INTRODUCTION

Venous thromboembolism (VTE), including deep venous thrombosis (DVT) and pulmonary embolism (PE), is generally considered a common and similar disease entity that expresses different clinical features [1,2]. VTE is a major cause of morbidity and mortality in most Western countries [3]. VTE is the leading cause of preventable early death with appropriate treatment. Hip fracture, major general surgery, major trauma, malignancy/chemotherapy, bed rest ≥3 days, and recent pregnancy (within 3 months of delivery) are well-known risk factors for the occurrence of VTE [4]. The incidence of VTE is lower in Asian countries than in Western countries. Several population-based studies have shown that, although the overall incidence of PE is reduced, the average mortality rate remains high at 14% to 30% [5].

VTE can be confirmed using computed tomography (CT) for PE and a combination of compression ultrasound (CUS) and CT for DVT. CUS is the most common imaging modality for DVT. For the diagnosis of proximal DVT, CUS shows a sensitivity of 90.1% and specificity of 97.3% [6]; however, recent advances in imaging technologies have replaced CUS with CT for diagnosing DVT.

The introduction of anticoagulant therapy reduces VTE-related mortality and morbidity [7]. The recent American College of Chest Physician guidelines recommend at least...
three months of a new oral anticoagulant (NOAC; such as dabigatran, rivaroxaban, apixaban, and edoxaban) alone over warfarin for acute VTE [8]. The advent of acute-phase anticoagulant treatment strategies might improve the clinical outcomes of patients with VTE. The absence of anticoagulation therapy is associated with a 3.2-fold increase in mortality [9].

This study aimed to analyze the clinical outcomes of VTE patients and identify the predictors of VTE-related unfavorable outcomes, such as major bleeding and 30-day all-cause mortality.

MATERIALS AND METHODS

From January 2016 to December 2020, 198 patients with confirmed VTE were enrolled. DVT was diagnosed using CUS or CT venography (CTV). PE was confirmed using CT pulmonary angiography (CTPA). All CTV and CTPA results were elucidated by two board-certified radiologists specializing in vascular imaging.

DVT was classified into proximal or distal. Proximal DVT was defined as a thrombus affecting the popliteal or proximal vein (Fig. 1). Each PE was diagnosed using CTPA (Fig. 2). Additionally, the simplified pulmonary embolism severity index (sPESI) was calculated. A high sPESI was defined as age >80 years; systolic blood pressure <100 mmHg; heart rate >110 bpm; O2 saturation <90%; or current diagnosis of cancer, heart failure, or chronic obstructive pulmonary disease (COPD) [10]. Anticoagulation regimens included unfractionated or low molecular weight heparin followed by oral vitamin K antagonist or NOACs for at least three months. An international normalized ratio of 1.5 to 2.5 was considered an appropriate therapeutic range.

In this study, patients with confirmed VTE were classified into isolated DVT or PE (PE with or without DVT) groups. Their clinical characteristics and risk factors (age >70 years; previous VTE; immobilization ≥3 days; history of trauma or surgery ≤4 weeks prior; history of malignancy and/or chemotherapy, hypertension, diabetes, coronary artery disease, heart failure, chronic kidney disease, cere-
brovascular accident, dementia, or COPD) for unfavorable outcomes and early all-cause mortality were evaluated.

A recent event was defined as any event that occurred within one month after a VTE diagnosis. VTE-related clinical outcomes were divided into unfavorable outcomes, major bleeding, and all-cause mortality. VTE-related unfavorable outcomes were defined when at least one of the following criteria was met: 1) hypotension (SBP <100 mmHg) or shock; 2) need for mechanical ventilation; 3) need for catecholamines to maintain organ perfusion; 4) need for cardiopulmonary resuscitation; and 5) all-cause death. Major bleeding was defined as life-threatening bleeding requiring transfusion of at least two units of packed red blood cells associated with a decrease in hemoglobin level >2 g/dL or the presence of retroperitoneal, intracranial, or intraocular bleeding. Massive PE was defined as PE associated with systemic hypotension (systolic blood pressure <90 mmHg), PE requiring cardiopulmonary resuscitation, or the need for catecholamines.

Clinical outcomes such as unfavorable outcome, major bleeding, and 30-day all-cause mortality for patients with VTE were analyzed, and the clinical characteristics were compared between the DVT and PE groups using Fisher’s exact test and the Chi-squared test. We also performed a univariate analysis of troponin I using enzyme immunoassay and d-dimer using enzyme-linked immunosorbent assay as risk factors for the development of unfavorable outcomes, major bleeding, and all-cause mortality.

Specified risk factors for unfavorable outcomes, major bleeding, and all-cause mortality within one month of diagnosis were analyzed using univariate and multiple logistic regression analyses. Candidate predictors (P<0.25 after univariate analysis) and several variables possibly associated with VTE outcome were included in each multivariate regression analysis. All P-values were two-tailed. Statistical significance was considered at P<0.05. All statistical analyses were performed using SPSS Statistics for Windows version 27 (IBM, Armonk, NY, USA).

