Incidence Rates of Postoperative Pulmonary Embolisms in Symptomatic and Asymptomatic Patients, Detected by Diagnostic Images

— A Single-Center Retrospective Study —

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Background: Pulmonary embolism (PE) is a serious complication during the perioperative period. However, because most previous studies on the incidence of postoperative PE are based on symptoms, asymptomatic occurrences of PE have been overlooked, and the absolute incidence of postoperative PE remains unknown. The aim of this study was to investigate the incidence of perioperative PE, regardless of its symptoms, by reviewing the clinical interpretations of the diagnostic images obtained during the postoperative period.

Methods and Results: This study included all patients aged at least 18 years who underwent operations under general and/or neuraxial anesthesia in our institution from 2013 to 2016. We reviewed all interpretations of the diagnostic imaging performed in the postoperative period. We analyzed the 90-day cumulative incidence of postoperative PE and the characteristics, risk factors, and symptoms of patients with and without postoperative PE. Among 21,763 operations, postoperative diagnostic imaging was performed in 1,168 patients, which found PE in 217 patients. Symptoms appeared in 11.1% (24/217) of the PE patients, and 66.7% of these symptoms were decreased levels of SpO_2 alone. Mortality from PE was 0.5% (1/217).

Conclusions: Diagnostic imaging found a number of postoperative PE cases, regardless of the presence of symptoms. Although symptomatic PE was not a frequent occurrence, these findings suggest that clinicians should be aware of postoperative PE even under current prophylaxis.

Key Words: Deep vein thrombosis; Postoperative complications; Pulmonary embolism; Venous thromboembolism

Venous thromboembolism (VTE), which includes pulmonary embolism (PE) and deep vein thrombosis (DVT), is a serious complication during the perioperative period. Because DVT is a precursor of PE, a life-threatening condition with sudden onset, prophylaxis of DVT is of importance and has been well studied. After the publication of guidelines,[1–3] the importance of DVT prophylaxis has been recognized nationwide, and decreased incidence has been reported. Without thromboprophylaxis, DVT occurs in approximately 10–40% of either medical or general surgical patients, and in 40–60% following major orthopedic surgery.[1] With prophylaxis under current guidelines, DVT incidence is reported to be 0.77% following abdominal surgery[4] and VTE incidence is reported to be 2.2% following colorectal surgery,[5] based on clinical databases searches.

Screening for DVT during the perioperative period is performed by either compression ultrasonography or contrast venography, and its incidence rate has been well studied.[6–9] However, screening for PE is often invasive and costly and requires radiation exposure, all of which leads to difficulty in performing it during routine examination. Thus, only symptomatic patients have been included in most studies reporting on the incidence of PE. According to the JSA-PTE study,[10] which is the largest study on perioperative symptomatic PE occurrences in Japan, the incidence in Japanese hospitals between 2002 and 2011 was 3.1 per 10,000 surgeries, with a mortality rate of 12.9% in 2011. Asymptomatic PE is thought to be much more prevalent than symptomatic PE; however, actual incidence during the perioperative period is difficult to track.

Although diagnostic examination of PE is usually performed only in symptomatic patients, there have been several studies reporting on the prevalence of asymptomatic PE, detected incidentally by multidetector computed tomography (MDCT). A meta-analysis reported that the

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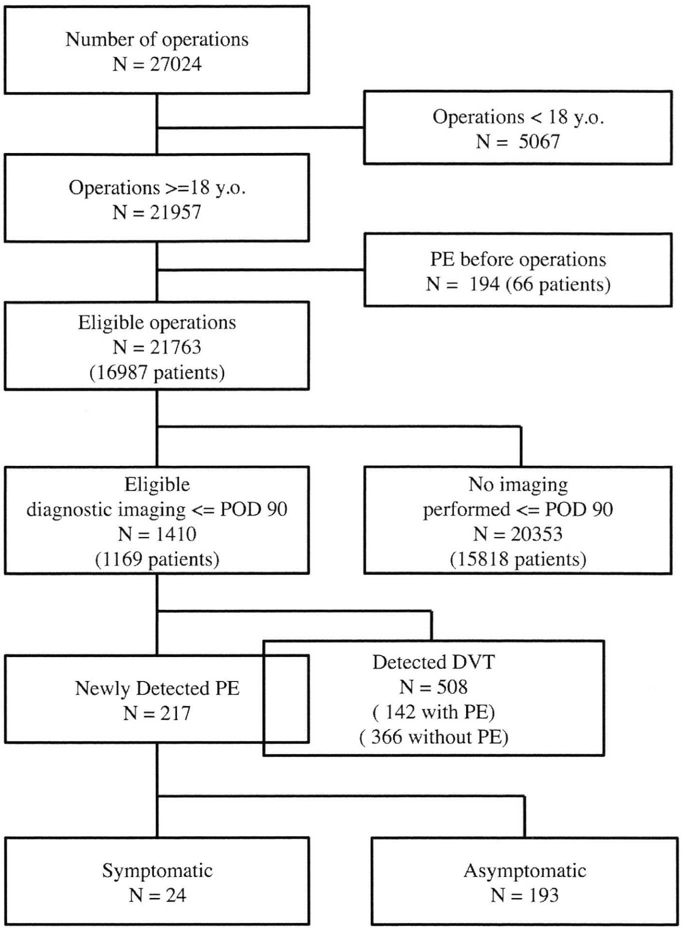

