

# Fatal pulmonary embolism in hospitalized patients: a large autopsy-based matched case-control study

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**OBJECTIVE:** Pulmonary embolism is an underdiagnosed major cause of death for hospitalized patients. The objective of this study was to identify the conditions associated with fatal pulmonary embolism in this population.

**METHODS:** A total of 13,074 autopsy records were evaluated in a case-control study. Patients were matched by age, sex, and year of death, and factors potentially associated with fatal pulmonary embolism were analyzed using univariate and multivariate conditional logistic regression.

**RESULTS:** Pulmonary embolism was considered fatal in 328 (2.5%) patients. In the multivariate analysis, conditions that were more common in patients who died of pulmonary embolism were atherosclerosis, congestive heart failure, and neurological surgery. Some conditions were negatively associated with fatal pulmonary embolism, including hemorrhagic stroke, aortic aneurism, cirrhosis, acquired immune deficiency syndrome, and pneumonia. In the control group, patients with hemorrhagic stroke and aortic aneurism had short hospital stays (8.5 and 8.8 days, respectively), and the hemorrhage itself was the main cause of death in most of them (90.6% and 68.4%, respectively), which may have prevented the development of pulmonary embolism. Cirrhotic patients in the control group also had short hospital stays (7 days), and 50% died from bleeding complications.

**CONCLUSIONS:** In this large autopsy study, atherosclerosis, congestive heart failure, and neurological surgery were diagnoses associated with fatal pulmonary embolism.

**KEYWORDS:** Atherosclerosis; Heart Failure; Neurosurgery; Pulmonary Embolism; Venous Thromboembolism.

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## INTRODUCTION

Venous thromboembolism (VTE) is a major cause of morbidity and mortality (10), and pulmonary embolism (PE) is responsible for up to 10% of hospitalized patient deaths (2). The estimates of PE prevalence in patients at risk for VTE have been derived from the results of randomized clinical trials, and prospective population-based analyses have provided additional insight into the risk of the population as a whole (1–4). However, the literature contains few studies that describe the incidence or the clinical characteristics of hospitalized patients who suffer from fatal VTE events.

Risk stratification and preventive strategies for both surgical and medical patients are presented in the American College of Chest Physicians Guidelines for VTE prophylaxis (3). Risk in surgical patients is based on age, the type of surgery, and the presence of other VTE risk factors. In medical patients, prophylaxis is recommended in cases of congestive heart failure (CHF) or severe respiratory disease and for bedridden patients with active cancer, previous VTE, sepsis, acute neurologic disease, or inflammatory bowel disease. Other guidelines recommend thromboprophylaxis for medical patients aged over 40 years who demonstrate reduced mobility associated with additional risk factors (4).

While the indications for thromboprophylaxis are well established, the diagnosis of PE remains a significant clinical challenge (5–8). Autopsy remains the gold standard for diagnosing fatal PE, but the number of autopsies performed has decreased substantially in many countries (9–11). In addition, recent studies have recognized PE as one of the most frequently missed diagnoses in living patients (12–15).

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In this retrospective matched case-control study, we analyzed the autopsy records of 13,074 patients with the primary objective of identifying conditions associated with fatal PE in hospitalized clinical and surgical patients. Our results may aid in identifying patients who could benefit from VTE prophylaxis and whose risks should be emphasized. The clinical suspicion of PE prior to death was also investigated.

## ■ MATERIALS AND METHODS

### Study population

This study was performed in a 1,100-bed university hospital at the Faculdade de Medicina da Universidade de São Paulo in Brazil, which admits adult medical and general surgery patients. Autopsies are routinely performed if requested by physicians and when considered necessary. This study was approved by the local ethical committee (protocol number 901/03).

