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Severe Intraabdominal Hypertension in Critically Ill COVID-19 Patients With Acute Kidney Injury

To the Editor:

COVID-19-induced acute respiratory distress syndrome has been described as an atypical form of the syndrome, notably by showing well-preserved pulmonary compliance in a large subset of patients.[1,2] Beyond the respiratory presentation of the disease, acute kidney injury (AKI) occurs in up to 25% of COVID-19 critically ill patients and is independently associated with a higher mortality rate, especially when renal replacement therapy (RRT) is required.[3] Clinicians' choices in both the ventilation strategy and the fluid stewardship of these patients could directly impact renal function, notably by changing intraabdominal pressure (IAP).[4] The use of mechanical ventilation with high positive end-expiratory pressure (PEEP) levels as well as fluid overload have been well demonstrated to be associated with intraabdominal hypertension (IAH) in ICU patients.[5] We aimed to assess IAH occurrence at the time of AKI development as well as IAP variation while changing fluid load and PEEP level in critically ill COVID-19 patients.

Methods

We screened all adult patients hospitalized in the ICU at the University Hospital of Reims (Northeastern France) between March 15 and May 15, 2020, with a diagnosis of COVID-19-induced ARDS requiring mechanical ventilation, who developed AKI, defined as stage 3 according to the Kidney Disease Improving Global Outcomes classification. Clinical data of all included patients were obtained by reviewing clinical charts and nursing records. Because of the well-known association between IAH and AKI, IAP was systematically monitored by intravesical pressure measurement with the Unometer Abdo-Pressure device every 8 hours in all patients developing AKI in our ICU according to a local protocol.[6] IAH was defined according to the World Society of Abdominal Compartment Syndrome as an increase in IAP above 12 mm Hg for more than 24 hours and graded as following: grade I, 12 to 15 mm Hg; grade II, 16 to 20 mm Hg; grade III, 21 to 25 mm Hg; grade IV, >25 mm Hg. IAH grades III to IV were considered as severe.[5] Management of IAH patients in our ICU included, when possible, a fluid-restrictive strategy and a decrease in PEEP level. Quantitative and qualitative data are reported as median [interquartile range] and number (percentage), and compared with Mann-Whitney test and χ^2 test with OR and 95% CI, respectively. $P < .05$ was considered statistically significant.

Results

Ninety-one COVID-19 patients were admitted to our ICU during the study period, and 64 (70.3%) required mechanical ventilation. Among the ventilated patients (median age, 69 [15.2] years; male, 51.6%), 20 (31.2%) developed stage 3 AKI during the ICU stay, all within the first 72 hours after admission (three patients were excluded because of missing data). Compared with non-AKI patients, patients with AKI were most likely to be men (88.2% vs 40.9%; OR = 10.8; 95% CI, 2.5-46.7; $P < .01$) and showed higher BMI (32.0 [6.7] vs 27.8 [6.8]; $P = .03$).

At the time of AKI development, all 17 (100%) included patients who developed AKI exhibited IAH with a median IAP of 23 (8) cm H_2O. Eleven (64.7%) had severe IAH and tended to show higher rates of both RRT requirement (54.6% vs 16.7%; OR = 6.0; 95% CI, 0.7-50.6; $P = .13$) and in-ICU mortality (72.7% vs 50%; OR = 2.7; 95% CI, 0.4-18.5; $P = .35$) compared with patients with nonsevere IAH (Table 1). At the time of AKI development, all included patients showed relatively preserved pulmonary compliance (44 [10] mL/cm H_2O) and were treated with high PEEP levels (12 [4] cm H_2O) and highly positive 24-hour fluid balance (2,070 [1,975] mL), whereas biochemical urinary analyses were mostly suggestive of prerenal aggression (Table 1). Our local protocol, including a decrease in fluid load (199.5 [1,962.8] vs 2,070 [1,975] mL; $P < .01$) and PEEP levels (10 [3] vs 12 [4] cm H_2O; $P < .01$), was associated with a decrease in IAP (13.5 [4] vs 23.0 [8] mm Hg; $P < .01$) and an increase in daily diuresis (1,510 [1,010] vs 925 [528] mL; $P < .01$) within 5 days (Fig 1).

