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Autopsies of COVID-19 deceased? Absolutely!

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ARTICLE INFO

Keywords:
 COVID-19
 SARS-CoV-2
 Pandemic
 Autopsy
 Post mortem

ABSTRACT

Autopsies are an essential tool for understanding new diseases. Against this background, it is incomprehensible why there is great reluctance worldwide to perform autopsies on COVID-19 deceased patients. The article provides an overview of the status of the autopsy series published worldwide and shows the path taken by the city of Hamburg in Germany, where autopsies are ordered by the health authorities in the interests of disease control. The risk of infection posed by SARS-CoV-2-positive deceased persons may be overestimated. The scientific benefit that can be drawn from experience with autopsies and further examination of tissue samples is immeasurable.

1. Introduction

At the end of 2019, the outbreak of a novel virus of the corona family, SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2), which causes COVID-19 (Corona Virus Disease 2019), began in Wuhan, China. Since then, a dynamic has developed worldwide, which first led to numerous cases of the disease in Asia and then in Europe. While in these parts of the world the infection activity has been contained for the moment by strong public restrictions (lockdown), the pandemic is now concentrated in North and South America, namely in countries such as the USA, India, Brazil, Chile and Peru. According to WHO data, there were 12,929,306 confirmed infections and 569,738 deaths worldwide on 14 July 2020 [1].

2. Autopsy activity in different countries

As soon as the pandemic reached the various countries, many of them began a wide range of scientific activities, focusing on the development of vaccines, the characterization of virus properties and clinical aspects of COVID-19. Initially, clinical and radiological data on the lungs of COVID-19 patients were available, but patho-morphological investigations were rarely undertaken. Naturally, the first publications on this subject came from China in February and March 2020, including results of lung biopsies of both living patients [2,3] and deceased patients [4] being examined. The first published full autopsy with macroscopic photographs in a COVID-19 patient was provided in a medico-legal journal from China in February 2020 [5]. Systematic examinations of autopsies were missing until then.

It is not quite clear why there has been a certain reluctance to perform autopsies of patients who died of COVID-19 until today. It is

true that in Germany the Robert Koch Institute (a German health monitoring institution) – at least in the initial phase of the pandemic – had advised against performing autopsies. However, the author is not aware of such clear votes against autopsies by other large health organizations such as the WHO, the Royal College of Pathologists (UK) or the CDC (USA). (Fulfillable) guidelines regarding minimum requirements for safe autopsies, e.g. concerning personal protection and room exhaustion, do exist, however [6–8].

Apparently autopsies are carried out here and there in the USA, which is particularly affected by COVID-19. Davis and Williamson published a letter in early June 2020, which deals with the risk of infection during COVID-19 autopsies [9]. A survey of 200 participating autopsy institutions has shown that at the time of writing there have been at least 225 autopsies in 14 states of the USA. For whatever reason, no major case series seem to have been investigated so far.

If publications on COVID-19 autopsy series are seen as an indicator for the autopsy frequency in the respective country, Germany, Italy, the USA, Switzerland, Austria and Great Britain seem to be countries where autopsies are performed at all – at least in individual centers. The studies used as a basis for this conclusion were PubMed-listed studies (search terms were COVID-19, SARS-CoV-2, autop* and post mort* in various combinations) whose case numbers go beyond mere case reports (which are of course also important) ($n > 2$; see Table 1). Postmortem study results also come from Brazil, China and France, but the tissue examined was obtained using different biopsy techniques (“minimally invasive autopsy”).

3. Procedure in Hamburg/Germany

In Germany, too, COVID-19 deaths have so far only been autopsied

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<https://doi.org/10.1016/j.legalmed.2020.101769>

Received 14 July 2020; Received in revised form 22 July 2020; Accepted 22 July 2020

Available online 26 July 2020

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Table 1

Autopsy series (n > 2) of COVID-19 deaths listed in PubMed. The terms COVID-19, SARS-CoV-2, autop* and post mort* were searched for in various combinations.