Figure 1. Flow chart of the study. All operations between 1 January 2013 and 31 December 2016 in the hospital were scrutinized. The exclusion criteria for the data are on the right side of the chart. DVT, deep vein thrombosis; PE, pulmonary embolism; POD, postoperative day.

prevalence of unsuspected PE was 4.0% in inpatients, which largely consisted of oncologic patients.[11] Additionally, in oncologic patients, 3.9–4.4% were found to have asymptomatic PE.[12,13] Intensive care unit patients were reported to have a 5% incidence.[14] However, there is a lack of research on the incidences of postoperative PE, especially in unsuspected, asymptomatic patients. Therefore, the aim of this retrospective study was to identify the incidence of postoperative PE, regardless of symptoms, by reviewing all interpretations of the diagnostic imaging performed during a perioperative period. We also investigated patient characteristics, risk factors, and any symptoms at the onset of PE.

Methods

Subjects

This was a single-center, retrospective, observational study, approved by the Ethics and Research Committee of Okayama University Hospital (#1705-011). All patients gave written informed consent before their operations and were given the opportunity to "opt-out" from the study. All authors could access the primary data. The VTE risk for all patients older than 18 years upon admission was assessed and all at-risk patients underwent prophylaxis for VTE in accordance with the Japanese Guidelines for the Diagnosis, Treatment and Prevention of Pulmonary Thromboembolism and Deep Vein Thrombosis.[2] The

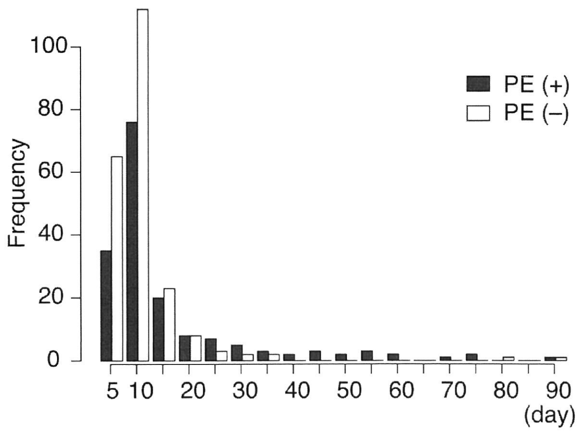

Figure 2. Histogram of the frequency of diagnostic imaging by postoperative day. The bars in black represent the PE(+) cohort, and the bars in gray represent the PE(–) cohort. PE, pulmonary embolism.

Table 1. Characteristics of the Patients With and Without PE, and 90-Day Cumulative Incidence of PE