Our study was approved by the Institutional Review Board of Seoul Medical Center (IRB no. 2021-05-001-002).

RESULTS

1) Clinical characteristics and outcomes

A total of 198 patients with VTE were enrolled, including 62 (31.3%) patients with isolated DVT, 100 (50.5%) with both DVT and PE, and 36 (18.2%) with PE alone. In addition, 49 (24.7%) had calf vein thrombosis and 113 (57.1%) had proximal DVT. The mean age was 71.6±15.06 years and the mean body mass index was 23.2±4.69. VTE-related unfavorable outcomes occurred in 26 (13.1%) patients, with a 30-day all-cause mortality of 17 (8.6%) patients. Of 62 patients with isolated DVT, 7 (11.3%) had unfavorable outcomes and 5 (8.1%) had all-cause mortality. Among 100 patients with DVT and PE, 13 (13.0%) had unfavorable outcomes and 8 (8.0%) had all-cause mortality. Among 36 patients with PE alone, 6 (16.7%) had unfavorable outcomes and 4

| Table 1. Demographic features |
|-------------------------------|
| Demographic feature          | All patient (n=198) | Isolated DVT (n=62, 31.3%) | PE (n=136, 68.7%) | P-value* |
| Age (y)                      | 71.58±15.06         | -                           | -                | -       |
| ≤50                          | 19 (9.6)            | 6 (9.7)                     | 13 (9.6)         | -       |
| 51-70                        | 55 (27.8)           | 20 (32.3)                   | 35 (25.7)        | -       |
| ≥71                          | 124 (62.6)          | 36 (58.1)                   | 88 (64.7)        | 0.370   |
| Body mass index              | 23.2±4.69           | -                           | -                | -       |
| >25                          | 64 (32.3)           | 20 (32.3)                   | 44 (32.4)        | 0.989   |
| Sex, male                    | 78 (39.4)           | 25 (40.3)                   | 53 (39.0)        | -       |
| Vital sign                   |                    |                              |                  |         |
| Pulse rate ≥110/min          | 27 (13.6)           | 3 (4.8)                     | 24 (17.6)        | 0.014   |
| Systolic blood pressure <90 mmHg | 20 (10.1)       | 6 (9.7)                     | 14 (10.3)        | 0.894   |
| Respiratory rate ≥30/min     | 16 (8.1)            | 3 (4.8)                     | 13 (9.6)         | 0.400   |
| Body temperature <36°C       | 3 (1.5)             | 0 (0.0)                     | 3 (2.2)          | 0.553   |
| Risk factor for VTE          |                    |                              |                  |         |
| History of VTE              | 16 (8.1)            | 5 (8.1)                     | 11 (8.1)         | 0.995   |
| Immobilization ≥3 days       | 106 (53.5)          | 40 (64.5)                   | 66 (48.5)        | 0.036   |
| Recent surgery <4 weeks      | 53 (26.8)           | 25 (40.3)                   | 28 (20.6)        | 0.004   |
| Active malignancy and/or chemotherapy | 46 (23.2)  | 10 (16.1)                   | 36 (26.5)        | 0.110   |
had all-cause mortality.

Several clinical characteristics showed statistically significant differences between the DVT and PE groups (Table 1). The prevalence of those with immobilization ≥3 days, recent surgery ≤4 weeks, the presence of COPD, pulse ≥110/ min, and a high sPESI was significantly higher in the PE group. Unfavorable outcomes (11.3% in the DVT group vs. 14.0% in the PE group, P=0.605) and all-cause mortality (8.1% vs. 8.8%, P=0.860) were lower in the DVT group than in the PE group, but the difference was not significant (Table 1).

