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1 The Prevalence of SARS-CoV-2 In Autopsy Tissue from Patients Dying Without Known COVID-19 Disease

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Disclosures: Adesola Akinyemi: None; Kathy Mangold: None; Linda Ernst: None

Background: Coronavirus disease 2019 (COVID), a respiratory illness (RI) caused by SARS-CoV-2 (CoV2) was first reported in Wuhan, China in December 2019. It spread rapidly and the US confirmed its first case in January 2020. Due to the novelty of CoV2 and COVID, little was known about the epidemiology, clinical course, and diagnostic methods. Since then, studies have shown that CoV2 originated from bats and COVID may have pre-existed undiagnosed outside China before the cases were first reported.

Our aim was to evaluate the prevalence of CoV2 in autopsy cases at our institution, where autopsy was not performed on known COVID cases.

Design: We searched our pathology database for adult autopsies performed on the lungs and heart in our institution from 6/1/19 – 6/30/20. Cases were divided into groups by cause of death (COD) possibly related to COVID, presence of a clinical RI, and autopsy findings of pneumonia (Pnx). CODs possibly related to COVID (COVID-possible) included bronchopneumonia and multisystem organ failure and CODs unlikely related to COVID (COVID-unlikely) included conditions such as acute myocardial infarction. Total RNA was extracted from archived formalin-fixed-paraffin-embedded (FFPE) lung tissue of all COVID-possible cases and COVID-unlikely cases with Pnx using a commercial kit and following the instructions in the kit. CoV2 RNA was tested for using CDC 2019-nCoV Real-Time RT-PCR Diagnostic Panel, testing the N1 region of the CoV2 genome and an RNA integrity control during amplification. An extracted CoV2 sample from our State Department of Health was used as positive control.

Results: 88 cases were included; 44 males and 44 females with an average age of 66 years. 42/88 (48%) cases were considered COVID-possible with 24/42 (57%) showing RI and/or Pnx. COVID as COD was considered unlikely in 46/88 (52%) with 34/46 (74%) showing no RI or Pnx. See Table 1. CoV2 PCR was performed on a total of 49 cases: 42 COVID-possible and 7 COVID-unlikely with Pnx. CoV2 PCR was negative in all 49 cases with appropriate positive control and RNA integrity in all cases.

Table 1. Classification Of Autopsy Cases by COD Possibly Related To COVID

	COVID-possible COD (N=42)	COVID-unlikely COD (N=46)
Age (years)	71.5 years	60.5 years
Male gender	20 (48%)	24 (52%)
Respiratory illness	15 (36%)	9 (20%)
Histologic pneumonia	17 (40%)	7 (15%)
Both RI and histologic pneumonia	8 (19%)	4 (9%)
Neither RI nor histologic pneumonia	18 (43%)	34 (74%)

Conclusions: In our single-institution autopsy cohort, CoV2 was not detected in FFPE lung tissue from any cases without a clinical diagnosis of COVID. Our data suggest that patients in our community who died between 6/1/2019 and 06/30/2020 without known COVID were unlikely to have had subclinical and/or undiagnosed COVID. Therefore, clinical examination and accurate laboratory testing likely identify the majority of cases of COVID.

2 Prevalence of ATTR Cardiac Amyloidosis in Elderly Americans: Impact of Gender and Comparison with a Finish Population-Based Autopsy Study

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Disclosures: Mayara Bearse: None; Isabela Delfino: None; James Stone: *Consultant*, Cook Medical

Background: Age-related ATTR cardiac amyloidosis is an idiopathic disease characterized by the deposition of misfolded wild-type transthyretin protein in the myocardium. There have been few large autopsy studies examining the prevalence of this disease. Clinically, the disorder is more common in men than women, but this gender predilection was not observed in prior autopsy studies.

Design: This study analyzed 483 autopsies performed in patients 80 years old or older, between 1996-2019. The diagnosis of ATTR amyloid was based on: 1) identification of amyloid in ventricular myocardial samples stained with Congo red showing apple-green birefringence with polarized light and 2) the amyloid showing immunoreactivity to transthyretin by immunofluorescence or immunohistochemistry. Cases with AL amyloidosis were excluded.

Results: Overall, ATTR cardiac amyloidosis was present in 132 (27%) of the 483 cases. The patients with ATTR were 80% Caucasian, 5% African-American, 2% Hispanic, and 14% other/unknown. The presence of ATTR was dependent on age in this elderly cohort, being present in 26% of patients age 80-94 and 52% of patients over the age of 94 ($P=0.002$). ATTR was more common in men than women for patients 80-94 years old (33% vs 18%, $P=0.0005$), but not in patients over 94 years in age (56% vs 50%, $P=1.00$). Compared with a previously reported Finnish study of 256 elderly patients, the rates of ATTR amyloidosis in this American cohort were systematically higher in all age and gender groups from age 85 to 99: women age 85-89 (19% vs 25%), men age 85-89 (9% vs 39%), women age 90-94 (19% vs 29%), men age 90-94 (45% vs 62%), women age 95-99 (31% vs 50%), men age 95-99 (36% vs 43%) (mean increase 15%, $P=0.01$).

Conclusions: ATTR cardiac amyloidosis is dependent on both age and gender and afflicts about half of the patients over the age of 94. The age and gender-specific rates of ATTR in this American autopsy cohort are significantly higher than those seen in a previous Finnish autopsy cohort. Hereditary ATTR due to known mutations in the gene encoding transthyretin (ATTRm) is relatively uncommon, and cannot account for the observed differences between the two cohorts. Further studies are required to understand this geographic dependency for the rate of age-related ATTR cardiac amyloidosis.

3 Effect of the COVID-19 Pandemic on Autopsy Rate

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Disclosures: Weibiao Cao: None

Background: Hospital autopsy rates have been steadily dropping over the past 50 years in the United States. It is unclear whether concerns of potential risks of exposure to SARS-CoV-2 through aerosols generated during dissection of lungs, infusion of formalin into lungs, and during opening skulls with an oscillating saw affect the overall autopsy rate.

Design: Autopsy rate was calculated during a period from March 2019 to February 2020 (before COVID-19 pandemic in Rhode Island) and that from March 2020 to February 2021 (COVID-19 pandemic period). Death and autopsy numbers were also analyzed.

Results: Autopsy rate over a year before the COVID-19 pandemic (between March 2019 and February 2020) was 8.4% (117/1391), whereas it was 9.1% (136/1492) during the COVID-19 pandemic (March 2020-February 2021). The difference was not statistically significant. During the COVID-19 pandemic between October 2020 and April 2021, the autopsy rate for non-COVID patients was 11%, whereas it was 8.6% in patients with COVID-19. The autopsy rate was slightly lower in COVID-19 patients, but the difference was not statistically significant. The death number and the percentage of death of patients with COVID-19 among all deaths reached a peak in December 2020, whereas the death number in non-COVID patients was relatively stable. The autopsy number also reached the peak in December 2020 and January 2021. From October 2020 to February 2021, the total autopsy number increased by 38-200%, when compared with one year ago (October 2019 to February 2020). The autopsy rate also increased from 7.9% before COVID-19 (from October 2019 to February 2020) to 10.7% during the same months of the COVID-19 pandemic, but the increase did not have the statistical significance.

Conclusions: The COVID-19 pandemic did not affect the overall autopsy rate, but it increased the number of autopsy cases.

4 Patterns of Inflammatory Cell Infiltration in the Lungs of Patients with COVID-19, An Autopsy Study

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Disclosures: Weibiao Cao: None

Background: SARS-CoV-2 causes diffuse alveolar damage, lymphocyte infiltration in the lungs and a cytokine storm. In this study we examined inflammatory cell infiltrates in the lungs of patients with COVID-19.

Design: Eighteen COVID-19 autopsy cases (COVID group), 9 non-COVID cases with diffuse alveolar damage (DAD, non-COVID group), and eleven controls without lung diseases were included. Immunostainings for CD3, CD4, CD8, CD68 and broad-spectrum keratins were performed.

Results: The average age of COVID-19 patients was 64.4 ± 2.1 years. The most common co-morbidities were hypertension (12/17, 70.6%), diabetes mellitus (9/17, 52.9%) and chronic kidney disease (3/17, 17.6%). The survival duration of 17 patients with available clinical information was 21.2 ± 3.4 days (range 7-53 days) after onset of symptoms. Patients younger than 67 years old (namely young patients thereafter, N=9) survived 26.4 ± 5.9 days after onset of symptoms, which was significantly longer than those greater than 67 years old (namely older patients thereafter, 15.2 ± 1.4 days, N=8, $P < 0.05$). The younger patients had significantly lower platelet counts ($107.7 \pm 33.2 \times 10^9/L$, N=8) than the older ones ($224.6 \pm 42.4 \times 10^9/L$, N=8, $P < 0.05$). Conversely, the younger patients had much higher absolute lymphocyte counts ($1.5 \pm 0.4 \times 10^9/L$, N=7) than the older ones ($0.7 \pm 0.1 \times 10^9/L$, N=8, $P < 0.05$). Interestingly, the patients with low platelet counts ($< 100 \times 10^9/L$) survived longer than those with higher platelet counts ($P < 0.05$). Patients with high troponin levels (> 0.2 ng/ml) had shorter survival duration after onset of symptoms (16.8 ± 1.9 days) than those with low troponin levels (30.8 ± 8.0 days, $P < 0.05$). Patients with macrophages $> 130/HPF$, CD3+ T cells $> 145/HPF$, CD8+ T cells $< 30/HPF$ and CD8+/CD4+ ratio < 1 had a shorter survival time compared to those with macrophages $< 130/HPF$, CD3+ T cells $< 145/HPF$, CD8+ T cells $> 30/HPF$ and CD8+/CD4+ ratio > 1 , respectively.

Conclusions: Patients' age > 67 years, blood troponin levels > 0.2 ng/ml, platelet count $> 100 \times 10^9/L$, lung macrophages $> 130/HPF$, CD3+ T cells $> 145/HPF$, CD8+ T cells $< 30/HPF$, and CD8/CD4 ratio < 1 were associated with shorter survival duration after onset of symptoms.

