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Reply to: "New imaging assisted methods for liver fibrosis quantification: Is it really favorable to classical transient elastography?"

Non-invasive assessment of liver fibrosis with impulse elastography: Comparison of Supersonic Shear Imaging with ARFI and FibroScan.

To the Editor:

We read with great interest comments by Dr. Lanthier *et al.* [1] regarding our article published in *Journal of Hepatology* [2]. We thank the authors for their kind interest in our work and welcome the opportunity to clarify points they raised.

First, in our study we did not apply nor even mention reliability criteria regarding the Supersonic Shear Imaging (SSI) technique. As Dr. Lanthier said, SSI is quite a recent technique, and to date, no study has focused on the description or definition of reliability criteria for this technique. In our study, interquartile range (IQR)/liver stiffness measurement (LSM) was <0.10 in 207 patients (69%), between 0.10 and 0.30 in 91 (30%), and >0.30 in 3 patients (1%). So, it is quite obvious that the reliability criteria of FibroScan® are probably not applicable to SSI, but we believe that the definition of such criteria requires a large multicentre study and should not be performed too hastily in a single centre study.

Second, we'd like to clarify the key point that the failure rate of FibroScan® in our study is low, around 2.6%, because the XL probe was used for obese patients (i.e. with body mass index $\geqslant$30 kg/m^2) (30% of patients of our study). In our experience, the failure rate of SSI is very close to that of the M probe of FibroScan®. Indeed, we can notice that the failure rate of SSI in our study (10.4% in the whole population; 28% for obese patients but only 2.6% for others) is close to the failure rate of the M probe described in the study by de Lédinghen *et al.* [3] among a patient population quite representative of our study population although with a slightly lower BMI (8.4% in the whole population; 26% for obese patients but only 2.5% for others). Unfortunately, as for ARFI and FibroScan®, the reliability of liver stiffness measurement with SSI is dependant on the quality of the shear wave transmission, which rapidly decreases as weight increases. This is likely to be evident in SSI and ARFI techniques where operators can notice the strong relationship between the reliability of the LSM and the quality of the spatial resolution on the B-mode US image.

Finally, as we've discussed, we agree that further studies are needed assessing the diagnostic performances and limits of SSI in specific aetiologies of chronic liver diseases. However, there is mounting evidence that SSI should be considered as an accurate and promising elastography technique in the field of chronic liver diseases.

To conclude, we are living in an era of great and frequent technological innovations, which is particularly exciting, but we have the duty to analyse, criticize and finally validate as quick as possible each new progress in order to ultimately provide the best diagnosis and treatment for all patients.

Conflict of interest

These authors have declared they have nothing to disclose regarding funding and conflict of interest with respect to this manuscript.

References

[1] Lanthier N, Stärkel P, Horsmans Y. New imaging assisted methods for liver fibrosis quantification: is it really favorable to classical transient elastography? J Hepatol 2015;63:765–766. http://dx.doi.org/10.1016/j.jhep.2015.04.027.
[2] Cassinotto C, Lapuyade B, Mouries A, Hiriart JB, Vergniol J, Gaye D, et al. Non-invasive assessment of liver fibrosis with impulse elastography: comparison of Supersonic Shear Imaging with ARFI and FibroScan. J Hepatol 2014;61:550–557. http://dx.doi.org/10.1016/j.jhep.2014.04.044.
[3] de Lédinghen V, Wong VW, Vergniol J, Wong GL, Foucher J, Chu SH, et al. Diagnosis of liver fibrosis and cirrhosis using liver stiffness measurement: comparison between M and XL probe of FibroScan. J Hepatol 2012;56:833–839. http://dx.doi.org/10.1016/j.jhep.2011.

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Albumin infusion in cirrhotic patients with infections other than spontaneous bacterial peritonitis: End of the story?

To the Editor:

We read with interest the recent manuscript by Thevenot *et al.* [1] which adds data to the debate on the potential beneficial effect of albumin administration during episodes of infections other than spontaneous bacterial peritonitis (SBP) in cirrhotic patients [2–4].

