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Forensic Imaging 21 (2020) 200378

Contents lists available at ScienceDirect

Forensic Imaging

journal homepage: www.sciencedirect.com/journal/forensic-imaging

Short communication

Implications for forensic death investigations from first Swiss post-mortem CT in a case of non-hospital treatment with COVID-19

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ARTICLE INFO

Keywords:
3D visualisation
SARS-COV-2
COVID-19
forensic pathology
3D reconstruction
Virtopsy

ABSTRACT

Case details: A case of a 50-year old HIV-positive man is presented, with focus on visualization of post-mortem computed tomography (PMCT) of the lungs, in comparison to a forensic control case. He had been found dead at home, a day after his nasopharyngeal swab had returned positive for SARS-COV-2, three days after the sample had been taken as an outpatient, over five weeks after first exhibiting possible symptoms. 3D-visualization was performed by visually discriminating correlates for aerated, poorly aerated and non-aerated lung regions. The visual side-by-side comparison with a control case shows the deterioration beyond any ”normal” post-mortem finding, however. The PMCT findings in the lungs resemble those of patients with acute respiratory distress syndrome (ARDS), while histologically identified inflammation also shows, in part binuclear, lymphocytes. In addition, acute liver dystrophy and acute tubular necrosis in the kidneys were found. Except coronary artery atherosclerosis, there appeared to be no remarkable pathology of the heart.

Comment: With the pandemic impact of SARS-COV-2, a range of issues unfolds, also for medicolegal investigations into deaths, as we report the first Swiss case with post-mortem CT where death had occurred due to a SARS-COV-2 infection, with features of a severe acute respiratory distress syndrome, as an outpatient. As this pandemic from the view of risk assessment does constitute a black swan, underestimated fat tails as technical reason should be addressed by also analyzing apparent extreme single observations. This case of an outpatient (without hospital or intensive-care treatment) shows a pulmonary progression beyond the typical findings of COVID-19, to a non-specific picture of ARDS, where histologically, in part binuclear lymphocytes were remarked. What appeared to be an initially slow progression with final rapid escalation raises the question whether nasopharyngeal swabs alone or added pulmonary CT might be better for screening high-risk patients. The reported symptoms and relatively late medical consultation in this case appeared to contrast with the extensive pathology, raising the question whether any search for super-spreaders should not just focus on asymptomatic but under-reported symptomatic patients, and whether their prolonged circulation in everyday life would justify measures such as for example more extensive face mask policies. As post-mortem testing for SARS-COV-2 may not be available for every case, PMCT may provide sensitive testing for lung changes related to COVID-19. In order to allow for more precise medicolegal investigations in the context of COVID-19, however, any more specific extra tests may have to be financed by stakeholders in epidemiology, infectious disease or policy.

Short Communication

Case details

Case history: A 50-year HIV-positive old man reportedly had been treated antibiotically for an unspecified pulmonary infection in Italy, up around five weeks prior to death (mid February, 2020). Eight days prior to death, he had noted fever up to 38,2°C, mild cough, and headaches. Three days prior to death, he thus visited and outpatient clinic and reported that he may have had contact with a workmate who had been tested positive for SARS-CoV-2. At the clinic, he did not seem to have dyspnea or thoracic pain, and oxygen saturation was good. On the day of his death, the clinic representative allegedly told him over the phone that his test had returned positive for SARS-CoV-2. As he then reportedly told of absence of fever, absence of dyspnea and thoracic pains, he was advised to remain in self-isolation. On the evening of the

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https://doi.org/10.1016/j.fri.2020.200378
Received 27 March 2020; Received in revised form 7 April 2020; Accepted 15 April 2020
Available online 18 April 2020