5 Fatal Disseminated Coccidioidomycosis: A Twenty-Year Academic Hospital's Experience of Autopsy Cases

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Disclosures: River Charles: None; Jingjing Hu: None

Background: Valley fever, also called coccidioidomycosis, is an infection caused by a fungus called *Coccidioides immitis* and *Coccidioides posadasii*. The fungus is spread through inhalation of soil arthroconidia endemic to the Southwestern United States, Mexico, and South America. Disseminated coccidioidomycosis (DC) is a rare cause of death and typically occurs in immunocompromised individuals. We analyzed our institutional autopsy experience of all DC cases over the past twenty years.

Design: A retrospective study of autopsies was performed on patients with DC at UC San Diego Jacobs Medical Hospital from 2001 to 2020. The pertinent clinical and pathologic data were reviewed.

Results: Among 2846 autopsy cases, five cases (0.17%) were found to have DC, including three males and 2 females. 4 of these cases occurred between 2001 and 2006, with only one case occurring between 2007 and 2021, indicating a downtrend in this fatal infection. The average age of death was 36.8 years (range 19 - 43 years). Of 5 patients, 4 were immunosuppressed (one with end stage AIDS, one with AIDS and s/p autologous bone marrow transplant, one s/p double lung transplant and one on high dose steroids in the setting of Acute Promyelocytic Leukemia). The non-immunosuppressed patient had a history of hypertension. The most commonly involved sites included lung (5/5, 100%), lymph nodes (4/5, 80%), spleen (4/5, 80%), liver (4/5, 80%), kidneys (2/5, 40%), CNS (2/5, 40%), adrenal (2/5, 40%), bone marrow (1/5, 20%), pancreas (1/5, 20%), heart (1/5, 20%), and skin (1/5, 20%). Microscopically, all patients had a granulomatous inflammatory response to the fungal organisms at least focally, except for the patient with end stage AIDS. One case had superimposed disseminated *Staph. Aureus* infection.

Conclusions: DC is a rare cause of death, typically occurring in immunosuppressed patients and more rarely in immunocompetent patients. DC most commonly involves the lungs, lymph nodes, spleen, and liver. A granulomatous inflammatory response is seen in the majority of cases with a minority of cases having necrotic purulent debris without granulomas. The incidence of DC appears to be decreasing over time.

6 Impact of COVID-19 on Autopsy Demographics at a Safety Net Hospital

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Disclosures: Manisha Cole: None; Tochukwu Ihejirika: None; Zahra Aryan: None; Elizabeth Duffy: None; Claire Trivin-Avillach: None; Brian Moore: None; Christopher Andry: None

Background: The ongoing COVID-19 pandemic has had a profound impact on death rates in this country, specifically on marginalized populations. As a metropolitan safety net hospital during a pandemic, we questioned if this increase of death rates had any effect on the demographics of completed autopsies at our institution. We aim to determine if there has been any significant change in the demographics of autopsy with the onset of the COVID-19 pandemic and, if so, what those changes were.

Design: A review of autopsy consent records from 2018-2021 was completed. Demographic data including gender, race, date of birth, and date of death was extracted from the medical record. Two cohorts were created: “Pre-COVID-19”, January 2018-February 2020 and “During COVID-19”, March 2020-September 2021. Data was collected and stored in Microsoft Excel. All analyses were performed in R (R-1.3.1056). P-values <0.05 were considered significant.

Results: A total of 184 autopsy reports were reviewed, but analysis was limited to autopsies of adults who were also patients at this institution, a total of 157. A total of 62 autopsies were completed prior to the pandemic, while 95 were completed during COVID-19. Females accounted for 45.2% of pre-COVID autopsies and 46.3% of autopsies during COVID. The average age dropped from 62.8 to 60.9, however, neither age, race, nor gender was found to change significantly in the setting of the COVID-19 pandemic.

Year	Before Pandemic	During Pandemic	p-value
Total	62	95	
Gender			1
Male	34 (54.8%)	51 (53.7%)	
Female	28 (45.2%)	44 (46.3%)	
Age			0.52
Average	62.8 (SD 12.9)	60.9 (SD 15.5)	
20-29	0	2 (2.1%)	
30-39	3 (4.8%)	10 (10.5%)	
40-49	7 (11.3%)	8 (8.4%)	
50-59	12 (19.4%)	16 (16.8%)	
60-69	23 (37.1%)	30 (31.6%)	
70-79	9 (14.5%)	20 (21.1%)	
80-89	8 (12.9%)	7 (7.4%)	
90-99	0	2 (2.1%)	
Race			0.77
Black	38 (61.3%)	57 (60.0%)	
Hispanic	2 (3.2%)	6 (6.3%)	
White	15 (24.2%)	23 (24.2%)	
Unknown	7 (11.3%)	9 (9.5%)	

Conclusions: The COVID-19 pandemic has not significantly impacted the demographics of patients undergoing autopsies at our institution. Of the adult autopsy consents reviewed, there was no significant demographic change between cohorts. The lasting effects of the pandemic on autopsies performed may be highlighted by a post-pandemic analysis.

7 Pathologic Features of Post-Acute Sequelae of COVID-19 (PASC) at Autopsy

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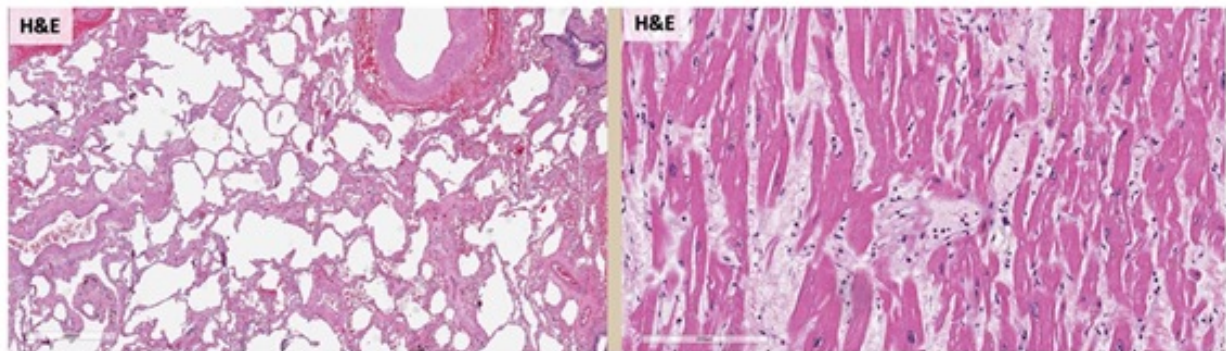
Disclosures: Fernanda Da Silva Lameira: None; Cameron Gabriel: None; Richard Vander Heide: None; Sharon Fox: None

Background: Across the globe, cases of post-acute sequelae of COVID-19 (PASC) are characterized by the delayed effects of SARS-CoV-2 infection in multiple organ systems. Patients may have appeared to recover from the initial infection, but experience sequelae of the disease weeks to months later. Autopsy studies of PASC have only initially begun. Our research aims to compare the pathology of cases in which patients experienced a prolonged, progressive decline, to the cases of patients who recovered from the initial infection of SARS-CoV-2, but experienced sequelae of the condition numerous weeks to months later.

Design: Autopsies were performed on 17 male and female decedents with an age range of 31-79 years with cause of death related to COVID-19 infection confirmed by SARS-CoV-2 PCR, and time between the onset of symptoms and death ranging from 30 to 112 days. Cases in which the time between the onset of symptoms and death exceeded 30 days, with evidence of initial recovery, were considered potentially PASC-related. The cases were separated into two groups based upon the timeline of first positive PCR to time of death: those who succumbed to the initial COVID-19 infection after an extended hospital course, and those with potential PASC-related disease. Clinical, gross and microscopic findings from both groups were compared, as well as PCR and IHC for SARS-CoV-2 at autopsy.

Results: The most common clinical comorbidity seen in both groups was hypertension (85.7%), followed by obesity and diabetes. Common microscopic findings in the lungs included proliferative to organizing diffuse alveolar damage (DAD). Findings in PASC-related cases included extensive alveolar fibrosis, fibrosing organizing pneumonia, and thrombi within medium-sized blood vessels. Two patients in their 30s presented with vasculitis/endotheliitis involving small blood vessels of the lungs and heart, consistent with Multisystem Inflammatory Syndrome. Additionally, late thrombotic events, and cardiac inflammation including macrophage infiltration appeared to be present in cases of PASC. Immunostaining for SARS-CoV-2 nucleocapsid and PCR at the time of autopsy did not reveal a persistence of virus in cases attributed to PASC.

Figure 1 - 7



PASC pulmonary and cardiac pathology (11 months following COVID-19 diagnosis)

Conclusions: Our findings suggest that there may be pathologic differences between a prolonged course of acute COVID-19, and PASC-related disease. Characteristics of PASC included evidence of new or continued small vessel inflammation, macrophage infiltration, and/or fibrotic disease of affected organs.

