Authors’ response

Umgelter and colleagues have reported that there is a general reluctance to treat cirrhotic patients with renal failure with volume resuscitation. Moreover, they are critical of the accuracy of diagnosing hepatorenal syndrome (HRS) using the infusion of pre-defined doses of albumin as recommended in our paper. Finally, they do not seem to share the opinion that HRS, once established, is no longer responsive to simple volume expansion, and therefore suggest investigating a goal-directed approach of treatment. We would like to take the opportunity to expand our discussion on the pathogenesis of HRS as well as on the therapeutic resources.

The fact that volume expansion is an essential component in the prevention and treatment of HRS has been confirmed in the past several years. For example, albumin is able to prevent HRS in patients with spontaneous bacterial peritonitis (SBP), and its prolonged administration is necessary to improve the efficacy of terlipressin or midodrine in reversing HRS type 1. This does not exclude, however, that simple volume expansion is insufficient to correct glomerular filtration rate in such patients.

From a pathogenetic standpoint, there are two types of functional renal failure in cirrhotic patients: one that is caused by an absolute loss of volume, as can occur after over-zealous diuretic use, gastrointestinal bleeding, diarrhoea or other dehydrating events. In these cases, renal failure is regarded as prerenal azotaemia, as hypovolaemia with reduced renal perfusion pressure is the only cause of renal failure. This type of renal failure is easily resolved by correction of the trigger and by volume restoration using albumin as well as crystalloids or colloids. The second type of renal failure is caused by renal vasoconstriction and this is what is defined as HRS. These patients have severe effective hypovolaemia that is not due to absolute volume loss, but rather to a maldistribution of the total blood volume with an excess of blood preferentially located in the dilated splanchnic vessels. The absolute blood volume of these patients is not necessarily decreased and the circulatory dysfunction is attributed to an exaggerated stimulation of cytokines, many of which are vasoconstrictors, such as the one that occurs with bacterial peritonitis. The reason why fluid administration corrects prerenal azotaemia but not HRS is probably due to the fact that in prerenal failure, the intravenous fluids administered are partly retained in the central circulation, thereby improving the total and the effective blood volume; whereas in the latter, the intravenous fluids are rapidly sequestered into the splanchnic circulation, or third spaced into the peritoneal cavity as increased ascites, rather than staying in the circulation to improve the effective blood volume. Accordingly, the response to blood volume expansion in cirrhotic patients has become one of the widely accepted criteria to separate HRS from other forms of functional renal failure.

Recent investigations suggest that, in addition to peripheral vasodilatation, the already elevated cardiac output as observed in patients with decompensated cirrhosis, is relatively insufficient for the extent of arterial vasodilatation and this may also contribute to the effective hypovolaemia in cirrhotic patients. The issue deserves new accurate investigations.
other simple measures such as plasma sodium and urine excretion could also be of help.

Francesco Salerno,1 Alexander Gerbes,2 Pere Gines,3 Florence Wong,4 Vicente Arroyo5

1 Department of Internal Medicine, Policlinico IRCCS San Donato, University of Milan, Italy; 2 Department of Internal Medicine II, Klinikum of the Ludwig-Maximilians-University/ Großhadern, University of Munich, Germany; 3 Liver Unit, Hospital Clinic, University of Barcelona, Spain; 4 Department of Medicine, Division of Gastroenterology, Toronto General Hospital, University of Toronto, Canada; 5 Liver Unit, Hospital Clinic, University of Barcelona, Spain

Correspondence to: Francesco Salerno, Department of Internal Medicine, Policlinico IRCCS San Donato, University of Milan, Italy, Via Morandi, 30, 20097 San Donato (MI), Italy; francesco.salerno@unimi.it

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Authors' response
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