

Acute Pulmonary Thromboembolism after Distal Gastrectomy: An Appraisal of the Guidelines for Preventing Pulmonary Thromboembolism/Deep Vein Thrombosis

Tetsuro Matsunobu^{1,2}, Masanori Watanabe^{1,2}, Hideki Bou^{1,2},
Naoto Takahashi³, Akira Tokunaga^{1,2} and Takashi Tajiri¹

¹Surgery for Organ Function and Biological Regulation, Graduate School of Medicine, Nippon Medical School

²Institute of Gastroenterology, Nippon Medical School Musashi Kosugi Hospital

³Department of Internal Medicine, Nippon Medical School Musashi Kosugi Hospital

Abstract

We report a case of acute pulmonary thromboembolism after gastrectomy. A 67-year-old woman was found to have gastric cancer and a giant lipoma in the ascending colon. We performed distal gastrectomy and enucleation of the ascending colon lipoma. On postoperative day 9, an acute pulmonary thromboembolism developed, and thrombolytic therapy was urgently performed. The 2004 Japanese guidelines for preventing pulmonary thromboembolism/deep vein thrombosis are discussed in relation to the present case.

(J Nippon Med Sch 2008; 75: 175–180)

Key words: guidelines for the prevention of venous thromboembolism, acute pulmonary thromboembolism

Introduction

Surgeons should monitor patients for pulmonary thromboembolism (PTE) during the perioperative period, as delayed treatment can result in an unfavorable outcome. In February 2004, the Japanese Society of Thrombosis and Hemostasis and the Pulmonary Embolism Study Association published guidelines for preventing PTE/deep vein thrombosis (DVT) (venous thromboembolism)¹. In April 2004, the National Health Insurance medical reward system was revised, and 305 points per admission were added as a preventive management fee for evaluating the need for PTE prophylaxis. Additionally, newspaper reports of sudden death

after surgery have captured the general public's interest. In Europe and the United States, PTE is the second most frequent disease, following coronary disease and cerebrovascular disorders. In Japan, however, the annual number of patients found to have PTE is 3,492, or approximately 1/25 of that in the United States². The adoption of a Western lifestyle in Japan may have increased the incidence of PTE, and several studies have indicated that the incidence in Japan is now similar to those in Europe and the United States, despite the low rate of clinical diagnosis in Japan³. In the present case report, we reconsider the Japanese guidelines and methods for preventing PTE during the perioperative period.

Correspondence to Tetsuro Matsunobu, MD, PhD, Institute of Gastroenterology, Nippon Medical School Musashi Kosugi Hospital, 1-396 Kosugi-cho, Nakahara-ku, Kawasaki, Kanagawa 211-8533, Japan

E-mail: nobu@nms.ac.jp

Journal Website (<http://www.nms.ac.jp/jnms/>)

Case Report

A 67-year-old woman with no complaints and a history of hypertension, atrial fibrillation, and iron-deficiency anemia was treated. She was taking propranolol, nifedipine, aspirin, sodium ferrous citrate, and digoxin. No relevant family history was noted. The patient was referred to our hospital because of a positive reaction on a fecal occult blood test performed at a local clinic. Endoscopy of the upper digestive tract revealed gastric cancer involving the antral region. Next, endoscopy of the lower digestive tract showed a giant lipoma in the ascending colon. Aspirin was discontinued 7 days before examination, in accordance with our hospital's regulations. A physical examination on admission revealed a standing height of 147 cm, a body weight of 53 kg, and a body-mass index (BMI) of 24.5 kg/m². The results of blood and biochemical examinations, including a coagulation test, were within the normal limits. The electrocardiographic findings were also within the normal ranges. Chest radiography revealed a cardiothoracic ratio (CTR) of 59.6%, suggesting cardiac hypertrophy. Echocardiography examination revealed an ejection fraction (EF) of 74%. The absence of thrombi was confirmed.

Distal gastrectomy (D2) and enucleation of the ascending colon lipoma were performed; the duration of the surgery was 4 hours and 9 minutes. The volume of blood loss was 500 mL. General anesthesia and epidural anesthesia were performed. For thrombus prevention, a graduated-compression elastic stocking was applied. However, pharmacological methods of thrombus prophylaxis were not performed.