8 Histology-proven Post-COVID Lung Fibrosis

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Disclosures: Jing Han: None; Shengjie Cui: None; Jihong Sun: None

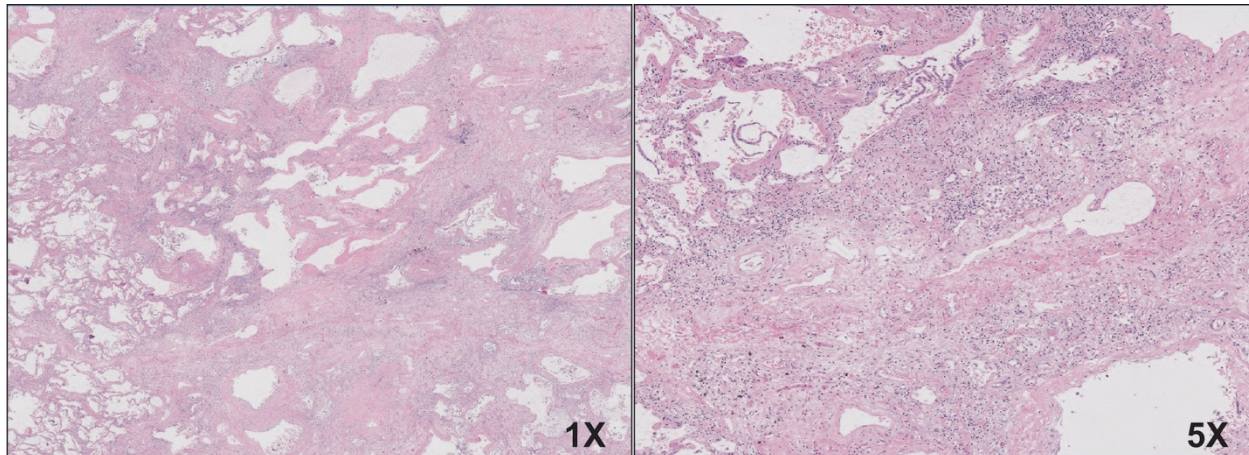
Background: Pulmonary fibrosis is a serious complication of viral pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). COVID-19 is believed to trigger substantial fibrotic consequences during acute infection. However, the extent to which lung fibrotic change could last and the degree of lung fibrosis in patients with complete resolution of infection still remain ambiguous. A predominant majority of reports on post-COVID-19 pulmonary fibrosis were drawn from radio imaging studies. By contrast, histological evidences of “post-COVID-19 pulmonary fibrosis” are paradoxically in significant shortage whilst they have higher diagnostic values. We herein report postmortem autopsies focusing on lungs from six patients with resolved SARS-CoV-2 infection.

Design: Eligible autopsy samples were collected from patients who died from diseases other than acute COVID-19 and who contracted SARS-CoV-2 virus but either had subsequent negative SARS-CoV-2 test (n=4) or the symptoms of COVID-19 no longer existed and died after at least 100 days after initial positive SARS-CoV-2 test (n=2).

Results: These patients included 4 men and 2 women with a mean age of 63 years (range 28 – 79 years). Two patients died from cardiovascular compromise, one patient died from venous thrombosis, one patient died from acute pneumonia, one patient died from post-COVID lung fibrosis, and one patient died from metastatic prostatic adenocarcinoma. Histology of lungs from all six cases showed different degree of fibrosis (Table 1). Remarkably, three of six cases showed extensive patchy interstitial fibrosis. Three of four cases with imaging data reviewed revealed consistent findings in CXR or CT (Table 1). Case (79 yo male) who died from post-COVID lung complications at 410 days after initial positive SARS-CoV2 test showed remarkably diffuse lung parenchyma damage with extensive fibrotic changes, honey combing, with an interstitial pattern (Figure 1).

Age (deceased)	sex	duration between deceased date and date tested positive	cause of death	Imaging	Histology	PMH
70	M	137	pulmonary venous thromboembolism	Not available	Right lung with subpleural and parenchymal scarring	HTN, KD
28	F	143	biventricular cardiac failure	X ray: Stable patchy areas of consolidation in both lungs, worse on the right side.	Sections of the lungs show patchy dense interstitial fibrosis, honeycomb change, and extensive calcifications in the septa and muscular walls, most prominent in the right upper lobe and left lower lobe. These findings are suggestive of interstitial lung disease.	ESRD s/p renal transplant, HTN, PE, stroke
64	M	116	Metastatic prostatic adenocarcinoma	X ray: The visualized lung fields are grossly clear.	Lungs show emphysema, fibrosis.	Prostate cancer, HTN
64	M	461	superimposed acute pneumonia	X ray: Moderately reduced lung volumes with diffuse coarsened interstitium with distortion of the parenchyma and bronchiectasis compatible with pulmonary fibrosis. There is persistent sizable consolidation throughout the majority of the left lung which could reflect superimposed pneumonia with some element of left pleural fluid also possibly present.	Section of lungs show patchy interstitial fibrosis with abrupt transition to normal lung parenchyma. Additional findings include areas of pleural fibrosis and focal acute inflammation.	HLD, DM, TB latent, post-COVID fibrosis
79	M	410	hypoxic hypercapnic respiratory failure secondary to lung fibrosis following COVID-19	CT: Redemonstration of bilateral interstitial reticulations, consistent with fibrosis and bronchiectasis. New finding of right upper lobe focal consolidation, abutting the horizontal fissure.	Lungs show diffuse lung parenchyma damage with extensive fibrotic changes, honey combing, leading to an interstitial disease-like pattern, possibly due to preceding COVID-19 infection. Left lower lobe also shows bronchopneumonia.	CAD, prostate cancer, DM
72	F	115	myocardial infarction	Not available	Sections of lung show areas of fibrosis, resolving diffuse alveolar damage and emphysematous changes.	CAD, DM, HTN

Figure 1 – 8



Conclusions: Post-COVID fibrotic lung change is present in some patients following resolution of COVID infection. The extent to which lung fibrotic change could last and the degree of lung fibrosis in patients with complete resolution of infection vary from case to case. However, the finding of significant histologically-proven fibrotic lung changes more than 400 days after the resolution of acute COVID-19 in the setting of autopsy provide insight into the pathogenesis and prognosis of long-lasting complications of COVID-19.

9 Cardiac and Pulmonary Pathology of Acute Cardiopulmonary Events in Patients Dying in the Setting of Recent Immune Checkpoint Inhibitor Treatment for Malignancy

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Disclosures: Cynthia Harris: None; James Stone: None

Background: Immune checkpoint inhibitor (ICI) associated myocarditis (ICIM) can be a severe, even fatal, consequence of ICI therapy. However, diagnosing ICIM clinically can be problematic, and the full spectrum of pathologic changes associated with acute cardiopulmonary events in patients on ICI therapy has not been well described.

Design: Autopsy records from 2013 to 2020 were searched for patients with cancer, and corresponding clinical records were searched for histories of ICI treatment. Inclusion criteria were: ICI-therapy within 180 days of death and evidence of an acute cardiopulmonary event, defined as: clinical diagnosis of ICIM, serum troponin level >30 ng/L, new acute-onset heart failure, and/or unexpected cardiac arrest with cardiopulmonary resuscitation.

Results: Of the 75 patients who received ICI-therapy within 180 days of death, 25 patients met inclusion criteria. One or more acute cardiopulmonary changes were identified in 18 patients [myocarditis (n=7), cardiac metastasis (CM) (n=10), aspiration pneumonia (n=4), pulmonary embolism (PE) (n=5)]. The patients were divided into 3 groups: ICIM (n=7), acute cardiopulmonary changes without ICIM (ACCW) (n=11), and no acute cardiopulmonary changes (NACC) (n=7). Patients with ICIM had higher median serum troponin levels compared to ACCW and NACC patients (976 ng/L, 100 ng/L, and 310 ng/L, respectively; $p=0.02$), were significantly more likely to have a serum troponin >500 ng/L (71%, 0%, and 29%, respectively; $p=0.009$), and had fewer median days from peak troponin to death (1, 3, 33, respectively; $p=0.02$). There were no significant differences in age, gender, type of cancer, or type of ICI treatment. Of the 7 patients clinically diagnosed with ICIM, 4 had pathologic ICIM at autopsy (concordant) and 3 did not (discordant). All 7 received immunosuppressant therapy. Compared with the discordant patients, the concordant patients were more likely to have a serum troponin >500 ng/L (100% vs 0%; $p=0.03$), were less likely to have CM (0% vs 100%; $p=0.03$), and trended towards fewer PE (0% versus 67%; $p=0.14$).

Conclusions: In the setting of ICI treatment, acute cardiopulmonary events are associated with multiple pathologic changes, including ICIM, CM, PE, and aspiration pneumonia. CM and/or PE may mimic ICIM clinically. Our findings indicate acutely and markedly elevated troponins (>500 ng/L) may serve as a useful aid in clinically identifying patients with pathologic ICIM.

10 The Density of CD-68 Positive Macrophages in the Epicardium Correlates with Covid-19 Infection in Deceased Patients

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Disclosures: Husam Jum'ah: None; Sirisha Kundrapu: None; Agnes Loeffler: None

Background: Angiotensin-converting enzyme 2, the target cellular receptor of SARS-CoV-2, is known to be present in adipose tissue. SARS-CoV-2 could enter the heart via the epicardium because the myocardium and the epicardium share the same microcirculation and are not separated from one another by a fascial layer. Previous studies demonstrated that macrophages play an important role in inflammation in adipose, including epicardial, tissue. In this study, we explore two hypotheses: a) there is no significant difference between the density of macrophages in the epicardium of patients who died with Covid-19 infection and those who died with non-Covid-19 acute lung injury, and b) the density of macrophages in the epicardium does not correlate with histological evidence of focal myocyte necrosis in patients who die of Covid-19 infection.

Design: We compared the density of macrophages in the epicardium of 10 patients who died of complications of Covid-19 infection to that in a control group of 10 decedents with non-Covid related acute lung injury. Further, macrophage densities of those with and without histological evidence of focal myocardial damage were compared within the Covid-19 group. Three blocks were routinely sampled from each case (right ventricle, left ventricle and septum). All the sections were stained with CD68 as a macrophage marker. The density of CD68-positive cells in the epicardium was determined by counting the number of cells in five "hot spot" regions (each 3 mm²) at 100x. Quantification was performed using imageJ and is expressed as cells/mm². The densities of CD68-positive macrophage were compared using T-test. The clinical characteristics between the groups were compared using Fischer exact test. P-value < 0.05 is significant.

Results: The density of CD68-positive macrophages in the epicardium is significantly higher in Covid-19 patients compared to the control group. The CD68-macrophage count is also significantly higher in hearts of Covid-19 decedents with histological evidence of focal myocyte necrosis than those with no evidence of myocyte necrosis. There are no significant differences in other characteristics between the groups (Table, Figure).