### Study design

All autopsy reports from 1995 to 2004 were screened, and autopsies in which PE was a finding (as determined by pathologists) were selected for review. We chose the years 1995 to 2004 because autopsies were much more common during this period compared to the following years (70% of total deaths), thereby avoiding selection bias. The autopsy protocol included a systematic search for pulmonary thrombi in all pulmonary lobes and a microscopic analysis of all suspect areas of the lungs. For each confirmed PE case, two additional patients matched by sex, age ( $\pm 5$  years), and year of death were selected as controls. Patients without PE but with deep vein thrombosis (DVT), as noted on the autopsy reports, were not eligible for use as controls. Pediatric and orthopedic patients were typically admitted to other institutes within the hospital complex and were not included in this study. All autopsy reports and discharge summaries were independently reviewed by two physicians from the research group (EFP and AL) to classify PE as the primary cause or a contributing factor of death ("fatal" and "non-fatal" PE), define the main reason for hospital admission, to identify whether a PE diagnosis was suspected before the autopsy. PE was considered fatal when the pathologists classified it as the only or main cause of death. The consensus reached between the two classifying physicians was 97%. When the two physicians disagreed, the case was reevaluated by both physicians together to reach a consensus.

All medical records were screened to determine whether VTE prophylaxis had been prescribed during hospitalization. Only unfractionated heparin (UFH) and enoxaparin were used for prophylaxis. UFH administered every 8 to 12 hours at a dose of 5,000 IU and enoxaparin administered once daily at a dose of 40 mg (or 20 mg if the creatinine clearance was below 30 mL/min/1.73 m<sup>2</sup>) were considered the proper treatment. For the prophylaxis to be considered adequate, the patients needed to have received the correct dose and could not have been subjected to 72 or more consecutive hours without prophylaxis during any period of hospitalization.

The entire patient group was considered for the analysis of PE incidence and the clinical accuracy of PE diagnosis before death. Only fatal cases and the appropriate controls

were included in the analysis of conditions associated with PE.

### Statistical analysis

A database was created using Microsoft Access Version 2003. Student's *t*-test, Fisher's exact test, and the chi-squared test were employed to compare characteristics between the cases and controls. Univariate and multivariate conditional logistic regressions were employed to estimate the association with fatal PE (OR and 95% CI). These regressions were performed by matching for sex, age, and year of death, and two controls were evaluated per case. The multivariate regression model included every variable that presented a *p*-value  $< 0.20$  in the univariate regression. Variables with *p*-values  $\geq 0.05$  were excluded sequentially according to decreasing *p*-values. The final multivariate model contained only variables with *p*-values  $< 0.05$ . The analyses were performed using the Stata 10.1<sup>TM</sup> software.

## ■ RESULTS

Autopsies were performed for 13,074 (71.2%) of the 18,359 deaths. Autopsies from 2002 were excluded because the hospital's computer system changed that year, and the new system was unable to transfer data from the old system. Table 1 shows how the autopsy rate decreased over the course of the study period, and a significant difference was found after 1999. The average percentage of deaths for which autopsies were performed between 1995 and 1999 was 87%, and it decreased to 53.9% between 2000 and 2004 (*p* = 0.005).

PE was detected in 502 autopsies (3.8%) and was considered the main cause of death (fatal PE) in 328 of these (2.5%) cases. There were no significant differences in the percentages of autopsies with PE or the percentage of PE cases classified as fatal or non-fatal over the course of the study period (Table 1).

The sensitivity of the clinical PE diagnosis was only 48.2% for the entire group, although it was higher in cases of fatal PE compared to non-fatal PE (61.9% *vs.* 22.4%, respectively, *p*  $< 0.001$ ). The specificity of the clinical diagnosis of PE was greater than 98% for all of the subgroups.

For the analysis of conditions associated with PE, 984 patients (328 fatal PE cases and 656 non-PE controls) were selected. The baseline characteristics are shown in Table 2. There were no significant differences in gender or age between the groups, which indicated successful matching. Arterial insufficiency, atherosclerosis, cancer, CHF, and chronic obstructive pulmonary disease (COPD) were more common in the fatal PE group, whereas acquired immunodeficiency syndrome (AIDS), aortic aneurism, cirrhosis, infections, pneumonia, and hemorrhagic stroke were more common in the control group.

Age and length of stay were analyzed according to the main disease groups to test the hypothesis that older patients and those with longer hospital stays would have greater risks for VTE (Table 3). The only significant difference was related to the mean hospital stay of patients with chronic renal failure, which was longer for those in the fatal PE group (18.7 days *vs.* 6.2 days in the non-PE group; *p* = 0.020).