On postoperative day 2, the patient did not sit up in bed, despite the physician's recommendation. On postoperative day 5, oral feeding (liquid diet) was resumed. Simultaneously, aspirin therapy was restarted. However, the patient's dietary intake was low, and vomiting was noted; therefore, the ingestion of the oral agent could not be confirmed. Furthermore, the patient did not sit up in bed, and the period of recumbency was prolonged.

On postoperative day 9, dyspnea rapidly developed when the patient stood up to walk to the rest room, resulting in hypoxemia. The patient was admitted to the intensive care unit for intensive

care/management. Under a tentative diagnosis of PTE, a detailed examination and treatment were started.

The laboratory data and the result of blood gas analysis at the time of PTE onset are shown in **Table 1**. The chest X-ray findings were compatible with a diagnosis of PTE, and the contrast-enhanced computed tomography (CT) images of the chest showed a giant thrombus shadow. The chest X-ray and CT findings are shown in **Figure 1**.

After stable respiratory/circulatory kinetics were confirmed under artificial respiration, the above examination procedures were performed, and the patient was confirmed to have PTE. Angiography was immediately performed. After confirming the absence of deep vein thrombosis (DVT), a giant-thrombus related complete occlusion of the right pulmonary artery and a partial occlusion of the left pulmonary artery were observed (**Fig. 2a**). Therefore, 1.4 million units of the tissue plasminogen activator (t-PA) (alteplase) was selectively administered for thrombolytic therapy, followed by suctioning (**Fig. 2b, 3**). After the patency of the right pulmonary artery was confirmed (**Fig. 2c**), 15,000 units of heparin was continuously infused, and a sheath was placed in the right inguinal region. The patient was readmitted to the intensive care unit. The following morning, the patient's respiratory and circulatory kinetics had stabilized. However, swelling and pain were noted at the sheath insertion site, and a venography of the lower limbs was performed. A DVT was observed in the lower part of the right thigh (**Fig. 4**), and a temporary inferior vena cava (IVC) filter was inserted for thrombolysis. The patient was then transferred to the intensive care unit of the Nippon Medical School Hospital for thrombolysis of the left pulmonary artery and for suctioning. A thrombus of the left pulmonary artery formed in the superior lobe and affected the artery's patency. The patency of the veins of the right lower limb was confirmed, and the patient was again transferred to Musashi-Kosugi Hospital. The patient's general condition stabilized, and the patient was discharged.

Discussion

According to the results of a survey regarding the perioperative onset of pulmonary embolism (2004),

Table 1 Laboratory data and blood gas analysis at onset

Laboratory data				Blood gas analysis	
WBC	12,180 / μ L	ALP	174 IU/L	pH	7.34
RBC	457×10^6 / μ L	GOT	28 IU/L	pCO ₂	33 mmHg
Hb	13.3 g/dL	GPT	14 IU/L	pO ₂	56 mmHg
Plt	24.6×10^3 / μ L	γ -GTP	7 IU/L	HCO ₃ ⁻	17.3 mmol/L
PT	15.1 sec	T-Bil	0.8 mg/dL	SBE	- 7.1 mmol/L
	65.9 %	D-Bil	0.3 mg/dL	anion gap	16.6 mmol/L
PT (INR)	1.31	LDH	370 IU/L	SatO ₂	87.4 %
APTT	29.1 sec	AMY	43 IU/L		
Fib	236 mg/dL	LAP	64 IU/L		
AT-III	55.8 %	CPK	82 IU/L		
FDP	481 μ g/mL	TP	6.1 g/dL		
D-dimer	203.6 μ g/mL	Alb	3 g/dL		
		BUN	12.1 mg/dL		
		Cre	0.3 mg/dL		
		Na	131 mEq/dL		
		K	3.6 mEq/dL		
		Cl	97 mEq/dL		
		BS	118 mg/dL		
		CRP	8.9 mg/dL		

