Excess out-of-hospital deaths during COVID-19 outbreak: evidence of pulmonary embolism as a main determinant

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Keywords

COVID-19, Pulmonary embolism, Deep Venous Thrombosis, Pandemic, Post-mortem imaging

Abbreviations

COVID-19	Coronavirus disease of 2019
CT	Computed Tomography
DVT	Deep Venous Thrombosis
IFMP	Institute of Forensic Medicine of Paris
IQR	Interquartile Range
OR	Odds-Ratio
PE	Pulmonary Embolism
PMCT	Post-Mortem CT
UD	Unexplained deaths

Manuscript

Coronavirus Infection Disease 2019 (COVID-19) deteriorates pulmonary function and can lead to acute hypoxemic respiratory failure. COVID-19 may also directly impact the cardiovascular system.[1] Cases of pulmonary embolism (PE) were reported in in-hospital settings[2–5] and in a small post-mortem autopsy series[6]. Our study investigates the relation between PE and out-of-hospital unexplained death (UD) during COVID-19 outbreak.

The Institute of Forensic Medicine of Paris (IFMP) regularly performs unenhanced Post-Mortem Computed Tomography (PMCT) on deceased subjects upon judicial request to investigate death causes. The study objective was to compare proximal PE rate on PMCT between subjects suspected of COVID-19 during the outbreak peak in Paris (from March 23rd to April 7th, 2020, COVID-19-suspected group) and subjects scanned during 2019 (control group).

We analyzed ≥18 years-old subjects presenting UD explored with PMCT, excluding traumas and putrefied bodies. During the COVID-19 outbreak peak, only subjects who were suspected to have contracted COVID-19 were included. As virologic tests were not performed due to prioritization of Reverse-Transcriptase Polymerase Chain Reaction tests to living patients, the COVID-19-suspected status was determined following clinical context and lung CT abnormalities which have demonstrated a high diagnostic value.[7] Thoracic and limb PMCTs were blindly read by two experts and disagreements were solved in consensus. Proximal PE and Deep Venous Thrombosis (DVT) were defined according to previous study criteria.[8] In accordance with French legislation, Ethics Committee approval was not needed for this retrospective, non-interventional study; commitment to compliance was filed (Reference Methodology MR-004, no.2617140420). Statistical analysis was performed with R software, using Fisher and Mann-Whitney-U tests for comparisons, and logistic regression to adjust Odds-Ratio (OR) on age and sex. Results are expressed as Median, IQR (Interquartile Range).

UD rate was strikingly higher during COVID-19 outbreak peak (68 [79%] of 86 deaths) than during the control year 2019 (70 [21%] of 334 deaths, OR=14.1, p<0.001). Among the 68 subjects with UD during COVID-19 outbreak peak, 4 without pulmonary COVID-19 lesions were excluded.

COVID-19-suspected subjects (n=64) were older (65 years, IQR 56-73, range 27-99) than control subjects (n=70, 55 years, IQR 40-65, range 19-91, p=0.0003). Sex ratio was not statistically different between groups (respectively 49/64 [77%] vs. 49/70 [70%] men, p=0.44). Most of the COVID-19-suspected subjects died at home, some presented with fever and/or cough before death, and the majority had suddenly lost contact with health care providers and/or family members 30 min to several hours earlier.

Proximal PE rate was higher in COVID-19-suspected group than in control group (15/64 [23%] vs. 5/70 [7%] respectively, p=0.014) (Figure 1). This was confirmed after adjustment on age and gender (OR 3.9 [95%CI:1.3-13.4], p=0.017). In subjects whose lower limbs were explored (50/64 COVID-19-suspected and all control subjects), DVT rate was higher in COVID-19-suspected group than in control group (9/50 [18%] vs. 3/70 [4%] respectively, p=0.026; Figure 1)

Our study showed that during the COVID-19 Paris outbreak, the IFMP diagnosed 3-fold more proximal PE in UD that in the entire year 2019. Moreover, UD rate was high and strikingly associated with COVID-19-related pulmonary PMCT lesions during the outbreak. Our findings have several clinical implications. First, we confirm that COVID-19 is associated with UD, highlighting the need of personal protective equipment for the resuscitation of a UD during the outbreak. Second, high PE rate in our UD series implies that it is a frequent cause of cardiac arrest, urging the resuscitated patient to be transferred to a cardiogenic shock center. Third, our results strongly suggest that PE should be explored in severe COVID-19 patients admitted to hospitals in order to start appropriate anticoagulation and to prevent death.

