Letter to the Editor

Liberal Versus Conservative Fluid Therapy in COVID-19 Patients: What is the Best Strategy for the Treatment of Critically ill Patients?

Dear Editor,

Fluid therapy is a key piece in the management of the critical patient.[1] Several studies have tried to compare a conservative fluid strategy with a standard care or liberal fluid strategy in critically ill patients in the intensive care unit (ICU). While a comprehensive analysis of these studies is beyond the scope of this article, improved outcomes have generally been reported with conservative fluid strategies in critically ill patients with acute respiratory distress syndrome (ARDS), sepsis, and shock.[2] The current pandemic associated with COVID-19 has represented a challenge for clinicians, especially when a large proportion of patients require treatment in ICUs.[3] Studies on its clinical characteristics, laboratory results and pathology findings, together with its clinical outcome, have shown that a large number of patients with the novel coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia die due to shock and acute lung injury (ALI) or ARDS.[4,5] However, optimal fluid strategy in the critical patients with COVID-19 has not been reported.

Currently, there are published guidelines on fluid management in patients with COVID-19. The main recommendations in these guidelines are based upon the Surviving Sepsis Campaign,[6] together with its specific update for COVID-19.[7] In the absence of direct evidence in patients with ARDS and shock from COVID-19, indirect evidence from other critically ill patients with ARDS and sepsis has been extrapolated to this context to support these recommendations, because it is plausible that these patients will respond to fluid administration similarly. A conservative strategy of fluid management in patients with ALI or ARDS, sepsis, or (systemic inflammatory response syndrome) has been associated in previous studies with improve of lung function, reduced the duration of mechanical ventilation, reduced length of ICU stay, improved prognosis, lower mortality, and better survival rates compared with a liberal strategy.[8,9] In contrast, a positive fluid balance has been associated with a worse oxygenation and ventricular dysfunction prolonged mechanical ventilation, longer ICU and hospital stay, and even higher mortality in critically ill patients,[10] especially in cases of ARDS[11] and septic shock.[12]

Considering the pathophysiological mechanism of new coronavirus, SARS-CoV-2 invasion leads to alveolar and vascular epithelial cells damage impelling the formation of minimal thrombus, increasing pulmonary venous pressure and vascular permeability and leading to massive fluid exudation causing pulmonary edema; this, in turn, leads to alveolar gas exchange disorders.[13] In this way, due to pulmonary edema in critical COVID-19 patients, excessive fluid therapy and a positive fluid balance in COVID-19 patients too could increase extravascular lung water due to pulmonary capillary leak and this affecting gas exchange, resulting in a worse prognosis;[14] therefore, according to this and in view of the benefit observed in other ARDS or sepsis populations, the consequences of a positive fluid balance, the possible reduction in the cost of administering less fluids, and the feasibility of the intervention, it has been suggested to use a conservative strategy over a liberal fluid therapy in critical patients with COVID-19. This conservative approach could reduce the occurrence of a positive fluid balance while ensuring tissue perfusion.[7,9,14]

However, as a new disease and lacking solid evidence to define the best fluid therapy strategy in COVID-19 patients, the general principles governing fluid management in ICU provide the basis for optimal fluid therapy in these times.[1] Strategies such as ROSE, supported by Malbrain *et al*.[15] allow and facilitate the comprehension of pathophysiological mechanisms of fluid therapy. In addition, in the current context, the shared experiences of colleagues and experts also play an important role, as they add and refine these concepts. Thus, in these times, the goals of resuscitation tend to constantly evolve. For example, as an anecdotal data, at the beginning of the pandemic, a very restrictive fluid strategy was controversial because to the effect of hypovolemia on the development of acute kidney injury in the patients with COVID-19.[16] Some experts even had suggested the potential risks of the conservative approach as the decreased cardiac output and impaired extra-pulmonary organ function. However, this did not truncate the conservative approach of fluid therapy but reinforced the idea of detect and correct hypovolemic states to prevent LRA in patients with COVID-19.[17]