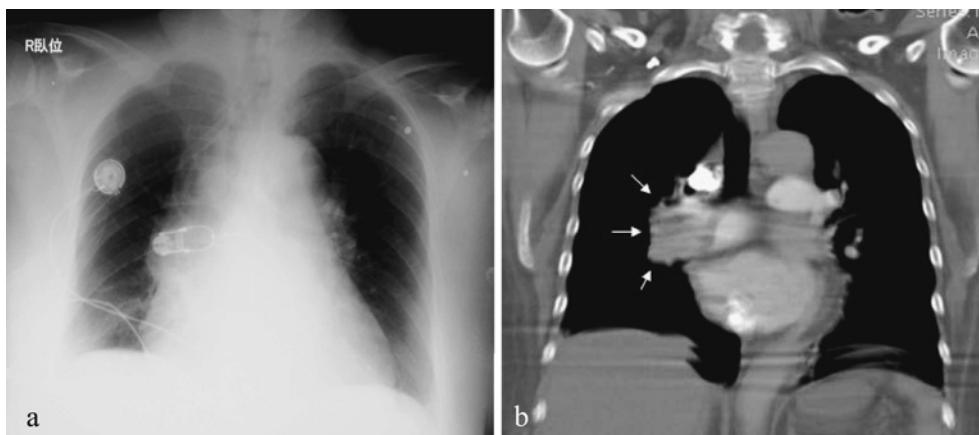


Fig. 1 **a:** X-ray showing right diaphragmatic elevation and the disappearance of a vascular shadow in the right lung. **b:** Contrast enhanced CT scan of the chest shows a giant thrombus shadow at the root of the right pulmonary artery (**arrows**) and blockage of blood flow into the right lung and left superior lobe.

reported by the Pulmonary Embolism Study Working Group, the Japanese Society of Anesthesiology, pulmonary embolism was observed in 409 of the 1,131,154 patients who were treated in departments of anesthetics at 642 hospitals from which survey responses were collected in 2004. PTE frequently occurred in women aged 66 to 85 years, who had undergone a laparotomy or hip or limb surgery. Furthermore, the risk factors for PTE included malignant tumors, obesity (BMI>25 kg/m²), and prolonged recumbency (>4 days)⁴. The

background of the present patient was consistent with these characteristics, suggesting typical PTE. With respect to the guidelines' risk levels, the present case was classified as a major surgery for cancer in a patient older than 40 years. According to the guidelines, intermittent pneumatic compression (IPC) or low-dose unfractionated heparin should have been used rather than elastic stockings to prevent PTE (**Table 2**). Institutional guidelines for the prevention of PTE have been prepared by some hospitals⁵, as reported by Nagasako et al.; these

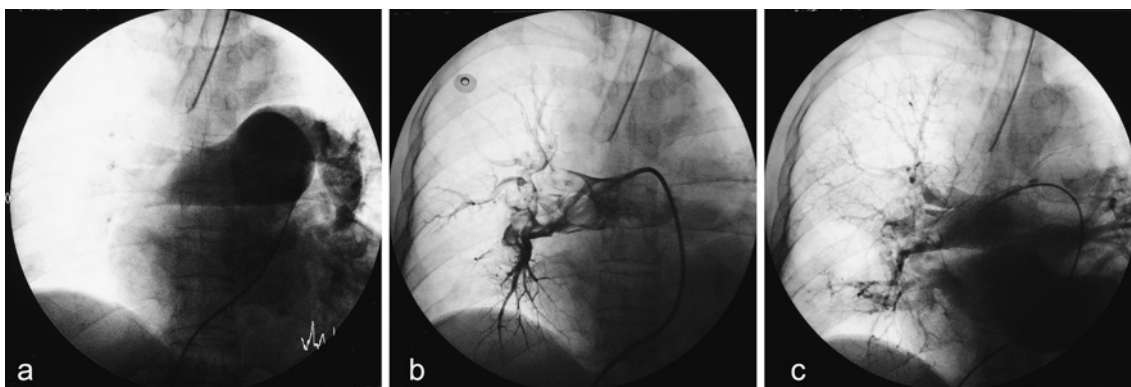


Fig. 2 **a:** A giant thrombus-related complete occlusion of the right pulmonary artery and partial occlusion of the left pulmonary artery are visible. **b:** View during selective thrombolytic and suction therapy. **c:** View after confirming the patency of the right pulmonary artery.



Fig. 3 Thrombus removed by suctioning after thrombus aspiration dissolution therapy.



Fig. 4 Venography of the lower limbs showing a DVT in the right lower thigh.

guidelines are usually based on risk scores and preventative strategies for identifying patients at high risk for perioperative PTE. In other hospitals, elastic stockings are combined with IPC for all patients, because interpretations of the guidelines differ in many respects among surgeons and anesthesiologists. In our hospital, elastic stockings are used from the day before surgery by all patients. However, surgeons may select additional strategies for individual patients after referring to the guidelines. Furthermore, most patients undergoing surgery in our department are older than 40 years and have digestive tract cancer, placing them in a high-risk category. In almost all our patients, IPC or low-dose unfractionated heparin should be used. However, for financial reasons, IPC cannot be performed in all patients. Our hospital is now holding study meetings to prepare an institutional

manual for preventing future relapses.