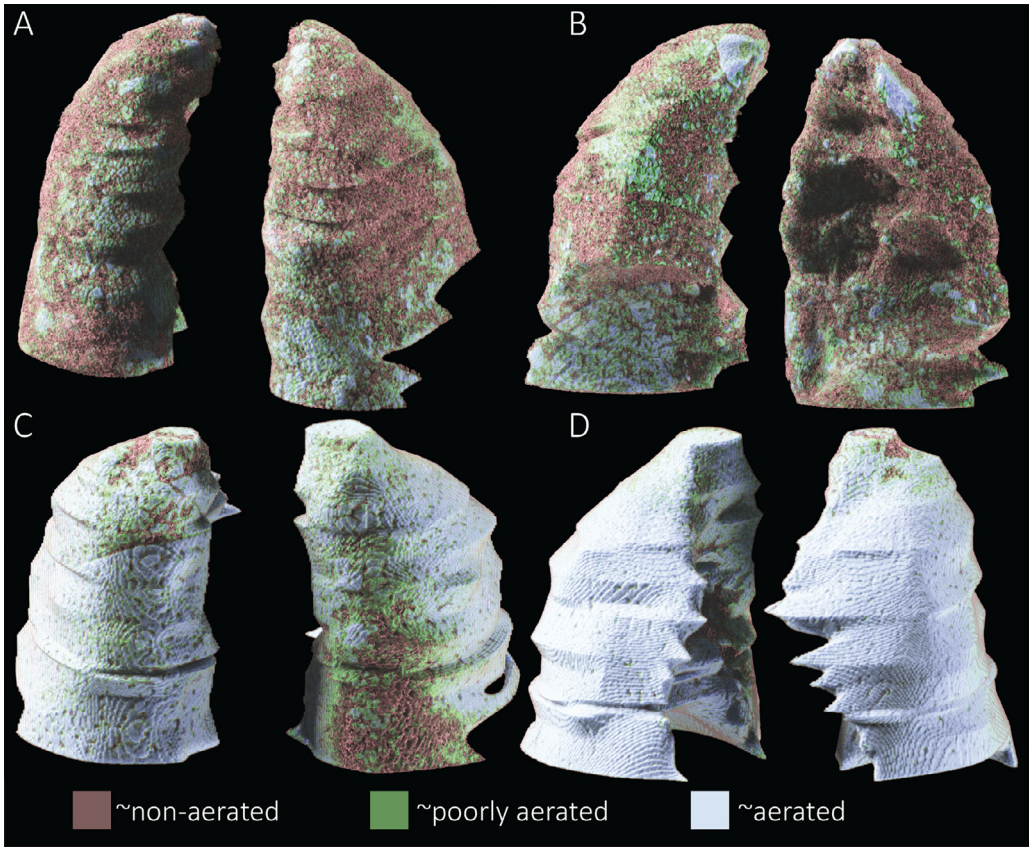

Fig. 1. Case of fatal pneumonia positive for SARS-COV-2 (**A, B**) with PMCT features of severe acute respiratory distress syndrome, versus a forensic control case with no such findings in pulmonary PMCT (**C, D**). Correlates for non-aerated (~ red), poorly aerated (~ green) and aerated (~ blue) lung regions (density ranges see text) were visualised three-dimensionally.

same day, he called the clinic again, now complaining of a racing heart [1], and was told to consult with the hospital at once. He never made it there, but was found dead at home on the following day. To clarify manner and cause of death, a medicolegal investigation into his death was opened. Before autopsy, PMCT was obtained (Fig. 1 and 2) that also showed absence of gas as indirect sign of probable absence of concurrent septicemia or bacterial infection [2–4]. The PMCT shows what appears to be a fatal case of a severe acute respiratory distress syndrome. The PMCT correlates for normally aerated lungs were identified between -900 and -500 Hounsfield units (HU), against which over-inflated (below -900 HU), poorly aerated (-500 to -100 HU) and non-aerated (above -100 HU) regions were differentiated on basis of density [5]. The visualizations in Figures 1 and 2 show a marked difference in the lung appearance compared to a control case. The details of the axial slice images are denoted in Figure 2; no reverse halo sign was identified. There appeared to be fluid in the maxillary and sphenoid sinuses. Bronchi and trachea appeared to be filled with fluid, whose PMCT surface characteristic was uneven, matching the autopsy finding of frothy fluid in the airways (see also Fig. 3). At autopsy, the heart of 340 g presented coronary artery atherosclerosis with pre-existing narrowing to 50% of the lumen of both the left anterior descending and right coronary arteries [6], no macroscopic signs of myocardial ischemia, and no relevant histological findings (such as contraction band necroses, infarction, or inflammation) were noted. The lungs with 1780 g weight showed extensive Tardieu spots and an increased consistency, with haemorrhagic foam or frothy fluid, in bronchi and trachea (Fig. 3). Microscopic features included congested blood vessels, some hyaline membranes, and patchy inflammation with lymphocytes (in part bi- and trinuclear). Histology of the liver that exhibited reduced consistency at autopsy was, other than macro- and microvesicular steatosis [7,8], a peracute liver dystrophy without inflammation; the kidney showed acute tubular necroses (Fig. 3). No signs of postmortem decomposition were noted on PMCT or at autopsy.

