A Postmortem Portrait of the Coronavirus Disease 2019 (COVID-19) Pandemic

A Large Multi-institutional Autopsy Survey Study

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• ***Context.***—**This study represents the largest compilation to date of clinical and postmortem data from decedents with coronavirus disease 2019 (COVID-19). It will augment previously published small series of autopsy case reports, refine clinicopathologic considerations, and improve the accuracy of future vital statistical reporting.**

Objective.—**To accurately reflect the preexisting diseases and pathologic conditions of decedents with SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) infection through autopsy.**

Design.—**Comprehensive data from 135 autopsy evaluations of COVID-19–positive decedents is presented, including histologic assessment. Postmortem examinations were performed by 36 pathologists at 19 medical centers or forensic institutions in the United States and Brazil. Data from each autopsy were collected through the online submission of multiple-choice and open-ended survey responses.**

Results.—**Patients dying of or with COVID-19 had an average of 8.89 pathologic conditions documented at autopsy, spanning a combination of prior chronic disease and acute conditions acquired during hospitalization. Virtually all decedents were cited as having more than 1 preexisting condition, encompassing an average of 2.88 such diseases each. Clinical conditions during terminal hospitalization were cited 395 times for the 135 autopsied decedents and predominantly encompassed acute failure of multiple organ systems and/or impaired coagulation. Myocarditis was rarely cited.**

Conclusions.—**Cause-of-death statements in both autopsy reports and death certificates may not encompass the severity or spectrum of comorbid conditions in those dying of or with COVID-19. If supported by additional research, this finding may have implications for public health decisions and reporting moving forward through the pandemic.**

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Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged from Wuhan, China, in 2019 and has since created a global pandemic.[1,2] The spectrum of disease caused by SARS-CoV-2 infection in humans is referred to as coronavirus disease 2019 (COVID-19); it includes pulmonary,[3] cerebral,[4] myocardial,[5] hepatic,[6] and renal[7] pathology, as well as clotting dysfunction.[8,9] Worldwide, SARS-CoV-2 has infected more than 100 million people and COVID-19 has killed more than 2 million people.[10] Until recently, the United States and Brazil were the 2 countries most affected by the virus; in the United States, more than 26 million people have been infected with greater than 400 000 deaths, and in Brazil, more than 9 million people have been infected and more than 220 000 people have died with the virus.

Since the first postmortem findings in a decedent with SARS-CoV-2 were reported in February 2020,[11] many articles documenting postmortem pathology and discussing pathophysiology in COVID-19 have been published[3,12–31] (Table 1). Most of these studies report findings from relatively small and homogenous patient populations, and many are limited in their scope of evaluation. Moreover, the vital role that autopsy plays in promoting accurate death certification in COVID-19 has been considered in only a subset of the publications.[16,17,25,29]

The present study is the largest compilation of demographic, clinical, and postmortem data in those dying of or with COVID-19 to date. It draws on a diverse patient population and the combined experience of numerous pathologists from across the United States and in Sao Paolo, Brazil. Comprehensive data from 135 postmortem evaluations of COVID-19 decedents are presented, including histologic evaluation of all organ systems in most cases. This study will augment previously published autopsy case reports, refine clinicopathologic considerations, and improve the accuracy of vital statistical reporting moving forward through the COVID-19 pandemic.

METHODS

Study Design and Participants

In April 2020, a written invitation to participate in this multi-institutional study was disseminated to all participants on the "COVID Autopsy Listserve"[32] by the first and last authors of this article. The 135 postmortem examinations in this study were performed by 36 resident and/or attending pathologists at 19 medical or forensic institutions across the United States and in Sao Paolo, Brazil; this participation represented roughly 20% of the listserve membership at that time. The examinations were conducted from circa February to March 2020 through the end of this study's data collection period in late May (data collection May 9–25, 2020). All contributing pathologists confirmed complying with applicable policies and procedures governing human subjects' research at their respective institutions, as well as obtaining appropriate consent for the autopsy procedure.