Screening for DVT/PTE is not mentioned in the guidelines. However, Goldhaber et al. have reported that DVT and PTE can be ruled out in patients with a D-dimer level of less than 500 ng/mL, suggesting the usefulness of this variable for preoperative screening⁶. In addition, Johanning et al. have reported that the D-dimer level can serve as an

Table 2 Risk classification and prevention of venous thromboembolism for surgery (extracted from the Japanese Guideline for Prevention of Venous Thromboembolism)

Risk level	Surgery	Prevention
Low risk	Non-major surgery in patients aged less than 60 years. Major surgery in patients aged less than 40 years.	Early recumbency and positive exercise.
Middle risk	Non-major surgery in patients aged over 60 years or with risk factors. Major surgery in patients aged over 40 years or with risk factors.	Elastic stocking or intermittent pneumatic compression.
High risk	Major surgery for cancer in patients aged over 40 years.	Intermittent pneumatic compression or low-dose unfractionated heparin.
Maximum risk	Major surgery in the presence of venous thromboembolism or a thrombotic predisposition.	Combination of low-dose unfractionated heparin and intermittent pneumatic compression, or the combination of low-dose unfractionated heparin and elastic stocking.

Instead of the combination of low-dose unfractionated heparin and intermittent pneumatic compression/elastic stocking, adjusted-dose unfractionated heparin and adjusted-dose Warfarin may be selected.

Thrombotic predisposition: Congenital predispositions such as anti-thrombin deficiency, protein C deficiency, and protein S deficiency; and acquired predispositions such as anti-phospholipid antibody syndrome

Major surgery: There is no close definition, but abdominal surgery and other procedures requiring 45 minutes or more are regarded as major surgery. This category is comprehensively evaluated based on anesthesia, the volume of blood loss, volume of transfused blood, and duration of surgery.

adjunct to screening for DVT and that emergency duplex ultrasound screening is not required if the D-dimer status is negative and the difference in the calf circumference is less than 2 cm⁷.

The onset of PTE is characterized by three signs: characteristic chest X-ray findings (diaphragmatic elevation, retention of pleural effusion, and the disappearance of a vascular shadow), a blood flow defect on contrast-enhanced CT, and single or multiple wedge-shaped perfusion defects on pulmonary blood flow scintigraphy⁸. Magnetic resonance angiography (MRA) has also been reported to be useful for the detection of PTE⁹. However, resuscitation and survival treatment is predominantly performed in patients with PTE and rapidly deteriorating conditions. When PTE is suspected, therapeutic angiography should immediately be performed as a standard procedure. Treatment often consists of thrombolytic therapy: selective thrombolytic therapy via the insertion of a Swan-Gantz catheter, pulse infusion thrombolytic therapy, or pulse spray thrombolytic therapy¹⁰⁻¹². In the present case, the contrast-enhanced CT findings and the D-dimer level suggested PTE, and an angiography was immediately performed.

Subsequently, selective thrombolytic therapy with t-PA (alteplase) and suction was successful. Therefore, we considered this treatment to be appropriate. However, why DVT occurred at the sheath insertion site of the lower limb despite heparinization after suction is unclear. Furthermore, the discontinuation of aspirin therapy before endoscopy or surgery may also have contributed to the development of PTE.

With the recent increase in medical malpractice lawsuits, guideline-based practice is essential. According to a survey conducted by the Pulmonary Thromboembolism Working Group, the Japanese Society of Anesthesiology, the incidence of PTE undergoing surgery (in 2003) to 3.61 (in 2004) after the preparation of guidelines in 2004 and the introduction of the preventive management fee. However, as described at the beginning of the guidelines, no evidence for the efficacy of PTE/DVT prevention has been obtained in Japan. The guidelines were prepared based on the basis of epidemiological data in Japanese people with reference to prevention guidelines established in accordance with the International Consensus

