RESEARCH LETTER

Postmortem Examination of Patients With COVID-19

Approximately 15% of individuals affected by coronavirus disease 2019 (COVID-19) develop severe disease, and 5% to 6% are critically ill (respiratory failure and/or multiple organ dysfunction or failure).[1,2] Severely ill and critically ill patients have a high mortality rate, especially with older age and coexisting medical conditions. Because there are still insufficient data on cause of death, we describe postmortem examinations in a case series of patients with COVID-19.

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Methods | Between April 4 and April 19, 2020, we conducted serial postmortem examinations in patients with proven severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection who died at the University Medical Center Augsburg (Germany). Autopsies were conducted according to published best practice.[3] Specimens from lung, heart, liver, spleen, kidney, brain, pleural effusion, and cerebrospinal fluid (CSF) were assessed. Postmortem nasopharyngeal, tracheal, bronchial swabs, pleural effusion, and CSF were tested for SARS-CoV-2 by reverse transcriptase–polymerase chain reaction. This study was approved by the local institutional review board, and written informed consent was obtained from next of kin.

Results | Of 12 consecutive patients with COVID-19 who died, postmortem examinations were conducted in 10. The median age was 79 years (range, 64-90 years); 7 patients were male. All cases tested positive for SARS-CoV-2 by nasopharyngeal swab at time of hospital admission. The median duration from admission to death was 7.5 days (range, 1-26 days). The most frequent initial symptoms included fever, cough, and dyspnea. In 9 patients, infiltrations with ground-glass opacity predominantly in middle and lower lung fields were detected by chest x-ray. Patients had a median of 4 known preexisting comorbidities (range, 0-6), with cardiovascular disease being most frequent (**Table**). Preexisting structural lung damage (eg, emphysema) was found in 2 patients. None of the patients had thromboembolic events in central vessels at autopsy or prior to death.

Table. Clinical Characteristics and Lung Pathology

Patient No.[a]	Known comorbidities	Symptom duration before admission, d	Time from admission to death, d	Duration of ventilator management, d	Stage of diffuse alveolar damage[b]		
					Acute	Organizing	End-stage
1	Chronic myelomonocytic leukemia, hypothyroidism	7	26	21	–	+	++
2	Arteriosclerosis, arterial hypertension, atrial fibrillation, chronic lymphocytic leukemia, coronary artery disease	14	15	14	+	++	–
3	Arterial hypertension, arteriosclerosis, chronic obstructive pulmonary disease, diabetes, fatty liver disease	7	7	6	+	++	–
4	Arterial hypertension, atrial fibrillation, chronic kidney failure, dilated cardiomyopathy, hypothyroidism, morbid obesity[c]	21	9	8	+	++	–
5	Hypertrophic cardiomyopathy	4	8	NA[d]	++	+	–
6	Arterial hypertension, arteriosclerosis, atrial fibrillation	6	3	NA[d]	+	++	–
7	Adenocarcinoma of the lung (stage IV), arterial hypertension, chronic kidney failure, hyperthyroidism	5	7	NA[d]	++	+	–
8	Chronic obstructive pulmonary disease, chronic kidney failure, diabetes, morbid obesity[c]	2	5	NA[d]	++	+	–
9	Arterial hypertension, arteriosclerosis, atrial fibrillation, dementia	3	1	NA[d]	++	+	–
10	Arterial hypertension, arteriosclerosis	2	8	NA[d]	++	+	–

Abbreviation: NA, not applicable.

