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ORIGINAL RESEARCH

Clinical Indicators to Guide Reoperation for Postoperative Hemorrhage After Pulmonary Resection for Malignancy: A Single-Institutional Experience of 22 Cases

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Background: This study investigated perioperative clinical information, surgical findings, and postoperative courses of patients who underwent reoperation due to bleeding after the surgery for pulmonary malignancies.

Methods: We identified patients who underwent reoperation due to postoperative bleeding from 6989 patients who had had operations for pulmonary malignancies between January 2007 and July 2019. Data were retrospectively collected from medical charts.

Results: Twenty-two patients (0.3%) underwent reoperation for hemostasis. The reason for reoperation was a shock state with minimum systolic blood pressure < 90 mm Hg in 12 patients (55%), persistent bloody drainage of 100 mL/h or more in 15 patients (68%), and intrathoracic hematoma on a chest X-ray image in 14 patients (64%). All those three findings were observed in five patients (23%), two in nine patients (41%), and one in eight patients (36%). The source of bleeding could not be identified during reoperation in four patients (18%). In the regression analysis, the coefficient of determination between the amount of drainage from a chest drain and the volume of intrathoracic hematoma found during reoperation was 0.31, indicating poor correlation. Postoperative complications and death occurred in two (9%) and zero patients, respectively.

Conclusion: Reoperation due to bleeding is required in certain cases. The amount of drainage from a chest drain does not necessarily reflect the volume of intrathoracic hematoma and it is hard to estimate the total amount of bleeding. The decision to perform reoperation for hemostasis should be comprehensively made on the basis of clinical signs and chest X-ray findings.

Keywords: bleeding, hemostasis, lung neoplasms, thoracic surgery, intraoperative complications, reoperation

Introduction

The incidence of serious complications after surgery for primary lung cancer was reported to be 7.9% (1491/18,800) according to the US Society of Thoracic Surgeons General Thoracic Database[1] and 5.6% according to 2014 analysis results of surgery cases from the National Clinical Database in Japan.[2] Among those cases, the incidence of reoperation was reported to be 1.0–4.6%.[3–5] Postoperative bleeding is the most common reason for reoperation and accounts for 27.3–73.3% of the cases.[3–5]

Precise assessment of patient's conditions is required for bleeding after pulmonary resection in order to promptly decide the necessity of adjustment of the infusion volume, administration of hemostatic agents, transfusion, or reoperation for hemostasis. Since the delay of reoperation for postoperative bleeding may cause serious complications including death, surgeons are required to properly decide the necessity of reoperation. Some studies reported risk factors for postoperative bleeding,[6,7] while very few studies examined clear criteria to decide if reoperation for hemostasis is necessary or not. Accordingly, such decision has been made on the basis of institutional criteria or each surgeon's experience. Clinical information used to assess patient's conditions, including the amount of drainage from a chest drain, image findings, blood

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test results, or vital signs, may well inform the decision on reoperation for postoperative bleeding, but they need to be validated as indicators. The persistent bloody drainage from a chest drain is suggestive of the postoperative bleeding. Reoperation may be indicated if 100 mL/h or more of the bloody drainage persists for two hours or longer.[8] However, surgeons often found a larger amount of bleeding than expected or formation of hematoma within the thoracic cavity during reoperation. The relationship between the amount of drainage from a chest drain and the volume of intrathoracic hematoma found during reoperation should be elucidated in order to validate the decision on reoperation for hemostasis made on the basis of the drainage amount from the chest drain. In addition, information on the source of bleeding commonly found during reoperation may be useful for surgeons to prevent reoperation for hemostasis as it shows the vessels at high risks of postoperative bleeding and allows surgeons to perform hemostasis more carefully and effectively at the initial surgery.

This study aimed to retrospectively investigate patients who underwent reoperation due to bleeding after the surgery for pulmonary malignancies in our hospital for their characteristics, perioperative clinical information, findings from reoperation for hemostasis, and courses after reoperation in order to prevent this rare but serious complication and establish proper treatment strategy. We also investigated the relationship between chest tube output and intrathoracic hematoma volume found at reoperation in order to validate the decision on reoperation for hemostasis.

