



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

prednisolone-equivalent mg/day was 46 (IQR 30-81) days. About half of the patients with ICPI-AKI had complete renal recovery (46%) defined as a return of SCr to 25% of the baseline within 3 months from AKI diagnosis. Interestingly, time to steroid initiation was shorter in patients who recovered kidney function (0, IQR 0-2 days) than in patients with non-recovery (9, IQR 2-23). ICPI was re-challenged after ICPI-AKI in 6 (21%) patients. AKI after the re-challenge re-occurred in 2 (33%) cases. The survival in patients with ICPI-AKI was 71%, with a median follow-up of 13 (IQR 7-33) months.

Conclusions: ICPI-associated AKI is not common but results in a high rate of hospitalisations and interruption of the treatment. Our study suggests that diagnostic investigations are infrequently performed. In our cohort, a more rapid start of steroids was associated with higher likelihood of renal recovery. In the majority of patients, ICPI-AKI led to a change in anti-cancer therapy. We suggest that more awareness is necessary and that diagnostic investigations should be included in screening tests during ICPI administration and during AKI assessment.

No conflict of interest

POS-210

POST-MORTEM MOLECULAR INVESTIGATIONS OF SARS-COV-2 IN AN UNEXPECTED DEATH OF A RECENT KIDNEY TRANSPLANT RECIPIENT



SIMMS, EL*¹, Chung, H², Oberding, L³, Muruve, D⁴, McDonald, B⁵, Bromley, A³, Pillai, DR³, Chun, J⁶

¹University of Calgary, Medicine, Calgary, Canada, ²University of Calgary, Snyder Institute for Chronic Diseases, Calgary, Canada, ³University of Calgary, Pathology and Laboratory Medicine, Calgary, Canada, ⁴University of Calgary, Department of Medicine, Calgary, Canada, ⁵University of Calgary, Critical Care, Calgary, Canada, ⁶University of Calgary, Medicine- Snyder Institute of Chronic Diseases, Calgary, Canada

Introduction: Solid organ transplant (SOT) recipients are vulnerable to severe infection during induction therapy. We report a case of a 67-year-old male who died unexpectedly 10 days after receiving a kidney transplant (KTx) on February 10, 2020. There was no clear cause of death, but COVID-19 was considered, retrospectively, as the death occurred shortly after the first confirmed case of COVID-19 in Canada. We confirmed the presence of SARS-CoV-2 components in the allograft and patient lung tissue using immunohistochemistry (IHC) for SARS-CoV-2 spike (S) protein and RNA scope *in situ* hybridization for SARS-CoV-2 RNA. Results were confirmed with the FDA EUA-approved Bio-Rad SARS-CoV-2 ddPCR for the kidney specimen. Our case highlights the importance of patient autopsies in an unfolding global pandemic and demonstrates the utility of molecular assays to diagnose SARS-CoV-2 post-mortem. SARS-CoV-2 infection during induction therapy may portend a severe or fatal clinical outcome. We also suggest COVID-19 may be transmittable via KTx.

Methods: We acquired autopsy specimens of the allograft and lung tissue for analysis by IHC (Figure 4A). RNA scope *in situ* hybridization and immunohistochemistry verified the presence of viral particles. Results were confirmed with RT-PCR and dd-PCR.

Results: Remarkably, antibodies directed against SARS-CoV-2 S protein were positive in the allograft and native lung tissue of the patient (Figure 4B). RNA scope *in situ* hybridization, RNA scope *in situ* hybridization was used to detect SARS-CoV-2 RNA in the allograft (Figure 4C) as previously described.^{3,7} With both IHC and RNAScope, we noted very few viral particles, with more in the donor kidney compared to native lung tissue. To confirm this finding, we used RT-PCR, but were unable to detect SARS-CoV-2 RNA (data not shown). Next, we turned to a FDA-EUA clinically validated BioRad ddPCR assay approved for human diagnosis, previously used to detect SARS-CoV-2 RNA in RT-PCR negative samples. Using ddPCR, we confirmed SARS-CoV-2 nucleocapsid N1 gene in the allograft (Figure 5). A smaller signal was observed in lung tissue, but lower than the clinically validated threshold (Figure 5).

Conclusions: Using three methods of viral protein and/or RNA detection we present a COVID-19 positive patient who died on February 10, 2020 which precedes the first confirmed case in Alberta, Canada and first Canadian COVID-19 fatality previously established as a travel-related case on March 5, 2020 and nursing home death on March 9, 2020, respectively. Our patient demonstrates the possibility of a severe adverse outcome for COVID-19 infection during induction therapy and the potential for SARS-Cov-2 renal allograft invasion mediated SOT transmission. This case carries significant epidemiologic consequences and highlights the vital role of autopsy in an unfolding pandemic in providing valuable diagnostic information. These sensitive methods can be applied to future disease outbreaks in the absence of pre-mortem testing.