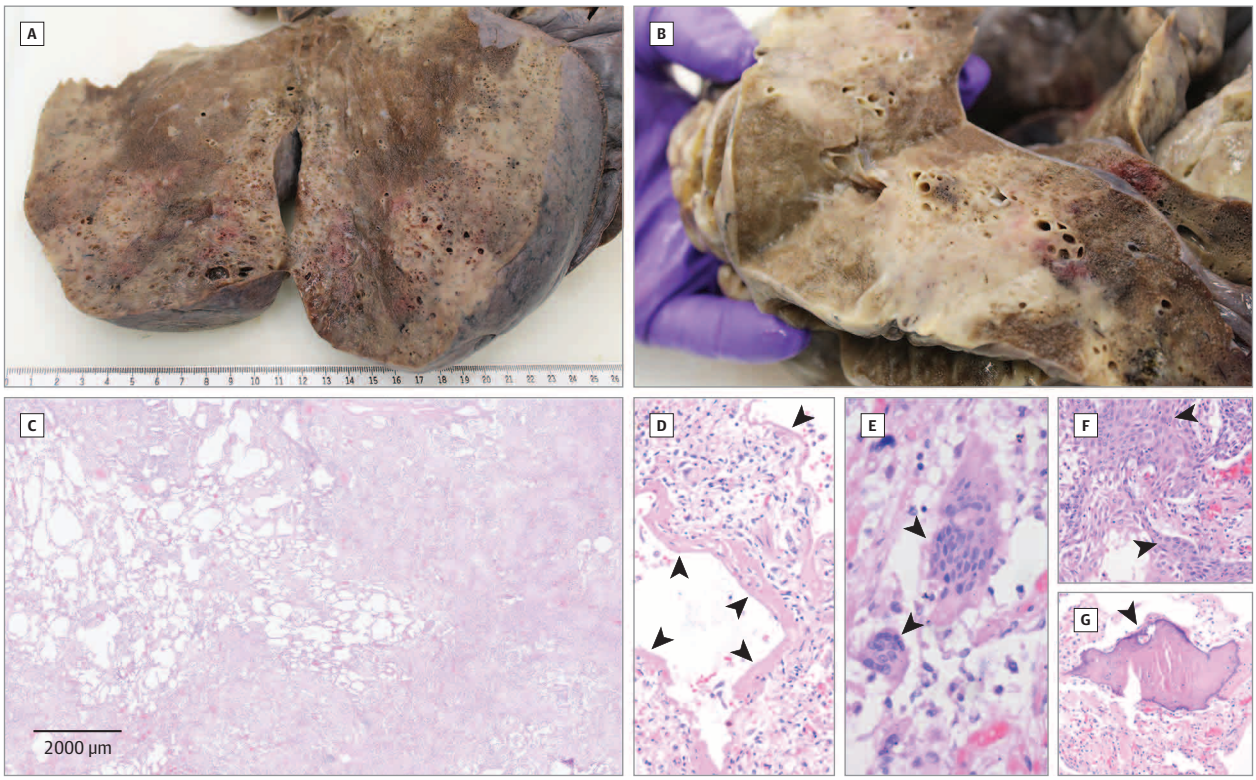
[a] Due to data privacy, patient numbers have been randomly assigned.

[b] Scale for predominant stage of acute alveolar damage: ++, strong; +, moderate; and –, weak/absent.

[c] Morbid obesity was defined as body mass index greater than 40 (calculated as weight in kilograms divided by height in meters squared).

[d] No invasive mechanical ventilation.

Figure. Macroscopic and Microscopic Findings in the Lung



Macroscopic (A and B) and histologic (C) images of organizing and end-stage diffuse alveolar damage (hematoxylin-eosin staining) with hyaline membranes (D, arrowheads, ×100), multinucleated giant cells (E, arrowheads, ×400), and squamous/osseous metaplasia (F and G, arrowheads, ×200) in a patient with a fatal course of coronavirus disease 2019.

In all cases, including 6 patients who did not receive invasive ventilation, disseminated diffuse alveolar damage at different stages (the histopathological correlate of acute respiratory distress syndrome) was the major histologic finding. Diffuse alveolar damage was detectable in all lobes but appeared unevenly distributed with pronounced manifestation in middle and lower lung fields (**Figure**, A-B). Signs of exudative early-phase acute diffuse alveolar damage with hyaline membrane formation, intra-alveolar edema, and thickened alveolar septa with perivascular lymphocyte-plasmocytic infiltration were consistently found. Organizing-stage diffuse alveolar damage with pronounced fibroblastic proliferation, partial fibrosis, pneumocyte hyperplasia leading to interstitial thickening and collapsed alveoles, and patchy lymphocyte infiltration was the predominant finding. In areas of organizing diffuse alveolar damage, reactive osseous and squamous metaplasia were observed (Figure, C-G). Fully established fibrosis was most prominent in patient 1, ultimately leading to almost complete destruction of pulmonary parenchyma. In 5 patients, minor neutrophil infiltration was indicative of secondary infection and/or aspiration.

Mild lymphocytic myocarditis and signs of epicarditis were detectable in 4 and 2 cases, respectively. Liver histology showed minimal periportal lymphoplasmacellular infiltration and signs of fibrosis. There was no morphologically detectable pathology in other organs. Specifically, no signs of encephalitis or central nervous system vasculitis were found.

At time of autopsy, SARS-CoV-2 was still detectable in the respiratory tracts of all patients. Polymerase chain reaction testing was positive in pleural effusion but negative in all CSF samples.

Discussion | In this postmortem evaluation of 10 patients with COVID-19, acute and organizing diffuse alveolar damage and SARS-CoV-2 persistence in the respiratory tract were the predominant histopathologic findings and constituted the leading cause of death in patients with and without invasive ventilation. Periportal liver lymphocyte infiltration was considered unspecific inflammation. Whether myoepicardial alterations represented systemic inflammation or early myocarditis is unclear; criteria for true myocarditis were not met. Central nervous system involvement by COVID-19 could not be detected.