Factor / Group	PE (–)	PE (+)	90-day cumulative incidence (%) (95% CI)
n	21,546	217	1.0 (0.9–1.1)
Age (years), median [IQR]	61 [43–71]	66 [56–75]	
n (%)			
<60	10,014 (46.5)	63 (29.0)	0.6 (0.5–0.8)
≥60 <70	5,377 (25.0)	66 (30.4)	1.2 (1.0–1.5)
≥70 <80	4,601 (21.4)	57 (26.3)	1.2 (0.9–1.6)
≥80	1,554 (7.2)	31 (14.3)	2.0 (1.3–2.8)
Sex, n (%)			
Female	11,700 (54.8)	117 (53.9)	1.0 (0.8–1.2)
Male	9,637 (45.2)	100 (46.1)	1.0 (0.8–1.2)
ASA-PS, n (%)			
1	6,856 (31.8)	38 (17.5)	0.6 (0.4–0.8)
2	10,792 (50.1)	114 (52.5)	1.0 (0.9–1.3)
3	3,554 (16.5)	55 (25.3)	1.5 (1.2–2.0)
4	321 (1.5)	9 (4.1)	2.7 (1.3–5.1)
5	23 (0.1)	1 (0.5)	4.2 (0.1–21.1)
BMI, median [IQR]	22.5 [20.2–25.0]	24.1 [21.9–27.3]	
n (%)			
<25	16,156 (75.0)	136 (62.7)	0.8 (0.7–1.0)
≥25 <30	4,427 (20.5)	58 (26.7)	1.3 (1.0–1.7)
≥30 <35	784 (3.6)	18 (8.3)	2.2 (1.3–3.5)
≥35	179 (0.8)	5 (2.3)	2.7 (0.9–6.2)
Operative duration (min), median [IQR]	136 [72–236]	204 [140–433]	
Anesthesia duration (min), median [IQR]	196 [120–311]	291 [205–544]	
n (%)			
<180	9,655 (44.8)	37 (17.1)	0.4 (0.3–0.5)
≥180 <300	6,061 (28.1)	77 (35.5)	1.3 (1.0–1.6)
≥300	5,830 (27.1)	103 (47.5)	1.7 (1.4–2.1)
Emergency, n (%)			
No	20,093 (93.3)	183 (84.3)	0.9 (0.8–1.0)
Yes	1,453 (6.7)	34 (15.7)	2.3 (1.6–3.2)
Surgical site, n (%)			
Hip and limb	2,762 (12.8)	93 (42.9)	3.3 (2.6–4.0)
Head and neck	3,408 (15.8)	20 (9.2)	0.6 (0.4–0.9)
Lower abdomen	4,890 (22.7)	17 (7.8)	0.3 (0.2–0.6)
Upper abdomen	2,155 (10.0)	17 (7.8)	0.8 (0.5–1.3)
Thorax	1,514 (7.0)	14 (6.5)	0.9 (0.5–1.5)
Thorax and abdomen	356 (1.7)	14 (6.5)	3.8 (2.1–6.3)
Brain	1,119 (5.2)	12 (5.5)	1.1 (0.5–1.8)
Spine	915 (4.2)	11 (5.1)	1.2 (0.6–2.1)
Chest/abdominal wall and perineum	2,343 (10.9)	7 (3.2)	0.3 (0.1–0.6)
Cardiovascular	838 (3.9)	7 (3.2)	0.8 (0.3–1.7)
Examination	76 (0.4)	2 (0.9)	2.6 (0.3–9.0)
Cesarean section	548 (2.5)	1 (0.5)	0.2 (0.0–1.0)
Other	622 (2.9)	2 (0.9)	0.3 (0.0–1.2)

ASA-PS, American Society of Anesthesiologists physical status; BMI, body mass index; CI, confidence interval; IQR, interquartile range; PE, pulmonary embolism.

records of all patients who underwent operations under general and/or neuraxial anesthesia in Okayama University Hospital between 1 January 2013 and 31 December 2016 were scrutinized for this study. All patients included in the study were admitted because ambulatory surgeries under general or neuraxial anesthesia by the anesthesiologists were not performed in this hospital. The records of patients who underwent minor surgeries under local anesthesia, administered by the surgeons, and patients with a history of PE were excluded from this study. Patients under 18 years were also excluded, because the Japanese guidelines[2] for VTE risk assessment are intended for patients older than 18 years and, therefore, they were not screened upon admission.