Authors	Journal	Cases	Extent of autopsy	Country	Notes
Edler et al. [10]	Int J Legal Med	80	Full	Germany	
Carsana et al. [11]	Lancet Infect Dis	38	Full	Italy	
Monteiro et al. [12]	Clinics (Sao Paulo)	31	Minimally invasive/punctures	Brasil	Technical report (no pathological results)
Han et al. [13]	Arch Pathol Lab Med	24	Full	USA	No pathological results
Menter et al. [14]	Histopathology	21	Full*	Switzerland	*full in 17/21
Dell'acquila et al. [15]	Arch Pathol Lab Med	12	Full	Italy	
Wichmann et al. [16]	Ann Intern Med	12*	Full	Germany	*Subset of Edler et al.
Schaller et al. [17]	JAMA	12	Full	Germany	
Lax et al. [18]	Ann Int Med	11	Partially	Austria	In situ technique, only 1 brain
Nunes duarte-neto et al. [19]	Histopathology	10	Mimimally invasive	Brasil	
Fox et al. [20]	Lancet Respir Med	10	full	USA	
Xu et al. [21]/Wu et al. [22]	Zhonghua Bing Li Xue Za Zhi	10	Minimally invasive	China	Focus on spleen and lung findings
Youd et al. [23]	J Clin Pathol	9	Full	Great Britain	
Ackermann et al. [24]	NEJM	7	Full	Switzerland/Germany	Focus on lung findings
Copin et al. [25]	Intensive Care Med	6	Minimally invasive (biopsies)	France	
Bösmüller et al. [26]	Virchows Arch	4	Full	Germany	
Buja et al. [27]	Forensic Sci Int	3	Full	USA	
Yao et al. [28]	Cardiovasc Pathol	3	Minimally invasive	China	

at a few locations. In Hamburg, the second largest city in Germany (1.8 million inhabitants), a special path was taken from the beginning. The health authorities of the districts ordered autopsies for all COVID-19 deaths according to the Infection Protection Act. Those autopsies have been performed in the Department of Legal Medicine of the University Medical Center Hamburg-Eppendorf. At the previous peak of the pandemic, it was not possible to autopsy all cases due to capacity reasons. Nevertheless, a full autopsy has been performed in 170 of the 231 deaths so far in Hamburg. Results of subsets are presented in various publications [16,29]. The world's largest series of 80 consecutive autopsies from the Hamburg Department of Legal Medicine was presented by Edler et al. [10].

4. Safety aspects

The main reason for the great reluctance worldwide to perform autopsies seems to be concerns about infectivity emanating from deceased persons. It remains somewhat unclear whether these concerns relate more to the health and safety of individual (forensic) pathologists, or to infection control in general. As far as the safety of the doctors and auxiliary staff involved in the autopsy is concerned, it must be objected that, in clinical pathology but particularly in forensic medicine every corpse must be considered potentially infectious. This starts with the risk of injuries, which can be an entry point for bacterial wound infections or viral diseases such as hepatitis C or HIV. But also diseases spread by air, such as meningococcal meningitis or tuberculosis, pose a real danger to the health of the autopsy staff. Often it is not even known that an infectious disease is present before the autopsy. Even if a disease like tuberculosis is known, an autopsy will still be performed with FFP2 or FFP3 mouthguards. Of course, other considerations apply in the case of highly infectious viral diseases with high mortality, such as Ebola.

Particularly in the case of sharply rising infection figures, as is currently the case in the USA or Brazil, the risk of encountering an unknown SARS-CoV-2-infected person if the autopsy is performed for other reasons, such as after homicide, is quite real. However, one will not be able to avoid such genuinely forensic autopsies with regard to latent risk of infection, which means that one must always protect oneself to a certain extent. But if the infection is known, specific precautions would be undertaken.