Control: Case of a 24 year old woman who had no acute respiratory distress syndrome related findings at all; there was post-mortem hypostasis dorsally at the right lung. The case allows for a comparison, as it may be seen as a ”normal” lung PMCT in a forensic caseload (Fig. 1 and 2).

PMCT: Lung PMCT was reconstructed from dedicated thorax/abdomen scans using a hard reconstruction kernel (Siemens, B60s). The data had been acquired on a dual-source CT (computed tomography) scanner (Somatom Definition Flash, Siemens, Erlangen, Germany). Standard protocols were employed [9]: for each case, whole body scans, thorax/abdomen scans as well as separate head scans were obtained. All scans used 120 kV and 128 x 0.6 mm collimation with automated dose modulation (CARE dose4D, Siemens, Erlangen, Germany). Thorax/abdomen scans were obtained at 400 reference mAs and for these, slice thickness was 1 mm with an increment of 0,6 mm. 3D-visualisation (Fig. 1) was performed after manual segmentation (Mevislab, Fraunhofer Institute, Germany).

Comment

The current SARS-COV-2[1]/COVID-19[2] pandemia constitutes a crisis in a number of ways [10,11]. Here, we argue that medicolegal specialists are privileged to a wider view, also on first-order and second-order effects, of SARS-COV-2, and, how even single extreme or rare observations should be relevant for policy-making.

Primarily, COVID-19 appears to concern clinical rather than forensic medicine: the direct impact of SARS-COV-2 is that it infects people where it may cause an illness with pneumonia in pandemic proportions that currently lacks specific treatment or vaccination. Then, it affects governments in that recommendations and emergency laws may be

[1] Severe acute respiratory syndrome coronavirus 2, cause of COVID-19
[2] Coronavirus disease 2019, caused by SARS-COV-2