| Demographic feature | All patient (n=198) | Isolated DVT (n=62, 31.3%) | PE (n=136, 68.7%) | P-value* |
|---------------------|---------------------|-----------------------------|-------------------|----------|
| Comorbidities       |                     |                             |                   |          |
| Hypertension        | 114 (57.6)          | 36 (58.1)                   | 78 (57.4)         | 0.925    |
| Diabetes mellitus   | 57 (28.8)           | 17 (27.4)                   | 40 (29.4)         | 0.774    |
| Coronary artery disease | 16 (8.1)      | 3 (4.8)                     | 13 (9.6)          | 0.400    |
| Chronic kidney disease | 9 (4.5)         | 3 (4.8)                     | 6 (4.4)           | >0.999   |
| Chronic heart failure | 11 (5.6)        | 1 (1.6)                     | 10 (7.4)          | 0.178    |
| Smoking             | 29 (14.6)           | 13 (21.0)                   | 16 (11.8)         | 0.089    |
| Pneumonia           | 38 (19.2)           | 6 (9.7)                     | 32 (23.5)         |          |
| Chronic obstructive pulmonary disease | 18 (9.1)   | 1 (1.6)                     | 17 (12.5)         | 0.014    |
| All pulmonary disease | 56 (28.3)        | 8 (12.9)                    | 48 (35.3)         | 0.001    |
| Cerebrovascular accident | 41 (20.7)     | 12 (19.4)                   | 29 (21.3)         |          |
| Dementia            | 29 (14.6)           | 9 (14.5)                    | 20 (14.7)         |          |
| Location of PE      |                     |                             |                   |          |
| Main & lobar arteries | 2 (1.0)          | 0 (0.0)                     | 2 (1.5)           |          |
| Segmental & subsegmental arteries | 45 (22.7) | 0 (0.0)                     | 45 (33.1)         |          |
| Massive PE          | 24 (12.1)           | 7 (11.3)                    | 17 (12.5)         | 0.809    |
| Location of DVT     |                     |                             |                   |          |
| Distal              | 49 (24.7)           | 16 (25.8)                   | 33 (24.3)         |          |
| Proximal            | 113 (57.1)          | 46 (74.2)                   | 67 (49.3)         |          |
| High sPESI          | 124 (62.6)          | 29 (46.8)                   | 95 (69.9)         | 0.002    |
| Inferior vena cava filter insertion | 40 (20.2) | 15 (24.2)                   | 25 (18.4)         | 0.345    |
| Anticoagulation treatment | 185 (93.4) | 55 (88.7)                   | 130 (95.6)        | 0.070    |
| Novel oral anticoagulants | 122 (61.6) | 32 (51.6)                   | 90 (66.2)         | 0.051    |
| Need for mechanical ventilation | 8 (4.0) | 2 (3.2)                     | 6 (4.4)           | >0.999   |
| Need for inotropics | 14 (7.1)            | 4 (6.5)                     | 10 (7.4)          | >0.999   |
| Need for thrombolysis or thrombectomy | 1 (0.5) | 0 (0.0)                     | 1 (0.7)           |          |
| Cardiopulmonary resuscitation | 3 (1.5) | 0 (0.0)                     | 3 (2.2)           | 0.553    |
| Unfavorable outcome | 26 (13.1)           | 7 (11.3)                    | 19 (14.0)         | 0.605    |
| Major bleeding      | 6 (3.0)             | 2 (3.2)                     | 4 (2.9)           | >0.999   |
| PE-related death    | 3 (1.5)             | 0 (0.0)                     | 3 (2.2)           | 0.553    |
| All-cause mortality | 17 (8.6)            | 5 (8.1)                     | 12 (8.8)          | 0.860    |

Total (n=133) DVT only (n=31, 23.3%) PE±DVT (n=102, 76.7%)

| Arterial saturation <90% | Total (n=158) DVT only (n=41, 25.9%) PE±DVT (n=117, 74.1%) |
|--------------------------|----------------------------------------------------------------|
| Total                    | 30 (22.6)                                                       | 7 (22.6)                                                      | 23 (22.5) |
| Elevated D-dimer         | 151 (95.6)                                                      | 38 (92.7)                                                     | 113 (96.6) |
| Elevated troponin I      | 36 (27.9)                                                       | 7 (22.6)                                                      | 29 (29.6) |

Values are presented as mean±standard deviation or number (%). DVT, deep venous thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism; sPESI, simplified pulmonary embolism severity score; -, not available.

*a Chi-squared test or Fisher exact test, logistic regression model.
Table 2. Characteristics of patients with unfavorable outcomes (n=26)