Patients and Methods

We identified patients who underwent reoperation due to postoperative bleeding from 6989 patients who had had operations for pulmonary malignancies performed at our hospital between January 2007 and July 2019 using our department's electric database. We excluded the patients who 1) underwent extrapleural pneumonectomy, 2) developed bleeding 30 days or more after the initial surgery, and 3) developed secondary bleeding due to pyothorax. We excluded patients who underwent extrapleural pneumonectomy (EPP) because postoperative management was different between EPP and other pulmonary resections. Clinical information and surgical findings of eligible patients were retrospectively investigated using medical charts. Classification and severity of complications of reoperation were determined according to the extended Clavien-Dindo Classification.[9] This study was conducted in compliance with the Declaration of Helsinki and the Japanese Ethical Guidelines for Epidemiological Research and approved by the Ethical Review Board of National Cancer Center Hospital, Tokyo, Japan (Approval No.: 2018–045, Approval date: 5/23/2018). This was a retrospective study with no invasive procedure or intervention and thus exempted from obtaining written consent from each patient.

Perioperative Management

Patients on anticoagulants before surgery (ie, warfarin and novel oral anticoagulants) stopped their anticoagulants and started continuous intravenous infusion of heparin. We used heparin because low-molecular-weight heparin was not covered by medical insurance in Japan. The heparin infusion was discontinued six hours before the surgery. The normalization of coagulation was evaluated by a coagulation blood test before surgery. Prophylactic hemostatic agents were not used routinely.

The surgical method used was small thoracotomy in combination with a thoracoscope in principle during the study period because of an institutional policy, although minimally invasive surgery is a preferable surgical method in the current guideline. We called our open procedure minimally invasive open surgery and reported satisfactory surgical outcomes.[10] Lobectomy was performed under direct view and assistance of the thoracoscope by performing posterolateral thoracotomy at the fourth or fifth intercostal space or axillary thoracotomy, as well as making a 1-cm port for a camera on the middle axillary line at the seventh or eighth intercostal space. At the end of the surgery, a 28Fr chest drain was inserted towards the apex of the lung from the camera port. General anesthesia was terminated at the end of the surgery after taking a chest X-ray image in the operation room and confirming that there was no abnormal finding. Patients were transferred to a recovery room and their arterial blood test results and wakefulness from anesthesia were evaluated. We start using epidural anesthesia for pain control just after the operation, monitor blood pressure in the recovery room before going back to the ward, and adjust for the dose of anesthetic agents to keep the blood pressure above 90 mmHg. Postoperative vital signs were monitored in combination with the invasive arterial pressure measurement until the day after the surgery. Patients were checked for the characteristics of drainage from the chest drain over

three hours after the surgery to confirm no postoperative bleeding occurred. Then, they received continuous heparin infusion at 400 units/h for preventing deep venous thrombosis at the discretion of a treating surgeon until they were confirmed to be ambulatory on the day after the surgery. We used heparin because low-molecular-weight heparin was not covered by medical insurance in Japan. Evaluation was performed in the early morning on the day after the surgery, consisting of blood count and biochemistry including arterial blood collection and chest X-ray. The blood tests and the chest X-ray were performed daily afterwards.

Administration of carbazochrome sodium sulfonate hydrate and tranexamic acid was considered for patients who had bloody drainage from the chest drain after surgery based on the discretion of attending surgeons. Transfusion or plasma products such as albumin were added as necessary. The indication for reoperation due to bleeding was defined as 1) a shock state with minimum systolic blood pressure < 90 mm Hg, 2) persistent bloody drainage from a chest drain of 100 mL/h or more, and 3) intrathoracic hematoma on a chest X-ray image. Attending surgeons were responsible for the decision to perform a reoperation for hemostasis or not on the basis of these findings.

Statistical Analysis

Continuous variables were reported as the medians with ranges and categorical variables as numbers of patients with percentages. Regression analysis was used for correlation between two continuous variables. JMP 13 (SAS Institute Inc., Cary, NC) was used for the statistical analysis. It was considered statistically significant when $p < 0.05$.