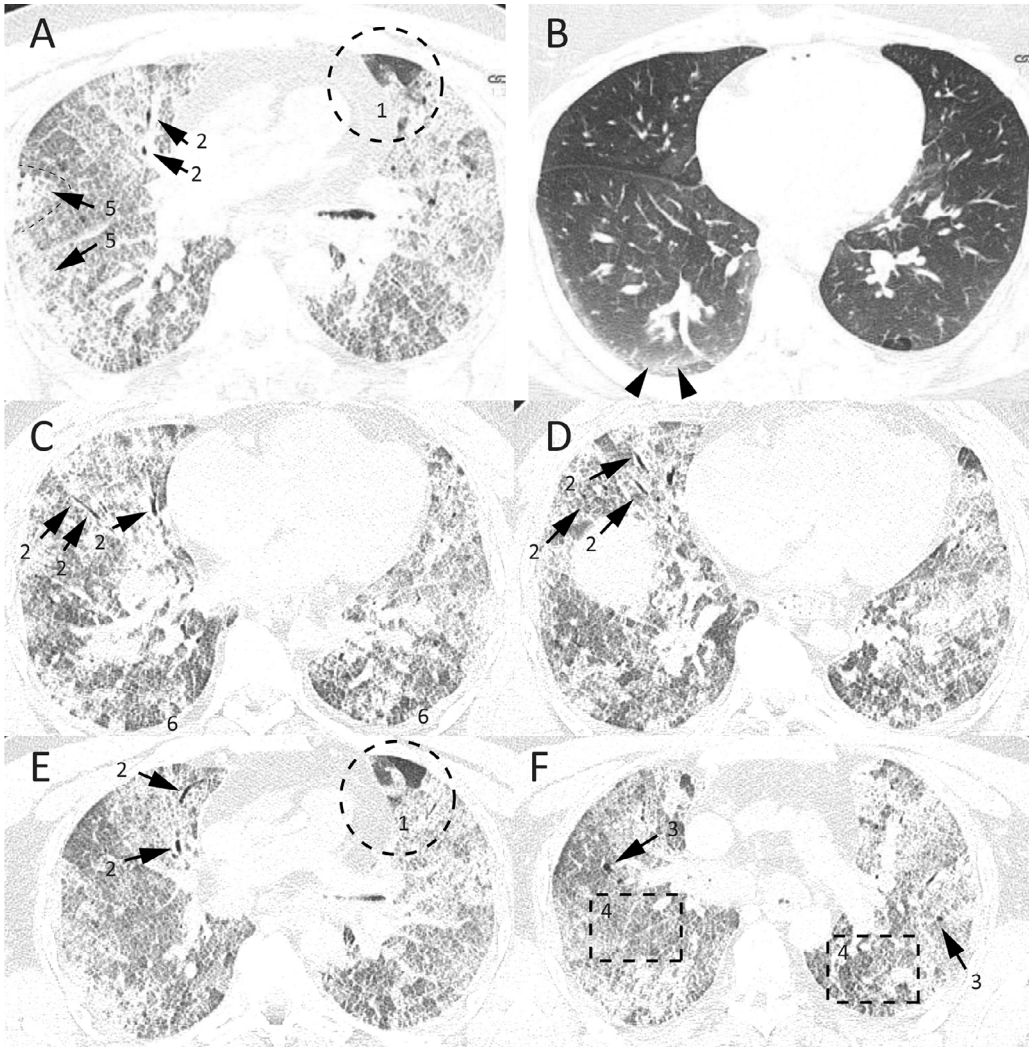

Fig. 2. Case of fatal pneumonia positive for SARS-COV-2 (axial PMCT images: **A, C-F**) versus a forensic PMCT control case (no signs of severe acute respiratory distress syndrome) (axial PMCT image: **B**). The gray-scale windowing setting was the same for all images. The SARS-COV-2 case (**A, C-F**) shows only few and small remaining regions as correlate for normal aeration (**1**), traction bronchiectasis (**2, 3**), crazy-paving with ground-glass opacities and septal thickening (for example, **4**) and multifocal consolidations (e.g., in the right lung, **5**) as well as small pleural effusions (**6**). These findings resemble those of patients with acute respiratory distress syndrome (ARDS). There appears to be no additionally visible post-mortem hypostasis. The control case shows dorsal location of post-mortem hypostasis (**B**: arrows).

issued, suspected patients may be recommended to report early symptoms, in order to follow procedures, in part also to medically observe and treat symptoms of COVID-19. Medicolegal complications of SARS-COV-2, however, mainly appear to derive from subsequent first-order and second-order effects.

There, the fear-based ”social distancing” as a government-imposed practice to lower risk of infection seems to provide a conceptual epicenter [12]: in combination with dramatic media reports [13], a current variety of ”social distancing” seems to also push irrational or aggressive behavior [14] while effectively exploiting fear to control the pandemic [13,15].

In considering its history, ”social distancing” had always been a well-established tradition, exerted upon various minorities, once even attributed with an individual fear-based graded 9-item scale of various levels (including items such as ”would keep away from”, ”would keep in an institution”, ”would send out of my country” and ”would put to death”) [16]: according to that paper, infectious disease outranked deafness, blindness or amputation, but not alcoholism or mental illness, as people to preferably stay away from.

