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ORIGINAL ARTICLE

Ligating the pulmonary vein at the pericardial reflection is useful for preventing thrombus formation in the pulmonary vein stump after left upper lobectomy

Takahito Nakano[1,2] · Hiroyuki Kaneda[1,2] · Takayuki Kawaura[3] · Tomoki Kitawaki[3] · Tomohiro Murakawa[2]

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Abstract

Objectives Thrombus formation in the pulmonary vein stump after left upper lobectomy is supposedly a risk factor for systemic thrombosis, resulting in a critical course for the patient. The purpose of this study was to assess the efficacy of the proximal ligation method preventing thrombus formation and thrombosis comparing the two groups of patients (those who did and those who did not undergo pulmonary vein ligation).

Methods We performed a surgical procedure to shorten the pulmonary vein stump in the left upper lobectomy. In this procedure, we first dissected the pericardium from the left upper pulmonary vein, and then we ligated the pulmonary vein at the pericardial reflection before stapling transection.

Results In the group that was not treated with the proximal ligation method, thrombus formation in the pulmonary vein stump was detected in all four cases. In contrast, thrombus formation in the pulmonary vein stump was detected in one only case of the eight cases treated with the proximal ligation method, which was significantly fewer than among those not treated with the ligation method ($p=0.010$). The logistic regression analysis revealed in both the univariate ($p=0.0014$) and multivariate analyses ($p=0.0071$) that the proximal ligation method was significantly associated with reduced thrombus formation in the pulmonary vein stump.

Conclusions Thrombus formation in the pulmonary vein stump was significantly reduced by ligating the pulmonary vein at the pericardial reflection.

Keywords Left upper lobectomy · Video-assisted thoracoscopic surgery · Pulmonary vein stump · Thrombosis

Introduction

Pulmonary lobectomy is performed worldwide as a curative treatment for patients with early stages of non-small cell lung cancer. Brain infarction is a postoperative complication that occasionally occurs after pulmonary lobectomy. Thrombus formation in the pulmonary vein stump after left upper lobectomy is supposedly a risk factor for systemic thrombosis [1–4]. However, the optimal treatment and prevention strategy for this complication have not been established [5, 6]. The long stump of the pulmonary vein that remains after left upper lobectomy is considered to be a risk factor for thrombus formation in the pulmonary vein stump [5]. We experienced a case of cerebral attack caused by a thrombus in the pulmonary vein stump that occurred after left upper lobectomy [7]. After this case, we performed contrast-enhanced computed tomography (CT) to evaluate thrombus formation in the pulmonary vein stump on the fifth to the seventh postoperative days for every patient who underwent left upper lobectomy. Surprisingly, contrast-enhanced CT revealed thrombi in all cases after left upper lobectomy. Therefore, we identified the need to develop a new surgical technique for use with the usual video-assisted thoracoscopic surgery (VATS) lobectomy to prevent thrombus formation in the pulmonary vein stump. In this study,

✉ Hiroyuki Kaneda
kanedah@takii.kmu.ac.jp

[1] Division of Thoracic Surgery, Kansai Medical University Medical Center, 10-15 Fumizonocho, Moriguchishi, Osaka 570-8507, Japan

[2] Department of Thoracic Surgery, Kansai Medical University, Hirakatashi, Japan

[3] Department of Mathematics, Kansai Medical University, Hirakatashi, Japan

we reviewed our experiences and assessed the efficacy of our surgical intervention.

Subjects

We retrospectively reviewed clinical charts, chest CT images, and surgical videos from consecutive patients who underwent left upper lobectomy with the VATS or open approach at Kansai Medical University Medical Center between June 2016 and January 2018. The study was approved by the Institutional Review Board of Kansai Medical University (approval date: April 3, 2018; approval number: 2017278). The requirement for informed consent was waived because of the retrospective nature of the study.

