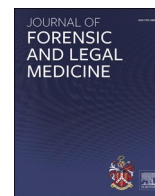




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Post-mortem routine practice in the era of the COVID-19 pandemic

Biagio Solarino, Davide Ferorelli^{*}, Alessandro Dell'Erba

Interdisciplinary Department of Medicine, University of Bari – Section of Legal Medicine, Bari General Hospital, Bari, Italy

At the beginning of March 2020 in a small town in Apulia (Southern Italy), a funeral ceremony for a 74-year-old man hit the news headlines because many people who attended the religious ceremony were subsequently found to be infected with severe acute respiratory syndrome coronavirus (SARS-CoV-2). Community transmission of the virus was attributed to the forensic pathologist who performed the routine post-mortem inspection of the man's body. The decedent died in his own home of natural causes. In the background history, the decedent reported that he was in Northern Italy during the initial outbreak of coronavirus disease 2019 (COVID-19). Diagnostic testing for detection of SARS-CoV-2 was performed before his death, but the forensic pathologist did not wait for the laboratory results and authorized a public funeral service. Two days later, the decedent's relatives were informed that they had tested positive for COVID-19 infection. The family were completely unaware that the decedent had infected most of his family members; consequently, many of the attendees at the funeral paid their respects to the family with kisses, hugs, and by shaking hands. Nearly 10,000 residents of the town were placed in quarantine, with the Italian Army surrounding the town to enforce the quarantine.

The COVID-19 pandemic represents a global burden for individuals and for a substantial number of healthcare providers who risk being infected during routine work in hospitals or in private clinical practice. The disease is caused by SARS-CoV-2, which mainly spreads from person to person, primarily via respiratory transmission.^{1,2}

The novel coronavirus was first identified in China and has now been detected in more than 200 countries. In recent weeks, Italy has reported many new deaths owing to SARS-CoV-2, being one of the worst-hit countries after China even in terms of mortality rate worldwide. An immediate lock-down of all public activities was implemented by the Italian government in a bid to contain the epidemic and reduce the burden and pressure on the healthcare system.³

The public has been continuously informed about the progression of the epidemic thorough daily updates regarding the number of infected and recovered individuals, as well as the number of deaths. In this respect, we aim to stress the role of forensic pathologists who are responsible for post-mortem management of the body in a decedent's

residence or in a hospital mortuary. The above-mentioned case reported in the media highlights the hazards and risks of such "routine" activities in the era of the COVID-19 pandemic.

In Italy, necropsy activity for people who died in the Hospital or in their own homes is managed by physicians who work in Forensic and/or Public Health and Hygiene Departments. If it is not possible to establish the cause and manner of death with a postmortem examination, a diagnostic autopsy is required. In case of suspicious death, a legal autopsy was order by Public Prosecutor. Forensic pathologists are often involved in crime scene investigations as well. Currently, all the international guidelines about autopsy procedures and specimens collections are routinely followed by practitioners but only few Hospitals have dedicated mortuary rooms for protecting against high risk of transmittable diseases.

In this sense, the case in Apulia points out not only the role of forensic pathologists in certifying the cause and manner of death but also the possible occupational hazards and risk of becoming infected when performing a necropsy and other autopsy procedures on the body of a deceased person infected with SARS-CoV-2.⁴

Claydon defined a high-risk necropsy as the "post-mortem examination of a deceased person who has had, or is likely to have had, a serious infectious disease that can be transmitted to those present at the necropsy, thereby causing them serious illness and/or premature death".⁵ Post-mortem examination requires taking a preliminary medical history for the decedent, which is often collected directly from close relatives in the location where the individual died or in a mortuary. It is now known that SARS-CoV-2 has been detected in asymptomatic individuals; therefore, relatives or funeral workers could be unaware of the risk of becoming infected with the virus.

According to the literature, SARS-CoV-2 is taking a disproportionate toll on older people in Italy, which has the oldest population in Europe and the second-oldest in the world after Japan. The older population is defined as people aged 65 years and over. In many cases, these older individuals have mild to serious degrees of pre-existing illnesses (such as diabetes, hypertension, cardiovascular disease, chronic respiratory disease, nephropathy, liver disease, cancer, and so on).