Data from each autopsy were collected through online submission of responses to a 49-question survey using a Microsoft Form designed by the first and last authors (see Supplemental digital content for elements of the survey at https://meridian.allenpress.com/aplm in the May 2021 table of contents). Some responses were characterized by a single letter or digit, while many required up to 50 text characters to provide sufficient information. All data were then compiled and analyzed in a Microsoft Excel workbook (Microsoft Corporation, Redmond, Washington). Nearly 25% of the data (questions No. 1–12) appear in Table 2. The remaining survey data (questions No. 13–49) were compiled and analyzed by first-hand observation of the authors and are summarized in Tables 3 through 5.

Diagnosis and Procedures

COVID-19 was diagnosed in 1 decedent (n = 1) by unspecified antemortem antibody testing and in all other decedents (n = 134) by polymerase chain reaction or Abbott Laboratories ID NOW assays for SARS-CoV-2. The 134 molecular assays were performed on antemortem (110), postmortem (12), or undesignated (1) nasopharyngeal swabs; postmortem lung tissue (5); postmortem tracheal and lung swabs (1); or a combination of these methods (5).

Postmortem evaluations were conducted by using various techniques including percutaneous/small-needle biopsy sampling (36) and at least in situ evaluation of body cavities and organs (99). Where biopsies were used, they included samples of lungs (multiple biopsies), liver, heart, kidneys, spleen, brain, skin, skeletal muscle, and testis.[22] Not all requested data were obtained in each evaluation, though most cases evaluated all organ systems histologically.

RESULTS

Database Demographics

The database breakdown by age, sex, and ethnicity, compared to available demographic figures from the United States, is provided in Table 2.[33] Although generally they are similar, our 135 cases capture a younger population (although maximum and minimum ages are very similar) with by far the largest statistical difference represented by the mode. The US statistical mode of greater than 85 y is extraordinarily high and reflects COVID-19's disproportionate mortality effect on the elderly. Our database reflects a population that is more male, more Black or African American, and less Hispanic, but approximately the same mix of white and Asian ethnicities. It should be noted that the US comparison statistics on ethnicity date to August 2020, whereas our survey period ended in May 2020; Hispanic prevalence increased later in the pandemic.[33]

Reported Preexisting Diseases and Clinical Conditions in SARS-CoV-2–Infected Decedents

SARS-CoV-2–infected decedents in our cohort harbored a high number of preexisting diseases, with total occurrences summarized in Table 3. Virtually all decedents were cited as having more than 1 preexisting disease; in fact, decedents in our database had an average of 2.88 diseases when they acquired COVID-19. Systemic hypertension was reported in 86 decedents (64% of the 135 cases). Diabetes mellitus was reported in 70 decedents (52%), and obesity was reported in 46 decedents (34%). Coronary artery disease was reported in 34 decedents (25%). Only 10 decedents (7%) had no preexisting conditions reported.

Clinical conditions during hospitalization were categorized in this survey by organ systems. These were reported a total of 395 times, and virtually all decedents had more than 1 concurrent disease. Unsurprisingly, 113 of the 135 decedents (84%) had acute respiratory disease, 73 (54%) acquired acute kidney dysfunction, and acute myocardial dysfunction was reported in 47 decedents (35%). Acute coagulopathies including disseminated intravascular coagulation affected 46 decedents (34%). Notably, concurrent infection with a pathogen other than SARS-CoV-2 was relatively rare, being noted in only 14 decedents (10%). Participants diagnosed concurrent infections by chart review for premortem cultures, by histologic evaluation, and in some cases by postmortem cultures.