Methods

Surgical procedure

Until March 2017, we transected the pulmonary vein using an automatic anastomotic device at the proximal site when technically possible for every lobectomy (Fig. 1a). In the method used previously, we did not dissect the pericardium from the left upper pulmonary vein. In April 2017, we changed the procedure for pulmonary vein dissection in the left upper lobectomy to shorten the pulmonary vein stump. In this procedure, we first dissected the pericardium from the left upper pulmonary vein, and then we ligated the pulmonary vein at the pericardial reflection. Finally, we transected the pulmonary vein using an automatic anastomotic device (Fig. 2a). To lower the risk for intra-pericardial bleeding, we did not open the pericardium and did not ligate the pulmonary vein inside of the pericardium. We performed ligation of the pulmonary vein at the pericardial reflection, which is the most proximal site in the thoracic cavity. This procedure is called the proximal ligation method. Other parts of the surgical procedure for lobectomy and perioperative management were unchanged. In brief, the surgeon stood on the front side of the patient, and the camera assistant stood on the back side. Two monitors were placed on the cranial side of the patient, with one monitor placed upside down. Lobectomy is performed via three ports: a 3–4-cm utility incision on the anterior axillary line in the fourth intercostal space, a 15-mm incision in the sixth intercostal space for the surgeon, and a 15-mm incision on the posterior axillary line in the fifth intercostal space for a camera with a 30° lens. The ribs were not resected or spread. The pulmonary arteries were dissected. Those > 7 mm thick were divided using a stapler and those < 7 mm thick were ligated by a 1–0 silk suture and divided. The bronchus was dissected using a stapler. Lymph node dissection was performed for mediastinal and hilar lymph nodes.

Data acquisition and statistical analysis

Contrast-enhanced CT was performed on the fifth to the seventh postoperative days after left upper lobectomy. Patients with renal dysfunction or with an allergy to the contrast medium were excluded from this analysis because they did not undergo contrast-enhanced CT. We measured the length of the pulmonary vein stump using the coronal plane on CT

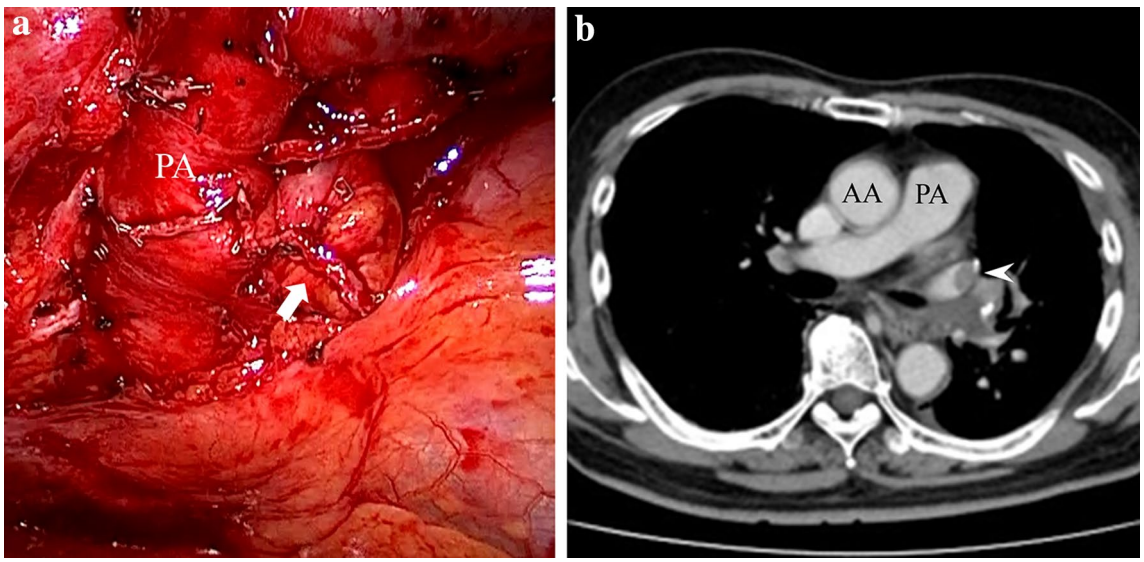

Fig. 1 A case from the group that was not treated with the proximal ligation method. **a** The pulmonary vein was transected by a stapler at the proximal site when technically possible using an intrathoracic approach (⇨). **b** Thrombus formation was detected in the pulmonary vein stump (➤). *AA* ascending artery, *PA* pulmonary artery