Statement, published by the Consensus Conference on Antithrombotic Therapy (American College of Chest Physicians [ACCP]) and the International Union of Angiology¹. Regarding these guidelines, although the risk levels in the Japanese guidelines were classified using the same risk factors used by the ACCP guidelines, the risk factors were stratified one rank lower than those in the ACCP guidelines, even in patients with the same risk factor profile; thus, risk-level-matched prevention is recommended. For the preventive guidelines, preventive methods have been recommended according to risk stratification, but individual patient factors, including differences related to technique and anesthesia, are important for surgeons; therefore, the selection of a preventative method may depend on the attending physician's judgment after guidelines for other disorders have been compared. For example, according to the Pulmonary Embolism Study Working Group, the Japanese Society of Anesthesiology, prevention and follow-up for a postoperative period of 1 week are needed in patients with malignant disorders⁴. Thus, the period of physical and pharmacological prevention may differ among various disorders. However, concrete situations are not described in the present guidelines. On August 9, 2007, The American College of Obstetrics and Gynecology (ACOG) updated its guidelines for DVT and PTE associated with gynecologic surgery. In this update, the ACOG showed a more concrete prevention and treatment strategy for DVT and PTE¹³. The guidelines are recognized as just that — guidelines, not a consensus — and are socially significant. Consequently, the guidelines should be revised to produce evidence-based, concrete preventive guidelines. Finally, the present case suggests that surgeons must utilize preventive strategies to avoid the development of DVT/PTE. At least we surgeons must follow these guidelines, then carry out preventive measures against DVT/PTE in individual patients.

Acknowledgements: We thank Dr. Tadashi Kaneshiro (Department of Radiology, Nippon Medical School Musashi Kosugi Hospital) and Dr. Takeshi Yamamoto (Intensive Care Unit, Nippon Medical School Hospital) for their cooperation.

References

1. Japanese guideline for prevention of venous thromboembolism: Editorial committee on Japanese guideline for prevention of venous thromboembolism, 2004 (in Japanese); Medical Front Int., Tokyo.
2. Nakamura M, Sakuma M, Yamada N, et al: Risk factors of acute pulmonary thromboembolism in Japanese patients hospitalized for medical illness: results of a multicenter registry in the Japanese society of pulmonary embolism research. *J Thromb Thrombolysis* 2006; 21: 131–135.
3. Kumasaka N, Sakamura M, Shirato K: Incidence of pulmonary thromboembolism in Japan. *Jpn Circ J* 1999; 63: 439–441. (in Japanese)
4. Kuroiwa M, Furuya H, Seo N, et al: Incidence and characteristics of perioperative pulmonary thromboembolism in Japan in 2004. *Masui* 2006; 55: 1031–1038. (in Japanese with English abstract)
5. Nagasako Y, Misawa K, Sano H, et al: Analysis of high risk group of perioperative pulmonary thromboembolism using risk score and precautionary measures. *Geka* 2005; 67: 453–458. (in Japanese)
6. Goldhaber SZ, Simmons GR, Elliot CG, et al: Quantitative plasma D-dimer levels among patients undergoing pulmonary angiography for suspected pulmonary embolism. *JAMA* 1993; 270: 2819–2822.
7. Johanning JM, Franklin DP, Thomas DD, et al: D-dimer and calf circumference in the evaluation of outpatient deep venous thrombosis. *J Vasc Surg* 2002; 36: 877–880.
8. Perrier A, Roy PM, Sanchez O, et al: Multidetector-row computed tomography in suspected pulmonary embolism. *N Engl J Med* 2005; 352: 1760–1768.
9. Altes TA, Mai VM, Munger TM, et al: Pulmonary embolism: comprehensive evaluation with MR ventilation and perfusion scanning with hyperpolarized helium-3, arterial spin tagging, and contrast-enhanced MRA. *J Vasc Interv Radiol* 2005; 16: 999–1005.
10. Kiyama T, Yoshioka M, Yoshiyuki T, et al: Acute pulmonary thromboembolism on 2 days after gastrectomy. *J Nippon Med Sch* 2002; 69: 504–507. (in Japanese)
11. Bookstein JJ, Fellmeth B, Roberts A, et al: Pulsed-spray pharmacomechanical thrombolysis: preliminary clinical results. *Am J Roentgenol* 1989; 152: 1097–1100.
12. Saito T, Taniguchi I, Nakamura S, et al: Pulse-spray thrombolysis in acutely obstructed coronary artery in critical situations. *Cath Cardiovasc Diag* 1997; 40: 101–108.
13. Thomas CK, Kristin KZ: Venous thromboembolism in obstetrics and gynecology. *Obstet Gynecol* 2007; 109: 761–777.

(Received, October 1, 2007)

(Accepted, March 6, 2008)