Apparent consequences of fear, leveraged through the tool of ”social distancing”, thus seem to surface, as fear will predispose to a whole range of individual reactions, rather than just the government-intended single reaction (”would keep away from” [16]). Medical personnel are now being evicted from their own housing, because landlords fear SARS-CoV-2 infection (reports from India, Switzerland, Great Britain [17–21]). Domestic violence has escalated world-wide [22,23], in one instance, a man allegedly killed his partner out of fear of getting infected (with both later testing negative [24]), and there seems to be a new SARS-CoV-2 related road rage [25,26]. Intentional murder charges were introduced [27], against infected people that are not respecting quarantine rules. With that, SARS-CoV-2-related issues are being pushed far into the domain of medicolegal investigation: particularly by leveraging fear in the public also through what is called ”social distancing:, a whole range of relevant meta-level consequences ensue despite good intentions [13,15].

From there, even single and extreme observations can and should influence statistical methods in order to improve policies. With regard to statistics, one may consider black swans as an ultimate consequence of underestimated fat tails [28,29]. The statistical models that are used for risk assessment [30] risk to be wrong if assumptions, as those about normal distributions, are met with differing realities [28,29]. With that, statisticians particularly outside medicine already now routinely consider single extreme observations to better characterize fat tails [31]. Medicolegal observations that seem to exceed a clinical view in significant ways may thus be well suited also to at least be considered in informing policies.

Some existing policies are already reasonably well-informed. As forensic medical doctors covering both clinical forensic medicine and forensic pathology, we may mostly not get funding for microbiological SARS-CoV-2 testing. Identifying possibly critical cases can be performed differently though. Forensic post-mortem CT (PMCT) imaging has become an increasingly valuable asset [32] whereas we perform PMCT