Table 1. International Literature Review of COVID-19[a] Autopsy Studies to Date

Source, y	Date in 2020	Location	No. of Cases With Histology	Age Range (Mean), y	M:F	COD	Primary Pathology Findings (Lung)	Secondary Pathology Findings	Background Chronic Disease
Xu et al,[11] 2020	2/15	China	1	50	1:0	No	DAD	Focal myocarditis	Liver
Su et al,[12] 2020	4/9	China	26 (kidney)	39–87 (69)	19:7	No	ATI	None	Kidney
Magro et al,[13] 2020	4/15	United States (New York)	2 (lung)	32–72 (55)	3:2	No	MT, lung hemorrhage, DAD	Skin vascular injury	None
Tian et al,[14] 2002	4/15	China	4	59–81	3:1	No	DAD, PNA	None	Liver, DM, hemat
Menter et al,[15] 2020	5/4	Switzerland	21	53–96 (76)	17:4	No	DAD, PNA, vasculitis	MI, ATI	Heart, kidney, liver
Barton et al,[16] 2020	5/5	United States (Oklahoma)	2	42, 77 (59)	2:0	Yes	DAD, PNA, MT	None	Heart, kidney, liver
Wichmann et al,[17] 2020	5/6	Germany	12	52–87	8:4	Yes	DAD, PE, PNA	Shock changes	None
Buja et al,[18] 2020	5/7	United States (Texas)	3	34–62 (48)	3:0	No	DAD, lung hemorrhage	MT kidney	None
Lax et al,[8] 2020	5/14	Austria	11	66–91 (80)	8:3	No	DAD, PNA, MT	MT heart	Heart, kidney, liver
Schaller et al,[20] 2020	5/21	Germany	10	64–90	7:3	No	DAD, PNA	Focal heart inflammation	Liver
Ackermann et al,[19] 2020	5/21	Germany	7 (lung)	68–96 (88)	5:2	No	DAD, MT	None	None
Bryce et al,[21] 2020	5/22	United States (New York)	25	34–94	NK	No	DAD, PNA, MT	ATI, MT kidney	Heart, kidney, liver
Nunes et al,[22] 2020	5/22	Brazil	10	33–83	5:5	No	DAD, PNA	MT heart, kidneys	Heart, kidney, liver
Fox et al,[23] 2020	5/27	United States (Louisiana)	10 (heart, lung)	44–78	NK	No	DAD, lung hemorrhage, MT	Rare heart inflammation	Heart
Rapkiewicz et al,[24] 2020	6/1	United States (New York)	7	44–65 (57)	4:3	No	MT, DAD, lung hemorrhage	Shock changes, MT	Heart
Edler et al,[25] 2020	6/4	Germany	12	52–96 (79)	46:34	Yes	DAD, PNA	Shock changes	Heart, lungs
Carsana et al,[3] 2020	6/8	Italy	38 (lung)	32–86 (69)	33:5	No	DAD, PNA, abscess	None	None
Youd & Moore,[26] 2020	6/30	United Kingdom	3	33–88 (77)	2:1	No	DAD	None	Heart, kidney, liver
Prieto-Perez et al,[27] 2020	7/3	Spain	33 (lung, marrow)	53–98	21:12	No	DAD, MT	None	None
Copin et al,[28] 2020	7/8	France	6	NK	NK	No	AFOP	None	None
Bradley et al,[29] 2020	7/16	United States (Washington)	14	42–84	6:8	Yes	DAD, PNA, MT	Focal heart inflammation, ATI	Heart, kidney, liver

Abbreviations: AFOP, acute fibrinous organizing pneumonia; ATI, acute tubular injury of kidney; COD, cause of death; COVID-19, coronavirus disease 2019; DAD, diffuse alveolar damage; DM, diabetes mellitus; hemat, hematologic; MI, myocardial infarction; MT, microthrombi; NK, not known; PE, pulmonic embolism; PNA, acute bronchopneumonia.

Table 2. Demographic Comparison of 135 COVID-Positive Autopsies to Available US COVID-19 Death Statistics

	135 Cases	US Statistics[a]
Age statistical measures, y		
Mean	61	65–74
Median	63	75–84
Mode	64	>85
Max	97	>85
Min	0.6	<1
Sex		
Male	59%[b]	54%
Female	41%	46%
Ethnicity		
Asian	3%	4%
Black or African American	30%	22%
Hispanic or Latino	17%	20%
White	50%	52%
Other	-	2%

Abbreviation: COVID-19, coronavirus disease 2019.