In this multicentre study, 193 cirrhotic patients with infections other than SBP, were randomly assigned to receive albumin infusion or no treatment in addition to antibiotics. The primary outcomes were renal failure and mortality rates. The study failed to show any beneficial effect on these outcomes, although albumin infusion delayed the onset of renal failure. However, in our opinion, some bias could have influenced the results. First, the prevalence of ascites was significantly higher in the patients randomized to albumin and antibiotics than in the patients assuming antibiotics alone (75.8 *vs.* 59.6%; $p = 0.017$). The development of infection and the consequent increase in vasodilatation may have influenced the rate of renal failure and prognosis of the former group differently from the control group in which the number of patients with ascites was lower. Second, the success or failure of antibiotic therapies were not analyzed and, as we know, the course of infections is a further important parameter for the prognosis of cirrhotic patients [5,6]. Third, as also discussed by the authors, many violations occurred in the protocol and 17 patients in the control group also received albumin for large volume paracentesis during the first week.

Thus, in our opinion, the results of the present study should not discourage further investigations in cirrhotic patients with infections also considering the wide range of potential benefits of albumin administration in this setting (antioxidant function, immunomodulation, anti-inflammatory activity and transport of many endogenous and exogenous substances), in addition to its well-known effect as plasma expander [7]. Among these additional properties, in particular, the effect of the albumin infusion during the therapy with moderately/highly protein-bound antibiotics should also be evaluated, considering the relevant role of hypoalbuminemia on the pharmacokinetics of these antibiotics [8].

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

References

[1] Thévenot T, Bureau C, Oberti F, Anty R, Louvet A, Plessier A, et al. Effect of albumin in cirrhotic patients with infections other than spontaneous bacterial peritonitis: a randomized trial. J Hepatol 2015;62:822–830.

[2] Guevara M, Terra C, Nazar A, Solà E, Fernández J, Pavesi M, et al. Albumin for bacterial infections other than spontaneous bacterial peritonitis in cirrhosis. A randomized, controlled study. J Hepatol 2012;57:759–765.

[3] Thevenot T, Monnet E, Di Martino V. Effect of albumin on survival in septic cirrhotic patients other than spontaneous bacterial peritonitis. The question remains open. J Hepatol 2013;58:638–639.

[4] Guevara M, Arroyo V, Ginès P. Reply to: "Effect of albumin on survival in septic cirrhotic patients other than spontaneous bacterial peritonitis. The question remains open". J Hepatol 2013;58:640.

[5] Arvaniti V, D'Amico G, Fede G, Manousou P, Tsochatzis E, Pleguezuelo M, et al. Infections in patients with cirrhosis increase mortality four-fold and should be used in determining prognosis. Gastroenterology 2010;139:1246–1256.

[6] Merli M, Lucidi C, Giannelli V, Giusto M, Riggio O, Falcone M, et al. Cirrhotic patients are at risk for health care-associated bacterial infections. Clin Gastroenterol Hepatol 2010;8:979–985.

[7] Caraceni P, Domenicali M, Tovoli A, Napoli L, Ricci CS, Tufoni M, et al. Clinical indications for the albumin use: still a controversial issue. Eur J Intern Med 2013;24:721–728.

[8] Roberts JA, Abdul-Aziz MH, Lipman J, Mouton JW, Vinks AA, Felton TW, et al. Individualised antibiotic dosing for patients who are critically ill: challenges and potential solutions. Lancet Infect Dis 2014;14:498–509
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Reply to "Albumin infusion in cirrhotic patients with non-SBP infections: End of the story?"

To the Editor:

We greatly appreciate the comments by Lucidi *et al.* [1]. Firstly, we acknowledge that, despite well-conducted randomization to reduce the risk of selection bias at trial entry [2], the presence of ascites was more frequently reported in the albumin (ALB) group as compared with the control group (75.8 *vs.* 59.6; $p = 0.017$). We have to remember that using an alpha risk of 5%, the probability of there being no imbalance between groups for any one baseline characteristic is 0.95. Assuming the characteristics are independent, there is a non-negligible $1 - (0.95)^n$ probability of observing a significant imbalance between groups when comparing n baseline characteristics. For instance, in Table 1 showing the baseline characteristics of patients [2], there were at least 10 independent variables meaning that the chance of at least one statistically significant imbalance was 0.40. In order to improve the precision of the treatment effect estimate, and to avoid any confounding, the two Cox multivariate analyses performed to determine predictive variables associated with renal failure and death at 3 months were adjusted for ascites, which was no longer significant.