Table 2. Unadjusted and Adjusted ORs of Postoperative PE

Factor	Bivariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (years)				
<60	Ref.		Ref.	
≥60 <70	1.95 (1.38–2.76)	<0.001	1.80 (1.25–2.60)	0.002
≥70 <80	1.97 (1.37–2.82)	<0.001	1.81 (1.22–2.68)	0.003
≥80	3.17 (2.06–4.89)	<0.001	3.03 (1.88–4.87)	<0.001
Sex				
Female	Ref.		Ref.	
Male	1.04 (0.79–1.36)	0.787	0.77 (0.58–1.02)	0.065
ASA-PS				
1	Ref.		Ref.	
2	1.91 (1.32–2.75)	0.001	1.15 (0.77–1.73)	0.490
3	2.79 (1.84–4.23)	<0.001	1.29 (0.81–2.07)	0.290
4	5.06 (2.43–10.60)	<0.001	1.71 (0.77–3.79)	0.190
5	7.84 (1.03–59.60)	0.046	2.66 (0.32–21.70)	0.360
BMI				
<25	Ref.		Ref.	
≥25 <30	1.56 (1.14–2.12)	0.005	1.56 (1.14–2.13)	0.006
≥30 <35	2.73 (1.66–4.48)	<0.001	2.88 (1.73–4.79)	<0.001
≥35	3.32 (1.34–8.20)	0.009	3.89 (1.53–9.92)	0.004
Anesthesia duration (min)				
<180	Ref.		Ref.	
≥180 <300	3.32 (2.24–4.91)	<0.001	3.32 (2.23–4.94)	<0.001
≥300	4.61 (3.16–6.72)	<0.001	5.14 (3.49–7.59)	<0.001
Emergency				
No	Ref.		Ref.	
Yes	2.57 (1.72–3.74)	<0.001	3.30 (2.21–4.94)	<0.001

OR, odds ratio; Ref., reference. Other abbreviations as in Table 1.

Data Collection

From the database of the departments of radiology and cardiology, we acquired the data from the examinations aimed at diagnosing VTE. The postoperative period was defined as within 90 days of the operation, as described in previous reports.[5,15–17] The following keywords, in either the requesting comments or interpretation reports by the attending doctors, were used to search for appropriate records: PE, pulmonary thrombosis, pulmonary thromboembolism, PE, PTE, venous thrombosis, deep vein thrombosis, and DVT. All imaging data, including CT scanning and ultrasound echocardiography data, discovered with the DVT searching protocol were also extracted. VTE was diagnosed by either board-certified radiologists, based on CT scanning data, or cardiologists, based on ultrasound echocardiography. All anesthesiologist reports within the observational time period were extracted and merged with the patient's imaging reports (patient records were cross-matched using patient names and identification numbers). The following patient characteristics (age, sex, American society of anesthesiologists physical status (ASA-PS), surgical site, duration of operation and anesthesia, body mass index (BMI), surgical priority (elective or emergency)), and presence of malignancy were obtained from the electronic medical and anesthetic records. The duration of general anesthesia was defined as the time between the administration of oxygen before anesthesia induction to discontinuing oxygen after extubation in the surgical theater. The duration of neuraxial anesthesia was defined as the time between the administration of local anesthetics to the end of the surgery.

Outcomes

The primary outcome of this study was the development of PE diagnosed by either a radiologist or cardiologist. Every thrombus, regardless of size (massive or small), location (proximal or distal), or type (segmental or subsegmental), was equally included in the PE(+) group. The symptoms of PE and the D-dimer value (normal limit <1.0 μg/mL, Sysmex, Kobe, Japan) in the PE(+) group, on the day of or day before the diagnosis, were analyzed as secondary outcomes. These symptoms included decreased SpO_2, changes in respiratory rate, dyspnea, chest pain or discomfort not related to the surgical wound, circulatory instability such as tachycardia, ST-T wave changes on ECG, and decreased blood pressure. These data were obtained from the electronic medical records.

Statistical Analysis

Continuous variables are expressed as median and interquartile range (IQR). Categorical variables are described as frequency count and percentage. Some continuous variables, including age, BMI, and anesthesia duration, were categorized for modeling. Categorization of the anesthesia duration was based on previous reports.[9,18] The number of categories for anesthesia duration was different in the analyses of the primary and secondary outcomes because of differences in the numbers of events. The 90-day cumulative