Table 4 shows the results of the conditional univariate logistic regression analysis performed to identify conditions



**Table 1 - Number and percentage of autopsies performed and PEs found during the study.**

Year	Deaths n	Autopsies n (%)	PE n (%)	Fatal PE n (%)	Non-fatal PE n (%)
1995	2189	1990 (90.9)	96 (4.8)	62 (3.1)	34 (1.7)
1996	2114	1767 (83.6)	70 (4.0)	38 (2.2)	32 (1.8)
1997	1905	1525 (80.1)	72 (4.7)	40 (2.6)	32 (2.1)
1998	1741	1502 (86.3)	38 (2.5)	33 (2.2)	5 (0.3)
1999	1654	1571 (95.0)	68 (4.3)	43 (2.7)	25 (1.6)
2000	1964	1345 (68.5)	42 (3.1)	28 (2.1)	14 (1.0)
2001	2248	1273 (56.6)	33 (2.6)	23 (1.8)	10 (0.8)
2003	2216	1063 (48.0)	57 (5.4)	40 (3.8)	17 (1.6)
2004	2328	1038 (44.6)	26 (2.5)	21 (2.0)	5 (0.5)
Total	18359	13074 (71.2)	502 (3.8)	328 (2.5)	174 (1.3)

PE: pulmonary embolism.

**Table 2 - Baseline characteristics in fatal PE and non-PE groups.**

Characteristic	Fatal PE	Non-PE	p-value
	n = 328	n = 656	
Age in years, mean (SD)	62.2 (16.4)	61.5 (16.5)	0.26
Male, n (%)	163 (49.7)	326 (49.7)	1.00
Length of stay in days, mean (SD)	10.8 (15.1)	11.7 (16.0)	0.200
AIDS, n (%)	7 (2.1)	38 (5.8)	0.009
AMI, n (%)	15 (4.6)	31 (4.7)	1.00
Aortic aneurism, n (%)	1 (0.3)	19 (2.9)	0.006
Arterial insufficiency, n (%)	17 (5.2)	15 (2.3)	0.020
Atherosclerosis, n (%)	7 (2.1)	4 (0.6)	0.049
Cancer, n (%)	135 (41.2)	196 (29.9)	0.001
Biliary tract, n (%)	6 (4.4)	11 (5.6)	0.80
Bladder, n (%)	2 (1.5)	3 (1.5)	1.00
Brain, n (%)	15 (11.1)	10 (5.1)	0.060
Breast, n (%)	9 (6.7)	8 (4.1)	0.32
Colorectal, n (%)	12 (8.9)	16 (8.2)	0.84
Esophagus, n (%)	4 (3.0)	9 (4.6)	0.57
Head and neck, n (%)	4 (3.0)	13 (6.6)	0.200
Kidney, n (%)	2 (1.5)	3 (1.5)	1.00
Leukemia, n (%)	5 (3.7)	15 (7.7)	0.160
Liver, n (%)	3 (2.2)	10 (5.1)	0.26
Lung, n (%)	12 (8.9)	26 (13.3)	0.29
Lymphoma, n (%)	10 (7.4)	20 (10.2)	0.44
Melanoma, n (%)	2 (1.5)	2 (1.0)	1.00
Myeloma, n (%)	3 (2.2)	2 (1.0)	1.00
Ovarian, n (%)	3 (2.2)	4 (2.0)	1.00
Pancreas, n (%)	9 (6.7)	9 (4.6)	1.00
Uterus, n (%)	10 (7.4)	9 (4.6)	0.40
Chronic renal failure, n (%)	6 (1.8)	10 (1.5)	0.80
CHF, n (%)	37 (11.3)	39 (5.9)	0.005
Cirrhosis, n (%)	3 (0.9)	58 (8.8)	<0.001
COPD, n (%)	16 (4.9)	13 (2.0)	0.020
Infections, n (%)	26 (7.9)	84 (12.8)	0.020
Pneumonia	8 (2.4)	39 (5.9)	0.020
Tuberculosis	6 (1.8)	11 (1.7)	1.00
Urinary	5 (1.5)	3 (0.5)	0.130
Endocarditis	3 (0.9)	8 (1.2)	0.76
Peritonitis	1 (0.3)	8 (1.2)	0.29
Others	4 (1.2)	15 (2.3)	0.33
Mesenteric ischemia, n (%)	3 (0.9)	12 (1.8)	0.41
Rheumatologic, n (%)	6 (1.8)	13 (2.0)	1.00
Stroke (hemorrhagic), n (%)	6 (1.8)	53 (8.1)	<0.001
Stroke (ischemic), n (%)	14 (4.3)	25 (3.8)	0.73
Others, n (%)	29 (8.8)	46 (7.0)	0.31

