and deciding which hemostasis method, such as silk ligation, suture, application of clip, and so on, should be made depending on the surgeon's experience. Cases with injuries less than 30% of the vessel circumference could be suture repaired primarily; cases with injuries between 30% and 50% of the vessel circumference might be patch repaired; cases with injuries more than 50% of the vessel circumference should be required either end-to-end anastomosis (if length is adequate), conduit interposition, or ligation (33). Various novel methods have been applied to troubleshoot intraoperative bleeding. Mei *et al.* introduced the suction-compressing angiorrhaphy technique to managing vascular injury (16). However, for selected cases with left main pulmonary artery injury, bleeding might not be controlled by this new technique due to anatomic limitations in attaining proximal control of the artery. According to Igai *et al.*, hemostasis could be mostly accomplished by attachment of the thrombotic sealant to the bleeding point (19). The use of sealants has been found to be suitable for patients with a small tear or in cases where the control by means of suture or ligation was complex (34). In the process, once it was found that hemostasis could not be achieved under the thoracoscope, surgeons should not hesitate to convert to open thoracotomy. In our study,

there were a total of 29 patients without unexpected conversions because of intraoperative bleeding. Conversion to thoracotomy was one of miscellaneous tips to manage and prevent intraoperative events (26). Surgeons should realize that minimally invasive surgery is not the goal of surgery itself, nor should it be a shame to convert to open thoracotomy. In terms of 5-year survival rate, compared with video-assisted thoracoscopic lobectomy, the patients with unexpected conversion to thoracotomy had a similar prognosis (35). The ultimate goal of intraoperative bleeding management is to control bleeding as soon as possible by reasonable application of various methods.

Prevention

Unexpected intraoperative bleeding can be avoided with careful preoperative planning and the application of intraoperative prevention strategies. For preoperative planning, attention should be paid to the inquiry of patient's history and then identifying patient-specific risk factors, such as history of chest surgery. On the other hand, rigorous radiologic assessment, including identifying tumor size, the relationship between lung lesion and pulmonary vessels (especially for central lung cancer), anatomical variation, calcification of lymph nodes, and so on, is an essential part of every thoracic surgeon's preoperative work. In our institution, according to the actual situation of every patient, different prevention measures may be applied during the operation. For all patients, attention to proper exposure, careful detection, and meticulous surgical manipulations of anatomical structures are the most critical elements for avoiding intraoperative injuries. Experienced surgeons highly value careful pulmonary artery manipulation, and extra care must be taken in use of energy devices to avoid inadvertent contact with pulmonary vessels. In addition, when a stapler is fired, surgeons need to adjust their force of retraction to minimize the tension on the pulmonary vessels (28). For patients whose lung lesion is closely related to or was not easily separated from the main pulmonary artery, or patients with tight adhesion between pulmonary artery and bronchus, the tourniquet should be used reasonably. For example, for the central lung cancer in the left upper lobe, the main and lower trunk of pulmonary artery can be dissociated in advance and the tourniquets may remain separately. If the pulmonary artery of left upper lobe is injured, the tourniquets can be tightened immediately to control bleeding, allowing us to deal with the bleeding point calmly. A similar method,

called pretreatment clamping of the pulmonary artery, was designed by Zhang *et al.*, which significantly reduced conversion rate, pulmonary artery repair time, and blood loss (36). In cases where thoracoscopic surgery is expected to be difficult to complete, the planned prolongation of incision, which means actively extending the surgical incision in order to better cope with complex situations, and thus reducing the risk of intraoperative bleeding, is better than unexpected conversion to thoracotomy. In our previous study (37), hybrid VATS, as a kind of minimally invasive approach somewhere between conventional thoracotomy and complete VATS, would be used for some complicated surgeries, and was shown to be a safe and feasible approach associated with better postoperative recovery and similar oncologic prognosis compared to conventional thoracotomy. For certain patients with swellings and calcified lymph nodes around pulmonary veins, in order to ensure safety, the hybrid VATS renders it unnecessary to deliberately ligate the effluent veins first. In accordance with the current literature, vein-first ligation might be related with improved survival outcomes in patients with lung cancer (38,39). However, a different opinion has been given that the sequence of pulmonary vessel interruption would not affect the oncological outcomes and survival (40). On the premise of minimizing the compression and traction of the tumor during the operation, a core principle was to do the easy one first instead of following the fixed sequence of ligation of vessels.

Limitation

The several limitations of this study were as follows. Firstly, as a retrospective study with relatively few cases, selection bias was inevitable. For example, the degree of swelling and calcification of the lymph nodes for every patient could not be evaluated, so that the relationship between lymph nodes and intraoperative bleeding could not be assessed. The relationship between surgical experience and intraoperative bleeding was not analyzed. There was no statistical difference in neoadjuvant therapy between IBG and RG. However, the influence of different neoadjuvant therapies on intraoperative bleeding was not further analyzed. Secondly, the relationship of type of resection and risk of intraoperative bleeding was not further analyzed in this paper. For many included cases, a special situation was often found, in which lobectomy or segmentectomy was combined with segmental or wedge resection of other lobes. Therefore, it was difficult to distinguish the

effects of different surgical resection types on bleeding. Thirdly, the data in this study were provided from a single institution, which was not universally representative to some extent. Fourthly, except pulmonary artery injury, there were relatively few cases of other vascular injuries, so the differences of hemostasis strategies depending on different sites of bleeding (such as pulmonary artery, pulmonary vein, bronchial vein and azygos vein) were difficult to further be obtained. Therefore, a prospective, well-designed, and multicenter trial with large sample size is needed.

Conclusions

In our study, the emergence of intraoperative bleeding was associated with history of chest surgery and T stage. Intraoperative vessel injury prolonged the operative time and postoperative hospital stay, increased the amount of intraoperative blood loss, and increased the incidences of intraoperative blood transfusion, conversion and postoperative complication. The predominant cause of vascular injury was accidental injury and the pulmonary arteries were the most vulnerable. Although intraoperative bleeding is unavoidable and dangerous, the risk is normally manageable. Based on surgeon's experiences and the specific circumstances of the individual patient, the ultimate goal is to select appropriate prevention and hemostasis strategies to successfully complete a surgery or deal with all kinds of emergencies. Prevention is more important than emergency measures. Avoiding unexpected intraoperative bleeding is subject to meticulous preoperative planning and the flexible application of intraoperative preventive measures, including the application of tourniquet, the planned prolongation of incision, and so on.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Liaoning Cancer Hospital & Institute (No. 20230421). Due to the anonymized nature of this study, the requirement for the informed consent of the patients was waived.

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