This led to considering the fact that COVID-19 patients present at different stages of their disease and it is important to determine the stage they are at because this provides an idea of the patient's volumetric status. Critical patients with COVID-19 who are admitted to the hospital in a late stage of the disease may have hypovolemia as a result of the fever, tachypnea, and breathing through the mouth, because this could cause a great loss of fluids and increase hypovolemia.[14] Similarly, although most patients present with respiratory symptoms, gastrointestinal

symptoms such as vomiting and diarrhea are also common and contribute to hypovolemia.[18] In addition, once in the ICU, depression, intubation, and sedation could exacerbate hypovolemia. Therefore, it is extremely important to make a detailed medical history (paying special attention to the onset of symptoms) and clinically evaluate the patient. However, clinicians cannot simply rely on clinical examination to detect hypovolemia and need actionable guidelines to rationalize fluid therapy.[17] In this way, fluid should be administered with caution only after assessing the responsiveness to fluids,[1] with a fluid challenge as through the passive leg lift maneuver in patients with suspected hypovolemia, and given the high incidence of myocardial dysfunction in COVID-19 which could limit the ability to handle large volumes of fluids, especially in elderly patients in the ICU.[14,18] Although it has been reported that conservative fluid strategy and liberal strategy have a similar incidence of AKI and the requirement for renal replacement therapy,[9] it is necessary to constantly monitor the kidney function, correct electrolyte balance and adjust acid-base balance.[14] Portable ultrasonography at the bedside (point-of-care ultrasound or POCUS) on critically ill patients with COVID-19, also may help to characterize volume status, pulmonary injury, and cardiac status. The findings found through this tool could then be interpreted in the context of hemodynamics and fluid balance to guide and rationalize fluid management in the COVID-19 times.[19] The establishment of specific goals adapted to the individual conditions of the patients seems to be a fundamental element in the treatment of these patients in the ICU.[1]

In summary, in the absence of data demonstrating a benefit from the use of liberal fluid strategies in critically ill patients with ARDS, sepsis or shock and considering that the majority of patients with severe COVID-19 in ICU may be complicated by this affections, a conservative approach has been suggested as fluid strategy in these patients.[14] In patients without shock, also conservative fluid management is recommended to avoid pulmonary edema and consolidation caused by open fluid therapy, which further aggravates oxidative disorders.[20]

It is important to carry out proper conservative administration of fluids while maintaining the average blood pressure and the perfusion of adequate organs with the appropriate use of diuretics and vasopressors. Therefore, it is necessary to assess fluid responsiveness and to evaluate ventricular function during fluid resuscitation.[20] On the basis of adequate fluid replenishment, early use of vasopressors and inotropes, close monitoring of changes in blood pressure, heart rate, urine output, lactic acid, and alkali residues; it is recommended to monitor the hemodynamics of COVID-19 critically ill patients, guide the use of infusion and vasoactive, and optimize tissue perfusion.

With the increase in our understanding of the adverse consequences of aggressive fluid administration and volume overload, conservative liquid strategies could reduce the occurrence of a positive fluid balance in critical ill patients with COVID-19, while ensuring adequate tissue perfusion; however, studies are needed to confirm such an approach and determine with certainty the best fluid strategy in these patients.

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José de Jesús Bohórquez-Rivero[1], Ezequiel García-Ballestas[2], Tariq M. Janjua[3], Luis Rafael Moscote-Salazar[4]

[1]Department of Research, GIBACUS Research Group, Faculty of Medicine, University of Sinú – Cartagena Sectional, [2]Center for Biomedical Research, Faculty of Medicine, University of Cartagena, [4]Latinamerican Council of Neurocritical Care, Colombia; [3]Critical Care Department, Critical Care Medicine, Regions Hospital, Saint Paul, Minnesota, USA

Address for correspondence: Dr. José de Jesús Bohórquez-Rivero, University of Sinú. Tv 54 #41-117, Santillana Campus, 13001, Cartagena de Indias, Colombia.
E-mail: josejbohorquez@gmail.com

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