PE: pulmonary embolism; AIDS: acquired immunodeficiency syndrome; AMI: acute myocardial infarction; CHF: congestive heart failure and COPD: chronic obstructive pulmonary disease.

related to fatal PE autopsy findings and adjusted for sex, age and admission time. Atherosclerosis (OR=4.65, 95% CI, 1.23–17.52,  $p=0.020$ ), cancer (OR=1.72, 95% CI, 1.28–2.32,  $p<0.001$ ), CHF (OR=2.14, 95% CI, 1.30–3.50,  $p=0.003$ ), and COPD (OR=2.75, 95% CI, 1.24–6.10,  $p=0.010$ ) were associated with fatal PE. Of the types of cancers documented, brain cancer (OR=2.91, 95% CI, 1.25–6.74,  $p=0.010$ ) and cancer of undetermined origin (OR=3.94, 95% CI, 1.17–13.28,  $p=0.030$ ) were most significantly associated with fatal PE. Fatal PE was negatively associated with AIDS (OR=0.30, 95% CI, 0.12–0.77,  $p=0.010$ ), aortic aneurism (OR=0.11, 95% CI, 0.14–0.88,  $p=0.040$ ), cirrhosis (OR=0.10, 95% CI, 0.03–0.33,  $p<0.001$ ), hemorrhagic stroke (OR=0.19, 95% CI, 0.08–0.47,  $p<0.001$ ), infection (OR=0.60, 95% CI, 0.38–0.97,  $p=0.040$ ), and pneumonia (OR=0.39, 95% CI, 0.18–0.85,  $p=0.020$ ). In the entire group (n=1,506), VTE prophylaxis was considered adequate in only 20.4% of cases. Lack of prophylaxis was not shown to be associated with fatal PE in the univariate analysis (Table 4).

The conditional multivariate logistic regression indicated that fatal PE was associated with atherosclerosis (OR=4.03, 95% CI, 1.06–15.01,  $p=0.040$ ), CHF (OR=1.77, 95% CI, 1.04–2.97,  $p=0.030$ ), and neurological surgery (OR=3.96, 95% CI, 1.48–10.65,  $p=0.006$ ). A negative association with fatal PE was found in patients with AIDS (OR=0.22, 95% CI, 0.08–0.60,  $p=0.003$ ), aortic aneurism (OR=0.12, 95% CI, 0.01–0.90,  $p=0.040$ ), cirrhosis (OR=0.08, 95% CI, 0.03–0.27,  $p<0.001$ ), pneumonia (OR=0.35, 95% CI, 0.15–0.79,  $p=0.010$ ), and hemorrhagic stroke (OR=0.09, 95% CI, 0.03–0.25,  $p<0.001$ ) (Table 5).

## DISCUSSION

VTE prevention in hospitalized patients has improved in recent years and now includes recommendations for improving the diagnosis of VTE and new algorithms for VTE prophylaxis (3,4,16). However, the percentage of patients whose deaths are the result of PE has not decreased, and this fact may be related to many factors, such as the increase in patient age or the large number of VTE risk factors (3,17). In addition, most doctors do not follow the appropriate thromboprophylaxis protocols (18,19). Thus, VTE remains a major cause of death for hospitalized patients, and a substantial number of VTEs discovered at autopsy are not diagnosed during hospitalization (14,20–23).

Autopsies remain invaluable for determining the effects of prophylaxis and diagnosing and treating VTE (9); unfortunately, the number of autopsies performed has decreased substantially in many countries (10,24). Although we observed a statistically significant decrease in the number of autopsies over the study period, the autopsy rate at our hospital was greater (71.2% of deaths) than that reported in other studies. Data from the United States National Center for Health Statistics over a similar time period showed that the autopsy rate was low in 1993 (9.7% of all deaths in the US) and further decreased to only 7.1% in 2003 (24).