No conflict of interest

POS-211

SAFETY AND EFFICACY OF BEDSIDE PLACEMENT OF TUNNELED HEMODIALYSIS CATHETERS IN PATIENTS WITH COVID-19 IN THE INTENSIVE CARE UNIT



SOHAIL, MA*¹, Lane, J², Hanane, T³, Vachharajani, T⁴

¹Cleveland Clinic Foundation, Internal Medicine, Cleveland, United States, ²Cleveland Clinic Foundation, Nursing Institute, Cleveland, United States, ³Cleveland Clinic Foundation, Critical Care Medicine, Cleveland, United States, ⁴Cleveland Clinic Foundation, Nephrology and Hypertension, Cleveland, United States

Introduction: Acute kidney dysfunction is common in critically-ill patients with coronavirus disease-2019 (COVID-19), which often necessitates the placement of a tunneled hemodialysis catheter (TDC) for kidney replacement therapy (KRT). The standard of care requires that the procedure be performed under ultrasound and fluoroscopic guidance to minimize complications and ensure optimal catheter tip positioning. This entails transfer of patients out of the intensive care unit (ICU) to the fluoroscopy suite, which poses the risk of viral transmission amongst numerous health care professionals. We hypothesized that bedside TDC placement by an experienced provider in the ICU, utilizing ultrasound and anatomic landmarks without fluoroscopic guidance, can be successfully accomplished without compromising patient safety or catheter function.

Methods: We conducted a retrospective chart review of all adult patients with COVID-19 in the ICU who selectively underwent right internal jugular (IJ) TDC placement at the bedside using ultrasound guidance with continuous cardiac monitoring by an experienced interventional nephrologist. The protocol for TDC insertion using anatomic landmarks was defined as: the manubrial sternal angle (MSA) topographically corresponds to the carina, with the insertion depth estimated by measuring the distance between the skin venipuncture site 1 to 2 cm above the clavicle and a point 5 cm below the MSA. One clinical safety indicator utilized was the guidewire 'recoil' sign, which signifies wire tip coiling in the right heart chambers. Outcomes included procedural complications such as bleeding, arterial puncture, venous air embolism, arrhythmias, pneumothorax, hemothorax and catheter tip malposition. The catheter tip position was confirmed with a post-procedure portable chest x-ray (CXR). TDC placement was considered to be successful when the inserted catheter was able to sustain the prescribed blood flow to perform a single hemodialysis treatment.

Results: We collected data on 10 patients with COVID-19 who had right IJ TDCs placed at the bedside, 3 of whom underwent simultaneous insertion of right IJ tunneled central venous catheters (CVC). The median age of the cohort was 66.5 years (interquartile range [IQR]:14.5); predominantly male (n=7) and African American (n=7). Comorbid conditions included chronic kidney disease (n=5), diabetes mellitus (n=6) and hypertension (n=10). The median Acute Physiology and Chronic Health Evaluation (APACHE II) score was 21.5 (IQR:5.25) and the median body mass index (BMI) was 28.3 (IQR:6.6). Continuous veno-venous hemodialysis (CVVHD) was the KRT modality employed in all patients. A median catheter blood flow rate of 200 ml/min (IQR:0)

	All Patients (N = 10)
Baseline Clinical Characteristics	
Age, median (IQR)	66.5 (14.5)
Male, n (%)	7 (70)
African American, n (%)	7 (70)
Comorbidities, n (%)	
Hypertension	10 (100)
Diabetes Mellitus	6 (60)
Chronic Kidney Disease	5 (50)
Body mass index, kg/m ² , median (IQR)	28.3 (6.6)
Use of Anti-platelet and/or Anti-coagulant medications within 72 hours of procedure, n (%)	
Aspirin	4 (40)
Rivaroxaban	1 (10)
Warfarin	1 (10)
None	5 (50)
APACHE II Score, median (IQR)	21.5 (5.25)

Table 1: Baseline Clinical Characteristics

was achieved in all patients without any deviation from the dialysis prescription. No catheter related complications were observed and none of the catheter tips were malpositioned on post-insertion CXRs, with the tip located either in the mid-right atrium (RA) (n=7) or at the junction of the superior vena cava and RA (n=3).