| Risk factor                                      | Unfavorable outcome (n=26, 13.1%) | Univariate P-value<sup>a</sup> | Multivariate P-value<sup>a</sup> | 95% CI       |
|--------------------------------------------------|-----------------------------------|--------------------------------|---------------------------------|--------------|
| **Age (y)**                                      | 74.5±13.2                         | 0.449                          | -                               | -            |
| ≥71                                              | 19 (73.1)                         | -                              | 0.305                           | 0.566-6.169  |
| **Body mass index**                              | 22.55±7.94                        | -                              | -                               | -            |
| >25                                              | 5 (19.2)                          | 0.126                          | 0.890                           | 0.255-3.277  |
| Symptom of DVT and PE                            | 20 (76.9)                         | 0.227                          | 0.415                           | 0.501-5.343  |
| Subjective leg symptom (edema)                   | 10 (38.5)                         | 0.650                          | -                               | -            |
| Subjective chest symptom                         | 11 (42.3)                         | 0.338                          | -                               | -            |
| **Risk factor for VTE**                          |                                   |                                 |                                  |              |
| History of VTE                                   | 2 (7.7)                           | >0.999                         | -                               | -            |
| Immobilization ≥3 d                              | 19 (73.1)                         | 0.032                          | 0.092                           | 0.849-8.644  |
| Recent surgery <4 wk                             | 7 (26.9)                          | 0.985                          | -                               | -            |
| Active malignancy and/or chemotherapy            | 8 (30.8)                          | 0.329                          | 0.457                           | 0.464-5.518  |
| **Comorbidities**                                |                                   |                                 |                                  |              |
| Hypertension                                     | 15 (57.7)                         | 0.990                          | -                               | -            |
| Diabetes mellitus                                | 11 (42.3)                         | 0.102                          | 0.637                           | 0.443-3.777  |
| Coronary artery disease                          | 3 (11.5)                          | 0.447                          | 0.228                           | 0.544-12.774 |
| Chronic kidney disease                           | 2 (7.7)                           | 0.336                          | -                               | -            |
| Chronic heart failure                            | 2 (7.7)                           | 0.641                          | -                               | -            |
| Smoking                                          | 5 (19.2)                          | 0.478                          | -                               | -            |
| Pneumonia                                        | 6 (23.1)                          | 0.589                          | -                               | -            |
| Chronic obstructive pulmonary disease            | 4 (15.4)                          | 0.266                          | 0.456                           | 0.082-3.072  |
| All pulmonary disease                            | 11 (42.3)                         | 0.102                          | -                               | -            |
| Cerebrovascular accident                         | 4 (15.4)                          | 0.608                          | -                               | -            |
| Dementia                                         | 6 (23.1)                          | 0.192                          | 0.385                           | 0.118-2.285  |
| **Vital sign**                                   |                                   |                                 |                                  |              |
| Pulse rate ≥110/min                              | 13 (50.0)                         | 0.001                          | <0.001                          | 3.418-44.744 |
| Systolic blood pressure <90 mmHg                 | 20 (76.9)                         | 0.001                          | -                               | -            |
| Respiratory rate ≥30/min                         | 8 (30.8)                          | 0.001                          | 0.013                           | 1.429-21.392 |
| Body temperature <36°C                           | 2 (7.7)                           | 0.046                          | 0.512                           | 0.108-86.780 |
| **Types of VTE**                                 |                                   |                                 |                                  |              |
| Isolated DVT                                     | 7 (26.9)                          | 0.605                          | -                               | -            |
| PE                                               | 19 (73.1)                         | 0.605                          | -                               | -            |
| Inferior vena cava filter insertion              | 6 (23.1)                          | 0.695                          | -                               | -            |
| Anticoagulation treatment                        | 23 (88.8)                         | 0.385                          | 0.075                           | 0.050-1.155  |
| (n=23, 12.4%)                                    |                                   |                                 |                                  |              |
| **Novel oral anticoagulants (total n=185)**       | 14 (60.9)                         | 0.583                          | -                               | -            |
| (n=24, 18.0%)                                    |                                   |                                 |                                  |              |
| **Arterial saturation <90% (total n=133)**        | 12 (50.0)                         | 0.001                          | -                               | -            |
| (n=22, 13.9%)                                    |                                   |                                 |                                  |              |
| Elevated D-dimer (total n=158)                   | 22 (100.0)                        | 0.594                          | -                               | -            |
| (n=24, 18.6%)                                    |                                   |                                 |                                  |              |
| Elevated troponin I (total n=129)                | 11 (45.8)                         | 0.030                          | -                               | -            |

Values are presented as mean±standard deviation or number (%). CI, confidence interval; DVT, deep venous thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism; -, not available.<sup>a</sup> Chi-squared test or Fisher exact test, logistic regression model.
1) Among 46 patients with malignancy±chemotherapy, lung cancer was the most common malignancy (n=11 [23.9%]), and the prevalence of PE was higher than that of DVT (78.3% vs. 21.7%). However, the difference between the two groups was not statistically significant (P=0.110).

2) Predictors for unfavorable outcome

VTE-related unfavorable outcomes were observed in 26 (13.1%) patients. Among the 16 patients with a respiratory rate ≥30/min, 8 (50.0%) showed an unfavorable outcome (Table 2). Univariate analysis of risk factors revealed that immobilization ≥3 days (P=0.032), pulse ≥110/min (P=0.001), respiratory rate ≥30/min (P=0.001), and temperature <36°C (P=0.046) were statistically significant risk factors (Table 2). In addition, the troponin I test was performed in 129 patients, and an elevated level was identified as a statistically significant factor for VTE-related unfavorable outcomes in the univariate analysis (P=0.030). We obtained arterial blood gas analysis data for 133 of 198 patients with VTE. An arterial saturation <90% was statistically significant in the univariate analysis (P=0.001). However, the presence of coronary artery disease and congestive heart failure, VTE type, VTE location, anticoagulation treatment, and elevated d-dimer levels were not significantly associated.

The multivariate analysis revealed that pulse ≥110/min (odds ratio [OR], 12.4; 95% confidence interval [CI], 3.4-44.7; P=0.001) and respiratory rate ≥30/min (OR, 5.5; 95% CI, 1.4-21.4; P=0.013) were statistically significant predictors of VTE-related unfavorable outcomes (Table 2).