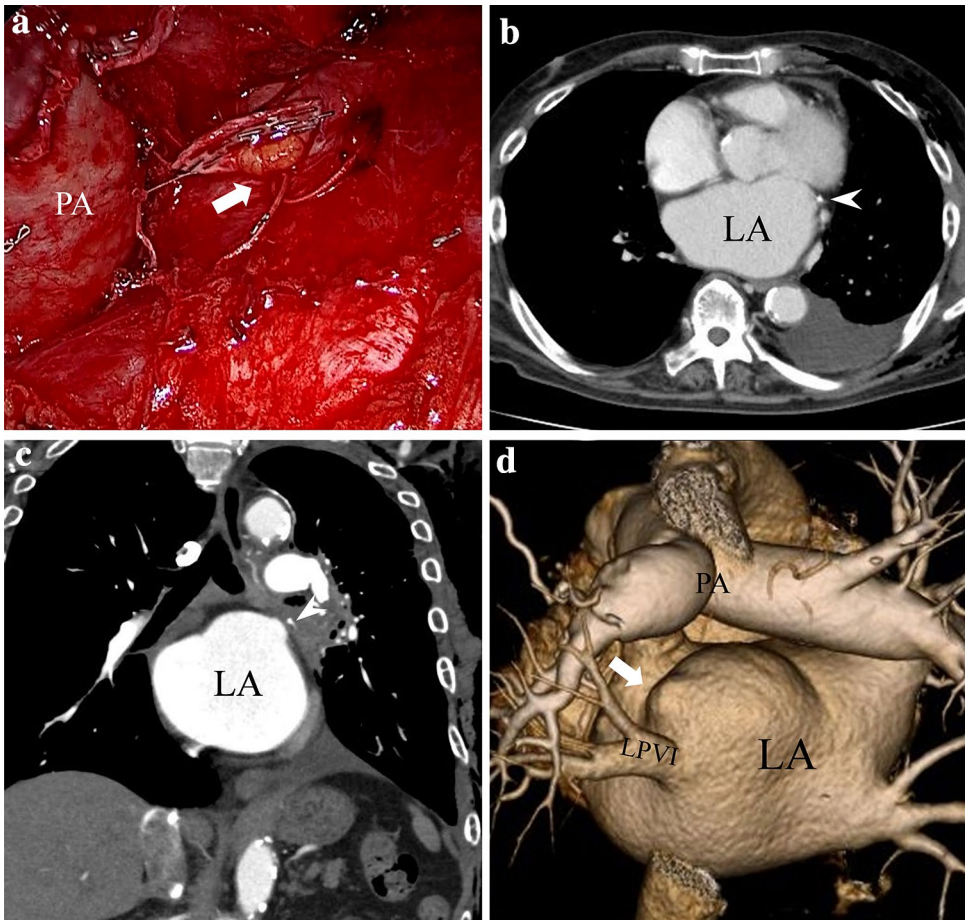

Fig. 2 A case from the group treated with the proximal ligation method. **a** The pulmonary vein was ligated at the pericardial reflection (⇨) and then transected by a stapler. **b, c** Thrombus formation was not detected in the pulmonary vein stump (➤). **d** A three-dimensional image reconstructed on postoperative computed tomography showed the pulmonary vein stump to have a round-shaped form (⇨). *PA* pulmonary artery, *LA* left atrium, *LPVI* left pulmonary vein inferior

as the standard, in which the long axis of the stump was visible or using the horizontal plane on CT if a suitable coronal plane image was not available. When thrombus formation was detected, oral anticoagulation therapy was administered for 3 months.

We compared two groups of patients (those who did and those who did not undergo pulmonary vein ligation) to assess the efficacy of the proximal ligation method for preventing thrombus formation and thrombosis. The Wilcoxon rank-sum test was used to compare continuous data, and Fisher's exact test was used to compare categorical data. Univariate and multivariate analyses were performed using logistic regression analysis. A p value of <0.05 was considered statistically significant. All statistical analyses were performed using JMP Pro software version 13.2.1 (SAS Institute, Inc., Cary, NC, USA).

Results

Four consecutive cases, in which the proximal ligation method was not used, and eight consecutive cases, in which the proximal ligation method was used, during the study period were included in this study. The patients' characteristics and postoperative outcomes are summarized in Tables 1 and 2, respectively.