The literature is dominated by appeals for more autopsies to be performed [23,30–33]. Pomara et al. are particularly insistent on the necessity of autopsies in the COVID 19 pandemic [34]: “Death can teach us not only about the disease, it might help with its prevention and, above all, treatment.” In this respect, it is actually hard to understand that there

are also publications that expressly oppose the performance of autopsies. Teresinski et al. claim [35]: “In general, in case of deaths caused by confirmed SARS CoV-2 infections, there are no medical indications to conduct a postmortem examination.” Sapino et al. recommend [36]: “Autopsies should be restricted to well-motivated cases [...]” – without specifying which cases this should be. However, both recommendations were made in the early stages of the pandemic.

Remarkably, Davis et al. registered only one case of infection in their survey after 225 autopsies, in which it is considered probable that the affected person was not infected by the autopsy but from community exposure [9]. Han et al. also report no disease symptoms in 6 participants after 24 COVID-19 autopsies [13].

In Hamburg, all autopsies were performed in a special autopsy room for infectious corpses (air suction directly at the autopsy table downwards). All persons involved wore FFP3 masks and the otherwise usual protective clothing. After more than 150 autopsies, there were no cases of disease or infection (PCR negative throat swabs, negative serology – unpublished data) among the approx. 25 persons involved (technical staff, doctors).

5. Autopsy results

The autopsies made it possible to examine COVID-19-associated deaths more closely than would have been possible by purely clinical observations. In Hamburg, it was noticed after only a few autopsies that the frequency of deep vein thromboses and fatal pulmonary embolisms in the deceased COVID-19 patients was much higher than initially suspected [10,16] (see Figs. 1 and 2). Many of the lungs examined were very large, extremely heavy and brittle. The pleura as well as the cut surfaces showed a patterned juxtaposition of pale and hyperemic areas

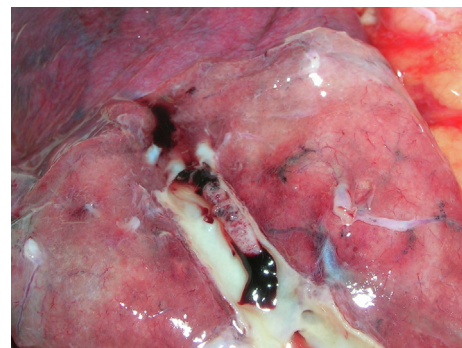


Fig. 1. Pulmonary embolism in a 91-year-old man.



Fig. 2. Deep vein thrombosis (same patient as Fig. 1).

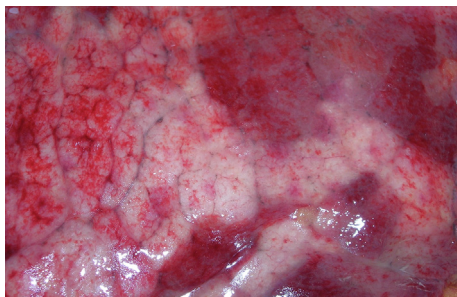


Fig. 3. Typical patchy aspect of the lung (cut surface), in a 56-year-old woman.

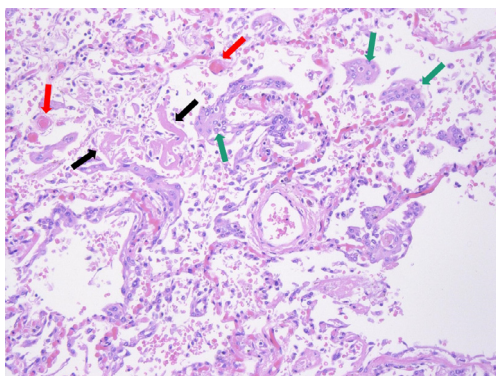


Fig. 4. Diffuse alveolar damage with abundant fibroblasts and pneumocytes in the alveoli, hyaline membranes (black arrows), squamous metaplasia (green arrows) and microthrombosis (red arrows) (H&E, $\times 80$). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

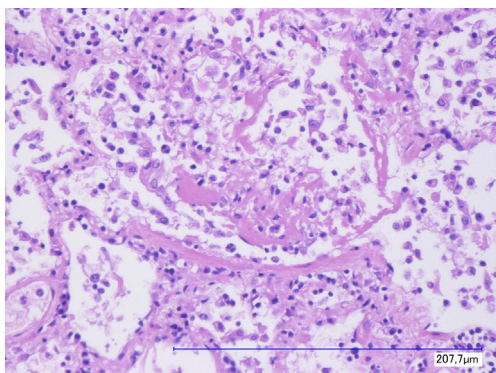


Fig. 5. Hyaline membranes (H&E, $\times 100$).

