



Is postoperative anticoagulation necessary after left innominate vein division in general thoracic surgery?

Hironobu Hoshino¹ · Takeshi Matsunaga¹ · Kazuya Takamochi¹ · Shiaki Oh¹ · Kenji Suzuki¹

Received: 4 June 2018 / Accepted: 1 October 2018 / Published online: 29 October 2018
© The Japanese Association for Thoracic Surgery 2018

Abstract

Objectives We encounter patients with mediastinal tumors invading the left innominate vein (LIV), and there is no evidence confirming whether the LIV should simply be ligated or reconstructed. The need for postoperative anticoagulant therapy after ligation of LIV is also controversial.

Methods 3209 patients with thoracic malignant tumors underwent surgical resection between 1994 and 2014 in our institute. Nineteen (0.6%) patients had mediastinal malignant tumors invading the LIV and underwent LIV resection. Of these patients, only 3 underwent reconstruction of LIV. We did not start anticoagulant therapy routinely after resection of LIV. The patients were divided into 2 groups: group A showed at least 50% patency of LIV by preoperative contrast-enhanced computed tomography (CECT) and group B showed less than 50%. We investigated the safety of resecting LIV and the need for postoperative anticoagulant therapy.

Results The 30-day and 90-day mortalities were zero in both groups. Thrombosis of the LIV stump and increased edema in the left neck and upper limb were observed in 2 (10.5%) patients only in group A. After initiating the anticoagulant therapy, the embolisms disappeared and weaning the patients off warfarin could be done in less than 1 year.

Conclusions In this study, there was no case of mortality or severe morbidity among the patients with LIV resection. Moreover, there was no need to initiate routine anticoagulant therapy after the LIV division as the frequency of embolism in the LIV stump was low and was expected to disappear prior to starting anticoagulant therapy.

Keywords Mediastinal malignant tumor · Division of left innominate vein · Anticoagulation

Introduction

Malignant thoracic tumors often invade surrounding vital organs, such as the aorta, superior vena cava (SVC), left innominate vein, pericardium, and lung parenchyma. Especially, in patients with malignant thoracic tumors invading the left innominate vein (LIV), we need to consider how to resect and reconstruct it, as there are few reports on the safety of LIV division. Chitoor et al. reported the safety of LIV division and needlessness of LIV reconstruction in cardiac surgery due to the lack of long-term morbidity.

Moreover, LIV division is recommended as an adjunct to improve exposure, in cardiac surgery as well as to facilitate en bloc resection of aggressive mediastinal tumors [1]. Bashist et al. showed that once the flow of LIV is interrupted, blood returns to the right side of the heart via the azygous/hemizygous system, internal mammary veins, the lateral thoracic and superficial thoracoabdominal veins, and the vertebral venous plexus [2].

It is also still controversial whether anticoagulant therapy should be started after reconstruction of SVC [3–5]. Previous reports have insisted that use of postoperative antithrombotic agents is inevitable, but 38% of grafts were occluded by thrombosis even after anticoagulant therapy postoperatively [6, 7]. On the other hand, the frequency of graft occlusion was not high when Oizumi et al. did not use postoperative antithrombotic agents. They therefore concluded that it is not necessary to routinely start anticoagulant therapy for patients who underwent reconstruction of SVC with artificial vessels [8]. Furthermore, to our knowledge, there have been

✉ Kenji Suzuki
kjsuzuki@juntendo.ac.jp

Hironobu Hoshino
hi-hoshino@juntendo.ac.jp

¹ Department of General Thoracic Surgery, Juntendo University School of Medicine, 1-3 Hongo 3-chome, Bunkyo-ku, Tokyo 113-8431, Japan

no reports on the need for anticoagulant therapy after LIV resection.

Thus, we retrospectively investigated the safety of LIV resection and the necessity of anticoagulation after surgery of malignant thoracic tumors invading LIV.

Materials and methods

Study population and design

A retrospective study was conducted on 3209 patients with thoracic malignant tumors, which were resected between 1999 and 2014 in our institute. Among them, 19 patients (0.6%) had mediastinal malignant tumors invading the LIV. This study was approved by the Juntendo University Institutional Review Board.