In a classic study by Lindblad, a systematic search for VTE identified PE in 26.4% of all autopsies (9.4% were considered fatal PE) (9). The percentage of PE patients in our patient sample (3.8% for all PE and 2.5% for fatal PE) was much lower. Differences in the percentages of autopsies found with PE in the different studies may be caused by



**Table 3 - Age and length of hospital stay according to reason for admission.**

Reason for admission	Mean age			Mean length of stay		
	Fatal PE, Years (n)	Non-PE, Years (n)	p	Fatal PE, Days (n)	Non-PE, Days (n)	p-value
AIDS	43.7 (7)	42.2 (38)	0.40	16.4 (7)	11.1 (38)	0.080
AMI	61.9 (15)	66.0 (31)	0.15	5.7 (15)	7.6 (31)	0.24
Aortic aneurism	65.0 (1)	66.1 (19)	-	99.0 (1)	8.8 (19)	-
Arterial insufficiency	74.1 (17)	75.1 (15)	0.40	8.5 (17)	13.9 (15)	0.070
Cancer	60.6 (135)	61.5 (196)	0.30	12.5 (135)	12.1 (196)	0.40
CHF	66.2 (37)	71.3 (39)	0.06	5.8 (37)	5.8 (39)	0.49
Chronic renal failure	59.2 (6)	53.5 (10)	0.29	18.7 (6)	6.2 (10)	0.020
Cirrhosis	56.3 (3)	56.6 (58)	0.49	3.0 (3)	15.7 (58)	0.060
COPD	69.3 (16)	68.9 (13)	0.47	5.6 (16)	10.5 (13)	0.060
Infection	66.5 (26)	65.9 (84)	0.43	13.9 (26)	15.8 (84)	0.34
Mesenteric ischemia	64.0 (3)	60.8 (12)	0.36	5.7 (3)	7.0 (12)	0.43
Rheumatologic disease	40.5 (6)	40.2 (13)	0.47	13.2 (6)	13.1 (13)	0.49
Stroke, hemorrhagic	54.7 (6)	62.2 (53)	0.15	13.5 (6)	10.6 (53)	0.36
Stroke, ischemic	69.6 (14)	64.6 (25)	0.16	9.0 (14)	8.4 (25)	0.43

PE: pulmonary embolism; AIDS: acquired immunodeficiency syndrome; AMI: acute myocardial infarction; CHF: congestive heart failure and COPD: chronic obstructive pulmonary disease.

different autopsy protocols, different hospital populations and the percentage of autopsies performed. We avoided selection bias by studying a period in which the percentage of autopsies was particularly high in our hospital, approximately 70% of the total number of deaths. The small difference between the number of total PE and fatal PE cases found in our series may be due to the autopsy protocol used to search for visible thrombi and perform microscopic analysis only of the areas with macroscopic findings. Because the main objective of this study was to identify conditions associated with fatal PE, this factor was not considered a major limitation.

Clinical suspicion of PE has a high specificity, but the reported sensitivity was approximately 30% (20–23). Sensitivity can also vary from less than 10% to more than 65%, depending on the related conditions. Diagnosis is typically more difficult in older patients and for those with respiratory diseases, specifically COPD and pneumonia (21). The severity of the PE episode may be another possible explanation for this variation, and this possibility was demonstrated in the present study, in which the sensitivity of antemortem diagnoses was much higher in patients with fatal PE (61.9%) compared to patients with non-fatal PE (22.4%).

Cancer, CHF, and COPD have long been considered important risk factors for VTE (3,4,25–27). In the present study, the association of these factors with fatal PE was noted in the univariate analysis, but only the association with CHF was confirmed in the multivariate analysis. The association between brain cancer and fatal PE was also lost in the multivariate analysis; however, brain cancer is considered one of the cancers most frequently associated with VTE complications. In one study, it was identified as the second most frequent VTE-related cancer (OR=2.37, 95% CI, 2.04–274) (28). Furthermore, neurological surgery has been shown to be associated with VTE (29), which was confirmed in our study.

Hemorrhagic stroke is considered to be highly associated with DVT and PE (3,4), but this was not the case in our study. In fact, we found a negative association with fatal PE in stroke patients, which may be explained by the severity of their conditions. In 48 of the 53 patients in the control group (90.6%), the hemorrhage itself was the main cause of death.