(Fig. 3). Even though most of the affected patients die clinically in respiratory failure, the patho-morphological images are quite differentiated. In many patients of the evaluated studies the classic signs of

diffuse alveolar damage (DAD), the pathological equivalent of Acute Respiratory Distress Syndrome (ARDS), were present in the sense of an atypical viral pneumonia (Figs. 4 and 5). However, this was not the case in all patients. Some had rather the findings of a purulent bronchopneumonia, so that one can ask whether SARS-CoV-2 in these cases rather was the basis for bacterial superinfection. Among the 80 cases published by Edler et al. there were also those which, after autopsy, showed an alternative, COVID-19-independent cause of death (e.g. pericardial tamponade in myocardial rupture after myocardial infarction), which, strictly speaking, were COVID-19 disease cases but not COVID-19 deaths in a narrower sense [10]. The authors proposed a four-level classification scheme according to pathological-morphological criteria to take into account the variability of the deaths (category 1: certain COVID-19 deaths, category 2: probable COVID-19 death, category 3: possible COVID-19 death with an equal alternative cause of death, category 4: SARS-CoV-2 detection with cause of death not associated to COVID-19).

In all post-mortem studies with larger case numbers, the average age of the deceased was quite high at about 80 years. A shift towards younger ages, as in Carsana et al. (69 years), one must probably assume a selection effect, since although the autopsies were performed in consecutive deaths, only patients from certain referral centres were considered [11]. In contrast, the study by Edler et al. is more representative for the general population because all COVID-19-associated deaths of patients known to the authorities outside the clinics were also examined [10]. Clinically already known or autopsically detected comorbidities (e.g. heart disease, lung disease, renal failure, diabetes, obesity, etc.) were frequently represented in all studies.

The study by Puelles et al. provided important findings, which were able to detect the virus in various organs such as kidneys, liver and brain [29]. Ackermann et al. were able to show that angiogenesis in the lungs of deceased COVID-19 patients was enhanced compared to influenza patients [24]. These are examples of how autopsies open the door to many important branches of research.

6. Conclusion

The results from the analyzed studies show that autopsies are essential in the COVID-19 pandemic. They enable a more differentiated assessment of mortality. More important than the determination of the cause of death, however, is the fact that only the autopsy (including histological and virological examinations) opens up the possibility of investigating the spread of the virus in the body, the involvement of various organ systems, but also the late effects of the disease – an aspect that is becoming increasingly important since, after more than 4 months of pandemic, there are many “recoveries” that may not have recovered as fully as had been hoped.

There are few valid reasons not to perform autopsies in COVID-19 deceased if the technical equipment meets certain minimum standards. It is easy to protect oneself against infection during the autopsy. Both clinical and forensic pathologists – preferably in cooperation – play an important role in gaining knowledge about the new disease as a basis for therapeutic measures and global pandemic control.

Acknowledgements

The funding source of the study is the University Medical Center of Hamburg-Eppendorf, Hamburg, Germany. I would like to thank the whole Corona Team of our Department, namely (in alphabetical order) Sven Anders, Eric Dietz, Carolin Edler, Carla Falk, Antonia Fitzek, Daniela Fröb, Moritz Gerling, Axel Heinemann, Fabian Heinrich, Anna Kammal, Anke Klein, Inga Kniep, Philine Lange, Felicia Langenwalder, Kay Uwe Liebsch, Larissa Lohner, Malin Luther, Chiara Marino, Kira Meißner, Anna Mitakoudis, Herbert Mushumba, Klaus Püschel, Carina Romich, Alexandra Ron, Julia Schädler, Alina Schneider, Ann Sophie Schröder, Sandra Wilmes, Tamara Zimmermann, and all cooperation

partners at the University Hospital.

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