3) Risk factors for major bleeding

Major bleeding occurred in 6 (3.0%) patients (Table 3). The major bleeding rate in patients with a history of recent surgery ≤4 weeks was higher than that in patients without a history [4/53 (7.5%) vs. 2/145 (1.4%)]. With regard to recent surgery, hip surgery was the most common (n=14 [26.4%]), followed by spine surgery (n=9 [17.0%]). Major bleeding occurred in the brain, hip joint, and stomach in each of those two cases. Risk factors for major bleeding were subjected to univariate analysis, and a history of recent surgery was statistically significant (P=0.045). However, in the multivariate analysis, diabetes was statistically significant (P=0.043).

4) Predictors for all-cause mortality

All-cause mortality was observed in 17 patients (8.6%). A history of malignancy±chemotherapy was present in 46 of 198 patients. Lung cancer was the most common (n=11 [23.9%]), followed by colon cancer (n=8 [17.4%]). Stage IV cancer was the most common (n=14 [30.4%]). Among the 24 patients with massive PE, all-cause mortality occurred in 10 (41.7%). Among the 124 patients with high sPESI, all-cause mortality occurred in 15 (12.1%). Anticoagulation treatment was administered to 185 (93.4%). All-cause mortality occurred in 4 (30.8%) patients not treated with anticoagulants and in 13 (7.0%) patients treated with anticoagulants. In addition, 6 of 8 (75.0%) patients who needed mechanical ventilation died within 30 days of their hospital stay. The univariate analysis revealed no NOACs, arterial

| Table 3. Characteristics of patients with major bleeding (n=6) |
|----------------------|----------------------|----------------------|
| **Risk factor** | **Major bleeding** | **Univariate** | **Multivariate** | **95% CI** |
| **Age (y)** | 71.83±16.52 | 0.364 | - | - |
| ≤50 | 0 (0.0) | - | - | - |
| 51-70 | 3 (50.0) | - | - | - |
| ≥71 | 3 (50.0) | - | - | - |
| **Body mass index** | 21.87±1.93 | - | - | - |
| >25 | 0 (0.0) | 0.180 | 0.996 | - |
| (n=5, 2.5%) | | | | |
| **Symptom of DVT and PE (total n=197)** | 3 (60.0) | >0.999 | - | - |
| Subjective leg symptom (edema) | 1 (20.0) | 0.661 | - | - |
| Subjective chest symptom | 2 (40.0) | >0.999 | - | - |
| **Risk factor for VTE** | | | | |
| History of VTE | 0 (0.0) | >0.999 | - | - |
| Immobilization ≥3 d | 5 (83.3) | 0.219 | 0.642 | 0.132-26.737 |
| Recent surgery <4 wk | 4 (66.7) | 0.045 | 0.254 | 0.407-29.980 |
| Active malignancy and/or chemotherapy | 1 (16.7) | >0.999 | - | - |
Table 3. Continued

| Risk factor                              | Major bleeding (n=6, 3.0%) | Univariate | Multivariate | 95% CI |
|------------------------------------------|---------------------------|------------|--------------|--------|
|                                          |                           | P-value     | P-value      |        |
| Comorbidities                            |                           |            |              |        |
| Hypertension                             | 2 (33.3)                  | 0.404      |              | -      |
| Diabetes mellitus                        | 4 (66.7)                  | 0.058      | 0.043        | 1.074-68.319 |
| Coronary artery disease                  | 1 (16.7)                  | 0.401      |              | -      |
| Chronic kidney disease                   | 0 (0.0)                   | >0.999     |              | -      |
| Chronic heart failure                    | 0 (0.0)                   | >0.999     |              | -      |
| Smoking                                  | 1 (16.7)                  | >0.999     |              | -      |
| Pneumonia                                | 2 (33.3)                  | 0.325      |              | -      |
| Chronic obstructive pulmonary disease    | 0 (0.0)                   | >0.999     |              | -      |
| All pulmonary disease                    | 2 (33.3)                  | >0.999     |              | -      |
| Cerebrovascular accident                 | 2 (33.3)                  | 0.606      |              | -      |
| Dementia                                 | 1 (16.7)                  | >0.999     |              | -      |
| Vital sign                               |                           |            |              |        |
| Pulse rate ≥110/min                      | 1 (16.7)                  | 0.590      |              | -      |
| Systolic blood pressure <90 mmHg         | 1 (16.7)                  | 0.477      |              | -      |
| Respiratory rate ≥30/min                 | 2 (33.3)                  | 0.076      | 0.113        | 0.589-147.536 |
| Body temperature <36°C                   | 0 (0.0)                   | >0.999     |              | -      |
| Types of VTE                             |                           |            |              |        |
| Isolated DVT                             | 2 (33.3)                  | >0.999     |              | -      |
| PE                                       | 4 (66.7)                  | >0.999     |              | -      |
| Inferior vena cava filter insertion      | 3 (50.0)                  | 0.098      | 0.089        | 0.702-140.721 |
| Anticoagulation treatment                | 5 (83.3)                  | 0.338      | 0.379        | 0.017-4.677 |
| (n=5, 2.7%)                              |                           |            |              |        |
| Novel oral anticoagulants (total n=185)  | 3 (60.0)                  | >0.999     |              | -      |
| (n=6, 4.5%)                              |                           |            |              |        |
| Arterial saturation <90% (total n=133)   | 2 (33.3)                  | 0.617      |              | -      |
| (n=4, 2.5%)                              |                           |            |              |        |
| Elevated D-dimer (total n=158)           | 4 (100.0)                 | >0.999     |              | -      |
| (n=4, 3.1%)                              |                           |            |              |        |
| Elevated troponin I (total n=129)        | 0 (0.0)                   | 0.576      |              | -      |