[a] Numbers and percentages reflect the period between February 1, 2020, and May 30, 2020.

[b] Percentages reflect the period between February 1, 2020, and August 8, 2020.

Organ Weights in SARS-CoV-2–Infected Decedents

Analysis of organ weights in decedents infected with SARS-CoV-2 showed few unexpected results. As expected, individual and combined lung weights were extremely heavy (mean combined weight, 1872 g; reference range, 685–1050 g).

The mean and median heart weights were 491 and 460 g, respectively; this mean value would lie within expected ranges only for men weighing more than 92 kg (203 lb) and women weighing more than 108 kg (238 lb).[34] Liver and kidney weights were nearly within normal ranges, but with outliers at both the maximum and minimum. As will be described, the increased heart, liver, and kidney weights likely reflect preexisting chronic conditions, rather than a direct effect of COVID-19.

Autopsy Pathology Findings

The number and diversity of pathologic conditions observed in these autopsies parallel both the variety of preexisting chronic conditions and the myriad disease processes complicating hospitalization (summarized in Tables 4 and 5). In the 74 brains with final neuropathologic evaluation available at the time of data analysis, no COVID-19–specific pathologic processes were observed, although some showed preexisting conditions. Most of these cases were examined by a neuropathologist. Our reporting of additional pathologic findings will focus on the principal organs examined at least by biopsy in all decedents. Electron microscopy was performed in a minority of 27 of the 135 cases (20%), and where any "viral-like particles" were identified they were predominantly located in the lungs.

Consistent with current literature, the most frequently demonstrated pulmonary pathology in 135 decedents was acute (101 [75%]) or organizing (63 [47%]) phases of diffuse alveolar damage (DAD), or both injury patterns together. At least focal pulmonary hemorrhage often accompanied DAD, while acute bronchopneumonia was reported in 55 decedents (41%). Interestingly, vasculitis was infrequently identified in pulmonary vessels in 5 (4%).

Macroscopic thrombi were only evaluable in 97 cases (after excluding needle biopsy procedures). However, on the basis of 135 cases used in other findings, pulmonary thrombi were identified in 28 decedents (21%), and thrombi in other sites were present in 14 decedents (10%). The term *microscopic thrombi* is being used interchangeably with intravascular fibrin or platelet-rich aggregates as defined in the study of De Michele and colleagues[35] of pulmonary findings in 40 autopsies. Nineteen autopsies included dissection of deep leg veins, and in 5 of these decedents

Table 3. Preexisting and Clinical Hospitalization Condition Findings in 135 COVID-19–Positive Autopsies

Preexisting Condition	No. Cited (n = 399)[a]	% Patients (n = 135)[b]	Hospitalization Condition	No. Cited (n = 395)[c]	% Patients (n = 135)[d]
Systemic hypertension	86	64	Acute respiratory disease	113	84
Diabetes mellitus	70	52	Acute kidney disease	73	54
Obesity	46	34	Acute myocardial disease	47	35
Coronary artery/vascular disease/hyperlipidemia	35	25	Acute coagulopathy/DIC	46	34
Neuromuscular disease	26	19	Acute liver disease	25	19
Heart disease	25	19	Acute neurological disease	24	18
Lung disease	23	17	Acute GI disease	19	14
Kidney disease	23	17	Other infection	14	10
Malignancy or rheumatologic disease	22	16	Other	25	19
Liver disease	7	5	Not provided	10	7
Other	26	19	-	-	-
Not identified	10	7	-	-	-

Abbreviations: COVID-19, coronavirus disease 2019; DIC, disseminated intravascular coagulation; GI, gastrointestinal.

[a] Virtually all patients were cited as having more than 1 preexisting condition at initial hospitalization, resulting in 2.88 preexisting conditions cited per patient.

