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# Postoperative thoracic hemorrhage after right upper lobectomy with thoracic wall resection during rivaroxaban anticoagulant therapy for deep leg vein thrombosis: A case report



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## ABSTRACT

**INTRODUCTION:** Postoperative pulmonary embolism (PE) is the one of the most important complications after thoracic surgery. This complication after the surgery is often treated by new anticoagulant drug, such as rivaroxaban, which does not need to the monitoring of blood coagulation system. We experienced postoperative bleeding case during anticoagulant therapy using rivaroxaban.

**PRESENTATION OF CASE:** The patient underwent a right upper lobectomy with lung and chest wall resection for lung cancer. On postoperative day (POD) 10, we started to use rivaroxaban to treat the deep vein thrombosis (DVT). Four days after starting the rivaroxaban treatment, severe surgical site hemorrhage occurred, which led to the need for the infusion of concentrated red cells (CRC). After stopping the rivaroxaban, the thoracic bleeding ceased. Because the event occurred so long after the surgery, and because the bleeding stopped after withdrawal of treatment, we believe that rivaroxaban induced the thoracic bleeding.

**CONCLUSION:** Some reports in the field of orthopedics (Turpie et al., 2009) have noted that rivaroxaban is effective to prevent postoperative DVT. However, there were few reports that invited the attention to postoperative bleeding be induced by rivaroxaban. Thus, we describe this case in order to alert clinicians to the potential bleeding risks associated with the administration of rivaroxaban postoperatively.

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## 1. Introduction

Postoperative pulmonary embolism (PE) is one of the most important acute and chronic complications after thoracic surgery. Deep vein thrombosis (DVT) often causes PE. Moreover, venous thromboembolism has been found to increase the 30-day mortality after cancer-related surgeries from 1.2% to 8.0% [2]. It was previously reported that the risk of DVT after lung cancer surgery within the first month postoperatively was 0.8% [3].

Rivaroxaban, a new, oral, direct factor Xa inhibitor, is an anticoagulant. In Japan, rivaroxaban is currently licensed for use in patients with non-valvular atrial fibrillation to prevent thrombosis. Moreover, rivaroxaban is used clinically after total hip arthro-

**Abbreviations:** DVT, deep vein thrombosis; POD, postoperative day; CRC, concentrated red cells; PE, pulmonary embolism; THA, total hip arthroplasty; VKA, vitamin K antagonists; CT, computed tomography; CXR, chest X-ray; Hb, hemoglobin; DIC, disseminated intravascular coagulation.

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plasty (THA) and knee replacement surgery for the prevention of venous thromboembolism [1]. The RECORD 1–4 Trials found that a once daily oral dose of rivaroxaban was more effective for extended prophylaxis than a once daily dose of subcutaneous enoxaparin in patients undergoing the surgeries mentioned above, with the two drugs having similar safety profiles [1]. Moreover, one report showed that rivaroxaban resulted in improvement satisfaction compared with enoxaparin/vitamin K antagonists (VKA) among patients with DVT [4]. However, although it had been reported that rivaroxaban was associated with a lower risk of severe bleeding [4] the main side effect associated with this new drug is severe hemorrhage [5].

We experienced the case of a patient with DVT who had undergone the resection of a lung and chest wall, who started treatment with rivaroxaban on POD 10 and developed thoracic hemorrhage on POD 14. No similar case has been reported previously, although the postoperative use of rivaroxaban has been suggested to be associated with the risk of bleeding in other situations. We therefore believe that this is the important case of thoracic hemorrhage induced by rivaroxaban, which was prescribed to treat DVT more than a week after surgery. We report this case to alert clinicians to the possibility that the postoperative use of rivaroxaban may

induce severe surgical site bleeding. The case report has been reported online with the SCARE criteria [6].

## 2. Presentation of case

A 74-year-old Japanese male underwent right upper lobectomy of the lung and mediastinal lymph node resection (ND2a-2) with costectomy of the second to fourth ribs and resection of the transverse process of the second to third thoracic vertebra for treatment of right lung cancer (pT3N0M0, stage IIIA, adenocarcinoma). This was performed after embolization of the feeding vessels (the second, third, fourth intercostal artery) to the tumor to reduce the bleeding during the surgery. There were many neovascular vessels and engorgement vessels on the chest wall near the tumor. We ligated and involved the second, third, fourth intercostal vessels. We restrained hemorrhage from the chest wall near the resection of the vertebra by using TachoSil. The length of the operation was 13 h and 45 min. The intraoperative blood loss was 7200 ml. We used 3640 ml of CRC transfusion, 3600 ml of fresh frozen plasma, 200 ml of platelet transfusion and 2000 ml of albumin during the operation. On POD 8, enhanced whole-body computed tomography (CT), which was performed to identify the cause of prolonged hypoxia, showed a right deep leg vein thrombosis (Fig. 1). However, the cause of the prolonged hypoxia was unclear. On POD 10, we started anticoagulant therapy with rivaroxaban (15 mg/day) to treat the DVT. On POD 12, the chest drain was removed after we made sure that there was normal pleural fluid and no air leaks and a chest X-ray (CXR) taken on POD 13 did not show marked increase of pleural effusion. However, because a CXR taken on POD 14 showed an acute increase of the right pleural effusion (Fig. 2) and because the patient's hemoglobin (Hb) level decreased to 2.2 g/dl we decided to reinsert the chest drain into the right pleural space.