Table: Comparison of density of epicardial macrophages and clinical characteristics between patients who died with and without Sars-CoV-2 infection (Covid-19).

Characteristic	Covid-19 decedent (N=10)	Non Covid-19 decedent (N=10)	P Value
Macrophage count/mm ² (mean)*	80.4	58.3	0.04
Age (mean)	64	58	0.17
Gender Male	7 (70)	5 (50)	0.64
Female	3 (30)	5 (50)	
Obesity	7 (70)	5 (50)	0.64
Hypertension	7 (70)	8 (80)	1.00
Diabetes Mellitus	6 (60)	3 (30)	0.18
Underlying cardiac disease (CHF and/or CAD)	4 (40)	4 (40)	1.00
Autoimmune Disorder	1 (10)	0 (0)	1.00
Characteristic	Covid-19 decedent with myocyte necrosis (N=5)	Covid-19 decedent without myocyte necrosis (N=5)	P Value
Macrophage count/mm ² (mean)#	99.2	61.6	0.01
Age (mean)	60	68	0.16
Gender Male	2 (40)	5 (100)	0.16
Female	3 (60)	0 (0)	
Obesity	4 (80)	3 (60)	1.00
Hypertension	4 (80)	3 (60)	1.00
Diabetes Mellitus	3 (60)	3 (60)	1.00
Underlying cardiac disease (CHF and/or CAD)	2 (40)	2 (40)	1.00
Autoimmune Disorder	1 (20)	0 (0)	1.00

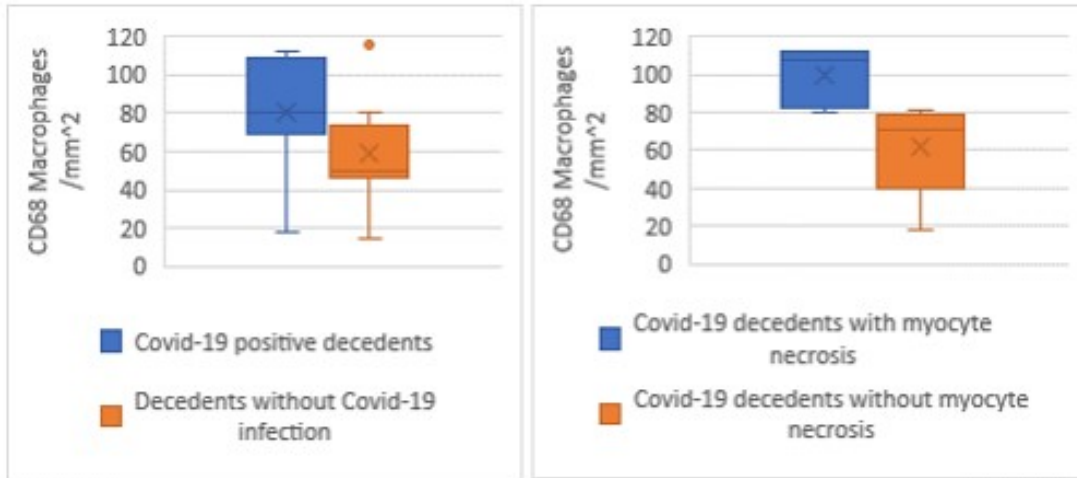
Note

Data refer to number of patients (%) unless specified. CHF: congestive heart failure. CAD: Coronary artery disease.

*One tailed T-statistic $t(18) = 1.8$

#One tailed T-statistic $t(8) = 2.7$

Figure 1 - 10



Conclusions: Contrary to our hypotheses, the density of CD68-positive macrophages is strongly correlated with Covid-19 infection and Covid-19 related myocyte necrosis. Further studies are needed to understand the pathophysiologic relationship between epicardial inflammation and myocyte necrosis.

11 Correlation of Clinical and Histopathological Findings with Viral Variant in the Gastrointestinal Tract of COVID-19 Autopsy Cases

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Disclosures: Zaid Khreefa: None; Jihuan Chen: None; Michael Webber: None; Wenjing Qiu: None; Maryam Sadough: None; Cameron Gabriel: None; Gordon Love: None; Sharon Fox: None

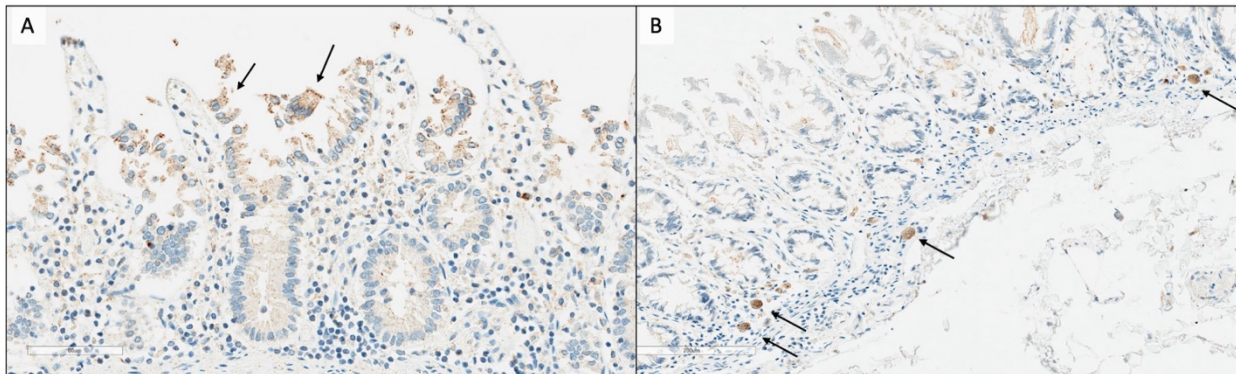
Background: Initial evidence has shown the occasional presence of SARS-CoV-2 in enterocytes in the intestines of patients with COVID-19. Our aim is to further assess the clinical and pathologic changes in the gastrointestinal tract caused by the highly contagious Delta (B.1.617.2) variant as compared to viral variants originating earlier in the pandemic.

Design: Intestinal samples from 32 patients with death due to COVID-19 were obtained at autopsy. Decedents were males and females, with an age range of 32-73 years. Twenty-one of the decedents self-identified as Black/African American, eight as Caucasian, and three as Hispanic. Two groups were differentiated by viral genome RNA sequencing from autopsy tissue: those with Delta variant (n=16), and those with non-Delta variant (n=16). SARS-CoV-2 expression in the intestine was evaluated by immunohistochemical (IHC) detection of the SARS-CoV-2 nucleocapsid protein (N-protein).

Results: Clinically, the Delta group reported diarrhea more frequently (25%) as compared to the non-Delta group (6%). Patients in the Delta group had a shorter time interval between the onset of gastrointestinal symptoms and death (mean = 19 days), as compared to the non-Delta group (mean = 25 days). Histologic examination revealed mostly normal to mild, non-specific chronic inflammation within the epithelium and lamina propria in both groups. Macrophages with positivity for N-protein IHC were present

beneath the epithelium, most notably within the Delta group. N-protein positivity occurred most frequently in small submucosal and mesenteric blood vessels. Patchy positivity for N-protein in enterocytes was seen frequently in cases of Delta variant in which the time from initial symptoms to death was short (<14 days).

Figure 1 - 11



A) Enterocytes, and B) Intestinal macrophages with positivity for SARS-CoV-2 from a decedent with Delta variant disease

Conclusions: As in prior studies, intestinal microscopic changes in COVID-19 were minimal, though our findings indicate that SARS-CoV-2 may be detected within enterocytes more frequently in the Delta group. Patients with the Delta variant experienced both a higher rate of diarrhea and a shorter interval between gastrointestinal symptom onset and death. Whether increased N-protein in enterocytes is a result of the Delta variant itself, or earlier intestinal sampling relative to symptoms in this group, remains to be determined. Autopsy studies can add to our understanding of the effects of COVID-19 on the digestive system, by allowing a greater volume of tissue sampling, as well as temporal sampling relative to disease onset that is not always possible at endoscopy.

12 Establishing Vitreous Glucose and Beta-hydroxybutyrate Thresholds to Assist in the Diagnosis of Hypothermia

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Disclosures: Tanner Mack: None; Jacqueline Parai: None; Christopher Milroy: None

Background: The diagnosis of hypothermia at autopsy is challenging because it lacks pathognomonic findings and there may be comorbidities that could cause death. Studies have established correlation between hypothermia and stress-related markers including glucose and beta-hydroxybutyrate (BHB), although they can overlap with controls. We seek to determine if vitreous glucose and BHB, in conjunction with hemoglobin A1c (HbA1c), can be used to diagnose death from hypothermia and establish a diagnostic threshold for these values.

Design: A retrospective case-control study was performed on medicolegal autopsy cases between May 2016 to December 2020. Cases were selected if the cause of death listed hypothermia as the primary or contributing cause. Controls were selected from non-hypothermic deaths occurring outdoors during months with an average environmental temperature less than 10°C. Data collected included demographic information, history of diabetes mellitus (DM) and alcoholism, postmortem HbA1c, vitreous glucose and BHB, cause and manner of death, history of prolonged resuscitation or hospitalization, temperature at the location and date of death and toxicologic results. Cases excluded included decedents below 18 years, extensive resuscitation, death from ketoacidosis, and no available vitreous fluid. To eliminate elevated vitreous glucose due to diabetes, prior to data analysis, deaths were excluded if HbA1c \geq 6.5% or if the decedent had a history of DM. Independent t-tests and χ^2 were performed to examine differences in continuous and categorical variables respectively. Receiver operating characteristic (ROC) curves were used to assess the predictive value of vitreous glucose, BHB, and glucose+BHB.