[b] Total does not equal 100% because virtually all patients were cited as having more than 1 preexisting condition at initial hospitalization and many patients were cited with the same condition.

[c] Virtually all patients were cited as having more than 1 clinical condition at terminal hospitalization, resulting in 2.85 clinical conditions cited per patient.

[d] Total does not equal 100% because virtually all patients were cited as having more than 1 clinical condition at terminal hospitalization and many patients were cited with the same condition.

Table 4. Pulmonary, Thrombosis, and Cardiac Pathologic Findings Cited in 135 COVID-19–Positive Autopsies

	No. Cited	% Patients
Pulmonary pathology	(n = 362)[a]	(n = 135)[b]
DAD - acute	101	75
DAD - organizing	63	47
Hemorrhage	58	43
Acute bronchopneumonia	55	41
Tracheitis/bronchitis/bronchiolitis	40	30
Mucus in airways	21	16
Emphysema	14	10
Edema or vasculitis	6	5
Not identified/assessed	4	2
Thrombosis	(n = 294)[a]	(n = 135)[b]
Macroscopic thrombosis[c]		
Lungs	28	21
Deep leg veins	8	6
Other	6	4
Not identified	59	44
Not assessed	39	29
Microscopic thrombosis		
Lungs	72	53
Kidneys	13	10
Other	12	9
Not identified	57	42
Cardiac pathology	(n = 275)[a]	(n = 135)[b]
Myocyte hypertrophy	104	77
Myocardial fibrosis	56	42
Coronary artery disease	34	25
Old myocardial infarction	22	16
Acute myocardial infarction	10	7
Myocarditis	8	6
Edema	4	3
Other	20	15
Not identified	9	7
Not assessed	7	5

Abbreviations: COVID-19, coronavirus disease 2019; DAD, diffuse alveolar damage.

[a] Virtually all patients were cited as having more than 1 pathologic condition at autopsy, resulting in 2.65 pulmonary, 1.03 thrombosis, and 1.92 cardiac conditions cited per patient.

[b] Total does not equal 100% because virtually all patients were cited as having multiple pathologic conditions at autopsy and many patients were cited with the same condition.

[c] Macroscopic thrombosis may be understated because in situ vascular assessments could only be performed in 97 autopsies (ie, excluding needle biopsy evaluations); moreover, deep leg vein dissection was only performed in 19 autopsies.

thrombosis was found both in the pulmonary arteries and deep leg veins. Microscopic thrombi were observed in the lungs of 72 of the 135 decedents (53%), whereas the kidneys and other sites showed much less frequent thrombosis with only 25 decedents (19%) having microscopic thrombi outside of the lungs.

Pathologic findings in the hearts included mainly sequelae of preexisting chronic disease in those dying of or with COVID-19. Myocyte hypertrophy affected 104 of the 135 hearts (77%), fibrosis and/or old infarction was present in 78 hearts (58%), and coronary artery disease was present in 34 hearts (25%). A striking finding was the paucity of

Table 5. Renal and Hepatic Pathologic Findings Cited in 135 COVID-19–Positive Autopsies

	No. Cited	% Patients
Renal pathology	(n = 292)[a]	(n = 135)[b]
Glomerulosclerosis		
Focal global	48	36
Diffuse global	18	13
Mesangial	19	14
Acute tubular injury	70	52
Arteriosclerosis	59	44
Interstitial fibrosis	28	21
Tubular atrophy	24	18
Diabetic changes	8	6
Not identified/assessed	17	12
Hepatic pathology	(n = 199)[a]	(n = 135)[b]
Ischemic changes/necrosis	56	41
Steatosis	50	37
Hepatitis/inflammation	26	19
Fibrosis	9	7
Congestion	8	6
Cirrhosis	7	5
Cholestasis	4	3
Other	11	8
Not identified	24	18
Not assessed	4	3

Abbreviation: COVID-19, coronavirus disease 2019.

[a] Virtually all patients were cited as having more than 1 pathologic condition at autopsy, resulting in 2.04 renal and 1.27 hepatic conditions cited per patient.