Postoperative thrombus formation and thrombosis

In the group that was not treated with the proximal ligation method, thrombus formation in the pulmonary vein stump was detected in all four cases. In contrast, thrombus formation in the pulmonary vein stump was detected in only one case of the eight cases treated with the proximal ligation method, which was significantly fewer than that among those not treated with the ligation method ($p=0.010$). The logistic regression analysis revealed in both the univariate ($p=0.0014$, Table 3) and multivariate analyses ($p=0.0071$, Table 3) that the proximal ligation method was significantly associated with reduced thrombus formation in the pulmonary vein stump.

Thrombosis occurred as a brain infarction in one patient in the group that was not treated with the proximal ligation method. This patient, who had thrombus formation in the pulmonary vein stump, had a repeated brain infarction while under anticoagulant therapy; the details of this case and its

Table 1 Patients' characteristics of the two groups in patients who did and who did not undergo the proximal ligation method

	Patients who did not undergo the proximal ligation method ($n=4$)	Patients who did undergo the proximal ligation method ($n=8$)	p value
Age, mean (range)	73 (66–81)	65 (50–76)	0.20
Sex, *n*			0.58
Male	3	4	
Female	1	4	
Preoperative comorbidity, *n*			
Brain infarction	0	1	1.0
Atrial fibrillation	0	2	0.52
Operative approach, *n*			1.0
VATS	3	6	
Thoracotomy	1	2	
Histological type, *n*			0.41
Adenocarcinoma	1	5	
Squamous cell carcinoma	2	2	
Small cell carcinoma	1	0	
Other	0	1	
Pathological stage, *n*			0.76
I	1	4	
II	1	2	
III	2	1	

VATS video-assisted thoracoscopic surgery

Table 2 Postoperative outcomes of the two groups of patients who did and who did not undergo the proximal ligation method

	Patients who did not undergo the proximal ligation method ($n=4$)	Patients who did undergo the proximal ligation method ($n=8$)	p value
Postoperative complication, *n*			
Brain infarction	1	0	0.33
Atrial fibrillation	1	2	1.0
Thrombus formation in the pulmonary vein stump, *n*	4	1	0.010
Length of pulmonary vein stump, mm, mean (range)[a]	19.1 (13.5–27.6)	8.5 (5–15.3)	0.014
Introduction of oral anticoagulation therapy, n	4	0[b]	0.0020

[a]The length of the pulmonary vein stump was measured using the coronal plane on CT in the 5 cases who underwent the proximal ligation method and using the horizontal plane in the remaining cases

[b]Anticoagulation therapy was waived due to hematuria caused by kidney disease

complicated clinical course have been reported previously [7]. No thrombosis was observed in the group of patients treated with the proximal ligation method over a postoperative follow-up period ranging from 5 to 21 months. No complications related to the surgical procedure for the proximal ligation method, such as critical bleeding, infection, and atrial fibrillation, were observed during the study period.

Risk analysis for thrombus formation: length and shape of the pulmonary vein stump

The mean length of the pulmonary vein stump in the group treated with the proximal ligation method was 8.5 mm, which was significantly shorter than that in the group

Table 3 Predicters of the thrombus formation in the pulmonary vein stump

	p value of univariate analysis	*p* value of multivariate analysis
Age	0.74	
Sex (male/female)	0.19	0.10
Preoperative history of cerebral infarction	0.29	
Preoperative atrial fibrillation	0.12	0.19
Operative approach (VATS/thoracotomy)	0.27	
Histological type (Ad/Sq/SCLC/Other)	0.37	
Pathological stage (I/II/III)	0.84	
Perioperative atrial fibrillation	0.73	
Proximal ligation method	0.0014	0.0071