Results

Patient Characteristics

Twenty-two patients (0.3%, 22/6989) underwent reoperation for hemostasis during the study period. The characteristics of all 22 patients are shown in Table 1. There was one patient who had an anticoagulant before surgery among the 22 patients included in this study. Primary diseases were primary lung cancer in 20 patients, and pulmonary mucosa-associated lymphoid tissue lymphoma and metastatic lung tumor in one patient each. The median amount of bleeding at the initial surgery was 49.5 mL. In one patient with a superior sulcus tumor, the amount of bleeding was exceptionally high at 5092 mL.

Table 1 Patient Characteristics (n = 22)

		n (%)
Sex	Man	15 (68%)
	Woman	7 (32%)
Age (year; median, range)		66 (42–85)
Smoking status	Current and former	14 (64%)
	Never	8 (36%)
Comorbidity: Hypertension		10 (46%)
Pathological diagnosis	Primary lung cancer	20 (91%)
	Other	2 (9%)
Initial surgery procedure	Pneumonectomy	2 (9%)
	Lobectomy	14 (64%)
	Segmentectomy	2 (9%)
	Wedge resection	4 (18%)
Heparin administration before the initial surgery		3 (14%)
Intrathoracic adhesion during the initial surgery	Yes	6 (27%)
	No	16 (73%)
Amount of bleeding during the initial surgery (mL; median, range)		49.5 (1–5092)
Heparin administration after the initial surgery		6 (27%)

Surgical Information and Outcome of Reoperation

Surgical information and outcome of reoperation were shown in Table 2. The median time from the end of the initial surgery to the start of reoperation was 9.8 hours (range: 0.5–94.1). The reoperation was performed within 24 hours from the initial surgery in 17 patients (77%). The reason for reoperation was a shock state with minimum systolic blood pressure < 90 mm Hg in 12 patients (55%), persistent bloody drainage of 100 mL/h or more in 15 patients (68%), and intrathoracic hematoma on a chest X-ray image in 14 patients (64%). All those three findings were observed in five patients (23%), two in nine patients (41%), and one in eight patients (36%). The median decrease of the hemoglobin level was 4.9 g/dL (range: 2.0–7.4) and transfusion was performed in 21 patients (96%). The median time from reoperation to discharge was 6.5 days (range: 3–36). After reoperations due to postoperative bleeding in 22 patients, complications of extended Clavien-Dindo Classification IIIa or higher occurred in two patients (9%) (one pulmonary edema and one pulmonary fistula). No death occurred within 30 days after the initial surgery. The median follow-up period after reoperation was 5.9 years ranging, 0.3 to 12.8 years. Eight patients experienced recurrence, and three died. Another patient died of a secondary malignancy. Thirteen patients survived without any evidence of malignancy. These findings suggest that quality of life was maintained after reoperation without long-term complications related to reoperation.

Source of Bleeding

Sources of bleeding identified during reoperation were shown in Table 3. In one patient, bleeding outside the pleural cavity penetrated into the pleural cavity, and the amount of drainage from a chest drain exceeded 1000 mL. Bleeding from the lung parenchyma noted in three patients, all occurred at the sites of resection which were closed using an automatic stapler. The source of the bleeding could not be identified during reoperation in four patients (18%).

Table 2 Surgical Information and Outcome of Reoperation (n = 22)

	n (%)
Time from the end of the initial surgery to the start of reoperation (hour; median, range)	9.8 (0.5–94.1)
Findings leading to consideration of reoperation	
Minimum systolic blood pressure < 90 mm Hg	12 (55%)
Bloody drainage from a chest drain of 100 mL/h or more	15 (68%)
Intrathoracic hematoma on a chest X-ray image	14 (64%)
Decrease in a preoperative hemoglobin level from the initial surgery to reoperation (g/dL; median, range)	4.9 (2.0–7.4)
Transfusion performed during reoperation	21 (96%)
Time from reoperation to discharge (day; median, range)	6.5 (3–36)

Table 3 Source of Bleeding (n = 22)

	n (%)
Bronchial artery	3 (14%)
Pulmonary parenchyma	3 (14%)
Chest wall	3 (14%)
Pulmonary ligament	2 (9%)
Pulmonary artery	2 (9%)
Intercostal artery	1 (5%)
Brachiocephalic vein branch	1 (5%)
Thoracodorsal artery	1 (5%)
Other	2 (9%)
Unknown	4 (18%)

