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Commentary

# Erectile dysfunction in patients with liver cirrhosis

O. Riggio, L. Ridola, S. Gioia, S. Nardelli*

*Dept. of Translational and Precision Medicine, "Sapienza" University of Rome, Rome, Italy*

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Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual performance [1]. The reported prevalence of ED ranges between 10% and 50% in the general population and is related to age, overall health status and emotional function [2,3]. Based on this high prevalence of ED and the progressive importance given to health related quality of life (HRQoL) of the patients, several investigations into the clinical and pathophysiologic mechanisms of sexual dysfunction have been carried out during the last decade [4,5]. Moreover, simple and well-validated tools for the evaluation of ED [6] are available such as the International Index of Erectile Function (IIEF5), which is now considered the gold standard for the diagnosis and evaluation of symptom's severity.

In the last years, many studies have reported an increased prevalence of ED in chronic liver diseases (chronic hepatitis C or B, alcoholic consumption or non alcoholic steatohepatitis) [7,8]. Among cirrhotic patients, the prevalence of ED is variable, depending on the severity of the disease and associated conditions such as diabetes, metabolic syndrome, heart diseases, smoking, chronic alcohol consumption and obesity [9]. Other important determinants may be psychological conditions, such as anxiety or depression, frequently observed in cirrhotic patients [10] as well as medications potentially acting on penile erection such as non selective beta-blockers, diuretics or antidepressants.

In a recent study by Paternostro et al. [11] the IIEF5 questionnaire was applied to 110 cirrhotic patients, thirty of them sexually inactive. Among the 80 sexually active cirrhotic patients, the variables independently associated to ED were arterial hypertension and diabetes but also MELD score and HVPG, pointing out the role of liver function and portal hypertension on sexual abnormalities. Interestingly, in this study, no significant difference in the distribution of beta-blockers intake was found among patients with or without ED, in line with the results of a metanalysis previously published. [12]

Recently, on this topic two more studies, conducted in Italy and in France, both published on DLD, became available.

In the first one, Maimone et al. [13] submitted 102 compensated cirrhotic patients (Child A) with a mean age of $63 \pm 10$ years, to 3 different questionnaires: the IIEF5 for ED detection, the Centre of Epidemiologic Studies Depression (CES-D) scale for the presence of depressive syndrome and the ANDROTEST for the presence of hypogonadism. The prevalence of ED resulted to be detectable in 56%, of the cirrhotic patients, similar to that expected in the general population of similar age. In this cohort, neither the clinical (varices, ascites, hepatocellular carcinoma) and the biochemical parameters related to the liver disease, nor the use of drugs (non selective beta-blockers, antihypertensive agents or diuretics), testosterone level or depressive symptoms were associated with ED. Older age (66 vs 60 years) and lower haemoglobin levels (13.6 vs 12.4 g/dl) were found in patients with ED vs no-ED respectively, and resulted to be the only two independent predictors of sexual dysfunction.

The second study by Phylonenco et al. [14] included cirrhotic patients with a wider range of liver failure and confirmed that the factors independently associated to ED were age and severity of liver disease. The novelty of the study consisted in the evaluation of minimal hepatic encephalopathy (MHE), as a possible risk factor for the development of ED, diagnosed by psychometric hepatic encephalopathy score (PHES) and the critical flicker frequency. In fact, MHE is known to be related to a poor quality of life and to other subtle modifications in behaviour such as depression, anxiety and alexitimia [10]. The study shows that patients with abnormal neurocognitive tests had a significantly higher prevalence of ED. This observation was not reported previously and opens an interesting perspective, especially because drugs able to reverse the cognitive impairment in liver cirrhosis [15] might consequently affect ED. In particular, the authors found that in the subgroup of patients with Child-Pugh A cirrhosis (n = 25), 100% of the patients with MHE

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* Corresponding author at: Dept. of Translational and Precision Medicine, Gastroenterology Unit, Sapienza University of Rome, Viale dell'Università 37, 00161, Roma, Italy.
*E-mail address:* nardelli.silvia@gmail.com (S. Nardelli).

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had ED (n = 16). Moreover, a statistically significant, although weak, correlation (r = 0.2459, p = 0.03) between PHES and IIEF5 was found. However, in the multivariate analysis, MHE was not identified as an independent risk factor for ED being age and liver failure the only 2 parameters associated with ED. These controversial results may be due to the small number of cases and to the consequent difficulty in distinguishing between the effects of two very well correlated variables such liver dysfunction and cognitive impairment. Therefore, at the moment, the association between neurocognitive impairment and erectile dysfunction proposed in the paper's title remains only an interesting hypothesis, especially because the cognitive impairment of cirrhosis, differently from age and other identified factors, is potentially treatable. Further studies aimed first at confirming this hypothesis on bigger series of cirrhotic patients and using other diagnostic tools such as neurophysiologic (evoked potentials or EEG) or computerized tests and especially aimed at studying the effect of the resolution of cognitive impairment on ED are therefore needed.

In conclusion, further investigations, with age matched control group and adequate sample size, are strongly necessary to estimate both the real prevalence of erectile dysfunction in cirrhosis and its correlation with the severity and complications of the disease. In future studies the presence of sarcopenia, which has been related to erectile dysfunction in diabetic patients [16], commonly observable in cirrhotic patients and strongly associated to the patients' cognitive impairment [17] should be also taken into consideration.

An important observation of the Phylonenco et al. study is that, despite the high prevalence of ED (85%), only 4 patients (4%) consulted a specialist for their specific problem, suggesting that ED is not often assessed and that patients do not readily discuss these symptoms during medical consultations. Given this background and the growing importance of quality of life in patients affected by chronic diseases, including liver cirrhosis, the evaluation of emotional aspects and sexual activity becomes mandatory in the overall management of the patients, in order to find the best customized treatment.

## Conflict of interest declaration

None declared.

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