

The effect of the COVID-19 pandemic on incidence and characteristics of pulmonary embolism

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Abstract: The coronavirus disease 2019 (COVID-19) pandemic has affected presentations of conditions unrelated to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection itself. We investigated the pandemic's effect on incidence and characteristics of pulmonary embolism (PE) cases without the infection. We retrospectively compared non-COVID PE patients during January 16-August 31, 2020 (COVID period) with PE patients during the same period in 2017-2019 (Pre-COVID period). The number of out-of-hospital onset cases was significantly higher during the pandemic than during each of the pre-COVID years. Also, the patients in the COVID period were older, more likely to be free of thrombotic predispositions, had higher mortality risks of PE, and were more likely to arrive at the hospital on emergency transport. Sedentary lifestyles during the pandemic seem to have had considerable effects on presentations of PE.

Keywords: COVID-19, venous thromboembolism, SARS-CoV-2, quarantine

The ongoing 2019 coronavirus disease (COVID-19) pandemic has altered people's habits and attitudes toward healthcare, causing a decreased use of health services for non-COVID-19 conditions (1). Pulmonary embolism (PE) is a common complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (2). However, few studies have analyzed PE in patients without COVID-19 during the pandemic. As people adopt more sedentary lifestyles due to stay-at-home restrictions, PE prevention is becoming more important. We investigated the effect of the COVID-19 pandemic on the incidence and clinical characteristics of PE in patients without COVID-19 in Tokyo, Japan.

We retrospectively examined adult patients with imaging-confirmed PE without COVID-19 treated at our tertiary-care hospital during the "COVID period" (January 16 to August 31, 2020) and the control "Pre-COVID period" (January 16 to August 31, 2017-2019). Patients with SARS-CoV-2 infection were excluded. Eligible patients were grouped according to onset and treatment: patients who received inpatient or outpatient treatment, and patients with in-hospital onset (*i.e.*, hospital-acquired) PE. For cases with out-of-hospital onset, we collected data on patient demographics (age, sex, and body mass index) and PE risk factors according to previous literature (3). To analyze PE severity, we calculated early mortality risk categories per European Society of Cardiology (ESC) guidelines (3) and also noted if emergency medical services (EMS) were used.

All data were collected from electronic medical records. Continuous and ordinal variables were compared using the Mann-Whitney *U* test, and nominal variables were compared using Pearson's chi-squared test. The study protocol was approved by the ethics committee of the National Center for Global Health and Medicine.

We identified 152 patients with PE during the control period and 77 during the COVID period, including 2 patients with positive SARS-CoV-2 tests that were excluded (from the analyses). The number of patients with non-COVID PE during the COVID period was significantly higher than during each of the pre-COVID years, with the highest increase in patients with non-hospital-acquired PE (Table 1a). Patients with non-hospital-acquired PE during the COVID period were older ($p = 0.013$), more likely to be free of identifiable thrombotic predispositions ($p = 0.012$), had a significantly higher ESC early mortality risk ($p < 0.001$), and were more likely to be transported to the hospital by EMS ($p = 0.019$) than patients during the pre-COVID control period (Table 1b).

PE in the COVID-19 era has been greatly affected by the pandemic. The fact that PE patients in the COVID period were more likely to be free of identifiable thrombotic predispositions suggests that lifestyle effects of the pandemic played a key role in the increase of non-hospital-acquired PE. The non-compulsory stay-at-home request in Tokyo was considered milder than that in other countries. Nonetheless, large-scale data collected from mobile devices indicate a reduction in mobility for an

Table 1a. Trend in all PE incidences during pre-COVID and COVID periods

Variables	Pre-COVID period			COVID period
	2017	2018	2019	2020
Total	50	44	58	75
Setting at onset				
Out-of-hospital onset	19	17	20	36
Outpatient treatment	7	12	11	12
Inpatient treatment	12	5	9	24
In-hospital onset	31	27	38	39

Table 1b. Comparison of out-of-hospital onset PE during pre-COVID and COVID periods