Discussion

The pathophysiology of COVID-19-related AKI remains incompletely elucidated and is probably

TABLE 1] Characteristics of the 17 Ventilated Patients With COVID-19 Developing Acute Kidney Injury in the ICU

Variables	All Patients With AKI N = 17	IAH Grade I-II n = 6	IAH Grade III-IV n = 11
Demographic data			
Age, y	70, 9	73, 7	69, 10
Men, No. (%)	15 (88.2)	6 (100)	9 (81.8)
Hypertension, No. (%)	13 (76.5)	4 (66.7)	9 (81.8)
Diabetes, No. (%)	7 (41.2)	3 (50)	4 (36.4)
BMI	32, 7	31, 3	32, 7
CKD, No. (%)	3 (17.6)	1 (16.7)	2 (18.2)
Baseline creatinine level, μmol/L	78, 34	81, 20	78, 35
RAAS blocker, No. (%)	9 (52.9)	4 (66.7)	5 (45.5)
Corticosteroid, No. (%)	6 (35.3)	2 (33.3)	4 (36.4)
Bacterial coinfection, No. (%)	7 (41.2)	3 (50)	4 (36.4)
Acute kidney injury			
Days from ICU admission, d	2, 1	2, 1	3, 1
Proteinuria, mg/mmol Creatinuria	48, 52	40, 28	63, 57
Urine sodium/potassium ratio <1	9 (52.9)	3 (50)	6 (54.5)
Urine/plasma creatinine ratio >30	15 (88.2)	5 (83.3)	10 (90.9)
Urine/plasma urea ratio >10	13 (76.5)	4 (66.7)	9 (81.8)
Fractional excretion of urea <35%	15 (88.2)	5 (83.3)	10 (90.1)
Respiratory parameters			
Compliance, mL/cm H_2O	44, 10	45, 11	44, 7
PEEP, cm H_2O	12, 4	11, 4	12, 4
ECMO, No. (%)	3 (17.6)	1 (16.7)	2 (18.2)
Hemodynamic parameters			
24-Hour fluid balance	2070, 1975	1945, 1867	2070, 2075
Norepinephrine > 0.25 μg/kg/min	14 (82.3)	5 (83.3)	9 (81.8)
Outcome			
Renal replacement therapy, No. (%)	7 (41.2)	1 (16.7)	6 (54.6)
Mesenteric ischemia, No. (%)	1 (5.9)	0	1 (9.0)
ICU mortality, No. (%)	11 (64.7)	3 (50)	8 (72.7)

Categorical and continuous variables are presented as No. (%) and as median with interquartile range, respectively. CKD = chronic kidney disease; ECMO = extracorporeal membrane oxygenation; IAH = intraabdominal hypertension; RAAS = renin-angiotensin-aldosterone system.

multifactorial.[7] The independent association between elevated IAP and renal function impairment has been well established and is mainly explained by renal venous congestion, which impairs glomerular filtration by decreasing renal plasma flow.[8] As previously reported, obesity, which concerns a large subset of critically ill patients with COVID-19, is an independent risk factor of IAH.[6] Describing a homogeneous population of ventilated patients with COVID-19 who developed severe AKI during ICU stay, we found that all of them had IAH at the time of AKI development. Additionally, although we did not find IAH grades III to IV to be significantly associated with worse outcomes, which might be attributable at least in part to our small sample size, patients with severe IAH tended to show higher rates of RRT and in-ICU death. Furthermore, we found that IAP decreased significantly in univariate analysis while decreasing fluid load and PEEP levels (both well-known IAH risk factors). The use of high PEEP level in patients with almost normal compliance has been widely criticized because it might increase transpulmonary pressures and decrease venous return without improving oxygenation.[1] As PEEP adjustments are transmitted to the abdomen, the use of high PEEP has also been reported to promote IAH