These patients also had short hospital stays prior to their deaths, which may have prevented the development of VTE. After excluding 1 patient who was in the hospital for 122 days, the average hospital stay of these patients was 8.48 days.

Aortic aneurism and cirrhosis were also found to have a negative association with fatal PE. Only 1 patient in the fatal PE group had an aortic aneurism, and his hospital stay was 99 days. Of the 19 patients in the control group, 13 (68.4%) died from the dissection or rupture of the aneurism, and 10 died prior to the third day of admission. Of the cirrhotic patients in the control group, 29 (50%) died from bleeding complications, and the median hospital stay prior to death for these patients was only 7 days.

One interesting finding of our study was the strong association between atherosclerosis and fatal PE (OR=4.03, 95% CI, 1.06–15.71,  $p=0.040$ ). Although atherosclerosis is not typically thought to be an independent risk factor for VTE (30,31), intriguing evidence from recent studies has suggested that statins may prevent VTE in healthy older adults (32,33). In a randomized, double-blind, placebo-controlled trial, 20 mg of rosuvastatin daily significantly reduced the occurrence of symptomatic VTE in outpatients with no cardiovascular disease histories. The PE rates were 0.09 in the rosuvastatin group and 0.12 in the placebo group (HR=0.77, 95% CI, 0.41–1.45,  $p=0.42$ ) (32). The anti-inflammatory effect of statins on the microvascular endothelium may be the possible mechanism of action (33). Another interesting finding was the negative association between pneumonia and fatal PE. Pneumonia has classically been considered a risk factor for VTE (3,4), and it is unclear why our data did not confirm this association.

AIDS is considered to present many risk factors for VTE, including frequent hospitalization, the use of central venous catheters, an age older than 45 years, and the activation of endothelial cells from infections with cytomegalovirus, herpes, and HIV itself (34,35). The mean age of the AIDS patients in our study was 43.7 years, and the average hospital stay of these patients was only 11.1 days. These findings may indicate that these patients presented to the hospital with serious conditions that did not allow enough time for PE to develop.



**Table 4** - Conditional univariate logistic regression of association between risk factors and fatal PE adjusted for sex, age and time of admission.

Factor Variable	Cases n	Controls n	Standard Error	OR	95% CI	p-value
AIDS	7	38	0.14	0.30	0.12-0.77	0.010
AMI	15	31	0.33	0.99	0.52-1.91	0.99
Aortic aneurism	1	19	0.12	0.11	0.14-0.88	0.040
Arterial insufficiency	17	15	0.72	1.93	0.93-4.00	0.080
Atherosclerosis	7	3	3.15	4.65	1.23-17.52	0.020
Cancer	135	196	0.26	1.72	1.28-2.32	<0.001
Biliary tract	6	11	0.60	1.11	0.38-3.21	0.85
Bladder	2	3	1.80	1.80	0.26-12.4	0.55
Brain	15	10	1.25	2.91	1.25-6.74	0.010
Breast	9	8	1.44	2.71	0.95-7.70	0.060
Colorectal	12	16	0.63	1.32	0.52-3.34	0.56
Esophagus	4	9	0.45	0.70	0.20-2.47	0.57
Head and neck	4	13	0.40	0.68	0.21-2.17	0.51
Kidney	2	3	1.68	1.59	0.20-12.5	0.66
Leukemia	5	15	0.40	0.73	0.25-2.13	0.56
Liver	3	2	0.38	0.56	0.15-2.11	0.39
Lung	12	26	0.34	0.88	0.42-1.86	0.75
Lymphoma	10	20	0.43	1.04	0.47-2.34	0.92
Melanoma	2	2	1.58	1.53	0.20-11.55	0.68
Myeloma	3	2	4.02	3.99	0.55-28.80	0.170
Ovarian	3	4	1.17	1.52	0.34-6.84	0.59
Pancreas	9	9	1.08	2.18	0.83-5.73	0.120
Prostate	6	6	1.18	1.98	0.62-6.38	0.25
Stomach	8	10	0.68	1.35	0.50-3.64	0.56
Undetermined	8	4	2.44	3.94	1.17-13.28	0.030
Uterus	10	9	1.16	2.42	0.95-6.21	0.070
CHF	37	39	0.54	2.14	1.30-3.50	0.003
Cirrhosis	3	58	0.06	0.10	0.03-0.33	<0.001
COPD	16	13	1.12	2.75	1.24-6.10	0.010
Chronic renal failure	6	10	0.63	1.22	0.44-3.36	0.70
Infection	26	84	0.14	0.60	0.38-0.97	0.040
Endocarditis	3	8	0.27	0.25	0.30-2.08	0.200
Peritonitis	1	8	0.46	0.57	0.12-2.82	0.49
Pneumonia	8	39	0.16	0.39	0.18-0.85	0.020
Tuberculosis	6	11	0.68	1.29	0.46-3.62	0.63
Urinary	5	3	2.21	3.01	0.71-12.74	0.140
Mesenteric ischemia	3	12	0.29	0.43	0.11-1.61	0.21
Surgery	57	98	0.22	1.17	0.80-1.69	0.42
Abdominal	15	36	0.24	0.75	0.40-1.42	0.38
Neurological	14	33	0.68	1.78	0.84-3.78	0.130
Thoracic	5	5	1.37	2.13	0.60-7.52	0.24
Vascular	12	24	0.33	0.84	0.39-1.81	0.65
Rheumatologic diseases	6	13	0.44	0.89	0.34-2.37	0.82
Stroke	20	78	0.12	0.44	0.26-0.74	0.002
Hemorrhagic	6	53	0.08	0.19	0.08-0.47	<0.001
Ischemic	14	25	0.33	0.91	0.44-1.84	0.79
VTE Prophylaxis	134	454	0.18	0.70	0.42-1.16	0.170