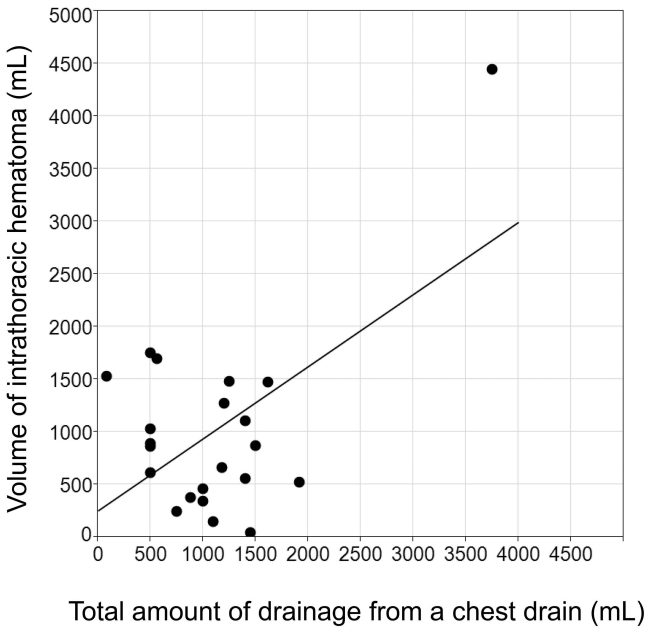

Figure 1 Relationship between the amount of drainage from a chest drain and the volume of intrathoracic hematoma found during reoperation. Dots and a line represent patients and a regression curve, respectively.

Relationship Between the Amount of Drainage from a Chest Drain and the Volume of Intrathoracic Hematoma

The median amount of drainage from a chest drain from the initial surgery to reoperation was 1050 mL (range: 80–3750). The median total volume of intrathoracic hematoma during reoperation was 865 mL (range: 40–4444). The volume of intrathoracic hematoma found during reoperation was greater than the amount of drainage from a chest drain in 10 patients (46%). The relationship between the amount of drainage from a chest drain and the volume of intrathoracic hematoma found during reoperation was shown in Figure 1. In the regression analysis, the coefficient of determination R^2 was 0.31, indicating poor correlation between the amount of drainage from a chest drain and the volume of intrathoracic hematoma.

Discussion

In this study, the incidence of reoperation for hemostasis was 0.3% (22/6989) of all surgery cases and lower than those in the previous reports (1.4–2.1%).[6,7,11–13] This low incidence was probably attributable to the extra caution taken during hemostasis using small thoracotomy for direct view in combination with a thoracoscope in our hospital.[10] We believe that VATS and open surgery have complimentary roles to view the surgical field, and the combination of these two different approaches resulted in the low incidence of reoperation for hemostasis in this study. The study in the US reported that 86.0% of the patients undergoing the surgery for primary lung cancer received preoperative administration of heparin for preventing deep venous thrombosis; of those received preoperative heparin, 1.6% required reoperation due to post-operative bleeding, which was significantly higher than 0.2% in those who did not receive heparin.[7] Preoperative heparin administration would increase the risk of reoperation due to postoperative bleeding. In our hospital, heparin was discontinued six hours before the surgery. The normalization of coagulability was evaluated before the surgery to reduce the risk of postoperative bleeding, which may also contribute to the low incidence of reoperation for hemostasis.

It is important to identify the source of bleeding commonly found during reoperation to ensure hemostasis during the initial surgery to prevent postoperative bleeding, although in clinical practice, we often have difficulty identifying the source of bleeding. In this study, the sources of bleeding found during reoperation substantially varied (Table 3). The study by Udelsman et al in 21 patients who underwent reoperation due to bleeding after lobectomy reported that the most bleeding occurred from diffuse or unknown sources (44%), followed by the chest wall (23%), the bronchial artery or lymph node (19%), and the pulmonary artery or lung parenchyma (15%).[6] In the study conducted by Dai et al on 57

patients, sources of bleeding included the area where adhesion was separated (29.8%), region of lymph node dissection (19.3%), and unknown (19.3%).[11] Considering the Results of this study and previous reports, it is important to explore the entire thoracic cavity without fail to ensure hemostasis during the initial surgery because the sources of bleeding found during reoperation substantially varied.