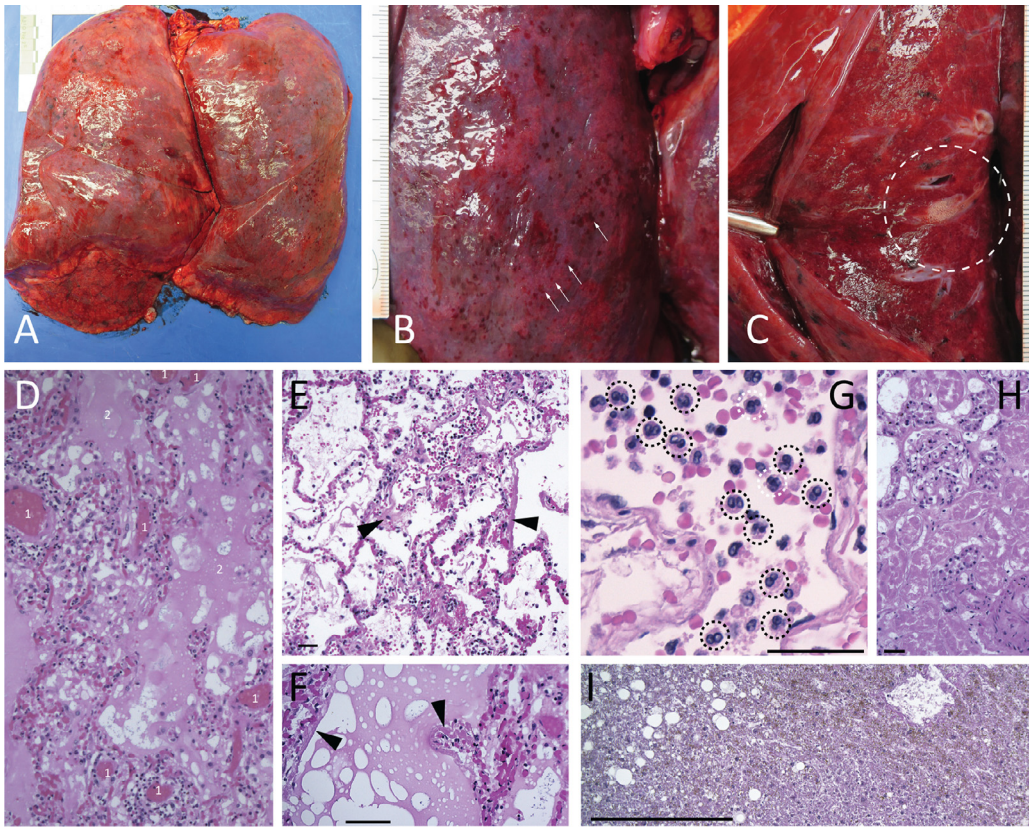

Fig. 3. At autopsy, the lungs of 1780 g weight (overview: **A**) showed pleural haemorrhages (**B**: Tardieu spots [a number of them are marked with arrows]). The cut surface exhibited foamy fluid in the airways (**C**, circle). Histology of the lungs (**D-G**) show a distorted septal and alveolar architecture (**D; 1**: congested vessels;**2**: correlate for edematous fluid), hyaline membranes (**E, F**: arrows) and lymphocytic infiltrates, in part binuclear (**G**: black circles) and trinuclear (**G**: white circles). Kidneys with acute tubular necroses (**H**). Liver with micro- and macrovesicular steatosis and what appears to be the correlate for acute dystrophy; scant lymphocyte accumulations in portal triads but no infiltrates (**I**). Bar 100μ (**E, F, G, H**), 1000μ(**I**).

scanning and data reporting on all bodies [33,34] before further steps, including autopsy, are done. One application of PMCT-based triage is to identify possible infectious disease prior to autopsy [35] and another one is to examine forensically relevant aspects of the lungs [36–38].

To the best of our knowledge, this report shares the first post-mortem computed tomography (PMCT) of a fatal course in a COVID-1 non-hospital patient. While one might interprete these to be extreme findings only because of their post-mortem nature, one should consider how a ”normal” PMCT may look like (Fig. 2 and 3). While this single SARS-CoV-2 fatality with what appear to be extreme findings should be seen within a wide forensic scope, we also stress the preliminary, early nature and necessarily incomplete nature of such communications as these.

While this man’s subjective report apparently did not include dyspnea, even less than a day prior to his death, the pulmonary pathology of this outpatient, as evidenced by PMCT, appears to extend beyond the severity shown in descriptions of currently published SARS-CoV-2-related fatalities, all of which apparently had obtained prior hospital and intensive-care treatment [39–41]. The extent of pulmonary affection in this case, both radiologically (see Fig. 2 and 3) and at autopsy, seems extensive in context of SARS-CoV-2 cases reported so far [42] but lies in the range of fatal SARS cases [43]. The findings appeared to be that of a per-acute respiratory distress syndrome, whereas no fibrosis and only some hyaline membranes were noted. Acute liver dystrophy and acute renal tubular necroses may be interpreted as consequences of acute right heart failure [44,45], which seems relevant in the context of possible COVID-19 related liver damage [46,47]. HIV-infection reportedly correlates with more frequent and more severe viral pneumonia [48,49]. The presence of binuclear lymphocytes as identified here may be considered as possibly enigmatic [50], whereas such cells had previously been reported in conjunction with polyclonal B-cell activation [51], also in MHV-A59 infections (Mouse Hepatitis Virus, also named Murine Coronavirus (MCoV) [52]) or EBV (Epstein-Barr-Virus [53]), whereas EBV also was reported to correlate with a more severe course of COVID-19 [54].

A first relevant policy aspect to consider is that of infectiousness in the light of COVID-19 [40]. Here, an individual appeared to have reported only relatively mild symptoms, and was advised to stay home only for the three days preceding death. Post-mortem examination however showed large amounts of frothy fluid in trachea, bronchi and paranasal sinuses, which also may indicate a wet cough [55,56] rather than a dry cough [40] in what appears to be a history with at least some symptoms stretching over around five weeks. Most of that time, this man can be assumed to have traveled and interacted freely with others. While over 99% in one series of COVID-19 patients [57] showed chest CT abnormalities, the frequencies of absent symptoms (no fever in 8,3%, no dyspnea in 73,3%, no cough in 25%) may also signify that there are those that under-report their illness and stay outside hospitals [58]. The reported symptoms and relatively late clinic consultation appeared to contrast with the extensive pathology, raising the question whether any search for super-spreaders should not just focus on so-called asymptomatic [59,60] but also on under-reported symptomatic patients (already suspected in those suffering from chronic cough [61]), and whether their prolonged circulation in everyday life would justify any measure of physical distancing, including the consideration of face masks [62,63]. At our institute [64], this has been taken into consideration for the latest recommendations regarding examination of deceased or live people in a forensic context. Thereby, in addition to usual protective gloves, surgical masks are recommended for all examinations for all people attending, whereas high-grade masks and a protective suit are required to protect the examiner in cases of known or strongly suspected COVID-19.