Table 3. Characteristics of the Patients With Postoperative PE

Factor / Group	Asymptomatic	Symptomatic
n (%)	193 (88.9)	24 (11.1)
Age (years), median [IQR]	65 [55–75]	72 [68.25–77]
n (%)		
<60	59 (30.6)	4 (16.7)
≥60 <70	63 (32.6)	3 (12.5)
≥70 <80	43 (22.3)	14 (58.3)
≥80	28 (14.5)	3 (12.5)
Sex, n (%)		
Female	106 (54.9)	11 (45.8)
Male	87 (45.1)	13 (54.2)
ASA-PS, n (%)		
1	31 (16.1)	7 (29.2)
2	106 (54.9)	8 (33.3)
3	48 (24.9)	7 (29.2)
4	7 (3.6)	2 (8.3)
5	1 (0.5)	0 (0.0)
BMI, median [IQR]	24.1 [21.8–27.4]	24.4 [22.6–26.7]
n (%)		
<25	121	15
≥25 <30	49	9
≥30 <35	18	0
≥35	5	0
Operative duration (min), median [IQR]	194 [137–391]	354 [211.5–592.75]
Anesthesia duration (min), median [IQR]	272 [197–504]	425.5 [288–677.5]
n (%)		
<300	107 (55.4)	7 (29.2)
≥300	86 (44.6)	17 (70.8)
Emergency, n (%)		
No	162 (83.9)	21 (87.5)
Yes	31 (16.1)	3 (12.5)
DVT, n (%)		
No	67 (34.7)	8 (33.3)
Yes	126 (65.3)	16 (66.7)
Malignancy, n (%)		
No	130 (67.4)	8 (33.3)
Yes	63 (32.6)	16 (66.7)
D-dimer (μg/mL), median [IQR]	13.0 [7.2–25.8]	14.7 [8.7–26.2]
Surgical site, n (%)		
Hip and limb	88 (45.6)	5 (20.8)
Thorax	10 (5.2)	4 (16.7)
Brain	8 (4.1)	4 (16.7)
Head and neck	17 (8.8)	3 (12.5)
Lower abdomen	14 (7.3)	3 (12.5)
Upper abdomen	15 (7.8)	2 (8.3)
Chest/abdominal wall and perineum	5 (2.6)	2 (8.3)
Thorax and abdomen	13 (6.7)	1 (4.2)
Spine	11 (5.7)	0 (0.0)
Cardiovascular	7 (3.6)	0 (0.0)
Examination	2 (1.0)	0 (0.0)
Cesarean section	1 (0.5)	0 (0.0)
Other	2 (1.0)	0 (0.0)

DVT, deep vein thrombosis. Other abbreviations as in Table 1.

incidence was expressed as percentage, with 95% confidence intervals (CI). The Mann-Whitney U test was used for comparisons of the patients' demographic characteristics. Fisher's exact test and logistic regression analyses were used to calculate odds ratios (OR). The correlation between anesthesia and operative duration was calculated using the Pearson's product-moment correlation formula. D-dimer values were not obtained from 3 asymptomatic patients (1.4%, 3/217) and, therefore, were not used for modeling. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan),[19] which is a graphical user interface for R (version 3.3.2, The R Foundation for Statistical Computing, Vienna, Austria). A P-value <0.05 was considered significant.

Results

Patient Population

In the study period, from 2013 to 2016, 27,024 operations under general and/or neuraxial anesthesia by anesthesiologists were performed. After exclusion of patients under 18 years old (n=5,067) and the patients with history of PE (n=194), data from 21,763 operations in 16,987 patients were included in the study (**Figure 1**). Among the eligible operations, VTE occurrence was assessed after 1,410 operations performed in 1,169 patients. Contrast-enhanced MDCT was performed for 1,168 of those patients in order to follow up the postoperative course and complications such as pneumonia, pleural effusion, anastomotic leakage, bleeding, and thrombotic events. Only 1 patient was diagnosed with PE solely by a cardiologist, based on ultrasound echocardiography without enhanced CT, because of unstable vital signs.

Primary Outcome

A histogram of the diagnostic imaging frequency during the postoperative period is shown in **Figure 2**. The examinations were performed between postoperative days 1 and 90 (median 7, IQR 5–11). The day of the detection of PE varied widely. These examinations found 217 newly detected PE cases (90-day cumulative incidence 1.0%, 95% CI 0.9–1.1) and 508 DVT cases as part of the CT angiography (2.3%, 95% CI 2.1–2.5) in patients. Of the 217 PE(+) patients, DVT was found in 142 and 75 patients were free of it (**Figure 1**). Patients' characteristics are shown in **Table 1**. Most of the cases of detected PE involved hip and limb surgeries (42.9% of PE). However, the cumulative incidence of PE was highest in thoracic and abdominal surgeries (3.8%, 95% CI 2.1–6.3), which were mostly esophageal surgeries; followed by hip and limb surgeries (3.3%, 95% CI 2.6–4.0). Both age and BMI were significantly higher in the PE(+) group than in the PE(−) group (P<0.001 for both), and the cumulative incidence of PE rose incrementally together with these parameters. OR calculations, as well as CIs and P-values, are summarized in **Table 2**. We included the indicated parameters to adjust for confounders. Although sex is controversial as a risk factor,[20,21] we found no difference in postoperative PE incidence between the sexes. Emergency cases were also associated with a higher incidence of postoperative PE. Higher ASA-PS was shown to be associated with a higher PE incidence in the bivariate analysis only, but the multivariate analysis revealed that higher ASA-PS was not an independent risk factor. In addition to these parameters, we analyzed the association between operation/anesthesia duration and the incidence of postoperative PE. Both the duration of the anesthesia and the operation were obviously correlated (correlation coefficient=0.98, 95% CI 0.98–0.981). We analyzed anesthesia duration as an indication of mandatory immobility. Longer anesthesia duration linearly correlated with higher incidence of postoperative PE as an independent risk factor.