All Patients (N = 10)	
CVVHD Prescription, median (IQR)	
Dialysate Flow Rate, ml/hr	2000 (575)
Blood Flow Rate, ml/min	200 (0)
Ultrafiltration Rate, ml/hr	200 (87.5)
Tunneled Dialysis Catheter Tip Positioning, n (%)	
Mid – Right Atrium	7 (70)
Superior Vena Cava – Right Atrium Junction	3 (30)
Catheter Malposition	0 (0)
Tunneled Dialysis Catheter Outcomes, n (%)	
Bleeding	0 (0)
Venous Air Embolism	0 (0)
Arrhythmias	0 (0)
Pneumothorax/Hemothorax	0 (0)

Table 2: CVVHD Prescription and Tunneled Dialysis Catheter Outcomes

Conclusions: In a select group of patients, preferential right IJ TDC placement at bedside, using ultrasound and anatomic landmarks without fluoroscopic guidance, may be a safe and viable option. Simultaneous insertion of tunneled CVCs can also be safely accomplished. Performing bedside TDC insertion may potentially reduce the risk of transmission of COVID-19 amongst health care workers.

No conflict of interest

POS-212

THE ROLE OF KIDNEY BIOPSY AND QUANTITATIVE COMPUTER MORPHOMETRY IN PREDICTING THE REVERSIBILITY OF DIALYSIS-DEPEND ACUTE KIDNEY INJURY DUE TO MYELOMA CAST NEPHROPATHY



KAZARINA, E¹, Stolyarevich, E*², Rekhina, I³, Kovrigina, A⁴, Dvirnyy, V⁵, Kulikov, S⁶, Mendeleeva, L⁷

¹National Research Center for Hematology, Intensive care and hemodialysis, Moscow, Russia, ²Moscow State University of Medicine and Dentistry, Nephrology, Moscow, Russia, ³National Research Center for Hematology, Chemotherapy of plasma cell dyscrasia, Moscow, Russia, ⁴National Research Center for Hematology, Pathology, Moscow, Russia, ⁵National Research Center for Hematology, Clinical diagnostic laboratory, Moscow, Russia, ⁶National Research Center for Hematology, Information and analytical, Moscow, Russia, ⁷National Research Center for Hematology, High-dose chemotherapy of paraproteinemic hemoblastoses, Moscow, Russia

Introduction: Myeloma cast nephropathy (MCN) is morphologically confirmed in 87–94% of patients with dialysis-dependent acute kidney injury (AKI) at multiple myeloma onset. However, kidney biopsy is necessary to detect paraprotein-related nephropathy. Recent studies have shown that kidney biopsy allows not only to establish the nature of damage, but also to determine severity and potential reversibility of pathological process. Clinically this can be helpful in choosing the optimal treatment program of MCN.

Methods: 25 patients aged 38 to 70 years (Me age=58 years) with dialysis-dependent AKI and newly diagnosed multiple myeloma were included. MCN was confirmed by kidney biopsy in all patients. The time from diagnosis of AKI to start of induction therapy did not exceed 3 months. Hematologic response was achieved on the first line of antimyeloma treatment in all cases. Hematologic and renal response were established according to IMWG criteria. Kidney biopsy samples were processed for light and immunofluorescence microscopy. The immunohistochemical study was performed to more accurately assess the condition of proximal tubules by measuring expression of epithelial-mesenchymal transition (EMT) markers: E-cadherin, vimentin, α -smooth muscle actin (α -SMA). The process of quantitative assessment is shown in Figure 1(B,D,F,H).