It is little difficult to measure the real length of LIV because it exists almost horizontally, thus we calculated

the patency of LIV, meaning the ratio of the real length and the expected length, before surgeries.

We divided them into the following 2 groups: group A showing a patency of LIV $\geq 50\%$ by preoperative contrast-enhanced computed tomography (CECT) and group B showing $\leq 50\%$ (Fig. 1). Group A consisted of 14 (74%) patients and group B of 5 (26%). In group A, 13 patients underwent division of left innominate vein (DLIV), and one patient underwent replacement of left innominate vein (RLIV). In group B, 3 patients underwent DLIV, and 2 patients underwent RLIV (Fig. 2). In the 3 RLIV patients, LIV was reconstructed with artificial graft between the LIV and right atrial appendage, and SVC was reconstructed with an artificial graft between the right innominate vein and SVC. We investigated the clinicopathological findings and postoperative complications to determine the safety of the resection of LIV and the need for postoperative anticoagulant therapy.

Fig. 1 CECT was performed on all patients preoperatively. In group A, patency of LIV was $\geq 50\%$, while in group B, it was $\leq 50\%$. CECT contrast-enhanced computed tomography, LIV left innominate vein

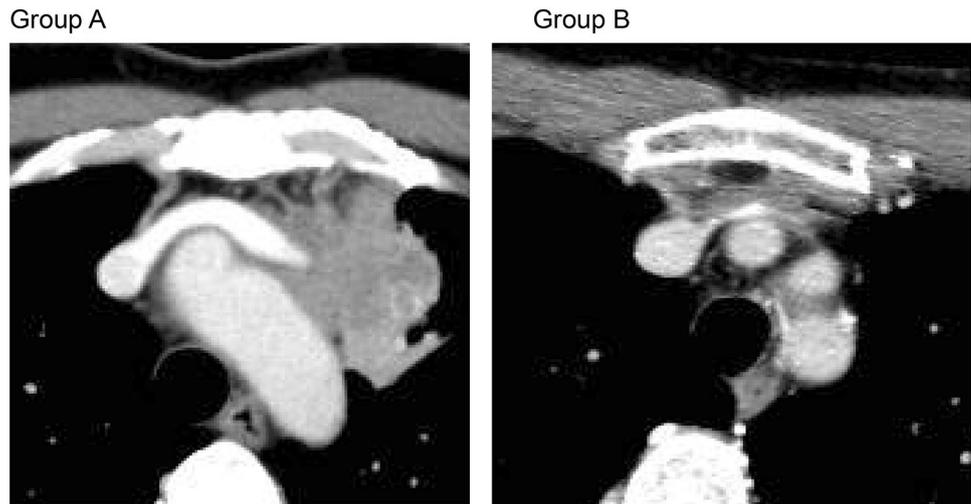
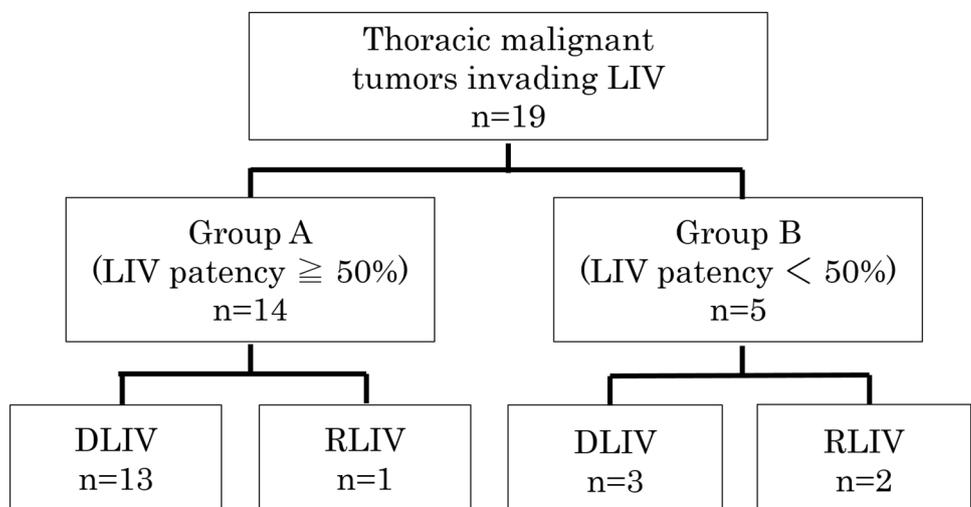