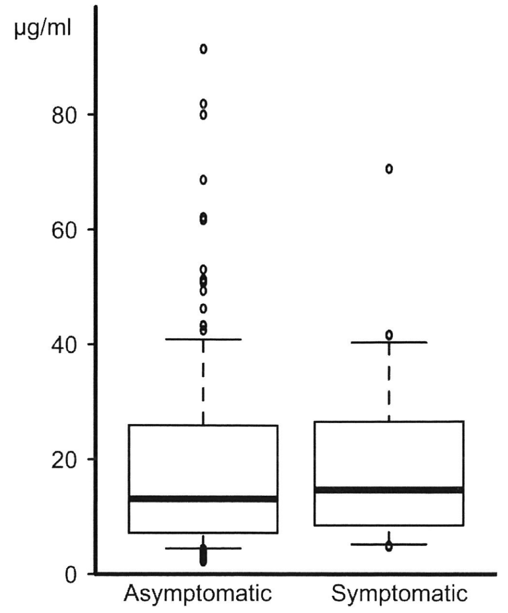

Figure 3. Box-and-whisker plot of the D-dimer concentrations in the patients with pulmonary embolism (n=190 in the asymptomatic group, and n=24 in the symptomatic group). Median and interquartile ranges are shown as bars and boxes. Whiskers show 10–90% of distribution. The circles indicate the individual data points outside of the distribution.

Secondary Outcomes

The symptoms related to PE in all of the PE(+) patients were obtained retrospectively from the medical records. **Table 3** shows the characteristics of both asymptomatic and symptomatic patients who developed postoperative PE. Most PE(+) patients (88.9%) did not exhibit any subjective or objective symptoms related to PE; 24 patients (11.1%) exhibited some PE-related symptoms. The cumulative incidence of symptomatic PE in all subjects was 0.1% (95% CI 0.1–0.2). D-dimer was measured in 214 patients in the PE(+) group, on either the day of or the day before the examinations. The median D-dimer value in all PE(+) patients was 13.1 µg/mL [7.2–25.9] (median [IQR]), which was within the range of the accepted postoperative values (the postoperative value varies by surgical procedure). D-dimer values were not significantly different between asymptomatic and symptomatic patients (13.0 [7.2–25.8] µg/mL vs. 14.7 [8.7–26.2] µg/mL, respectively, P=0.556). **Figure 3** shows the D-dimer values of the asymptomatic and symptomatic patients, and **Table 4** summarizes the symptoms of these patients. Two-thirds (16/24) of symptomatic patients exhibited decreased SpO_2 alone without any other complaints. The other one-third (8/24) of patients exhibited either subjective symptoms or cardiovascular events. One patient died from PE on the day of onset.

Table 4. Symptoms and D-Dimer Values in Symptomatic PE Patients

Symptoms	n (%)	D-dimer (μg/mL), median [IQR]
Decreased SpO_2 alone	16 (66.7)	18.35 [9.78–27]
Decreased SpO_2 and dyspnea	1 (4.2)	
Decreased SpO_2, dyspnea and chest pain	1 (4.2)	
Decreased SpO_2, dyspnea and tachycardia	1 (4.2)	
Chest pain	1 (4.2)	
Tachypnea	1 (4.2)	9.75 [5.3–34.43]
Tachycardia	1 (4.2)	
Decreased blood pressure	1 (4.2)	
Death	1 (4.2)	

Abbreviations as in Table 1.

