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3 The role of hepatic enzymes in Crohn's disease

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32 Abstract

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64 Keywords: biopsy, Crohn disease, elastography, histology, inflammatory bowel

65 diseases, liver

66 Sir,
67 a systematic review has reported that, in Crohns' disease (CD) patients, the prevalence of cholelithiasis ranged
68 from 11% to 34%, that of primary sclerosing cholangitis (PSC) from 1.2% to 3.4%, that of fatty liver
69 disease 23% and hepatic amyloidosis occurred in <1% [1]. In a prospective, single-blind study we evaluated the
70 prevalence of histological changes in the liver of patients with CD, without alterations of both liver biochemical
71 tests and ultrasound, and their prognostic significance. The patients underwent liver biopsy at the time of
72 intestinal resection. Exclusion criteria were a known liver disease. Thereafter, patients were clinically monitored
73 every 6 months, upper abdomen ultrasound was performed at least every 12 months. Finally, after a mean
74 interval of 14 years from liver biopsy, these patients were assessed using the Fibroscan[®] (Echosens[®], Paris,
75 France). Ultrasound examination in the pre-operative step showed steatosis in 10 (29%) patients. At biopsy
76 specimens alterations in 60% of patients, without serious liver injuries, were found. No evidence of a significant
77 liver damage progression after a mean period of 14 years were found. The average result (5.2 ± 1.2 kPa)
78 obtained performing Fibroscan[®] was comparable to that (5.30 ± 1.45 kPa, $p = 0.63$) reported in healthy subjects
79 [2].

80 A recent interesting retrospective study was performed in 383 CD patients newly diagnosed (not treated). One
81 patient with chronic liver disease (small duct PSC) was excluded. Of the 383 patients included in this study, 131
82 had liver test abnormalities (34.1%), but liver diseases were not found, apart from liver steatosis in 6% of
83 patients [3] (*versus* 29% in the previous study [2]).

84 The two studies [2, 3] agree that, considering the cost/benefit ratio, patients with CD should be considered as
85 healthy from the liver perspective, without the need for additional biochemical and instrumental examinations
86 than the general population, unless the presence of clinical or biochemical suspicion of liver disease.

87 In the more recent study [3], however, the authors found that, patients with liver test abnormalities, without an
88 hepatic disease, more often developed complicated CD behaviour and more often needed hospitalization or
89 surgery within 5 years of diagnosis than patients without liver test abnormalities. Patients with a C-reactive
90 protein (CRP) <16 mg/L but with liver test abnormalities had a higher risk of developing complicated disease
91 compared to those without liver test abnormalities. This demonstrates that the presence of liver test abnormalities
92 does not merely reflect a higher CRP concentration, but may be a more sensitive indicator of an increased risk of
93 complicated disease behaviour than CRP. At multivariate analysis, the presence of liver test abnormalities was
94 independent risk factors for complicated disease behaviour; additionally, the presence of liver test abnormalities

95 was independently associated with an increased risk of hospitalizations (HR 1.7, $p = 0.023$) as well as surgery
96 (HR 2.3, $p = 0.015$) [3].

97 In conclusion, in the absence of a known liver disease or of a risk factor for hepatic injury (e.g., a potentially
98 hepatotoxic drugs), liver enzymes in CD do not need to be routinely measured. However, when increased, liver
99 enzymes could predict a more aggressive CD behaviour.

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101 **Compliance with ethical standards**

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103 **Funding** None to declare.

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105 **Conflict of Interest** None to declare.

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107 **Ethical approval** The study was conducted in accordance with ICH Good Clinical Practice
108 guidelines, the Declaration of Helsinki, and local laws and regulations.

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110 **Informed consent** Informed consent due to the observational study has been obtained in the
111 cited studies.

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120 **References**

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