We diagnosed a right thoracic hemorrhage because of the bloody drainage. There was no clinical evidence of postoperative disseminated intravascular coagulation (DIC) (international normalized ratio of prothrombin time, 1.18; activated partial thromboplastin time, 43.7 s; fibrin degradation products, 22.5 µg/mL). There was 2730 ml of bloody drainage. The rivaroxaban treatment was stopped immediately, and 280 ml of CRC was infused. On POD 19, we removed the drain because the bloody drainage had stopped. We observed that the patient had no further exacerbations of the thoracic hemorrhage after stopping the rivaroxaban treatment.

## 3. Discussion

We herein reported the case of thoracic hemorrhage apparently induced by rivaroxaban, which was administered for the treatment of DVT after resection of the right lung and chest wall. We want to draw attention to the fact that even if there is a low risk of postoperative bleeding because a long time has elapsed since surgery, it is not beyond the realm of possibility that the use of rivaroxaban in the perioperative period may cause postoperative bleeding.

It had been reported that rivaroxaban can prevent DVT after THA and knee replacement surgery, and is also useful for the treatment of DVT [1]. Moreover, 10 mg of oral rivaroxaban once daily was reported to be associated with the same risk of postoperative bleeding as 40 mg of enoxaparin administered subcutaneously once daily (the risk of bleeding in the rivaroxaban group was 6.1%, that in the enoxaparin was 5.9%) [1]. On the other hand, it was reported that four weeks after THA, the patients taking rivaroxaban to prevent DVT were more likely to have acute-onset severe gastrointestinal tract hemorrhage [5]. However, we could not find any previous case reports of postoperative surgical site hemorrhage during rivaroxaban treatment.



Fig. 1. Enhanced inferior limb CT on POD 8. This CT scan shows that the right leg vein had localized vasodilations and deficits (arrow).

It was extremely improbable that our case did have continued postoperative bleeding, because the chest drain had serous drainage of fluid on POD 10. In addition postoperative DIC did not exist when the thoracic bleeding occurred. For these reasons, and because stopping treatment led to resolution of the bleeding, we strongly suspect that rivaroxaban induced the surgical site bleeding. We hypothesized that the patient's postoperative condition caused vascularization, and that the new blood vessel growth induced bleeding. There were several likely contributors to this finding. First, we performed an invasive surgery, which included chest wall resection. Second, this case had prolonged postoperative pneumonia [7]. Third, we performed embolization of the feeding vessels to the tumor [8]. Some anticoagulation monitoring is essential for conventional anticoagulant therapy after surgery, such as that involving warfarin, heparin or low molecular weight heparin.



**Fig. 2.** A chest X-ray (CXR) on POD 14 shows that the right pleural fluid increased rapidly, and the right lung field had permeability decay.

On the other hand, rivaroxaban does not require such monitoring. Thus, in postoperative anticoagulation therapy after a highly invasive surgery, such as our case, we believe that it is safer to use conventional anticoagulant therapy than rivaroxaban, although some previous reports [1,4] suggested that rivaroxaban is associated with a risk of postoperative bleeding equivalent to that of conventional anticoagulant therapy. It is likely that the indications for rivaroxaban will be expanded to include not only the field of orthopedics, but also other fields after surgery to prevent DVT.

#### 4. Conclusion

We want to raise the alarm that using rivaroxaban after an invasive surgery, such as that performed in our case, requires careful attention, and that patients treated with the agent after such surgeries should be closely monitored.

#### Conflict of interest

There were no conflicts of interest or financial interests for any of the authors.

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#### Ethical approval

We got ethical approval from ethical committee of University Occupational and Environmental health, Japan.

#### Consent

Written and signed consent form the patient to publish a report has been obtained.

#### Authors' contributeons

Taiji Kuwata; Study design, writing.  
 Masatoshi Kanayama; Data collection.  
 Ayako Hirai; Data collection.  
 Shuichi Shinohara; Others.  
 Masaru Takenaka; Others.  
 Soichi Oka; Others.  
 Yasuhiro Chikaishi; Others.  
 Naoka Imanishi; Others.  
 Koji Kuroda; Others.  
 Fumihiko Tanaka; Study design.

#### Guarantor

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