

**Figure 1** The number of hospital admissions for acute heart failure (AHF) in weekly intervals to Vanderbilt University Medical Center decreased both compared to the same time period in 2019 and in current year as confirmed cases of COVID-19 began to rise.<sup>5</sup> The 'stay-at-home' order for the state of Tennessee (TN) was signed on April 2, 2020.

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

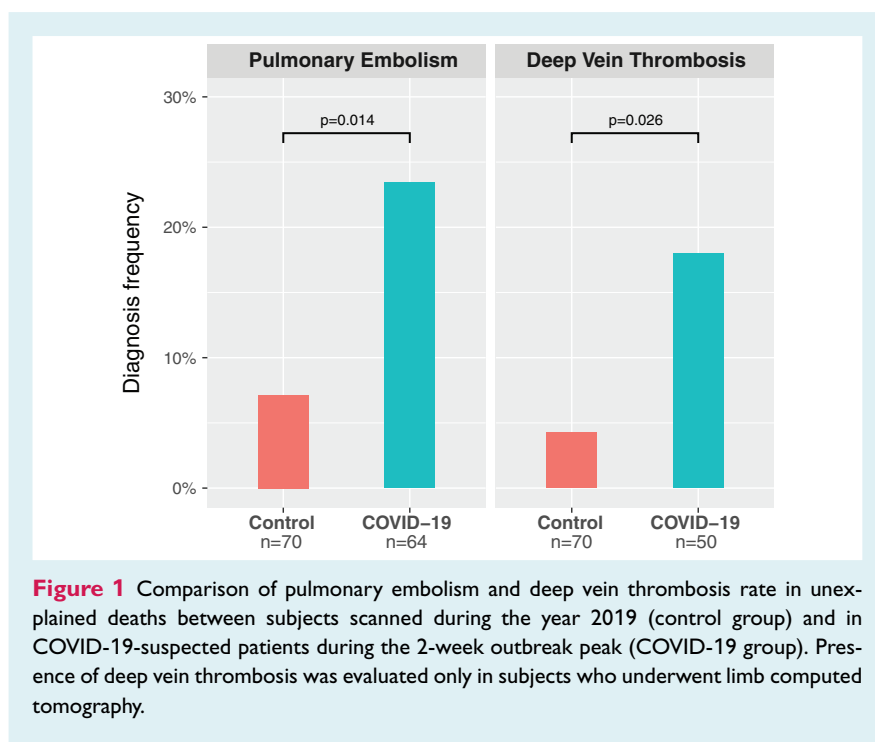
Coronavirus disease 2019 (COVID-19) deteriorates pulmonary function and can lead to acute hypoxaemic respiratory failure. COVID-19 may also directly impact the cardiovascular system.<sup>1</sup> Cases of pulmonary embolism (PE) were reported in in-hospital settings<sup>2–5</sup> and in a small post-mortem autopsy series.<sup>6</sup> Our study investigates the relation between PE and out-of-hospital unexplained death 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 23 March to 7 April 2020, COVID-19-suspected group) and subjects scanned during 2019 (control group).

We analysed  $\geq 18$ -year-old subjects presenting unexplained death 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 computed tomography abnormalities which have demonstrated a high diagnostic value.<sup>7</sup> Thoracic and limb PMCTs were blindly read by two experts and disagreements were solved in consensus. Proximal PE and deep vein thrombosis (DVT) were defined according to previous study criteria.<sup>8</sup> 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 and interquartile range (IQR).

The unexplained death rate was strikingly higher during COVID-19 outbreak peak [68 (79%) of 86 deaths] than during the control



**Figure 1** Comparison of pulmonary embolism and deep vein thrombosis 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 deep vein thrombosis was evaluated only in subjects who underwent limb computed tomography.

year 2019 [70 (21%) of 334 deaths; OR 14.1,  $P < 0.001$ ]. Among the 68 subjects with unexplained death during COVID-19 outbreak peak, four 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 significantly different between groups [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.

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

Our study showed that during the COVID-19 Paris outbreak, the IFMP diagnosed threefold more proximal PE in unexplained

death that in the entire year 2019. Moreover, the unexplained death 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 unexplained death, highlighting the need for personal protective equipment for the resuscitation of an unexplained death during the outbreak. Second, the high PE rate in our unexplained death series implies that it is a frequent cause of cardiac arrest, urging the resuscitated patient to be transferred to a cardiogenic shock centre. 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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