Table 5. Unadjusted and Adjusted ORs of PE Symptom Manifestation

Factor	Bivariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Age (years)				
<60	Ref.		Ref.	
≥60 <70	0.70 (0.15–3.27)	0.653	0.60 (0.13–2.88)	0.524
≥70 <80	4.80 (1.48–15.60)	0.009	5.23 (1.50–18.30)	0.009
≥80	1.58 (0.33–7.54)	0.566	2.28 (0.44–11.80)	0.324
Sex				
Female	Ref.			
Male	1.44 (0.62–3.37)	0.401	0.85 (0.32–2.29)	0.749
Anesthesia duration (min)				
<300	Ref.		Ref.	
≥300	3.01 (1.12–8.98)	0.017	3.08 (0.98–9.65)	0.054
Malignancy				
No	Ref.		Ref.	
Yes	4.13 (1.68–10.20)	0.002	2.54 (0.89–7.30)	0.083

Abbreviations as in Tables 1,2.

The mortality rate of symptomatic PE cases was 4.2% (1/24), whereas that of all PE cases was 0.5% (1/217). Because the PE patients in the present study were largely asymptomatic, we sought to identify risk factors related to the severity of postoperative PE. There was no significant difference in D-dimer values between the patients with minor symptoms (decreased SpO_2 alone, n=16) and those with major symptoms (any respiratory or circulatory signs other than decreased SpO_2, n=8) (18.35 [9.78–27] μg/mL vs. 9.75 [5.3–34.43] μg/mL, respectively, P=0.49, **Table 4**). **Table 5** shows the bivariate and multivariate ORs of symptom manifestation in the postoperative PE patients. Unlike in the analysis of the risk factors associated with the development of postoperative PE (**Table 2**), BMI was not related to the development of symptoms. Although the incidence of postoperative PE linearly increased with age, only patients in their 70s had a significant risk of symptom presentation. Anesthesia duration >300 min and the presence of malignancy seemed to correlate with the risk of symptomatic PE in the bivariate analysis. However, the multivariate analysis suggested that these were not independent factors.

Discussion

It is not practical to perform routine PE screening for all surgical patients during the postoperative period to investigate the incidence rate. Therefore, we estimated the incidence of postoperative PE from the interpretations of diagnostic images taken during the postoperative period. In the present study, 1,168 diagnostic imaging cases among 21,763 operations found 217 postoperative PE. The 90-day cumulative incidence of postoperative PE was at least 1.0%, which was 30-fold higher than that in a previous nationwide study[10] based on symptomatic PE in Japanese patients. Our study indicated the insufficiency of the current prophylaxis guidelines for postoperative VTE in preventing the development of postoperative PE. However, symptomatic PE was only seen in 11.1% of all PE patients, and most of their symptoms were very mild. This result implied that, despite the frequent occurrence of PE, clinically significant PE is an uncommon event. However, whether we should update the guidelines in order to prevent asymptomatic PE in the postoperative period remains unknown.

The main strength of this study is that we included both symptomatic and asymptomatic PE events during the postoperative period. Unlike previous reports on postoperative PE, based on some clinical manifestations, our approach revealed the risk factors associated with the postoperative development and the incidence of symptoms in all PE patients. A Japanese national survey (JSA-PTE study) reported an incident rate of 0.03% for the development of symptomatic PE in all types of surgical procedures.[10] The incidence of PE with major symptoms in the present study (n=8, 0.04%) was comparable to the incidence of symptomatic PE in the JSA-PTE study. The National Surgical Quality Improvement Program reported a 0.3–0.6% incidence rate.[4,22] Even after hip and knee arthroplasty, which are one of the highest risk procedures, incidence rates of symptomatic PE were reported as 0.14–0.27% under recommended prophylaxis.[23] These symptom-based studies inevitably underestimate the incidence of PE. Although we likely missed some instances of PE in our cohort, the proportion of asymptomatic cases in the present study implied that symptom-based studies have missed approximately 90% of postoperative PE cases. This proportion is in line with previous reports;[13,24] incidental PE was found in 4.4% of oncologic patients based on routine CT imaging, and 11.1% of patients (2/18) complained of related symptoms.[13] The ratio of asymptomatic DVT to symptomatic VTE has been reported to range from 5:1 to 10:1 in most studies.[24]

Improvements in diagnostic imaging have contributed to the higher incidence of postoperative PE detection. Auer et al[25] reported that chronological increases in PE diagnoses corresponded to increases in the rate of high-resolution MDCT performance; the frequency of high-resolution CT scans during the postoperative periods has increased over time from 6.6 scans/1,000 postoperative patients in 2000 to 45 scans/1,000 patients in 2005. In their results, increased use of MDCT detected more cases of peripheral PE, without increases in the number of cases of central and/or fatal PE, which could account for the increased detection of asymptomatic PE in our study, as 64.8 scans/1,000 operations were performed during our study period.