^{*} Corresponding author. Policlinico di Bari Hospital, University of Bari, Piazza G. Cesare 11, 710124, Bari, Italy.
E-mail address: davideferorelli@gmail.com (D. Ferorelli).

It is not an easy task to establish whether an old man who died at home with no previous hospitalization and who had only mild symptoms that are commonly seen in people of a comparable age range should be reported as a suspected case of COVID-19 infection. This is particularly troublesome in the context of a virus epidemic because it is possible that the decedent had contact or lived with infected but asymptomatic individuals. A question in such cases arises concerning the need to request post-mortem virus testing and/or autopsy to confirm or disprove the diagnosis. The same problem occurs in all cases, even for example, a suspected homicide victim with no external signs of traumatic injury, where it is impossible to establish the cause and manner of death. We suggest preliminary application of the medical record criteria provided by the World Health Organization, which is widely discussed in the literature for identifying possible cases of COVID-19 infection. If COVID-19 is indeed suspected according to the circumstances of death, it is mandatory to request post-mortem virus testing and autopsy.

Monitoring the overall population mortality at this stage is essential, to assess the impact of the epidemic. Under the state of emergency declared by the Italian government, elective surgeries have been cancelled and non-urgent procedures postponed. Family doctors are considerably limited in their practice with respect to identifying possible COVID-19 cases, and the access to hospital emergency departments must be limited to urgent conditions. Under this scenario, the risk is that patients with multiple unrelated diseases who remain at home may die without adequate healthcare. A point of debate has arisen regarding the accuracy of epidemiological data, especially the criteria for evaluating confirmed COVID-19-related deaths. Undoubtedly, CT scan findings of bilateral and multifocal ground-glass opacity with peripheral/posterior distribution progressing to acute respiratory distress syndrome (ARDS), together with specific symptoms and progressive respiratory failure in patients with a positive diagnostic COVID-19 test represents a valid method for establishing the cause of death.⁵ Otherwise, in nearly all deaths, the decedents (mainly over age 80 years) had underlying chronic medical conditions, sometimes so severe as to generate legitimate doubt about the independent correlation between death and SARS-CoV-2 infection. The question is whether we can consider deaths caused by COVID-19 to be all cases in which the result of virus detection testing was positive.

Currently, only one published study has reported macroscopic findings, observed during an autopsy performed in a 85-year-old patient with COVID-19.⁷ The authors describe lung damage with excess production of mucus spilling out from the alveoli, indicating COVID-19-related pathological changes in the alveoli and deep airways similar to those observed in SARS and Middle East respiratory syndrome (MERS). Analogous conclusions were reported by Xu and co-authors, who discuss the histopathological findings obtained using biopsy samples taken from lung, liver, and heart tissue of a 50-year-old patient who died 2 weeks after being infected with COVID-19.⁸

Learn from the dead is an aphorism that underlines the need to reverse the diminished reliance on autopsy rates that has taken place in recent decades.⁹ The fear of malpractice litigation, the need to reduce healthcare costs, and the belief that advances in modern antemortem diagnostic tools have rendered autopsy obsolete are among the many reasons for this decline. Nevertheless, it is an undisputed fact that the value of autopsy is widely recognized as a means of advancing scientific knowledge, assessing the quality of care, and establishing the truth, such that a complete autopsy with collection of specimens remains the gold standard for the control of infectious disease outbreaks.¹⁰

Autopsy findings are critical not only for determining the cause of death in a patient with COVID-19 infection but also for providing new insights into the pathogenesis of SARS-CoV-2 related respiratory disease. Although it is well known that the novel coronavirus affects the respiratory system, autopsy will help to further understanding regarding the involvement of other organs, such as those of the digestive system, and outcomes correlated with pre-existing diseases such as cancer or chronic liver conditions.¹¹

It has been assumed that patients who are severely affected by SARS-CoV-2 may have cardiac complications, including cardiac arrest, myocardial infarction, acute-onset heart failure, and myocarditis.¹² In such cases, only a complete evaluation of macroscopic and histopathological findings, with additional analyses when necessary, such as toxicological, biochemical, microbiological, and genetic testing, with permit determination of whether cardiac system involvement is secondary to COVID-19 or another pre-existing disease.