The decision on reoperation due to postoperative bleeding has been conventionally made on the basis of the amount of drainage from a chest drain. It is suggested to consider reoperation for hemostasis if the bloody drainage of 100 mL/h or more persists for two hours or longer.[8] However, this study showed that there was no correlation between the amount of drainage from a chest drain and the volume of intrathoracic hematoma found during reoperation and the latter was greater than the former in 46% of the patients. These results suggested that the amount of drainage from chest drains alone is insufficient to decide the necessity of reoperation for hemostasis and should be used as a guide as inadequate drainage may be caused by the occlusion due to hematoma, bending, and improper placement of a chest drain, or the posture of a patient. The poor correlation between the amount of drainage from a chest drain and the volume of intrathoracic hematoma found during reoperation suggests there might be other unexplored factors that may influence the decision for reoperation, and surgeons need to consider in-depth consideration.

Decision on reoperation due to bleeding should be made promptly and precisely. It was reported that postoperative complications or death may be reduced if the reoperation for hemostasis is performed within 24 hours after the initial surgery.[11] The median time from the initial surgery to reoperation was 9.8 hours in our hospital and reoperation for hemostasis was performed within 24 hours after the initial surgery in 17 patients (77%). These outcomes were attained by the comprehensive decision on reoperation made according to not only the amount of drainage from a drain but also postoperative conditions of patients. Only five patients (23%) showed all three findings of 1) a shock state, 2) bloody drainage of 100 mL/h or more, and 3) intrathoracic hematoma formation on a chest X-ray image as the reasons for reoperation. Prompt decision-making resulted in the excellent outcome with the median hospital stay from reoperation to discharge of 6.5 days and no in-hospital death after the surgery. We believe that reoperation due to postoperative bleeding should be positively considered if there is at least one of three findings of 1) a shock state, 2) bloody drainage of 100 mL/h or more, and 3) intrathoracic hematoma formation on a chest X-ray image.

The limitation of this study is that this is a 13-year single-center case series study and treatment policy may have been changed as surgical techniques advanced over time. The retrospective data collection from medical charts might introduce biases and inaccuracies, and providing more details on the specific criteria used by attending surgeons to decide on the necessity of reoperation beyond the three general indicators mentioned was difficult because of the retrospective nature of our study. The study's single-institutional focus may limit the generalizability of its findings because factors such as surgical techniques, patient populations, and institutional practices can significantly vary between medical centers. A multicenter approach or validation with external datasets could enhance the reliability of the identified clinical indicators. In addition, we did not investigate the incidence or treatment courses of patients with postoperative bleeding who received only conservative therapy without reoperation.

In conclusion, reoperation due to bleeding after the surgery for pulmonary malignancies is required not often, but in certain cases. Multiple steps, including the addition of a chest tube and careful management of anticoagulants in patients who are at high risk of postoperative bleeding, will be warranted. The amount of drainage from a chest drain does not necessarily reflect the volume of intrathoracic hematoma and it is hard to estimate the total amount of bleeding. The decision to perform reoperation for hemostasis should be comprehensively made on the basis of vital signs and chest X-ray findings of patients. Furthermore, the incidence of postoperative complications was low and no postoperative death occurred in this study. Accordingly, we suggest that the decision to perform reoperation for hemostasis should be promptly and positively made for appropriately selected patients.

Conclusions

Reoperation due to bleeding is required in certain cases. The amount of drainage from a chest drain does not necessarily reflect the volume of intrathoracic hematoma and it is hard to estimate the total amount of bleeding. The decision to perform reoperation for hemostasis should be comprehensively made on the basis of clinical signs and chest X-ray findings.

Ethics Approval and Informed Consent

This study was conducted in compliance with the Declaration of Helsinki and the Japanese Ethical Guidelines for Epidemiological Research and approved by the Ethical Review Board of National Cancer Center Hospital, Tokyo, Japan (Approval No.: 2018-045, Approval date: 5/23/2018).

This was a retrospective study with no invasive procedure or intervention and thus exempted from obtaining written consent from each patient. The data was anonymized and maintained with confidentiality.

Consent for Publication

All authors have approved the manuscript and agree with its submission to the journal.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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