Although the risk factors associated with the development of VTE have been well studied, those associated with symptom manifestation are still unknown. Our results showed that being aged in the 70s is an independent risk factor of symptomatic PE and the OR for age in the 80s was smaller than that for the 70s. This might reflect differences in the types of surgery, surgical procedures such as lymph node dissection, and postoperative coagulability. In addition, the multivariate analysis implied that there were some confounders relating to longer anesthesia duration and presence of malignancy. These factors are related not only to a longer period of immobility but also more invasive procedures. Because of the small number of the events, a larger study is required to investigate this further.

Regarding symptomatic PE, both the incidence and mortality rates were lower in our study than in a previous study.[10] One likely reason is that most patients in the present study had small thrombi located in the peripheral pulmonary arteries. We hypothesize that less frequent central PE occurrence, with the current prophylaxis guidelines, could prevent development of massive thrombi in large veins. In addition to mechanical prevention, novel anticoagulants, especially direct oral anticoagulants (DOACs), have been marketed in Japan and permitted for VTE prevention (Fondaparinux in 2007, Enoxaparin in 2008, Edoxaban in 2011, Rivaroxaban and Apixaban in 2015). A previous study showed chronological decreases in the incidence of symptomatic PE together with the emergence of these drugs,[10] and the current guidelines recommend administration of these drugs for high-risk patients.[2] Our institution follows these guidelines for all surgical inpatients, which might have contributed to the decrease in PE occurrence. However, the effect of these approaches on the alleviation of symptoms still requires further assessment.

D-dimer is the most useful biomarker for thrombotic events, with a superior negative predictive value.[26] However, we cannot argue for the diagnostic value of D-dimer for PE risk, because we only studied D-dimer values in patients with PE. We found that the D-dimer values did not differ between symptomatic and asymptomatic patients. Additionally, there was no difference among patients with minor and major symptoms in the symptomatic cohort. Given these results, and the fact that D-dimer in the postoperative period is significantly affected by the surgical procedure, we cannot recommend the prediction of the severity of PE symptoms from this value. However, we recommend basing treatment decisions on other factors, such as the size of thrombi in the images and the patient's risk factors, as mentioned in the guidelines for treatment of VTE.[27,28]

Study Limitations

First, the rates of performing postoperative diagnostic imaging affected the results. Additionally, there was a considerable difference between the types of surgeries that included postoperative diagnostic imaging because decisions to request these examinations were at the discretion of the attending physicians. Although the patients undergoing surgeries at high risk for VTE, such as total knee and hip arthroplasty and esophageal surgery, are frequently evaluated for PE occurrence after the surgery, low-risk patients were examined only when PE was suspected by either symptoms or laboratory data, such as an unusual elevation in D-dimer level. This may exaggerate the risk of PE in "high risk" surgeries and underestimate it in "low risk" surgeries. Our approach to estimating the incidence rate of PE cannot be generalized to other hospitals, because we should be minimizing patients' radiation exposure and medical costs. Second, this is a single-center study, resulting in biased patient ethnicities and backgrounds. More than 99% of patients were Asian-Japanese, which likely affected the incidence rates and weakened the generalizability of our findings, because a difference in VTE incidence between the races is well recognized.[10,20,29] In addition, the institution is a core hospital in the area, so operative procedures are likely become more invasive, and we are more likely to be referred patients with severe complications. No ambulatory surgeries were included in this study. Therefore, the patients' status could contribute to the higher incidence rates of PE compared with previous Japanese nationwide studies. However, the ratio of symptomatic to asymptomatic patients in the present study was comparable to previous well-designed studies. We believe that our results are informative for all clinicians.

In conclusion, we report an incidence of postoperative PE diagnosis that was higher than reported by previous studies based on our detailed review of postoperative imaging data. The current guidelines for the prevention of VTE do not eliminate the development of small, asymptomatic, and postoperative PE. However, because most of our PE patients had either no or mild symptoms, our study findings emphasize the need for future studies on whether updating the current prophylaxis guidelines to both detect and prevent asymptomatic PE during the postoperative period can would improve overall prognosis.

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Disclosure of Conflicts of Interest

All authors have no conflicts of interest to disclose. There are no funding sources to declare for this study.

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