Results: After exclusions, 39 controls and 34 hypothermia cases were analyzed. No statistical differences were found between the groups for gender (p=0.538), age (p=0.095) or ambient temperature (p=0.097). Hypothermia deaths versus controls, had higher mean vitreous glucose (2.93 vs. 1.14 mmol/L; p<0.0001), BHB (1.89 vs. 1.35 mmol/L, p=0.010), and glucose+BHB (4.83 vs. 2.46

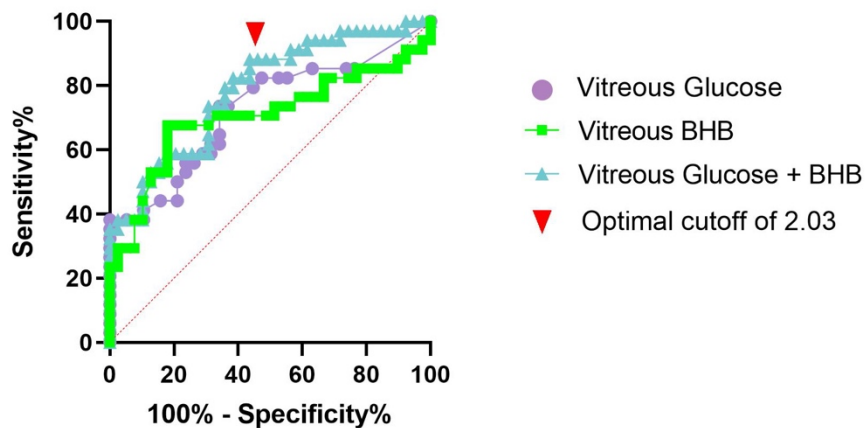
mmol/L; $p < 0.0001$). The ROC curve of vitreous glucose+BHB had the largest area under the curve of the three (0.787); with an optimum threshold of 2.03 mmol/L (sensitivity 88.2%; specificity 56.4%).

Table 1. Summary of demographic characteristics and ambient temperature between hypothermia cases and controls

	Hypothermia cases	Controls	P value	Total study population
Number of cases	34	39	-	73
Prevalence (%)	46.6	53.4	-	100
Age (years)	54.6 +/- 20.7	46.7 +/- 19.2	0.095	
Number of males	24	30	0.538	54 (74%)
Number of females	10	9	0.538	19 (26%)
Ambient temperature (°C)	-2.3 +/- 9.2	1.0 +/- 7.5	0.097	

Figure 1 - 12

ROC curve of vitreous glucose, BHB and glucose and BHB combined



Conclusions: This study shows combined use of postmortem biochemistry can be used in the identification of hypothermia at autopsy.

13 CAUSE of Death Assignment Using Minimally Invasive Tissue Sampling in Low Resource Settings: A Cross-Sectional Study from The University Teaching Hospital of Kigali, Rwanda

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Disclosures: Marie Claire Ndayisaba: None; Belson Rugwizangoga: None; Gervais Ntakirutimana: None

Background: Complete diagnostic autopsy (CDA) is the gold standard post-mortem examination of the body for Cause of Death (CoD) determination but is rarely performed in low-resource settings. Minimally invasive tissue sampling (MITS) involves systematic collection of needle biopsies for laboratory tests to determine the CoD and is among alternative methods to CDA. We aimed to assess the usefulness of MITS for the CoD assignment at a large public hospital in Rwanda.

Design: This is a cross-sectional study and MITS included brain, lungs and liver core needle tissue biopsies for histopathology and brain, lungs, liver cores, nasopharyngeal and rectal swabs; blood and CSF collection for microbiological culture. The corpses were preserved in a morgue refrigerator at -2°Celsius that was cleaned and disinfected using 1% bleach after each case. Medicolegal cases were excluded. CoD was assigned for each case by a multidisciplinary team of 6 medical professionals using ICD-10 startup mortality list, clinical data and MITS findings.

Results: We enrolled 60 females and 40 males aged from 6 days to 96 years (mean=50years, mode=26, SD=23). 91% of studied cases died in the hospital. 83 % of MITS were performed in less than 24 hour-death-autopsy interval. The overall sampling for targeted tissue for histopathology was satisfactory at 90%, majority exhibited non-significant histopathological changes. *Escherichia coli* and *Klebsiella species* were the most common pathogens identified in positive cultures. Differences in immediate CoD attribution before and after MITS were noted in 24% of the cases including 10% with unknown CoD assigned before autopsy. Leading immediate CoD included: Certain infectious and parasitic diseases (34%), diseases of circulatory system (16%), diseases of respiratory system (16%), neoplasms (10%) and endocrine, nutritional and metabolic disease (6%). HIV, diabetes mellitus, hypertension, liver cirrhosis and malnutrition were the top five underlying conditions noted.

Conclusions: Interpretation of MITS findings coupled with antemortem clinical data provided useful insights on CoD among studied cases at a large public hospital in Rwanda. MITS autopsy can reduce uncertainty around CoD but the risk of missing a localized lesion or false positive microbiology due to post-mortem bacterial translocation is high. MITS can offer an opportunity to integrate the involvement of a multidisciplinary team for CoD assignment and a step forward to initiate autopsy practice in low resource settings.

14 Routine Cranial Cavity Assessment in Autopsy Examinations? Think Outside the Box

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Disclosures: Diarmuid O'Connor: None; Eoghan O'Connor: None; Kevin O'Hare: None

Background: Autopsy pathology is an evolving area of medicine, with multiple advances in the recent past allowing for more accurate, focused and detailed assessment of cases. In particular, the use of modern ancillary investigations such as toxicology and biochemical analysis provides a new paradigm for the evolution of autopsy practice. However, the performance of a three cavity autopsy remains standard practice for the majority of cases in the Republic of Ireland. The purpose of this study was to critically assess the value of performing a routine cranial cavity examination in autopsy practice at our institution.

Design: We reviewed 339 autopsy cases completed at our institution between 2018-2019, in order to assess if a cranial cavity examination was performed and if any positive findings were identified. All reports were analyzed on our internal laboratory system.

Results: Of all 339 autopsies completed during this time period, 98.8% (n=335) had a cranial cavity examination performed. Of these autopsies, only 13.7% (n=46) demonstrated significant intracranial pathology that contributed to the cause of death, with 86.2% (n=289) showing an intracranial examination not contributing to the cause of death. Other intracranial pathologies not contributing to the cause of death included a benign meningioma and a small ependymoma. Furthermore, of the 46 autopsy cases which demonstrated significant intracranial pathology, a specific indication to assess the cranial cavity was present in 91.3% of cases (n=42). The majority of these indications involved confirmed intracranial pathology on imaging studies. Of all autopsy cases where the cranial cavity was examined, only 1.2% (n=4) of cases demonstrated significant intracranial pathology that was not identified before the autopsy was performed. 3 of these cases were of subarachnoid hemorrhages secondary to ruptured cerebral aneurysms and 1 was of an intracranial bleed secondary to systemic hypertension. Importantly, all 4 cases were of patients pronounced dead before arrival to the hospital setting.

Analysis of Autopsy Cases

Total Number of Cases with CNS Examined	335
Significant Intracranial Pathology with an Indication Present	42 (12.5%)
Significant Intracranial Pathology without an Indication	4 (1.2%)
Unexpected Non-Significant Intracranial Pathology	2 (0.5%)

Conclusions: This study confirms that only a small percentage of autopsy cases demonstrated unexpected intracranial pathology which was of significance to the cause of death. Examination of the cranial cavity retains a very critical role in the autopsy examination if an indication is present. However, we believe this study has shown that the routine examination of the cranial cavity, without a specific indication, is of limited value in the vast majority of cases.

15 Molecular Methods in the Identification of Pulmonary Pathologic Traits of the SARS-CoV-2 Delta Variant at Autopsy

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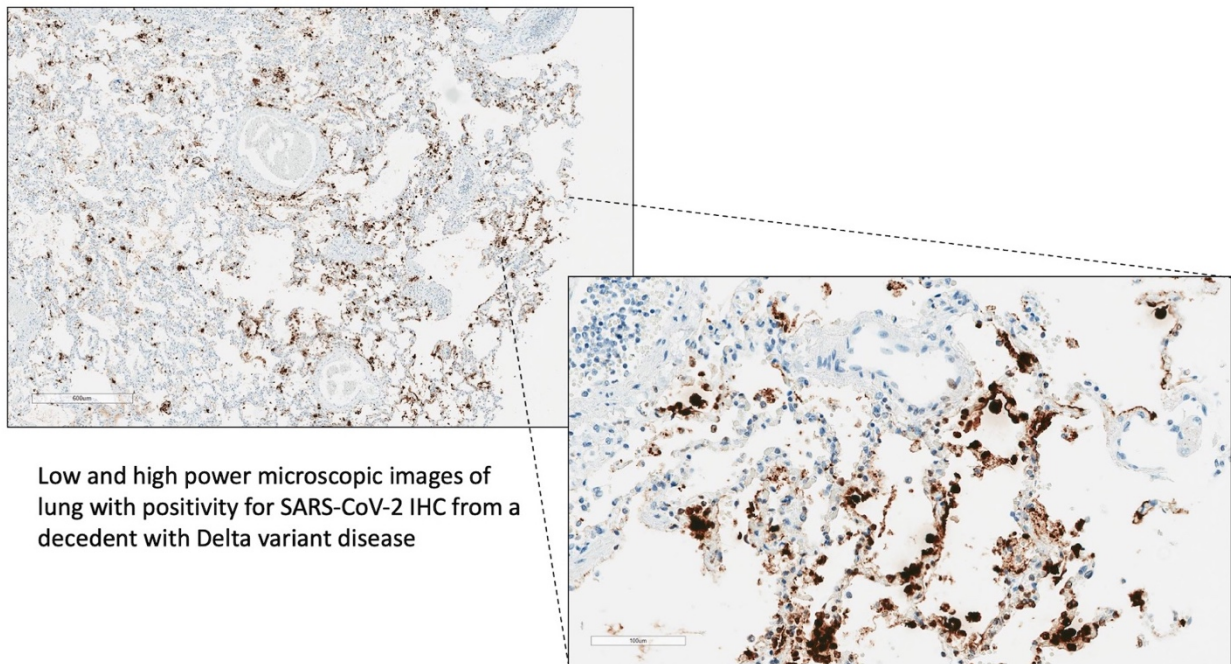
Disclosures: Wenjing Qiu: None; Jihuan Chen: None; Michael Webber: None; Zaid Khreefa: None; Judy Crabtree: None; Grace Athas: None; Gordon Love: None; Sharon Fox: None

Background: The highly contagious Delta variant of COVID-19 accounts for more than 80% of SARS-CoV-2 cases in the fall of 2021. Our aim was to determine whether molecular methods for variant and lineage detection could be utilized at autopsy to examine pathologic findings of Delta variant as compared to non-Delta variant cases.