Values are presented as mean±standard deviation or number (%).
CI, confidence interval; DVT, deep venous thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism; -, not available.
*Chi-squared test or Fisher exact test, logistic regression model.

saturation <90%, history of malignancy±chemotherapy, pulse ≥110/min, systolic blood pressure <90 mmHg, respiratory rate ≥30/min, massive PE, high sPESI, anticoagulation treatment, need for mechanical ventilation, need for inotropics, and cardiopulmonary resuscitation were risk factors for all-cause mortality (Table 4). Multivariate regression analysis showed that a history of malignancy±chemotherapy (OR, 7.38; 95% CI, 1.219-44.681; P=0.030), anticoagulation treatment (OR, 0.061; 95% CI, 0.006-0.590; P=0.016), and need for mechanical ventilation (OR, 235.220; 95% CI, 4.954-11168.024; P=0.006) were statistically significant predictors of all-cause mortality (Table 4).

**DISCUSSION**

VTE, including DVT and PE, is common in hospitalized patients. DVT and PE have the same disease processes but different clinical manifestations. However, few studies have reported the overall clinical outcomes of VTE. Despite recent advances in medicine, the 30-day all-cause mortality of VTE remains high around 8% to 11% [9,11]. Our study findings also indicated that the 30-day all-cause mortality rate was relatively high (8.6%). Tagalakis et al. [11] reported that the 30-day mortality rate after VTE was 10.6%. The all-cause mortality rates of DVT and PE were similar (8.1%
vs. 8.8%).

Our multivariate analysis showed that a high pulse and respiratory rate were statistically significant predictors of unfavorable outcomes. As expected, tachycardia and tachypnea were early signs of shock and cardiopulmonary resuscitation. This should be interpreted as physicians employing aggressive intervention for tachycardia and tachypnea in VTE patients to prevent unfavorable outcomes.

In several randomized controlled trials, the incidence of major bleeding at 3 to 6 months is as high as 4% [12,13]. In the present study, 30-day major bleeding occurred in 6 of 198 (3.0%) of the enrolled patients, a rate slightly lower than that reported in previous studies. Of the 185 patients who underwent anticoagulation treatment, 5 (2.7%) had major bleeding. Our multivariate analysis showed that diabetes mellitus was the only predictor of VTE-related major bleeding. The present study found that major bleeding was not associated with all-cause mortality.

Several studies have reported that increased age is associated with mortality [14,15]. In our study, 14 of 124 (11.3%) patients older than 70 years and 3 of 74 (4.1%) patients younger than 70 years died; the difference was not statistically significant. Those with a systolic blood pressure <90 mmHg at the initial event showed a higher all-cause mortality rate (30.0% vs. 6.2%). In addition, massive PE (41.7%), high sPESI (12.1%), and a respiratory rate >30/min (30.0%)