A second policy aspect to consider is that of diagnostic effort to screen for COVID-19. What appeared to be an initially slow progression with final rapid escalation in this case raises the question whether nasopharyngeal swabs are sufficient or if pulmonary CT might be a sensible addition for screening high-risk patients early into the course of suspected COVID-19. In this case, disease progression appears to be

characterized by a particularly fast deterioration, in comparison to at least one other fatal SARS-CoV-2 case with a known detailed timeline [8]: whereas it seems to be typical that shortness of breath may precede death by a few days, here, the cardinal symptom preceding imminent death reportedly was that of a "racing heart" [65]. One has to consider that naso-pharyngeal swabs and ensuing RT-PCR[3] evaluation may delay the diagnosis, while also turning out significant portions of false negatives [66]. If available, additional early pulmonary CT appears to offer both a relatively high speed and sensitivity [67], albeit at lower specificity [68]. For forensic post-mortem examinations, we had already previously identified triage PMCT as valuable, particularly and also in the context of screening for correlates of possible infections [35]. As post-mortem RT-PCR testing for SARS-CoV-2 in a forensic setting may not be available or too slow, PMCT may identify lung changes possibly related to COVID-19. With that, it is also relevant to note that forensic PMCT may show correlates of pathology that differ from a clinical setting [69].

This case was exceptional also in the way it was handled as "reportable death", because forensic work typically focuses on whether a crime was committed, without spending extra cost or effort. A conservative handling of Swiss procedures with regard to "reportable deaths" [70] risks to list most probable natural deaths as a result of assumed or possible acute cardiac failure. As relevant as that may appear to forensic investigations, this seems rather uninformative otherwise, and may definitely entail under-reporting of COVID-19 cases [58] when in fact, death *with* COVID-19 (as in: fall from great height, intoxication, road traffic accident, etc.), death *caused by* COVID-19 (as in: death of SARS-CoV-2 related ARDS, etc.), and death *with or of* COVID-19 *under medical treatment* (as in: experimental or cross-label medication was administered), might become a relevant distinction. Differentiating virus strains may be important, from view of epidemiology, rather than simple binary testing, seeing as if the clinical picture of COVID-19 and illness severity may differ across different viral strains (or subtype, or genetic variant) [71], with a majority of fatal COVID-19 cases possibly including additional microbial agents, whose pathophysiological role may yet have to be clarified; there, elevated serum procalcitonin as possible indicator of bacterial (rather than viral) infection [72] had already been identified to correlate with clinical severity [73].

So, more research, also with regard to aspects of previously unreported cases with COVID-19, may be needed, in order to identify where policies may require adaptation or extensions. In order to allow for more precise medico-legal investigations in the context of COVID-19, more specific testing may have to be financed by stakeholders in epidemiology, infectious disease or policy.

Competing interests

The authors declare that they have no competing interests.

Acknowledgements

The authors express their gratitude to Emma Louise Kessler, MD for her generous donation to the Zurich Institute of Forensic Medicine, University of Zurich, Switzerland. Data was published after having obtained a waiver by the Ethics Committee of the Canton of Zurich (15-0686) and with explicit permission of the investigating state attorney.

[3] This acronym refers to real-time reverse transcription polymerase chain reaction test that is used to qualitatively detect nucleic acid of the SARS-CoV-2 in specimens of the lower and upper respiratory tract, such naso-pharyngeal swabs.

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