This study has limitations, including the small number of cases from a single center and missing proof of direct viral organ infection.

The pulmonary histologic characteristics of COVID-19 resembled those observed in diseases caused by other *Betacoronavirus* infections such as severe acute respiratory syndrome[4] and Middle East respiratory syndrome.[5]

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Accepted for Publication: May 11, 2020.

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Published Online: May 21, 2020. doi:10.1001/jama.2020.8907

Author Contributions: Drs Schaller and Claus had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Schaller and Hirschbühl contributed equally as first authors. Drs Märkl and Claus contributed equally as senior authors.
Concept and design: Schaller, Hirschbühl, Braun, Trepel, Märkl, Claus.
Acquisition, analysis, or interpretation of data: Schaller, Hirschbühl, Burkhardt, Märkl, Claus.
Drafting of the manuscript: Schaller, Hirschbühl, Braun, Trepel, Märkl, Claus.
Critical revision of the manuscript for important intellectual content: Schaller, Hirschbühl, Burkhardt, Trepel, Märkl, Claus.
Statistical analysis: Claus.
Obtained funding: Braun.
Administrative, technical, or material support: Schaller, Hirschbühl, Burkhardt, Trepel, Märkl.
Supervision: Claus.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the physicians from the intensive care unit (Michael Wittmann, MD, and Ulrich Jaschinski, MD), and the Department of Radiology (Thomas Kröncke, MD) of the University Medical Center Augsburg. We thank Jürgen Schlegel, MD, from the Department of Neuropathology, School of Medicine, Institute of Pathology, Technical University Munich, for sampling brain tissue. Technical support was provided by Alexandra Martin, AMLT, Christian Beul, AMLT, and Elfriede Schwarz, AMLT, from the Institute of Pathology and Molecular Diagnostics, University Medical Center Augsburg. No compensation was received for their roles in the study.

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Prevalence of SARS-CoV-2 Among Patients Admitted for Childbirth in Southern Connecticut

Developing an approach to care for pregnancy and childbirth during the coronavirus disease 2019 (COVID-19) crisis is a priority to (1) provide safe care to pregnant women and newborns and (2) protect health care workers from infection. A study conducted in New York City reported a 13.5% prevalence of asymptomatic infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in women presenting for childbirth.[1] On March 30, 2020, an initially asymptomatic woman admitted to the Yale New Haven Health system developed cough and fever soon after childbirth; testing confirmed SARS-CoV-2 infection. This event prompted the development of a SARS-CoV-2 screening and testing program of patients presenting for childbirth; we report the prevalence detected in the first weeks of the program.

Methods | From April 2, 2020, to April 29, 2020, screening and testing of patients admitted for childbirth was initiated at 3 Yale New Haven Health hospitals in southern Connecticut. Screening consisted of questions related to travel, contacts, and symptoms of COVID-19. All patients without a prior diagnosis of COVID-19 underwent SARS-CoV-2 polymerase chain reaction (PCR) testing of nasopharyngeal swabs, with rapid testing available. Patients scheduled for cesarean birth were screened and tested at preoperative visits.

Hospital policies recommended universal mask use on clinical units by clinicians, patients, and support persons and limited each patient to 1 support person visitor for childbirth. For patients with symptoms of COVID-19, clinicians wore N95 respirators and appropriate personal protective equipment

Table 1. Demographics and Characteristics of Patients Tested for SARS-CoV-2 on Admission for Childbirth[a]

Characteristics	SARS-CoV-2 PCR result	
	Positive (n = 30)	Negative (n = 740)
Age, y		
<30	14 (46.7)	199 (26.9)
30-34	10 (33.3)	310 (41.9)
≥35	6 (20.0)	231 (31.2)
Nulliparity	16 (53.3)	323 (43.7)
Site of hospital		
Greenwich	8 (26.7)	204 (27.6)
Bridgeport	11 (36.7)	129 (17.4)
New Haven	11 (36.7)	407 (55.0)
Gestation <37 wk at birth	0	62 (8.4)
Cesarean delivery[b]	10 (33.3)	275 (37.2)
Apgar score		
<7 At 1 min	0	40 (5.4)
<7 At 5 min	0	12 (1.6)
Neonatal birth weight, mean (SD), g	3370 (621)	3331 (568)
Neonatal SARS-CoV-2 positive test result[c]	0	

Abbreviations: COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a] Data are expressed as No. (%) of participants unless otherwise indicated. Excludes patients diagnosed with COVID-19 prior to admission, including those considered recovered (defined as ≥14 days from onset of symptoms and ≥72 hours afebrile).

[b] Mode of birth was determined by routine obstetric indications.

[c] Neonatal testing by PCR of nasopharyngeal swabs was performed at 24 hours of age.