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Commentary

Mechanisms of Kidney Dysfunction in the Cirrhotic Patient: Non-hepatorenal Acute-on-Chronic Kidney Damage Considerations

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Cirrhosis is a worldwide health problem: by 2019, cirrhosis was associated with 2.4% of global deaths, with obesity and alcohol consumption becoming its leading etiologies as improved outcomes in the treatment of Hepatitis C and hepatitis B virus decreases the number of viral hepatitis associated cirrhosis.

Among patients who live with chronic liver disease, kidney dysfunction spectrum, including kidney frailty, subclinical acute kidney Injury (SAKI), acute kidney injury (AKI), Acute Kidney Disease (AKD), Chronic Kidney Disease (CKD) and End Stage Kidney Disease (ESKD) are among the most common extrahepatic complications along the natural history of cirrhosis.

Given the known nature of the human body as a complex unified homeostatic system, it has been largely recognized that multiple organ involvement is an expected phenomenon in pathologies affecting primarily a specific organ, both because of clinical observation and theoretical biological sense.

However, only in the last decades, advances in molecular biology, imaging technology and large clinical trials have allowed the physiopathological pathways of multiorgan crosstalk to be described.

In cirrhotic patients specifically, kidney involvement has been largely explained in terms of hepatorenal syndrome. However, given the complex natural history of cirrhosis, a myriad of clinical events, as well as newly described histopathological pathways should also be taken into account when evaluating a specific clinical scenario, as multifactorial is the most plausible etiology for most kidney injury events, and mutually exclusive physiopathological pathways are rarely seen.

As an example, during an acute-on-chronic liver failure episode, a single patient may present with both Hepatorenal Syndrome and bile cast nephropathy, while also at risk for contrast-media induced AKI during the diagnostic approach.

In 2020, the manuscript "Mechanisms of Kidney Dysfunction in the Cirrhotic Patient: Nonhepatorenal Acute-on-Chronic Kidney Damage Considerations." briefly summarizes some of the most important non-prerenal, non-HRS considerations regarding acute-on-chronic kidney dysfunction in cirrhotic patients, including renal manifestations related to non-alcoholic steatohepatitis (NASH), viral hepatitis, cardiorenal syndrome, cirrhotic cardiomyopathy, and corticosteroid-deficiency associated renal dysfunction.

The manuscript highlights the importance of multiorgan crosstalk pathways to be considered as interconnected gears to be understood and described when approaching the clinical trajectory of renal function within the natural history of cirrhosis and, more importantly, within the clinical trajectory of multiorgan interaction during a specific patient's clinical course.

As an example, endocrine dysfunction—including thyroid dysfunction, metabolic dysfunction-associated steatohepatitis (MASH), and obesity-related kidney dysfunction—should be considered in both the chronic and acute liver dysfunction follow-up of an obese cirrhotic patient.

Most importantly, a change in the basic clinical paradigm must be taken into account, as modern medicine has made evident the existence of the human body as an open homeostatic system, in which changes in the microbiota, pharmacological interventions, surgical procedures, extracorporeal therapies, and even transplantation physiological consequences must also be considered.

Hopefully, within the years to come, the use of computer systems, novel biomarkers and further understanding of multiorgan crosstalk will make feasible the development of novel, more efficient therapeutic approaches for the surveillance, preservation, and restoration of both liver and kidney function in cirrhotic patients, as well as the replacement of both liver and kidney function by either extracorporeal therapies, bioartificial organs, or transplantation [1-23].

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