Design: We evaluated the lungs from 20 decedents with death due to SARS-CoV-2 confirmed by antemortem nasopharyngeal RT-PCR in July and August 2021 (Delta wave), as well as from 40 autopsy cases prior to February 2021 with death due to SARS-CoV-2. The patient population included males and females, with an age range of 37-67 years in the Delta group, and 44-79 in the non-Delta group. The population demographic was considered at risk for death due to COVID-19, and only one decedent, with immunosuppression, was known to be vaccinated. Lung specimens were examined on H&E and with SARS-CoV-2 nucleocapsid immunostain (IHC).

Results: The time from initial symptoms to death averaged 9 days within the Delta wave and 16 days in non-Delta cases. Steroids, anticoagulation, antibiotics, and monoclonal antibody infusion were frequently part of the clinical treatment of Delta wave cases. Notably, SARS-CoV-2 PCR of lung swabs at autopsy were positive in all but one case examined in the Delta variant group, and viral genome RNA sequencing from lung at autopsy confirmed Delta variant lineage. In both groups, gross features of the lungs included edema, while grossly identifiable thrombi were more commonly seen in non-Delta variant cases. Histologic examination revealed diffuse alveolar damage (DAD) in all cases, most commonly early stage DAD in Delta variant cases. SARS-CoV-2 IHC demonstrated patchy to strong positivity in the alveoli of the majority of Delta variant cases – a finding not frequently seen in non-Delta cases.

Figure 1 - 15



Low and high power microscopic images of lung with positivity for SARS-CoV-2 IHC from a decedent with Delta variant disease

Conclusions: Our study is the first to incorporate PCR and viral genome sequencing from the lung at autopsy to correlate the Delta variant wave with histopathologic findings – a technique that may be useful in identifying important pathologic features of future variants. While the finding of DAD remains the same across viral variants, the majority of Delta cases showed a significant presence of SARS-CoV-2 in the lung by IHC, with minimal inflammatory infiltrate and reduced thrombotic

complication. Whether these findings are the result of a shorter time interval between disease onset and death, therapeutic intervention, or increased viral load remains to be determined.

16 A Case-Control Autopsy Series of Liver Pathology Associated with Novel Coronavirus Disease (COVID-19)

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Disclosures: Fabiola Righi: None; Richard Vander Heide: None; Rondell Graham: None; Marie-Christine Aubry: None; Jorge Trejo-Lopez: None; Melanie Bois: None; Anja Roden: None; Robert Reichard: None; Joseph Maleszewski: *Consultant*, Edwards Scientific; Mariam Priya Alexander: None; Reade Quinton: None; Christopher Hartley: None; Catherine Hagen: None

Background: COVID-19, the disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), continues to be a global health emergency. Although well-known for pulmonary injury, COVID-19 is a systemic process. Previous autopsy case series have speculated about, although not clearly defined, patterns of hepatic injury, with steatosis being reported in many patients. This retrospective study is the first case-control study investigating hepatic pathology in a large cohort of deceased COVID-19 patients.

Design: Consented autopsy cases at two institutions, between 4/2020 and 2/2021, were retrospectively searched for documentation of COVID-19 as a contributing cause of death. A control group of 40 consecutive consented COVID-19(-) autopsy cases during the same period was identified. The autopsy report and electronic medical records were reviewed for clinical information. H&E-stained liver sections were examined for selected histologic features.

Results: 54 COVID-19(+) (mean age 72, M:F=3.2:1) were included in the study. The 40 control cases had a mean age of 64 years and a M:F=1.4:1. The study group was significantly older (p=0.0095) but there was no significant difference in sex. The control group had a higher rate of chronic alcoholism and underlying malignancy, with no difference noted in BMI or other comorbidities. The study group was more likely to have received steroid (72.2% vs. 30%, p<0.0001) and anticoagulation therapy (75.9% vs. 47.5%, p=0.009). Histologically, the study group showed a higher incidence of clinically insignificant steatosis (≤5%), (33.3% vs 12.5%; P = 0.03). Presence of clinically relevant (>5%) steatosis or zonal distribution of steatosis was not significantly different between the groups. Mild nonspecific lobular inflammation and acidophil bodies were also more common in COVID-19 cases (51.9% vs 30.0%; P = 0.04). No significant difference was noted among other histologic features, including vascular changes (Table 1).

Table 1: Comparison of histologic features between control group and COVID-19 group

	Control group (n=40)	COVID-19 group (n=54)	P-value
Steatosis			
• 1-5%	5 (12.5%)	18 (33.3%)	0.03
• >5%	20 (50.0%)	24 (44.4%)	0.68
Steatosis type	n=25	n=42	
• Macro large droplet	16 (64%)	26 (62%)	0.28
• Macro small droplet	1 (4%)	6 (14%)	
• Macro mixed large and small droplet	4 (16%)	8 (19%)	
• Mixed macro and micro steatosis or micro only	4 (16%)	2 (5%)	
Predominant zone involved	n=25	n=42	
• Zone 2-3	9 (36%)	24 (57.2%)	0.22
• Zone 1	3 (12%)	1 (2.4%)	
• Panlobular	3 (12%)	3 (7.1%)	
• Nonzonal	10 (40%)	14 (33.3%)	
Ballooning present	6 (15%)	2 (3.7%)	0.07
Cholestasis	9 (40.9%)	10 (18.5%)	0.08
Portal inflammation	31 (77.5%)	45 (83.3%)	0.6
Lobular inflammation and/or acidophil bodies	12 (30%)	28 (51.9%)	0.04
Vascular changes	7 (17.5%)	7 (13.0%)	0.57
Advanced fibrosis (stage 3 or 4)	8 (20%)	8 (14.8%)	0.58
Centrilobular congestion	30 (75%)	46 (85.2%)	0.29

Conclusions: Mild nonspecific lobular necroinflammatory activity is a common finding in deceased COVID-19 patients, suggestive of COVID-19 hepatitis. COVID-19 is unlikely a cause of clinically significant steatosis. However, patients with COVID-19 are more likely to have low levels of steatosis ($\leq 5\%$) compared to controls. The high rate of steroid therapy in this population may be a possible source of this minor component of steatosis.

17 Subclinical Thyroid Nodular Disease. Trends and Prevalence in Autopsies from Mexico

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Disclosures: Javier Ríos-Valencia: None; Armando Gamboa-Dominguez: None

Background: Prevalence of thyroid nodules is 3-4% in cohort studies, but autopsy series have shown it to be higher. Thyroid palpation to escorts of patients in a general hospital in Mexico, has shown 1.4% prevalence of nodules. However, iodine addition to salt since 2004 in this country, could be associated with higher prevalence.

Design: Autopsies performed and studied from 1992-2019 already concluded (Figure 1), but with formalin fixed thyroid remnants in postmortem archives were considered. After re-grossing, thyroids with >10 tissue blocks for microscopic analysis were included. Autopsy protocols were reviewed for demographic information, age, gender, thyroid weight/gross aspect, body mass index and cause of death. Cases with premortem known thyroid pathology were excluded. Both authors review H-E slides in a two head microscope and, a nodule was diagnosed when the gland histology was distorted (any size for malignancies, 5mm for benign/borderline pathology).

Results: The study included 492 autopsies without known thyroid pathology and with extended sampling in 263/53.4% women and 229/46.5% men, with a mean age of 47 years (13-101 y). The mean death age in women was 42y and 65y in men. Thyroid nodules were observed in 203/41.2% autopsies. Nodular glands had higher weight when compared with glands without nodules (18.37g vs 16.79g), and showed a 1.9:1 female to male ratio. No increase in thyroid nodules was observed after year 2004 when iodine was added to table salt in Mexico (prevalence of nodules 0.22 vs 0.19). The median age when autopsy was performed in patients with nodules was 49y for male and 51y for female. Papillary thyroid carcinoma (PTC) was observed in 46/9.3% glands, partially oxyphilic nodules in chronic lymphocytic thyroiditis in 16/3.2%, non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) in 8/1.6% and the rest were conventional colloid/hyperplastic nodules. All but two carcinomas were microcarcinomas without lymph node metastases.

Thyroid Nodules Found in 203/492 Autopsies. Prevalence 41.2%		
Hyperplastic/colloid	133	27%
PTC	46	9.3%
Oxyphilic nodule in chronic thyroiditis	16	3.2%
NIFTP	8	1.6%

Figure 1 - 17

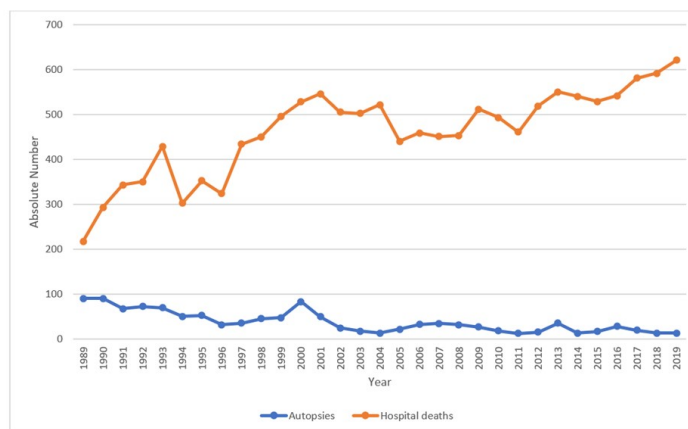


Figure. Hospital Deaths and Autopsies in a Teaching Hospital. A decline from 70% to 2% in performed autopsies (-97%) was documented since 1989 through 2019.