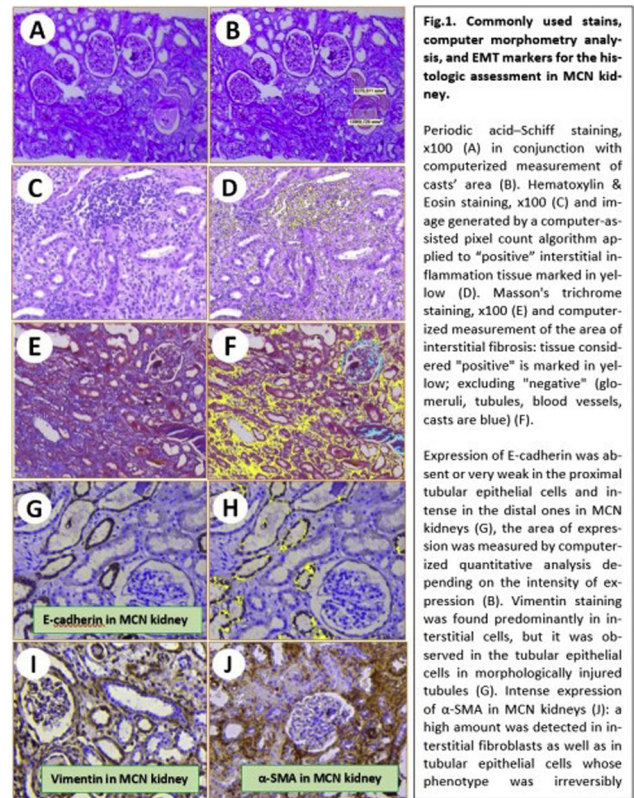


Fig.1. Commonly used stains, computer morphometry analysis, and EMT markers for the histologic assessment in MCN kidney.

Periodic acid-Schiff staining, x100 (A) in conjunction with computerized measurement of casts' area (B). Hematoxylin & Eosin staining, x100 (C) and image generated by a computer-assisted pixel count algorithm applied to "positive" interstitial inflammation tissue marked in yellow (D). Masson's trichrome staining, x100 (E) and computerized measurement of the area of interstitial fibrosis: tissue considered "positive" is marked in yellow; excluding "negative" (glomeruli, tubules, blood vessels, casts are blue) (F).

Expression of E-cadherin was absent or very weak in the proximal tubular epithelial cells and intense in the distal ones in MCN kidneys (G), the area of expression was measured by computerized quantitative analysis depending on the intensity of expression (B). Vimentin staining was found predominantly in interstitial cells, but it was observed in the tubular epithelial cells in morphologically injured tubules (G). Intense expression of α -SMA in MCN kidneys (J): a high amount was detected in interstitial fibroblasts as well as in tubular epithelial cells whose phenotype was irreversibly

All biopsy samples were assessed using standard semi-quantitative method and by computer quantitative color image analysis (digital module Leica). Statistical software package SAS 9.4 was applied for calculations. All estimates are shown with 95%CI.

Results: Renal minimal response or better occurred in 17 (68%) of patients during of Me 68,5 (16–183) days. At the same time, complete renal response (GFR > 60 ml/min) was achieved only in one case. There are some quantitative pathological findings associated with renal response in Table.

Table. Computer quantitative pathological findings associated with renal response

Prognostic value of quantitative renal biopsy findings	Renal responders (n = 17)	Non-renal responders (n = 8)	P
Total sclerotic glomeruli, Me (range)	16,7% (0–50)	20,4% (12,5–55,6)	0,4
Median number of casts per field, Me (range)	6,4 (1,3–36,5)	6,4 (4–31)	0,6
Area of Casts obstruction from tubulo-interstitium, Me (range)	14,9 (7,5–23,6)	16,3 (10,7–24,6)	0,9
Interstitial inflammation, Me (range)	5,2% (0–22,6)	4,3% (2,6–17,5)	0,12
Interstitial fibrosis, Me (range)	22,8% (12,9–39,3)	45,9% (19,1–59)	0,001
Area of E-cadherin expressing from proximal tubules, Me (range)	28,8% (16,2–41,2)	10,5% (0–13,6)	0,002
Area of E-cadherin expression from tubulo-interstitium, Me (range)	18,9% (7,9–27,4)	7,2% (3,8–11)	0,005
Distal tubules expressing E-cadherin, Me (range)	37,6% (26,6–53,9)	40,4% (21,1–62,5)	0,7
Area of vimentin expression from tubulo-interstitium, Me (range)	22,9% (6,3–43,9)	23,5% (11,1–48,4)	0,8
Area of α -SMA expression from tubulo-interstitium, Me (range)	37,7% (18,6–56,5)	45,1% (31,8–61,1)	0,3

There were less area of interstitial fibrosis (22,8% vs 45,9%, respectively, $p=0,001$), larger area of E-cadherin expression in proximal tubules (28,8% vs 10,5%, respectively, $p=0,002$) and of tubulo-interstitium (18,9% vs 7,2%, respectively, $p=0,005$). The median number of casts per field was the same (6.4 and 6.4, $p=0.6$) as well as the area of casts obstruction from tubulo-interstitium (14,9% and 16,3%, $p=0,9$). It has been shown number and area of casts are not prognostic criteria for the reversibility of AKI in MCN and eliminates after effective treatment. It was confirmed that expression of EMT markers is multidirectional (Figure 1 G,I,J). It has been proven that saved expression of E-cadherin in epithelium of proximal tubules is a prognostic marker of AKI reversibility in MCN (Table). Compared with semi-quantitative analysis, computer morphometry made