VATS video-assisted thoracoscopic surgery, *Ad* Adenocarcinoma, *Sq* Squamous cell carcinoma, *SCLC* Small cell lung cancer

that was not treated with the proximal ligation method (19.1 mm of mean length, $p = 0.014$). Figure 1 shows the thoracoscopic (a) and CT (b) images that reveal a thrombus formation in the pulmonary vein stump in a case that was not treated with the proximal ligation method. The pulmonary vein was transected with a stapler at the proximal site via the intrathoracic approach (Fig. 1a). A 12-mm thrombus was detected in the pulmonary vein stump (Fig. 1b). Figure 2 shows thoracoscopic and CT images of a case that was treated with the proximal ligation method. The pulmonary vein was ligated at the pericardial reflection and then transected with a stapler (Fig. 2a). Thrombus formation was not detected in the pulmonary vein stump (Fig. 2b, c). A three-dimensional image reconstructed by postoperative CT was available in this case, and it showed the pulmonary vein stump as a round-shaped form (Fig. 2d). Figure 3 shows a case from the group treated with the proximal ligation method, in which thrombus formation was detected on postoperative CT; the length of the pulmonary vein stump was 15 mm.

Discussion

To prevent thrombus formation in the pulmonary vein stump, a surgeon proposed transecting the pulmonary vein inside the pericardium [3, 8]. However, this transection procedure inside the pericardium is technically difficult in the thoracoscopic setting. Since April 2017, we have been making the pulmonary vein stump as short as possible, ligating the pulmonary vein at the pericardial reflection and then transecting the pulmonary vein at the distal site with a stapler. The pulmonary vein was ligated before stapling transection because traction of the upper lobe toward the opposite side from the mediastinum allows the ligation to locate a more proximal site than ligation of the vein after stapling transection.

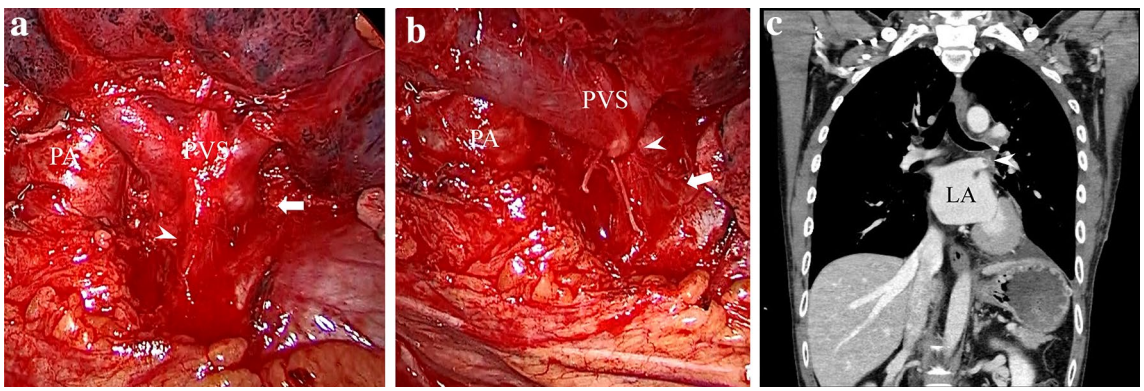

Fig. 3 A case from the group treated with the proximal ligation method. **a** A tent-like adhesion (➤) remained at the pericardial reflection (⇨). **b** The ligation point (➤) was placed toward the peripheral side from the pericardial reflection (⇨). **c** Thrombus formation was detected in the coronal plane on postoperative computed tomography (➤). The length of the pulmonary vein stump was 15 mm. *PA* pulmonary artery, *PVS* pulmonary vein superior, *LA* left atrium

In this study, the prevention of thrombus formation in the pulmonary vein stump was statistically significant in patients who were treated with the proximal ligation method. The length of the pulmonary vein stump was < 10 mm in most cases treated with the proximal ligation method, which appears to be favorable for preventing thrombus formation, according to a previous study that reported the relation between the length of the pulmonary vein stump and thrombus formation [5]. Furthermore, a round-shaped stump of the pulmonary vein formed by ligation with threads may contribute to the prevention of turbulence from blood flow, which has been surmised as a cause of thrombus formation [9].

Thrombus formation was detected in one case in the group treated with the proximal ligation method. We reviewed the surgical video and retrospectively observed that a tent-like adhesion between the pulmonary vein and pericardium was not dissected sufficiently and remained in the ventral side of the left upper pulmonary vein (Fig. 3a). The ligation point was moved toward the distal side from the pericardial reflection, in contrast to our usual goal (Fig. 3b). The length of the pulmonary vein stump in this case was 15 mm in the coronal plane of a postoperative CT, which was as long as that transected without the proximal ligation method in our study. As a result, we now consider that sufficient dissection between the pulmonary vein and pericardium at the cranial site is as important as ligating the pulmonary vein for shortening the pulmonary vein stump (Fig. 4).