[b] Total does not equal 100% because virtually all patients were cited as having multiple pathologic conditions at autopsy and many patients were cited with the same condition.

myocarditis, documented in only 8 decedents (6%). Two of these were in adolescents with clinical findings consistent with multisystem inflammatory syndrome (MIS-C), and most remaining cases involved patients dying of causes other than COVID-19.[36]

The most prevalent finding in the liver was ischemic changes/necrosis, consistent with the frequent history of intensive care unit stays and low perfusional states before death. As with the heart, other hepatic findings were frequently sequelae of preexisting diseases, including steatosis in 50 of 135 livers (37%) and fibrosis to cirrhosis in 16 (12%). There were no unique liver findings that appeared to be a direct result of SARS-CoV-2 infection.

The kidneys also demonstrated a heavy burden of chronic pathology, including various patterns of glomerulosclerosis in 85 of 135 decedents (63%), arteriosclerosis in 59 (44%), and interstitial fibrosis in 28 (21%) and tubular atrophy in 24 (18%), all reflecting the high prevalence of systemic hypertension and diabetes mellitus in our cohort. Most decedents had 3 or more pathologic conditions in their kidneys (average number of pathologic conditions per decedent was 2.04). Acute tubular injury was seen in 70 decedents (52%), again consistent with the frequent history of low perfusional states before death. As in other organs, inflammation was infrequently observed.

Causes of Death

Cause-of-death determinations by surveyed autopsy pathologists were categorized into primary (ie, underlying)

and contributing causes of death for ease of analysis. It should be noted that cause-of-death statements are similarly formulated in the United States and Brazil for autopsy reports and death certification. For the majority—101 of 135 decedents (75%) in our cohort—the primary cause of death was categorized as acute respiratory disease, most often cited as "COVID-19 pneumonia" or "acute lung injury." However, among the remaining deaths that did not include acute respiratory disease as the primary cause of mortality, COVID-19 was only listed as a contributing cause of death in 6 cases. Seven cause-of-death statements listed "COVID-19" without further specification. In spite of the high incidence of acute kidney disease during hospitalization, renal pathology was never listed as a primary cause of death and was only reported as a contributing cause of death once. Acute myocardial disease was provided as the primary or contributing cause of death in only 6 and 7 autopsies, respectively. Acute coagulopathy/disseminated intravascular coagulation was not listed as a contributing cause of death for any case. Obesity and diabetes mellitus were each referenced as contributing causes of death in fewer than 10 cases. In sum, neither preexisting diseases nor the panoply of medical conditions that arose in our decedent population was adequately represented in the cause-of-death statements prepared by autopsy pathologists in our cohort.

DISCUSSION

We report findings from 135 postmortem evaluations performed in geographically and sociopolitically diverse areas of the United States and Brazil, encompassing both hospital and forensic autopsy practices. Although there was no centralized review of rendered diagnoses, the survey format included both multiple-choice selections and many opportunities to add items not included in the choices. All cases were performed or supervised by experienced autopsy pathologists, some of whom have already published small case series pertaining to autopsy in COVID-19. There was likely less selection bias in our cohort's autopsied population owing to efforts early in the pandemic to evaluate as many suspected COVID-19 deaths as possible. It is possible that our cohort is younger owing to selection artifact, that is, younger decedents may have been more likely to undergo autopsy. In spite of the relatively younger age of our study cohort compared to those dying of COVID-19 in the United States, our database is comparable to the (largely international) literature in age ranges and means and sex breakdown (Table 1). The proportions of people from each ethnic group dying of or with COVID-19 in our cohort appear comparable to those in the United States during the period of the survey.