Fig. 2 First, thoracic malignant tumors invading LIV were divided into two groups; in group A, LIV patency was $\geq 50\%$, in group B, it was $\leq 50\%$. Next, each group was subdivided into two groups according to division or replacement of LIV. In group A, 13 patients were in the DLIV group and 1 in the RLIV group. In group B, 3 patients were in the DLIV group and 2 in the RLIV group. LIV left innominate vein, DLIV division of left innominate vein, RLIV replacement of left innominate vein



Perioperative care

All patients were extubated after the operation and transferred to the ICU. We did not start anticoagulant therapy routinely. Due to spreading and worsening of edema of the left neck and left upper limbs, we performed CECT scan to confirm the presence of thrombosis in the LIV. That was then followed by anticoagulant therapy. First, we started with heparin with the aim of increasing the activated partial thromboplastin time (APTT) ratio to 2.0. Next, we switched it to warfarin or a novel oral anticoagulant to set the level of prothrombin time–international normalized ratio (PT–INR) at around 2.0 as the edema was decreasing.

Results

Median age was 51 years and 68% of patients were male. Table 1 showed that there were 5 thymomas, 3 thymic cancers, 2 yolk sac tumors, 2 squamous lung cancers, 2 atypical carcinoids, 2 seminomas, 1 Hodgkin lymphomas, 1 malignant lymphoma (uncategorized), and 1 adenocarcinoma. A median sternotomy was used in 13 (68%) patients. The hemiclamsell incision was chosen for 6 patients. There

was no 30-day or 90-day mortality, and no case of severe morbidity such as cerebral infarction, coronary infarction, pulmonary thrombosis, acute respiratory distress syndrome and re-operation due to postoperative bleeding. Thrombosis in the LIV stump was observed in 2 (10.5%) patients only and both were in group A.

Case 1

Case 1 was an 80-year-old female who belonged to group A, in that her LIV was still open over 50% by CECT. She underwent surgery of thymoma by hemiclamsell incision and her left upper lobe and LIV was resected. On postoperative day (POD) 6, edema of her left neck and upper limb appeared and CECT was performed. Her left internal jugular vein and left subclavian vein were occluded by embolism occurring from the LIV stump (Fig. 3). On the same day, 10,000 units of heparin were given to control the APTT ratio at approximately 1.5–2.5. We switched the treatment to warfarin as the edema was decreasing. We performed CECT after 6 months to confirm its disappearance and stopped the warfarin (Fig. 4). Twelve months later, we confirmed that it had disappeared and performed CECT, once again.

Table 1 The patients' characteristics of group A and B

Case	Age	Sex	DLIV or RLIV	Embolism	Diagnosis	Tumor size (mm)	Operating time (min)	Blood loss (ml)
Group A								
1	30	Male	DLIV	–	Yolk sac tumor	115	440	1071
2	53	Male	RLIV	–	Thymic carcinoma	87	310	905
3	62	Female	DLIV	–	Thymoma	97	308	275
4	52	Male	DLIV	–	Thymoma	90	190	300
5	57	Male	DLIV	–	Thymoma	45	265	120
6	60	Male	DLIV	–	Sq. with neuroendocrine differentiation	130	285	1055
7	34	Male	DLIV	–	Hodgkin lymphoma	100	230	190
8	45	Male	DLIV	–	Atypical carcinoid	102	291	400
9	59	Male	DLIV	–	Thymic carcinoma	55	341	750
10	80	Female	DLIV	+	Thymoma	92	281	520
11	33	Male	DLIV	–	Malignant lymphoma	110	386	2007
12	56	Male	DLIV	–	Adenocarcinoma	125	265	460
13	36	Female	DLIV	–	Thymic carcinoma	75	169	100
14	44	Female	DLIV	+	Thymic carcinoma	35	183	250
Group B								
1	50	Male	RLIV	–	Seminoma	50	415	900
2	51	Female	DLIV	–	Atypical carcinoid	120	260	1783
3	71	Female	DLIV	–	Thymoma	100	145	230
4	45	Male	RLIV	–	Thymoma	140	453	3860
5	31	Male	DLIV	–	Thymoma	70	356	460