No intraoperative or postoperative complications related to the proximal ligation method were observed in our study. Cardiac complications after pulmonary lobectomy commonly include arrhythmia, congestive cardiac failure, and myocardial infarction [10, 11], and some cases of bleeding or cardiac tamponade caused by transecting the pulmonary vein around the pericardial reflection have been reported [12, 13]. The proximal ligation method does not require complicated handwork, and vascular stapling is safely performed without the risk of injuring mediastinal structures. Therefore, we considered that the proximal ligation method is especially useful in the thoracoscopic setting.

Our study has several limitations. First, this study showed short-term outcomes for preventing thrombus formation in the pulmonary vein stump. Its efficacy in the long-term needs to be examined further because thrombosis after pulmonary resection does not occur only in the perioperative period [14]. Second, the length of the pulmonary vein stump was evaluated with some variability on CT. In all cases that were not treated with the proximal ligation method, and in some cases that were treated with the proximal ligation method, the length of the pulmonary vein stump was measured on the horizontal plane of CT because the coronal plane was not available, which may have caused the length to be underestimated. Finally, this is a retrospective study from a single institution that included a relatively small number of patients. We confirmed the acceptability of our statistical analysis even with the relatively small number of patients with the co-authors, who are biostatisticians. In our series of patients, thrombus formation in almost all cases was prevented by the proximal ligation method; however, in some patients, anatomical variations may influence the efficacy of the proximal ligation method. For example, the long intrapericardium course of the pulmonary vein may lead to technical difficulties in shortening the pulmonary vein stump. On the other hand, in patients who have a common trunk of the left upper and left lower pulmonary vein, the ligation at the proximal site of the left upper pulmonary vein would be easier to perform. Therefore, the findings of this study need to be confirmed by a prospective, large-scale study. However, although the findings in this study are based on a small number of patients, we believe that the conclusions of this study are worth reporting, as our technique may play a role in preventing thrombosis after left upper lobectomy.

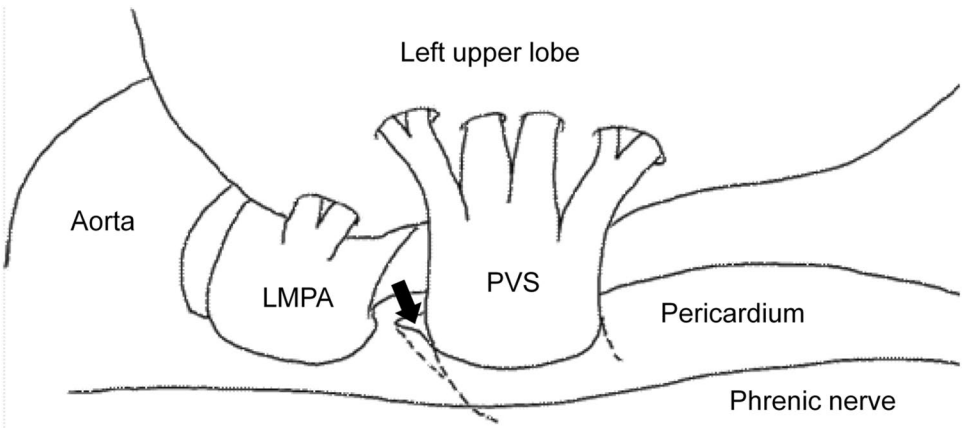

Fig. 4 Figure of the dissection of a pulmonary vein. The arrow shows the dissection point of the cranial side of the pulmonary vein from the pericardium. *LMPA* left main pulmonary artery, *PVS* pulmonary vein superior

Conclusion

In conclusion, thrombus formation in the pulmonary vein stump was significantly reduced by ligating the pulmonary vein at the pericardial reflection. We think that this method is useful for preventing thrombus formation in the pulmonary vein stump and consequent systemic thrombosis. The procedure is technically feasible not only during open surgery but also during thoracoscopic surgery.

Compliance with ethical standards

Conflict of interest The authors have declared that no conflict of interest exists.

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