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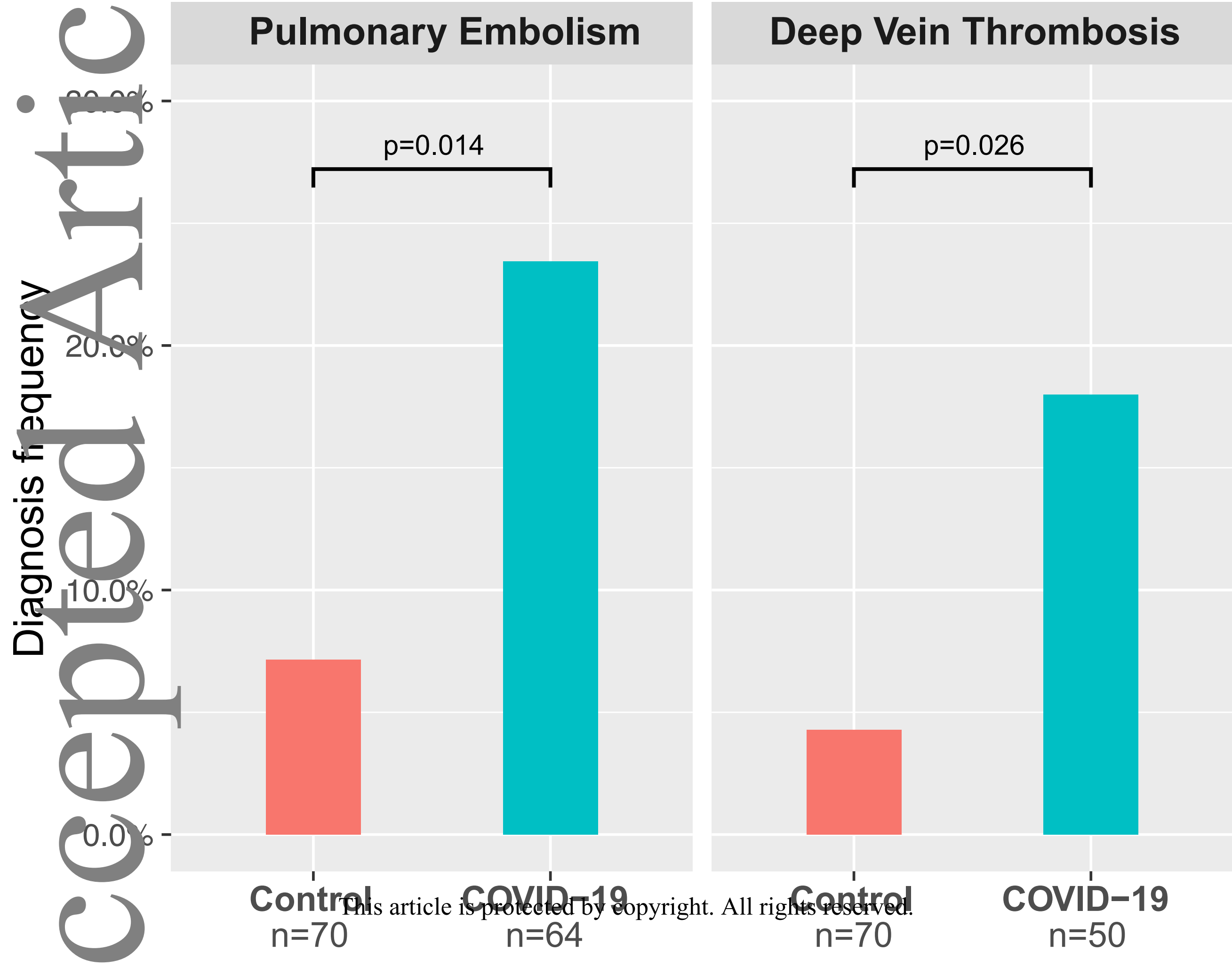
Figure captions

Figure 1. Comparison of pulmonary embolism and deep vein thrombosis (DVT) rate in unexplained deaths between subjects scanned during the year 2019 (control group) and in COVID-19-suspected patients during the 2-week outbreak peak (COVID-19 group). Presence of DVT was evaluated only in subjects who underwent limb CT.


Pulmonary Embolism
Deep Vein Thrombosis
Diagnosis frequency
0.0%
10.0%
20.0%
p=0.014
p=0.026
Control
n=70
COVID−19
n=64
Control
n=70
COVID−19
n=50