DLIV division of left innominate vein, RLIV replacement of left innominate vein

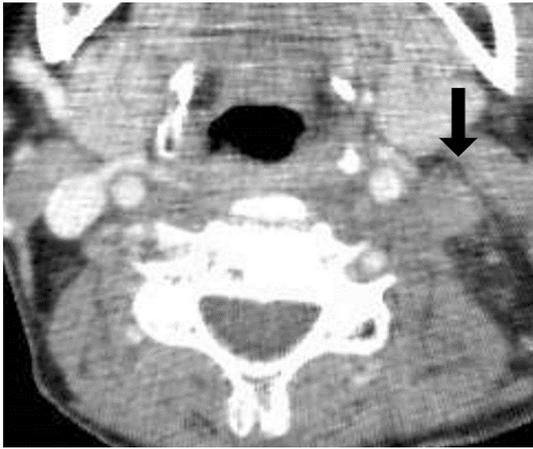


Fig. 3 CECT showed that her left internal jugular vein was occluded by embolism on POD 6. CECT contrast-enhanced computed tomography, POD postoperative day



Fig. 4 After we administered anticoagulation to her, the embolism disappeared

Case 2

Case 2 was a 44-year-old female who underwent surgery for thymic cancer by median sternotomy and her LIV was divided. On POD 5, edema of her left neck and left upper limb appeared and CECT was performed on the same day. There was embolism from the limit of LIV to both the left internal jugular vein and left external jugular vein. On that day, anticoagulant therapy was carried out using heparin. We switched it to warfarin as the edema was decreasing. We confirmed its disappearance and performed CECT after 6 months, and stopped the warfarin. Twelve months later, we confirmed that it had disappeared and performed CECT, once again.

Discussion

The mediastinum includes many important organs called “vital organs”, such as, the aorta, SVC, and LIV. In thoracic surgery, tumors sometimes invade mediastinal vital organs and make it difficult and challenging to achieve complete resection. In this study, we focused on patients with mediastinal tumors invading the LIV. After dividing the LIV to remove tumors en bloc, surgeons are faced with the problem of whether to start anticoagulant therapy to prevent embolism. Thus, we need to consider the risks and benefits of anticoagulation after dividing the LIV and we think that it would be safer to withhold anticoagulation than to routinely start it postoperatively because of two reasons. First, postoperative bleeding and intra cranial hemorrhage induced by anticoagulation are rare, but they are much more crucial and irreversible than edema of the left neck and upper limb induced by embolism of LIV [9–11]. Second, once edema is observed, it is not too late to start anticoagulation treatment as the edema is expected to disappear. In this study, 19 patients with tumors invading the LIV were registered and anticoagulation was not initiated after surgery. As such, only 2 patients had edema due to embolism, which disappeared after anticoagulant therapy was administered.

The reason why we categorized patients into two groups based on their preoperative LIV patency was because preoperative LIV flow could be one of the risk factors of postoperative embolism. As mediastinal tumors increase and invade LIV gradually, the patency of LIV occludes, and collateral flow develops [12]. In patients with poor blood flow in the LIV (group B), the blood flow of the collateral almost could not change because it developed after the LIV resection, which was not the case in patients with normal blood flow in the LIV (group A).

Usually, we thoracic surgeons do not routinely administer anticoagulant therapy postoperatively to patients who underwent lobectomies as embolism in the PV stump is not expected. Similarly, we do not generally expect embolism in the LIV stump and are therefore not inclined to initiate anticoagulation routinely after division of LIV. However, Ohtaka et al. showed that thrombosis developed in 13.5% of patients who underwent LUL. They presumed that “turbulent flow or stasis of blood occurs in the long PV stump and develops into thrombosis in stump”. The risk of thrombosis in the stump is correlated with the length of PV stumps, and longer PV stumps tend to create thrombosis more frequently [13–15]. Thus, we need to observe the findings of increasing edema of left neck and upper limbs after dividing the LIV as “turbulent flow or stasis of blood occurs in long LIV stumps and develop into thrombosis in the stump”.

