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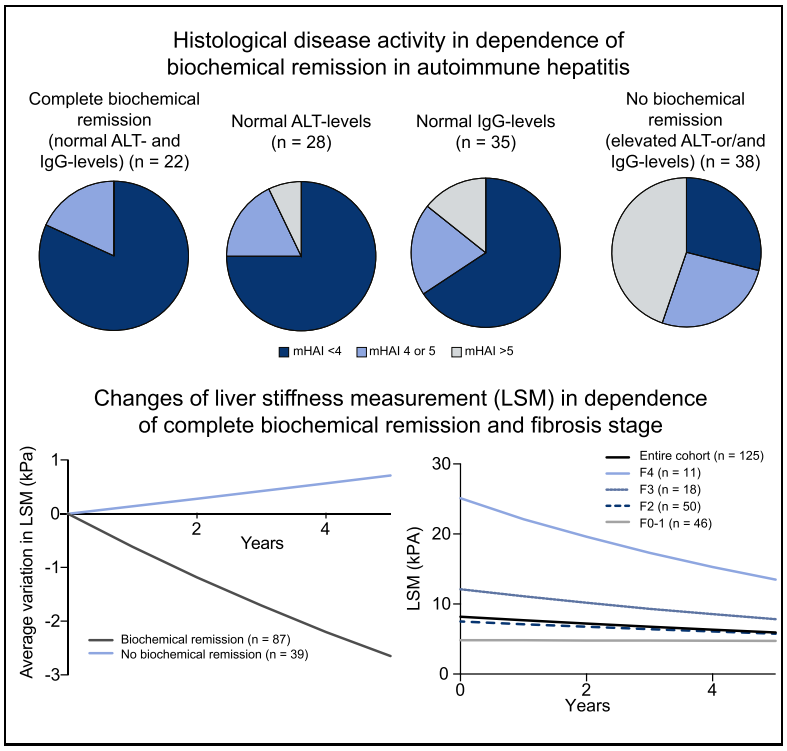
Research Article
Cholestasis and Autoimmune Diseases

Usefulness of biochemical remission and transient elastography in monitoring disease course in autoimmune hepatitis

Graphical abstract



Highlights

- Complete biochemical remission is a reliable surrogate of low histological disease activity.
- Transient elastography is a non-invasive tool to monitor fibrosis development in autoimmune hepatitis.
- These study results may improve treatment monitoring in patients with autoimmune hepatitis.
- Patients with autoimmune hepatitis have a high chance of fibrosis regression if inflammation is suppressed.

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Lay summary

Autoimmune hepatitis is an inflammatory disease of the liver, which often progresses to cirrhosis if left untreated or in the case of insufficient treatment response. Current guidelines have defined biochemical remission (normalisation of biochemical markers for liver inflammation) as a major goal in the treatment of AIH. However, data on the prognostic relevance of this definition are scarce. Herein, we demonstrate that the current definition of biochemical remission is a reliable surrogate for low disease activity on histological assessment and for a beneficial long-term disease course. In addition, we establish transient elastography, a non-invasive ultrasound-based method of measuring scarring of liver tissue, as a reliable tool to monitor disease course in AIH.

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Usefulness of biochemical remission and transient elastography in monitoring disease course in autoimmune hepatitis

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Background & Aims: Liver fibrosis regression but also progression may occur in patients with autoimmune hepatitis (AIH) under treatment. There is a need for non-invasive surrogate markers for fibrosis development in AIH to better guide immunosuppressive treatment. The aims of the study were to assess the impact of complete biochemical remission defined as normalisation of aminotransferases and IgG on histological activity and fibrosis development, and the value of repeat transient elastography (TE) measurement for monitoring disease progression in AIH.

Methods: A total of 131 liver biopsies from 60 patients with AIH and more than 900 TE from 125 patients with AIH, 130 with primary biliary cholangitis (PBC) and 100 with primary sclerosing cholangitis (PSC), were evaluated. Time intervals between TE were at least 12 months. Patients with AIH were treated for at least six months at first TE.

Results: In contrast to PBC and PSC, a decrease of liver stiffness (LS) was observed in the whole group of patients with AIH (−6.2%/year; 95% CI −12.6% to −0.2%; $p = 0.04$). The largest decrease of LS was observed in patients with severe fibrosis at baseline (F4: −11.7%/year; 95% CI −19% to −3.5%; $p = 0.006$). Complete biochemical remission was strongly linked to regression of LS ("remission": −7.5%/year *vs.* "no remission": +1.7%/year, $p < 0.001$). Similarly, complete biochemical remission predicted low histological disease activity and was the only independent predictor for histological fibrosis regression (relative risk 3.66; 95% CI 1.54–10.2; $p = 0.001$). Patients with F3/F4-fibrosis, who remained in biochemical remission showed a considerable decrease of fibrosis stage (3.7 ± 0.5 to 1.8 ± 1.7; $p = 0.007$) on histological follow-up.

Conclusions: This study demonstrates that complete biochemical remission is a reliable predictor of a good prognosis in AIH and leads to fibrosis regression that can be monitored by TE.

Lay summary: Autoimmune hepatitis is an inflammatory disease of the liver, which often progresses to cirrhosis if left untreated or in the case of insufficient treatment response. Current guidelines have defined biochemical remission (normalisation of biochemical markers for liver inflammation) as a major goal in the treatment of AIH. However, data on the prognostic relevance of this definition are scarce. Herein, we demonstrate that the current definition of biochemical remission is a reliable surrogate for low disease activity on histological assessment and for a beneficial long-term disease course. In addition, we establish transient elastography, a non-invasive ultrasound-based method of measuring scarring of liver tissue, as a reliable tool to monitor disease course in AIH.

Introduction

Autoimmune hepatitis (AIH) is a chronic disease, which harbours a significant risk of fibrosis progression when treatment is insufficient.[1,2] Some patients may progress despite immunosuppressive treatment.[3,4] Therefore, AIH patients require close, life-long follow-up. In daily practice, treatment monitoring is mainly guided by biochemical surrogate markers for hepatic inflammation. Besides serum aminotransferases, it has been demonstrated that selectively elevated IgG levels also indicate ongoing inflammatory activity in AIH.[5] Therefore, complete biochemical remission has been defined as repeatedly normal serum aminotransferase and IgG levels. Although the prognostic relevance of this definition is uncertain, current treatment guidelines have incorporated this definition as the goal of immunosuppressive treatment in AIH.[6–8] Since complete biochemical remission is hard to achieve in some patients and requires high doses of immunosuppressants in others, it is important to validate the prognostic significance of this definition.

Monitoring treatment response and disease progression by biochemical markers may have limitations, since a proportion of patients may display relevant inflammatory activity on liver histology despite normal biochemical markers.[4,5] In addition, AIH is characterised by a fluctuating disease course, which may mask repeated flares and disease progression if laboratory values are controlled infrequently. Therefore, although not generally recommended by current guidelines, many experts per-

Keywords: Autoimmune hepatitis; Biochemical remission; Fibrosis regression; Transient elastography; Fibroscan; Liver stiffness; IgG.
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