Conclusions: In contrast with the 1.4% prevalence of thyroid nodular disease identified in clinical studies and the 19.6% observed in ultrasonographic studies in this country, autopsy data showed a 41.2% prevalence of nodules. Not increases of thyroid nodular disease was associated with iodine salt addition since 2004.

Thyroid nodular disease was more frequent in females. Malignant (PTC) and premalignant (NIFTP) lesions were identified in 11% of autopsies. A useful information when screening thyroid nodules.

18 COVID-19 Patients with GI Manifestations May be Associated with Extensive Microthrombosis in the Small Intestine, a Study from 13 Autopsy Cases

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Disclosures: Shahram Saberi: None; Lawrence Lin: None; Kristen Thomas: None; Luis Chiriboga: None; Suparna Sarkar: None; Wenqing (Wendy) Cao: None

Background: More than 20% of COVID-19 patients have gastrointestinal (GI) symptoms, among which diarrhea is the most commonly seen symptom. Studies have suggested that patients with severe disease are more likely to have abdominal manifestations. Recent studies have also implicated that coagulopathy and thromboembolic as the major pathophysiological event leading to higher mortality. Besides thrombus in larger vessels, microthrombi appears to occur systemically and plays an important role in multiple organ dysfunction. However, fewer studies have focused on microthrombosis in the GI system.

Design: 13 bronchial SARS-CoV-2 PCR proven autopsy cases were included in the study. Small intestinal specimens were obtained, and processed to routine hematoxylin and eosin (H&E) and CD61 immunohistochemistry (IHC). Related clinical and laboratory data were collected from patient charts. H&E and IHC slides were reviewed by two GI pathologists to evaluate histopathology and microthrombi. The degree of microthrombosis was graded as no microthrombi, focal (1- 2 per 10x), scattered (3-5 per 10x), and diffuse (≥6 per 10x).

Results: Out of 13 patients (11 males, 1 female, age range 22-89 years old), 6 had diarrhea as the initial GI symptom, while others (7 patients) did not report any GI manifestations. Sections from the small intestine showed no acute inflammation in all cases. CD61 positive microthrombi was seen in all small intestine specimens, mainly located in the microvasculature of mucosa, and occasionally submucosal tissue. Patients who had diarrhea, 4/6 (66.7%) showed diffuse (greater than 6 per 10x field) microthrombi in the small intestine. In contrast, patients without GI symptoms, only 2/7 (28.5%) had diffuse microthrombi. Data from lab tests showed the D-dimer appeared to be higher in patients with diarrhea (median, 4067, range from 867 to 10000 ng/ml) compared to patients without diarrhea (median, 2820, range from 298 to 10000 ng/ml). There was no significant difference between median levels of C-reactive protein, prothrombin time (PT) and partial thromboplastin time (aPTT) between patients with or without diarrhea.

Conclusions: Our study highlights that microthrombi frequently occurs in the GI system as reported in other organs. COVID-19 patients with initial GI manifestations, may develop severe microthrombosis and progress to severe disease.

19 Suicide Deaths in Cook County, Illinois Before and During the COVID-19 Pandemic

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Disclosures: Joanna Solarewicz: None; Fernando Alekos Ocampo Gonzalez: None; Benjamin Soriano: None; Ponni Arunkumar: None

Background: To combat the COVID-19 pandemic, the Governor of Illinois signed a stay-at-home order that took effect on March 21, 2020 and extended through the end of May 2020. Mental health was an important consideration during this time as the health impact of the pandemic and the measures taken, including physical distancing and isolation at home, disrupted people's daily lives. Consequently, deaths due to suicide were a concern for public health officials.

Design: We performed a retrospective review of the Cook County Medical Examiner's Office electronic database for all suicide cases during the first year of the COVID-19 pandemic (April 2020-March 2021) and compared those findings with the previous corresponding time period (April 2019-March 2020). Patient demographics and mechanism of death were analyzed.

Results: A total of 478 and 445 suicide deaths occurred during the time period of 4/1/2019 – 3/31/2020 and 4/1/2020 – 3/31/2021, respectively (Table 1). In the first year of the pandemic, deaths due to gunshot wounds increased by 10%, deaths due to hanging decreased by 6% (Figure 1) and deaths in the Black population increased by 5%. During the stay-at-home order, there was a decrease in overall suicide deaths compared to the previous year (Figure 2). During both time periods, all mechanisms of suicides were markedly higher for men than women, except in the drug/alcohol toxicity mechanism. Deaths due to gunshot wounds increased by 6% in the 18-30 age group during the first year of the pandemic. Deaths due to drug/alcohol toxicity increased by 11% in the Black population, and this involved mostly Black women. Deaths due to impact by a train decreased 12% overall during the first year of the pandemic; however, there was a 10% increase seen both in the Black and Asian populations compared to the previous year.

Time Period		Time Period	
4/1/2019 – 3/31/2020		4/1/2020 – 3/31/2021	
All Suicide Deaths		478	445
Age Range (years)	8 - 95	Age Range (years)	9 - 94
White	64%	White	59%
Black	15%	Black	20%
Latino	15%	Latino	15%
Asian	6%	Asian	6%
Other	1%	Other	1%
Hanging Deaths			
Average age (years)	43	Average age (years)	42
White	64%	White	57%
Black	13%	Black	19%
Latino	17%	Latino	17%
Asian	6%	Asian	7%
Other Asphyxia Deaths			
Average age (years)	54	Average age (years)	52
White	81%	White	77%
Black	13%	Black	8%
Latino	0%	Latino	15%
Asian	6%	Asian	0%
Gunshot Deaths			
Average age (years)	49	Average age (years)	48
White	55%	White	58%
Black	25%	Black	23%
Latino	16%	Latino	17%
Asian	3%	Asian	1%
Other	2%	Other	1%
Multiple Injuries Deaths			
Average age (years)	41	Average age (years)	46
White	70%	White	57%
Black	7%	Black	18%
Latino	13%	Latino	5%
Asian	8%	Asian	17%
Other	2%	Other	3%
Drug/Alcohol Toxicity Deaths			
Average age (years)	48	Average age (years)	48
White	74%	White	62%
Black	10%	Black	21%
Latino	10%	Latino	11%
Asian	5%	Asian	6%
Other	1%	Other	0%
Sharp Injury Deaths			
Average age (years)	54	Average age (years)	49
White	67%	White	73%
Black	5%	Black	7%
Latino	24%	Latino	13%
Asian	5%	Asian	7%

Figure 1 - 19

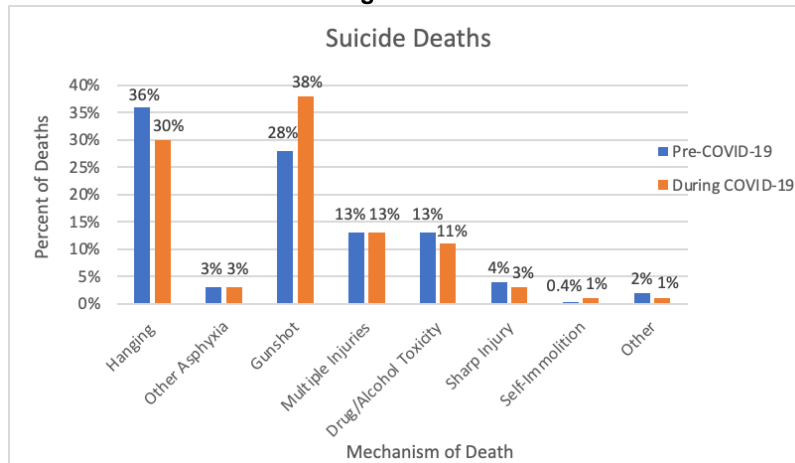
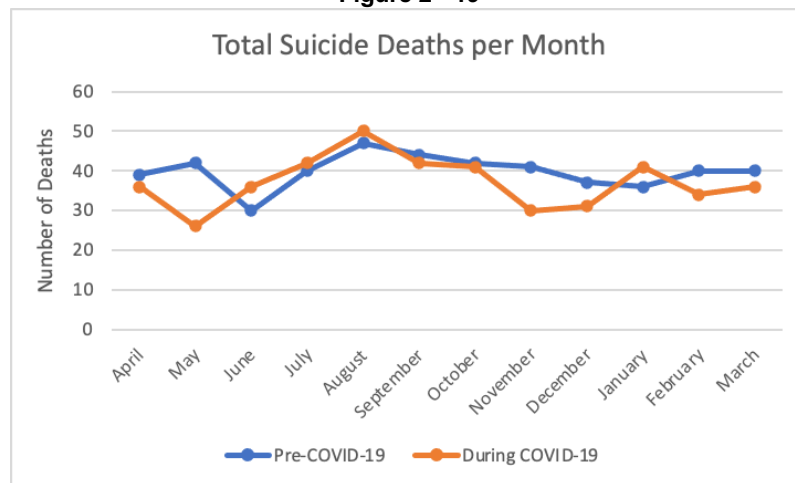


Figure 2 - 19



Conclusions: Our study did not find an increase in number of suicide deaths during the first year of the COVID-19 pandemic. However, future suicide prevention requires an assessment of factors that influence suicide risk. In Cook County, there was a significant rise in gunshot suicides in the overall population and an increase in drug/alcohol toxicity suicides among Black women during the first year of the pandemic. Our study shows how changes in lifestyle, access to drugs and transportation method used influence the mechanism of suicide deaths. Future analyses should continue to examine changes in mechanism of death and demographic trends.

20 End-Stage Kidney Disease is Underreported in Death Certificates

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Background: End-stage kidney disease (ESKD) impacts more than 785,000 Americans and often occurs with multiple comorbid conditions, especially cardiovascular diseases, which are the most common cause of death (COD) in ESKD. Many complications directly arise from ESKD, but its deadly impact can be overlooked. At our institution, the death certificate is completed by clinicians and a majority by clinical house staff. We reviewed the death certificates of ESKD autopsies to understand the clinicians' perspectives on the range of CODs in this clinical setting.