The limitation of this study is that the number of cases is limited and a statistical analysis could not be performed

on these patients. There is an urgent need to accumulate evidence to clarify many clinical questions statistically, such as the risk factors of embolism. Meanwhile, these situations were rare in our study and our results were tangible. As such, they will likely contribute in determining the perioperative treatment strategy for patients with mediastinal tumors invading the LIV. However, we need to investigate the results in a multicenter study in the near future. In conclusion, division of the LIV was safe as there was no mortality or severe morbidity. Moreover, there was no need to start routine anticoagulant therapy after dividing the LIV because the frequency of the embolism in the LIV stump was low and any embolism was expected to have disappeared prior to starting anticoagulant therapy.

Compliance with ethical standards

Conflict of interest None declared.

References

1. Chitoor B, Sudhakar SAJ. Safety of left innominate vein division during aortic arch surgery. *Ann Thorac Surg* 2000;70:856–8.
2. Bashist B, Parisi A, Frager D, Suster B. Abdominal CT findings when superior vena cava, brachiocephalic vein or subclavian vein is obstructed. *Am J Roentgenol*. 1996;167:1457–63.
3. Suzuki K, Asamura H, Watanabe S, Tsuchiya R. Combined resection of superior vena cava for lung carcinoma: prognostic significance of patterns of superior vena cava invasion. *Ann Thorac Surg*. 2004;78:1184–9 (discussion 9).
4. Spaggiari L, Leo F, Veronesi G, Solli P, Galetta D, Tatani B, et al. Superior vena cava resection for lung and mediastinal malignancies: a single-center experience with 70 cases. *Ann Thorac Surg*. 2007;83:223–9 (discussion 9–30).
5. Lanuti M, De Delva PE, Gaissert HA, Wright CD, Wain JC, Allan JS, et al. Review of superior vena cava resection in the management of benign disease and pulmonary or mediastinal malignancies. *Ann Thorac Surg*. 2009;88:392–7.
6. Sekine Y, Suzuki H, Saitoh Y, Wada H, Yoshida S. Prosthetic reconstruction of the superior vena cava for malignant disease: surgical techniques and outcomes. *Ann Thorac Surg*. 2010;90:223–8.
7. Shintani Y, Ohta M, Minami M, Shiono H, Hirabayashi H, Inoue M, et al. Long-term graft patency after replacement of the brachiocephalic veins combined with resection of mediastinal tumors. *J Thorac Cardiovasc Surg*. 2005;129:809–12.
8. Oizumi H, Suzuki K, Banno T, Matsunaga T, Oh S, Takamochi K. Patency of grafts after total resection and reconstruction of the superior vena cava for thoracic malignancy. *Surg Today*. 2016;46:1421–6.
9. Alberts MJ, Bhatt DL, Smith SC Jr, Rother J, Goto S, Hirsch AT, et al. Risk factors and outcomes for patients with vascular disease and serious bleeding events. *Heart*. 2011;97:1507–12.
10. Tempaku A. Intracranial hemorrhage during administration of a novel oral anticoagulant. *J Rural Med*. 2016;11:69–72.
11. Inoue H, Uchiyama S, Atarashi H, Okumura K, Koretsune Y, Yasaka M, et al. Post-marketing surveillance on the long-term use of dabigatran in Japanese patients with nonvalvular atrial fibrillation: preliminary report of the J-dabigatran surveillance. *J Arrhythm*. 2016;32:145–50.
12. Yonei A, Sari A. Reversal of blood flow in the internal jugular vein. *Anesthesiology*. 1991;74:634–5.
13. Ohtaka K, Hida Y, Kaga K, Kato T, Muto J, Nakada-Kubota R, et al. Thrombosis in the pulmonary vein stump after left upper lobectomy as a possible cause of cerebral infarction. *Ann Thorac Surg*. 2013;95:1924–8.
14. Ohtaka K, Hida Y, Kaga K, Takahashi Y. Left upper lobectomy can be a risk factor for thrombosis in the pulmonary vein stump. *J Cardiothorac Surg*. 2014;9:5–9.
15. Ohtaka K, Takahashi Y, Umemura S. Blood stasis may cause thrombosis in the left superior pulmonary vein stump after left upper lobectomy. *J Cardiothorac Surg*. 2014;9:159–65.