Variables	Pre-COVID period	COVID period	p value
Total	56	36	
Patient demographics			
Age, years	65 [47.5-72]	74 [58-79.25]	0.013
Male sex, n (%)	30 (54%)	18 (50%)	0.74
BMI, kg/m ²	22.13 [15.3-25.41]	22.04 [19.99-24.24]	0.55
Any thrombotic medical condition [§] , n (%)	43 (77%)	23 (64%)	
Cancer, n (%)	26 (46%)	11 (31%)	
Diabetes mellitus, n (%)	4 (7%)	7 (19%)	
Obesity, n (%)	6 (11%)	0 (0%)	
Congestive heart failure or chronic respiratory disease, n (%)	6 (11%)	6 (17%)	
Orthopedic condition [‡] , n (%)	7 (13%)	6 (17%)	
Oral contraception or hormone therapy, n (%)	3 (5%)	3 (8%)	
Recent long travel, n (%)	7 (13%)	0 (0%)	
None of the above risk factors, n (%)	2 (4%)	7 (19%)	0.012
PE severity			
ESC early mortality risk			< 0.001
Low risk, n (%)	42 (75%)	14 (39%)	
Intermediate-low risk, n (%)	11 (20%)	13 (36%)	
Intermediate-high risk, n (%)	1 (2%)	6 (17%)	
High risk, n (%)	2 (4%)	3 (8%)	
Use of EMS, n (%)	12 (21%)	16 (44%)	0.019

[§]Thrombotic medical conditions: autoimmune diseases, cancer, chronic respiratory disease, congestive heart failure, diabetes mellitus, infection, inflammatory bowel disease, obesity, paralytic stroke, previous venous thromboembolism, thrombophilia, varicose veins. [‡]Orthopedic conditions: fracture of lower limb, hip or knee replacement, major trauma, spinal cord injury. Abbreviations: BMI, body mass index; ESC, European Society of Cardiology; EMS, emergency medical service. Data are expressed as number (%) or median [interquartile range].

extended time following the first wave of the pandemic (4). Limited ambulation is the most common risk factor of PE and is present in 45% of patients with venous thromboembolism (VTE) (5), and sedentary lifestyles are widely recognized to be closely associated with VTE (6). This study demonstrates that even lenient approaches to contain the pandemic impact other health domains.

Previous studies have reported that the elderly population exhibited the most significant decrease in physical activity due to self-quarantines (7,8). Staying indoors is generally accepted as essential for the elderly population, who are more susceptible to COVID-19. Quarantines are especially reinforced in nursing homes. However, it is important to also consider that older adults, even without comorbidities, carry a higher risk of developing severe PE. The public must be made aware of the risks of sedentary behavior during the pandemic.

This study is limited by its retrospective approach and inclusion of patients from a single institution. Multi-

center studies are needed to confirm if this is a national or global trend.

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References

1. Jeffery MM, D'Onofrio G, Paek H, Platts-Mills TF, Soares WE 3rd, Hoppe JA, Genes N, Nath B, Melnick ER. Trends in emergency department visits and hospital admissions in health care systems in 5 states in the first months of the COVID-19 pandemic in the US. *JAMA Intern Med.* 2020; 180:1328-1333.
2. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and thrombotic or thromboembolic disease: implications

- for prevention, antithrombotic therapy, and follow-up: JACC state-of-the-art review. *J Am Coll Cardiol.* 2020; 75:2950-2973.
3. Konstantinides SV, Meyer G, Becattini C, *et al.* 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). *Eur Heart J.* 2020; 41:543-603.
 4. Yabe T, Tsubouchi K, Fujiwara N, Wada T, Sekimoto Y, Ukkusuri SV. Non-compulsory measures sufficiently reduced human mobility in Tokyo during the COVID-19 epidemic. *Sci Rep.* 2020; 10:18053.
 5. Spencer FA, Emery C, Lessard D, Anderson F, Emani S, Aragam J, Becker RC, Goldberg RJ. The Worcester Venous Thromboembolism study: a population-based study of the clinical epidemiology of venous thromboembolism. *J Gen Intern Med.* 2006; 21:722-727.
 6. Shirakawa T, Iso H, Yamagishi K, Yatsuya H, Tanabe N, Ikehara S, Ukawa S, Tamakoshi A. Watching television and risk of mortality from pulmonary embolism among Japanese men and women. *Circulation.* 2016; 134:355-357.
 7. Yamada K, Yamaguchi S, Sato K, Fuji T, Ohe T. The COVID-19 outbreak limits physical activities and increases sedentary behavior: A possible secondary public health crisis for the elderly. *J Orthop Sci.* 2020; 25:1093-1094.
 8. Yamada Y, Uchida T, Ogino M, Ikenoue T, Shiose T, Fukuma S. Changes in older people's activities during the coronavirus disease 2019 pandemic in Japan. *J Am Med Dir Assoc.* 2020; 21:1387-1388.
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