OR: odds ratio; CI: confidence interval; AIDS: acquired immunodeficiency syndrome; AMI: acute myocardial infarction; CHF: congestive heart failure and COPD: chronic obstructive pulmonary disease.

**Table 5** - Conditional multivariate logistic regression of the association between risk factors and fatal PE, adjusted for age and time of admission.

Factor Variable	Cases n	Controls n	Standard Error	OR	95% CI	p-value
AIDS	7	38	0.11	0.22	0.08-0.60	0.003
Aortic aneurism	1	19	0.12	0.12	0.01-0.90	0.040
Atherosclerosis	7	3	2,80	4.03	1.06-15.71	0.040
CHF	37	39	0.47	1.77	1.04-2.97	0.030
Cirrhosis	3	58	0.05	0.08	0.03-0.27	<0.001
Pneumonia	8	39	0.15	0.35	0.15-0.79	0.010
Neurological surgery	14	33	2.00	3.96	1.48-10.65	0.006
Stroke, hemorrhagic	6	53	0.05	0.09	0.03-0.25	<0.001

OR: odds ratio; CI: confidence interval; AIDS: acquired immunodeficiency syndrome and CHF: congestive heart failure.



One recent publication that evaluated the adequacy of VTE prophylaxis in 37,356 hospitalized patients across 32 countries reported that thromboprophylaxis was prescribed for only 50% of these patients (18,19). In our hospital, the use of VTE prophylaxis has only increased during recent years, which suggests that we would expect to observe low rates of prophylaxis during the period studied. This finding proved accurate, as only 20.4% of patients in this study received adequate prophylaxis. This low prophylaxis rate may explain why no association between prophylaxis and fatal PE was found.

This study evaluated a large number of autopsies performed on hospital patients who had been admitted for general medical care or surgery; atherosclerosis, CHF, and neurological surgery were found to be associated with fatal PE. AIDS, aortic aneurism, cirrhosis, and hemorrhagic stroke were negatively associated with fatal PE, and this finding may be explained by the severity of these conditions, which often led to patient death after a short hospital stay and before PE could develop.

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### AUTHOR CONTRIBUTIONS

Bricola SA and Lichtenstein A were responsible for the study conception and design, data acquisition, critical review and final approval of the manuscript. Paiva EF contributed to the study conception and design, data acquisition, analysis and interpretation, drafting and final approval of the manuscript. Gianini RJ and Neto JE were responsible for the data analysis and interpretation, critical review and final approval of the manuscript. Duarte JG and Shinjo SK were responsible for the data acquisition, critical review and final approval of the manuscript. Martins MA contributed to the study conception and design, data analysis and interpretation, critical review and final approval of the manuscript.

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