Design: We searched our database for autopsies of adult ESKD patients (2012-2021) that had accessible death certificates. COVID-positive cases were excluded. We evaluated the COD section of death certificates and correlated them with autopsy findings. The frequency of autopsy findings directly identifying CODs or resulting in amendments of death certificates was also noted.

Results: Of 68 autopsy reports, the majority of CODs reported in death certificates were related to sepsis/infection (30%), and cardiovascular diseases (26%). There was no documentation of ESKD in the majority (78%, 53/68) of death certificates. Of these 53 cases, 89% had COD either due to fatal complications of ESKD (98%) or increased mortality of another comorbid condition due to the underlying ESKD. The remaining 11% had COD unrelated to ESKD. Among the fatal complications of ESKD, cardiovascular complications were the most commonly noted (72%) followed by sepsis (20%). Autopsy findings were used to identify the COD on death certificates in only 6% of cases. No amendments were made on any of these death certificates.

Conclusions: ESRD is often not mentioned in death certificates, which underestimates its mortality burden. The death certificate is a source for mortality statistics and used by government for public health policy and allocation of research funding. Hence, accurate accounting of death certificates is essential for this complex and silent disease.

21 Prevalence of Amyloidosis by Fat Pad Biopsy: A Single Institution Autopsy Study

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Disclosures: Jasmine Vickery: None; Michael Billips: None; David Chapel: None; Jeffrey Mueller: None

Background: The amyloidosis refer to a group of disorders of protein misfolding characterized by aggregated β -pleated sheet protein fibrils which deposit in extracellular tissue. The most common and severe type of systemic amyloidosis is amyloid (AL) amyloidosis due to immunoglobulin light chain production, but dozens of others are also described. The abdominal fat pad fine-needle aspiration biopsy (FNAB) is considered the method of choice for confirmation of systemic amyloidosis. Despite having a minimally invasive procedure with relatively high sensitivity to demonstrate tissue deposits of amyloid the epidemiology of amyloidosis has not been well characterized.

Design: We studied abdominal fat pad aspirates from 40 randomly selected decedents on whom we performed a complete autopsy from 2019-2020. The patients had a variety of clinical presentations and none had a pre-mortem diagnosis of amyloidosis. Prior to evisceration, samples were obtained from the abdominal wall, inferior and lateral to the umbilicus. Three to five passes were made with a 22-gauge, 1.5-inch needle. The presence of visible fragments of adipose tissue on direct air-dried and alcohol-fixed smears was used to determine adequacy. The tissue was then stained with Congo Red using the commercially available Leica kit and overlaid with a glass coverslip. All sections were polarized and reviewed by two independent observers with complete concordance. An autopsy case of massive cardiac amyloid deposition was used as a control.

Results: 8 of the 40 samples showed strongly positive perivascular orangeophilic to red material on brightfield examination using a standard microscope. The cases displayed apple-green birefringence when examined with polarized light.

Conclusions: In our limited sample, we found that the incidence of systemic amyloidosis detectable by FNAB is as high as 20%. None of the decedents had a clinical suspicion of amyloidosis, of note 1 of the 8 patients did have a medical history of lymphoplasmocytic lymphoma. Given that fine-needle aspiration biopsy of the abdominal fat pad is reported in the literature to have a sensitivity of 53-100% it is possible that the incidence and prevalence of systemic amyloidosis is greatly underestimated. Amyloidosis did not directly contribute to the decedents cause of death in any of our cases, these results also suggest that fat pad FNAB for amyloidosis may be less specific for clinically significant amyloidosis than previously thought.

22 University of Chicago Pathology Novel SARS-CoV-2 Autopsy Protocol

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Disclosures: Jasmine Vickery: None; Jeffrey Mueller: None

Background: While all autopsies pose a potential risk of exposure to infectious agents, the recent emerging SARS-CoV-2 (COVID) pandemic reminds us of this elevated potential. During this outbreak there are still few detailed protocol recommendations, limited data, and much uncertainty about how exactly to handle such a case. Furthermore, it has been estimated that SARS-CoV-2 autopsies take at least three times longer than a standard autopsy. We designed an institutional autopsy protocol to mitigate occupational risk, increase efficiency, limit exposure, and maximize educational value.

Design: The personal protective equipment (PPE) for the evisceration component of the autopsy consisted of Powered Air Purifying Respirator (PAPR), two layers of long cuff disposal gloves, plastic apron, fluid proof gown, and fluid resistant leg covers. All SARS-CoV-2 autopsies were conducted by a limited number of trained personnel including an attending pathologist, resident and pathologist assistant using the Virchow evisceration method. The cranium was opened using a bone saw with an integrated vacuum. Organ retrieval, weight, and photographing of the cut surface were performed on the day of evisceration and could be completed within one hour, including cleaning of the autopsy suite. Sectioning was performed after fixation for 48-72 hours in 10% neutral buffered formalin. On the day of sectioning, a PAPR was replaced with a N95 respirator.

Results: Over 10 members of our department have contributed to performing 40 COVID autopsies since 2019. No personnel became infected with SARS-CoV-2. Our complete protocol has provided our institution with resources to further study the pathogenesis of COVID in humans. It also differs from other modifications by for example, having multiple body cavities open at a time and not having autopsy rooms dedicated only to infected cadavers. Using these methods we have been able to supply numerous institutional labs with organ sections for various research protocols.

Conclusions: Although post-mortem examination of COVID-infected decedents has inherent risk, only complete autopsies are a source of invaluable and irreplaceable information. This protocol was originally designed for SARS-CoV-2, but we recognize the potential application for other high-risk infectious cases. It is our hope that as more practical evidence-based biosafety guidance is disseminated the need for limited autopsies and partially or completely suspended autopsy services will be obviated.

23 Not Without Risk: Post-procedural MitraClip Device Embolization to the Right Coronary Artery causing Fatal Myocardial Infarction

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Disclosures: Brianna Waller: None; Mary Kelly: None; John DeWitt: None

Background: Mitral valve disease affects more than 4 million people in the United States. The gold standard of treatment is surgical repair or valve replacement. Although surgical options are the treatment of choice for patients with severe mitral regurgitation (MR), up to 50% of these patients are denied surgery due to advanced age, poor left ventricle function, or other comorbidities. In the last decade, numerous transcatheter therapies, such as MitraClip, have been developed to overcome the increased number of subjects with symptomatic severe MR and high surgical risk.

Design: A 71 year old male with a past medical history significant for severe MR, heart failure, hypertension, hyperlipidemia, and type II diabetes mellitus presented for a MitraClip insertion. There were no procedural complications and he was discharged home. On post-procedure day 5, the patient presented to the emergency department for worsening dyspnea and was diagnosed with an acute myocardial infarction (MI). The patient arrested and cardiopulmonary resuscitation was unsuccessful. Consent was obtained from the next of kin and an autopsy was performed.

Results: Gross examination during autopsy revealed cardiomegaly (910 grams) with biventricular hypertrophy and a right-dominant posterior coronary circulation. Examination of the coronary vessels revealed evidence of MitraClip embolization to the proximal right coronary artery (Fig. 1) causing a complete obstruction. In the remaining coronary vessels, there was minimal to moderate atherosclerotic coronary artery disease.

Figure 1 - 23

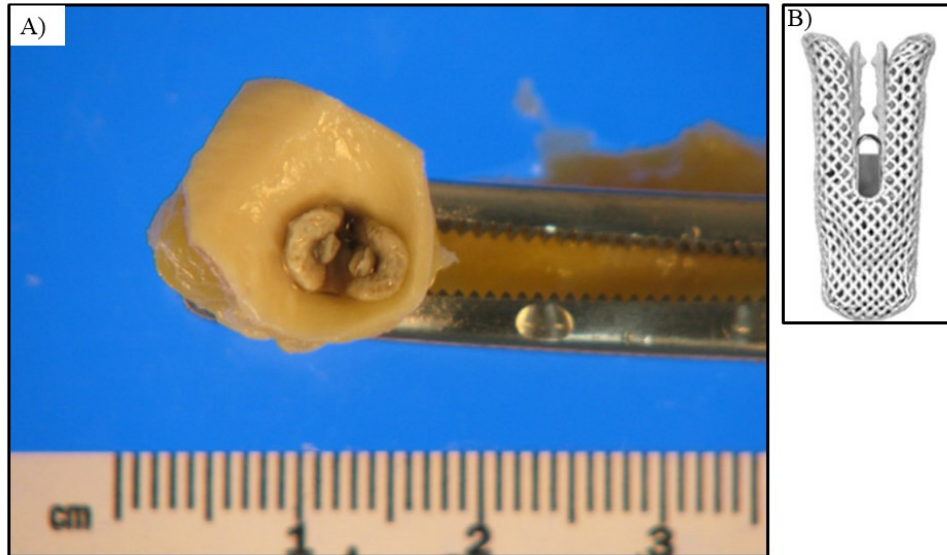


Figure 1: A) Right coronary artery with MitraClip embolus causing 100% occlusion B) MitraClip Device

Conclusions: While minimally invasive, the MitraClip procedure is not without risk. Partial clip detachment, device embolization, mitral valve stenosis, and clip entanglement in the chordae, amongst others, have been identified as potential complications. In the EVEREST II trial, it is estimated that 4.8% of patients may have partial detachment of the device within the first 12 months. Complete detachment and embolization is even rarer, occurring in 0.1-0.7% of patients. Putative risk factors include procedural technical difficulties and severe leaflet flail, both of which occurred in our decedent's case. Few case reports exist in the literature describing device embolization with even rarer cases resulting in right coronary artery embolization with subsequent MI and death. In patients presenting with an acute coronary syndrome after MitraClip, device complications could be a consideration during the resuscitative process.