### Table 4. Demographics of all-cause mortality (n=17)

| Risk factor                                      | All-cause mortality (n=17, 8.6%) | Univariate P-value | Multivariate P-value | 95% CI      |
|--------------------------------------------------|----------------------------------|--------------------|----------------------|-------------|
| Age (y)                                          | 76.24±14.83                     | 0.24               | -                    | -           |
| ≤50                                              | 1 (5.9)                          | -                  | -                    | -           |
| 51-70                                            | 2 (11.8)                         | -                  | -                    | -           |
| ≥71                                              | 14 (82.4)                        | -                  | 0.242               | 0.376-48.124|
| Body mass index                                  | 22.36±5.19                       | -                  | -                    | -           |
| >25                                              | 3 (17.6)                         | 0.277              | -                    | -           |
| Symptom of DVT and PE                            | 11 (68.8)                        | 0.842              | -                    | -           |
| Subjective leg symptom (edema)                   | 7 (43.8)                         | 0.418              | -                    | -           |
| Subjective chest symptom                         | 5 (31.3)                         | 0.808              | -                    | -           |
| Risk factor for VTE                              |                                  |                     |                      |             |
| History of VTE                                   | 2 (11.8)                         | 0.633              | -                    | -           |
| Immobilization ≥3 d                              | 10 (58.8)                        | 0.648              | -                    | -           |
| Recent surgery <4 wk                             | 3 (17.6)                         | 0.568              | -                    | -           |
| Active malignancy and/or chemotherapy            | 8 (47.1)                         | 0.015              | 0.030               | 1.219-44.681|
| Comorbidities                                    |                                  |                     |                      |             |
| Hypertension                                     | 12 (70.6)                        | 0.256              | -                    | -           |
| Diabetes mellitus                                | 5 (29.4)                         | 0.953              | -                    | -           |
| Coronary artery disease                          | 3 (17.6)                         | 0.146              | 0.070               | 0.847-48.882|
| Chronic kidney disease                           | 1 (5.9)                          | 0.562              | -                    | -           |
| Chronic heart failure                            | 3 (17.6)                         | 0.057              | 0.299               | 0.321-40.396|
| Smoking                                           | 4 (23.5)                         | 0.284              | -                    | -           |
| Pneumonia                                         | 4 (23.5)                         | 0.747              | -                    | -           |
| Chronic obstructive pulmonary disease             | 3 (17.6)                         | 0.190              | >0.999              | 0.084-11.891|
| All pulmonary disease                            | 6 (35.3)                         | 0.535              | -                    | -           |
| Cerebrovascular accident                          | 1 (5.9)                          | 0.206              | 0.071               | 0.003-1.272 |
| Dementia                                          | 4 (23.5)                         | 0.284              | -                    | -           |
| Vital sign                                        |                                  |                     |                      |             |
| Pulse rate ≥110/min                              | 7 (41.2)                         | 0.001              | 0.484               | 0.180-37.384|
| Systolic blood pressure <90 mmHg                 | 6 (35.3)                         | 0.001              | -                    | -           |
| Respiratory rate ≥30/min                         | 5 (29.4)                         | 0.001              | 0.213               | 0.466-30.763|
| Body temperature <36°C                           | 1 (5.9)                          | 0.237              | 0.783               | 0.000-8562.725|
had higher all-cause mortality rates. Regarding the anticoagulant treatment strategies, the NOAC group showed a lower mortality rate than the other anticoagulant groups (3.3% vs. 14.3%). The better results in the NOAC versus vitamin K antagonist group are thought to be attributed to the convenience of use, minor drug and food interactions, consistent pharmacokinetics and pharmacodynamics, and good compliance [16]. The multivariate regression analysis showed that a history of malignancy±chemotherapy, anticoagulation treatment, and need for mechanical ventilation were statistically significant predictors of all-cause mortality. This group of patients should be monitored closely, and aggressive interventions are needed to prevent mortality.

**CONCLUSION**

VTE-related mortality and morbidity rates remained high (8.1%–8.8%). In cases of tachycardia and tachypnea, early aggressive treatment is needed to prevent unfavorable outcomes. Patients with a history of malignancy, no anticoagulation use, and need for mechanical ventilation should be monitored closely to prevent mortality.

**FUNDING**

None.

---

**Table 4. Continued**

| Risk factor                                      | n=17 (8.6%) | Univariate | Multivariate | 95% CI          |
|-------------------------------------------------|-------------|------------|--------------|-----------------|
| Types of VTE                                     |             |            |              |                 |
| Isolated DVT                                    | 5 (29.4)    | 0.860      | -            | -               |
| PE                                              | 12 (70.6)   | 0.860      | -            | -               |
| Massive PE                                      | 10 (58.8)   | 0.001      | 0.795        | 0.047-54.305    |
| High sPESI                                      | 15 (88.2)   | 0.033      | -            | -               |
| Inferior vena cava filter insertion             | 3 (17.6)    | >0.999     | -            | -               |
| Anticoagulation treatment                       | 13 (76.5)   | 0.017      | 0.016        | 0.006-0.590     |
| Novel oral anticoagulants                       | 4 (23.5)    | 0.583      | -            | -               |
| Need for mechanical ventilation                 | 6 (35.3)    | 0.001      | 0.006        | 4.954-11168.024 |
| Need for inotropics                             | 8 (47.1)    | 0.001      | 0.754        | 0.061-47.367    |
| Need for thrombolysis or thrombectomy           | 0 (0.0)     | >0.999     | -            | -               |
| Cardiopulmonary resuscitation                   | 2 (11.8)    | 0.020      | 0.291        | 0.098-2310.987  |
| Major bleeding                                  | 1 (5.9)     | 0.421      | -            | -               |
| Arterial saturation <90%                        | 9 (60.0)    | 0.001      | -            | -               |
| Elevated D-dimer                                | 15 (100.0)  | >0.999     | -            | -               |
| Elevated troponin I                             | 7 (50.0)    | 0.051      | -            | -               |

Values are presented as mean±standard deviation or number (%). CI, confidence interval; DVT, deep venous thrombosis; PE, pulmonary embolism; VTE, venous thromboembolism; sPESI, simplified pulmonary embolism severity score; -, not available.

