Diagnostic value of liver stiffness as marker of hepatic amyloid deposition in systemic AL amyloidosis

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INTRODUCTION

Liver involvement is common in patients with systemic AL amyloidosis and is often reflected by increased levels of alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT), however these are nonspecific markers. ^{123}I-labeled serum amyloid P component (SAP) scintigraphy is a specific and sensitive method to detect liver amyloid deposition but is not widely available. Transient elastography is a rapid, non-invasive and reproducible method for measuring liver stiffness (LS) (**figure 1**). Amyloid deposition in the liver increases LS.

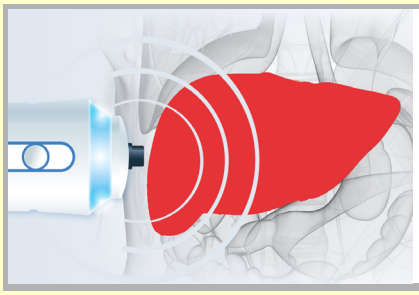

Figure 1. Transient Elastography: measurement of liver stiffness.
A 50-MHz wave is passed into the liver from a small transducer on the end of an ultrasound probe. Shear wave (m/s) as it passes through the liver is measured. Shear wave velocity can be converted into liver stiffness (kPa).

OBJECTIVE

To assess the diagnostic value of LS for liver involvement in AL amyloidosis using SAP-scintigraphy as gold standard.

PATIENTS AND METHODS

LS was measured using transient elastography in 43 consecutive patients with AL amyloidosis visiting the outpatient clinic of the Groningen Amyloidosis Centre of Expertise. SAP scintigraphy, laboratory assessments including ALP, GGT, N-terminal pro-B-type natriuretic peptide (NTproBNP) and fat aspiration biopsy for semi-quantification and typing of amyloid was performed in all patients. SAP liver uptake was visually scored and semi-quantified.

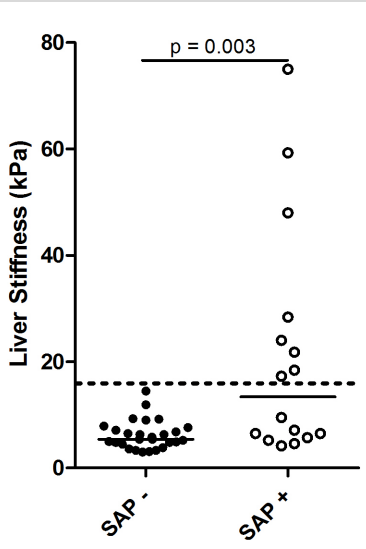

Figure 2. LS in patients with (SAP+) and without (SAP-) liver involvement based on visually scored SAP-uptake. The middle lines represent the median. The dashed line represents the cut-off value of 15.9 kPa.

RESULTS

Median LS was significantly increased in AL patients with liver involvement compared to patients without liver involvement (based on visually-scored SAP-uptake: 13.4 kPa vs 5.4 kPa; p=0.003, based on semi-quantified SAP-uptake: 9.5 kPa vs 5.6 kPa; p=0.009) (**figure 2**). LS was significantly related to NT-proBNP (r=0.3, p=0.03), load of amyloid in fat tissue (r=0.4, p=0.009), ALP (r=0.4, p=0.005), GGT (r=0.7, p<0.001) and semi-quantitative SAP-uptake (r=0.5, p=0.001) and visually scored SAP-uptake (r=0.5, p<0.001). In a linear regression model using semi-quantitative SAP-uptake as dependent variable and ALP, GGT, NTproBNP and amyloid load in fat tissue as independent variables, LS is an independent predictor. A cut-off value of 15.9 kPa yielded a specificity of 100% with a sensitivity of 50% for detecting liver involvement based on visually-scored SAP-uptake (AUC 0.78, p=0.003) (**figure 3**) and a specificity of 96% with a sensitivity of 47% for detecting liver involvement based on semi-quantitative SAP-uptake (AUC 0.75, p=0.008).

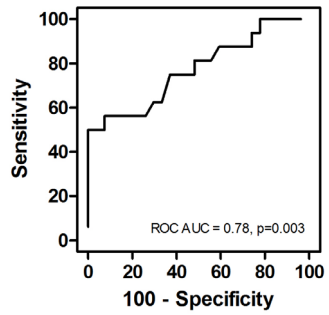

Figure 3. ROC curve comparing the visually scored SAP uptake (positive or negative) and LS value in kPa. A cut-off value of 15.9 kPa yielded a specificity of 100% with a sensitivity of 50% for detecting liver involvement.

CONCLUSIONS

- **LS is increased in AL amyloidosis patients with SAP-scintigraphy proven liver involvement.**
- **The finding of a high LS value (>15.9 kPa) is specific for hepatic amyloid deposition**
- **A LS value <15.9 does not exclude liver involvement.**
- **LS as marker of for hepatic amyloid deposition has additional value compared to ALP en GGT.**
- **The value of LS as individual follow-up marker will be investigated**

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GUARD