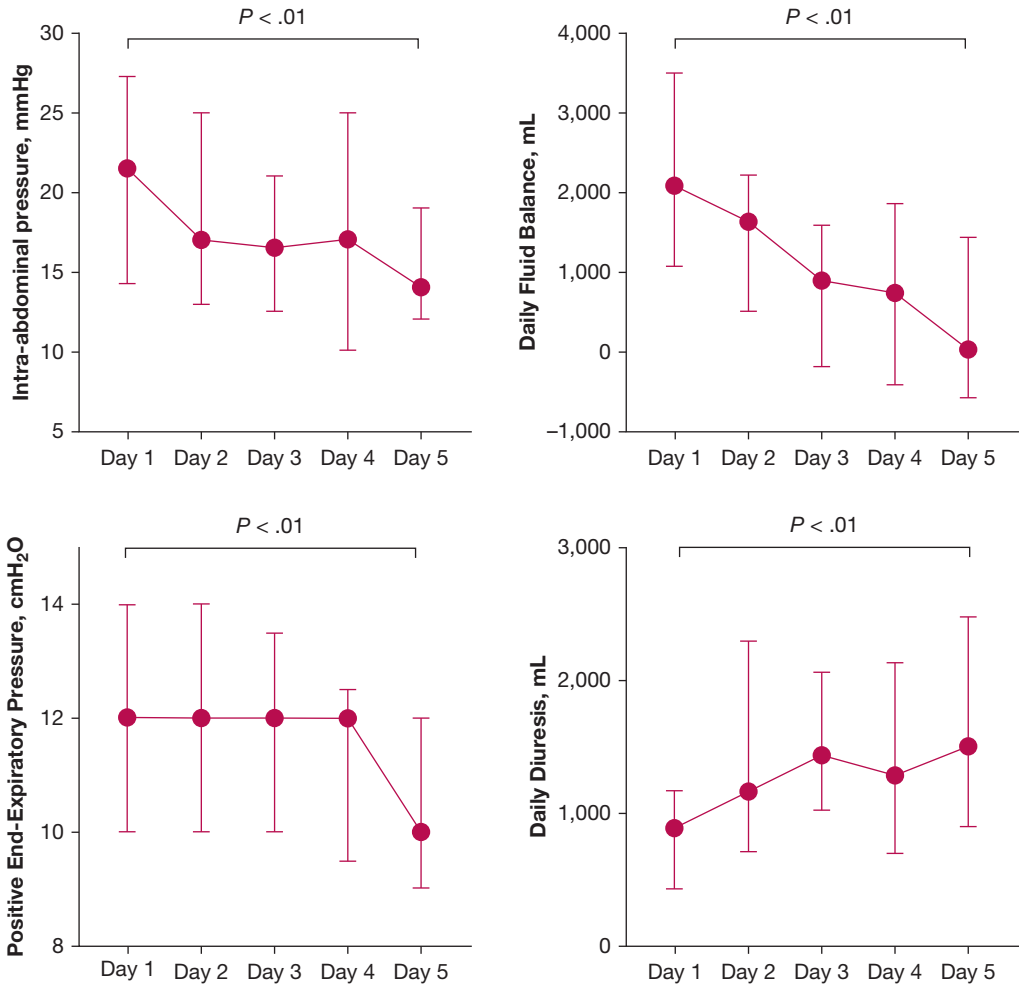

Figure 1 – *Evolution of fluid load, positive end-expiratory pressure, intraabdominal pressure, and daily diuresis within 5 days after AKI development in ventilated patients with COVID-19. Data are presented as median with interquartile range. Mann-Whitney test was used to compare each variable between day 1 (AKI development) and day 5.*

in patients under mechanical ventilation.[4,5] A liberal fluid therapy strategy might promote the development of visceral edema as well as right-sided heart failure, thus contributing to IAH.[9] Thus, the optimal fluid and respiratory stewardship remains to be established by prospective studies in COVID-19 patients with preserved pulmonary compliance to avoid the adverse effects of either underhydration or overhydration and positive pressure ventilation on kidney function in this setting.[10]

Despite the inherent limitation of its retrospective design, and small sample size, our study is the first to highlight the high frequency of severe IAH in patients with COVID-19 developing AKI. Although the clinical benefit of IAH prevention/treatment in terms of renal function remains to be established by interventional studies, bedside clinicians should be aware of IAH importance in critically ill patients with COVID-19 and AKI. Future larger studies are needed to prospectively assess this issue to improve outcomes, notably in ventilated patients with COVID-19.

Vincent Dupont, MD
Claire Gamblin, MD
Mathieu Bard, MD
Gautier Julien, MD
Michel Bonnivard, MD
Vanessa Champenois, MD
Antoine Goury, MD
Bruno Mourvillier, MD, PhD
Reims, France

AFFILIATIONS: From the Medical Intensive Care Unit, University Hospital of Reims.

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CORRESPONDENCE TO: Vincent Dupont, MD; email: vdupont@chu-reims.fr

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