*aChi-squared test or Fisher exact test, logistic regression model.

---

**CONFLICTS OF INTEREST**

The authors have nothing to disclose.

**ORCID**

Han Young Lee  
https://orcid.org/0000-0002-6509-4154  
Tae Hoon Yeo  
https://orcid.org/0000-0002-6705-3540  
Tae Kyung Heo  
https://orcid.org/0000-0001-8275-2377  
Young Gyu Cho  
https://orcid.org/0000-0001-9665-0945  
Dong Hui Cho  
https://orcid.org/0000-0003-4515-521X  
Kyung Bok Lee  
https://orcid.org/0000-0003-1111-118X

**AUTHOR CONTRIBUTIONS**

Conception and design: HYL, KBL. Analysis and interpretation: HYL, KBL. Data Collection: THY, TKH. Writing the article: HYL, KBL. Critical revision of the article: YGC, DHC. Final approval of the article: all authors. Statistical analysis: KBL. Obtained funding: None. Overall responsibility: KBL.
REFERENCES

1) Schulman S, Ageno W, Konstantinides SV. Venous thromboembolism: past, present and future. Thromb Haemost 2017;117:1219-1229.
2) Tritschler T, Kraaijpoel N, Le Gal G, Wells PS. Venous thromboembolism: advances in diagnosis and treatment. JAMA 2018;320:1583-1594.
3) Arcelus JI, Caprini JA, Monreal M, Suárez C, González-Fajardo J. The management and outcome of acute venous thromboembolism: a prospective registry including 4011 patients. J Vasc Surg 2003;38:916-922.
4) Anderson FA Jr, Spencer FA. Risk factors for venous thromboembolism. Circulation 2003;107(23 Suppl 1):I9-I16.
5) Nakamura M, Fujioka H, Yamada N, Sakuma M, Okada O, Nakanishi N, et al. Clinical characteristics of acute pulmonary thromboembolism in Japan: results of a multicenter registry in the Japanese Society of Pulmonary Embolism Research. Clin Cardiol 2001;24:132-138.
6) Bhatt M, Braun C, Patel P, Patel P, Begum H, Wiercioch W, et al. Diagnosis of deep vein thrombosis of the lower extremity: a systematic review and meta-analysis of test accuracy. Blood Adv 2020;4:1250-1264.
7) Hyers TM, Agnelli G, Hull RD, Morris TA, Samama M, Tapson V, et al. Antithrombotic therapy for venous thromboembolic disease. Chest 2001;119(1 Suppl):176S-193S.
8) Kearon C, Akl EA, Ornelas J, Blaivas A, Jimenez D, Bounnameaux H, et al. Antithrombotic therapy for VTE disease: CHEST guideline and expert panel report. Chest 2016;149:315-352.
9) Nakamura M, Miyata T, Ozeki Y, Takayama M, Komori K, Yamada N, et al. Current venous thromboembolism management and outcomes in Japan. Circ J 2014;78:708-717.
10) Spirk D, Husmann M, Hayoz D, Baldi T, Frauchiger B, Engelberger R, et al. Predictors of in-hospital mortality in elderly patients with acute venous thromboembolism: the SWIs Venous ThromboEmbolism Registry (SWIVTER). Eur Heart J 2012;33:921-926.
11) Tagalakis V, Patenaude V, Kahn SR, Susa S. Incidence of and mortality from venous thromboembolism in a real-world population: the Q-VTE Study Cohort. Am J Med 2013;126:832.e13-832.e21.
12) Fiesinger JN, Huisman MV, Davidson BL, Bounnameaux H, Francis CW, Eriksson H, et al. Ximelagatran vs low-molecular-weight heparin and warfarin for the treatment of deep vein thrombosis: a randomized trial. JAMA 2005;293:681-689.
13) Büller HR, Davidson BL, Decousus H, Gallus A, Gent M, Piovella F, et al. Fondaparinux or enoxaparin for the initial treatment of symptomatic deep venous thrombosis: a randomized trial. Ann Intern Med 2004;140:867-873.
14) Heit JA, Silverstein MD, Mohr DN, Petterson TM, O’Fallon WM, Melton LJ 3rd. Predictors of survival after deep vein thrombosis and pulmonary embolism: a population-based, cohort study. Arch Intern Med 1999;159:445-453.
15) Andresen MS, Sandven I, Brunborg C, Njaastad AM, Strekerud F, Abdelnoor M, et al. Mortality and recurrence after treatment of VTE: long term follow-up of patients with good life-expectancy. Thromb Res 2011;127:540-546.
16) Mekaj YH, Mekaj AY, Duc i SB, Miftari El. New oral anticoagulants: their advantages and disadvantages compared with vitamin K antagonists in the prevention and treatment of patients with thromboembolic events. Ther Clin Risk Manag 2015;11:967-977.