Chronic disease has been calculated to contribute to 60% of the worldwide overall 56.5 million deaths and is predicted to rise to 73% in 2020.[37] In America, approximately 60% of adults have at least 1 chronic disease, and 1 in 4 of them has 2 or more chronic conditions.[38] The patients dying of or with COVID-19 in our cohort had a striking spectrum of illnesses, with 399 total reported conditions, prominently including systemic hypertension, diabetes mellitus, obesity, and coronary artery disease. Only 10 COVID-19 decedents in our database had no recorded preexisting conditions and the average was 2.88 diseases per decedent. It is likely that these preconditions set the stage for the complex hospital courses of these decedents (average 2.85 conditions during terminal hospitalization) and the numerous pathologic conditions observed at autopsy. Some contrasts between clinically reported conditions and autopsy findings are also of interest; for example, obesity was reported as a preexisting condition in 46 decedents (34%), but 55 decedents (41%) had a calculated body mass index that was in the obese to morbidly obese range at autopsy (body mass index of 30.0 or higher).

Our database confirms that DAD is the primary lung pathology in COVID-19 as reported in the existing literature. Fluid imbalances likely contributed to the 3- to 4-fold increase in lung weights, which was frequently observed. Most other lung findings in our cohort (hemorrhage, tracheitis, edema) result from this same process of acute lung injury, explaining why decedents had an average of 2.65 pulmonary autopsy findings each. Interestingly, acute bronchopneumonia was much less common in this group than previously reported in the literature (Table 1). It is not yet clear whether acute pneumonia represents an aspect of the reaction to viral infection or bacterial superinfection in most cases. Most pathologists providing data to this article attributed acute pneumonia to superinfection. Macroscopic and microscopic thrombosis mainly appeared in the lungs. Nearly all cases with microscopic pulmonary thrombi also had DAD. Formation of thrombi has been associated with localized alterations in coagulation[39] as well as SARS-CoV-2–associated endothelial injury,[19] though investigation of deep leg veins for gross thrombi remains an important component of a complete autopsy procedure.

Our cohort showed extraordinarily little prevalence of myocarditis. Though myocyte damage from inflammation in COVID-19 has received a great deal of discussion, especially in the popular press, studies do not show a high frequency of the disease, with only 12 to 14 cases reported in 2 recent meta-analyses of the literature.[40,41] Our cohort of decedents had an average of 1.92 cardiac diseases and, with the exception of a minority of acute myocardial infarctions (possibly attributable to shock), these were chronic preexisting conditions. If COVID-19 patients have long-term cardiac effects, it appears that these may result, not from inflammation, but rather from some other viral action in a background of underlying disease. SARS-CoV-2 in general does not appear to characteristically produce a prominent cellular inflammatory response in tissue or in vasculature, even in the lungs.

The decedents' histories, clinical courses, and pathologic findings all speak to the heavy burden of comorbid conditions both before SARS-CoV-2 infection and during the subsequent disease course. In our large autopsy sample, patients dying of or with SARS-CoV-2 infection carried more aggregated preconditions than the general population. This was true even though on average the population examined was younger than that of COVID-19 decedents in the United States. Patients in our cohort had an average of 8.89 pathologic conditions documented at autopsy, spanning both prior chronic disease and acute conditions acquired during hospitalization. Although these comorbidities were revealed in the decedents' histories and by the pathology of their organs, they were generally not listed in the cause-of-death statements prepared by the autopsy pathologists. Cause-of-death statements in both autopsy reports and death certificates, therefore, may not encompass the severity or spectrum of comorbid conditions in those dying of or with COVID-19. This has serious implications

for public health decisions including allocation of resources and reopening of essential public functions. Future studies will more rigorously compare available death certificate data with clinicopathologic information and autopsy findings in this cohort to illuminate the extent of this information gap.

Large autopsy samples are crucial to studying an emerging disease entity such as SARS-CoV-2. Assumptions about disease, such as the apparent ubiquity of myocarditis, based only on small samples and clinical conclusions, may affect both the course of treatment and directions of future research. Pathologists trained and willing to undertake the important work of providing detailed postmortem analysis of deaths resulting from a pandemic such as COVID-19 should be supported at local, national, and international levels in a medical landscape that will almost certainly include more novel infectious diseases in the years to come.

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