Therefore, we believe that autopsy in cases of COVID-19 infection represents an essential component in the peer review process, with a thorough comparison between clinical and pathological findings. The value of post-mortem results might also help physicians to formulate a timely therapeutic strategy for patients with COVID-19.

Considering that the number of deaths is increasing daily worldwide, we acknowledge that it will be difficult to perform autopsy in all cases; therefore, we can choose to perform autopsy at random, such as in certain unique cases. In addition to the difficulties in organizing a mortuary that cannot cope with hundreds of coronavirus deaths each day, another reason for the reluctance to perform autopsy is owing to the risks posed by an infectious disease like COVID-19 for forensic pathologists.

A mortuary can be a dangerous place¹³: the main reason is that the forensic pathologist's staff often do not know in advance if the deceased is affected by a transmissible infectious disease. Hence, a standard precautions and well-equipped facilities should be applied in all post-mortem examinations.

The term high-risk autopsy refers to those in which there is a high risk of transmission of an infectious agent to autopsy practitioners.¹⁴ The high-risk agents that elicit the greatest concern include human immunodeficiency virus (HIV), hepatitis B and C virus (HBV, HCV), *Mycobacterium tuberculosis*, and the causative agent of Creutzfeldt-Jacob disease; these are included in Hazard Group 3 (HG3) with other and rare agents.^{4,15} Except for the prion responsible for CJD and transmissible spongiform encephalopathy, which is extremely resilient to formalin and routine methods of decontamination, the risk of occupational acquisition of viral and bacterial infections during autopsy are extremely low, and there is no universal scientific agreement about the possibility that a cadaver can spread infection to humans although the contrary has not yet been proven.¹⁶ A potentially advantageous alternative for pathologists is the use of minimally invasive autopsy (MIA), which is assumed to pose less risk than a full autopsy involving highly contagious infectious agents.^{17,18}

However such procedure often need to be combine with Resonance Magnetic imaging (MRI) and computed tomography (CT) scan for performing imaging-guide biopsy and this imply an effort in terms of mortuary organization and health care costs.¹⁹

It is our opinion that conventional autopsy performed with appropriate protective measures remains the most valuable tool also in such cases.

For safe post-mortem practice on cadavers known or suspected to be affected by an infectious agent, the Royal College of Pathologists (RCP) recommend safety protocols that have been updated with brief guidance following the outbreak of COVID-19 infection in China.²⁰

COVID-19 is considered an HG3 pathogen that may be acquired via inhalation; it remains unclear whether the virus is spread by skin contamination. To safely and satisfactorily perform autopsy on the body of a person with suspected or confirmed COVID-19 infection, a list of standard precautions are recommended with respect to the autopsy suite, procedure, the minimum number of staff, and personal protective equipment (PPE). Interim guidance by the US Centers for Disease Control and Prevention (CDC) states that autopsies in known or suspected COVID-19 cases should be conducted only in a specialized mortuary with an isolation room: this recommendation is not mandatory according to the RCP.²¹ The post-mortem samples collected for diagnosing cases of COVID-19 are the same as those used for the diagnosis of living patients, i.e., upper and lower respiratory tract specimens. The

respiratory sites to be fixed in formalin during autopsy include the trachea and central lung with bronchi and lung parenchyma. Specific precautions for the collection and handling of post-mortem clinical and pathological specimens are reported in the literature.^{22,23}

Italy is currently registering the highest number of COVID-19-related deaths worldwide. If we consider it difficult to protect the general public from infection, the same holds true for protecting healthcare workers, including forensic pathologists and all mortuary staff.

As mentioned before, most of the mortuaries in Italy lack this safety recommendations, especially regarding the presence of dedicated negative-pressure isolation room.²⁴ For this reason the Government did not recommend to perform autopsies in patients with SARS-CoV-2 infection and suggest to reduce the period of post mortem observations.²⁵

Nevertheless we believe that in the era of the COVID-19 pandemic, post-mortem practice has a fundamental role in better defining the cause of death and advancing scientific knowledge regarding the pathogenesis of SARS-CoV-2 related diseases, toward developing future therapies. Practitioners involved in necropsy must minimise the risks of COVID-19 infection by applying standard precautions.

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