On the assessment and impact of liver fibrosis in patients with chronic Hepatitis C

Akademisk avhandling

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This thesis is based on the following studies

I. Ydreborg M, Söderström A, Håkansson A, Alsiö Å, Arnholm B, Malmström P, Hellstrand K, Westin J and Lagging M. Look-back screening for the identification of transfusion-induced hepatitis C virus infection in Sweden. *Scand J Infect Dis. 2011 Jul;43(6-7):522-7.*

II. Ydreborg M, Westin J, Lagging M, Castedal M, Friman S. Impact of donor histology on survival following liver transplantation for chronic hepatitis C virus infection: a Scandinavian single-center experience. *Scand J Gastroenterol. 2012 Jun;47(6):710-7.*

III. Ydreborg M, Lisovskaja V, Lagging M, Brehm Christensen P, Langeland N, Rauning Buhl M, Pedersen C, Mørch K, Wejstål R, Norkrans G, Lindh M, Färkkilä M, Westin J. A novel fibrosis index comprising a non-cholesterol sterol accurately predicts HCV-related liver cirrhosis. *Submitted*

IV. Ydreborg M, Westin J, Rembeck K, Lindh M, Norrgren H, Holmberg A, Wejstål R, Norkrans G, Cardell K, Weiland O, Lagging M. Impact of IL28B-related single nucleotide polymorphisms on liver transient elastography in chronic hepatitis C infection. *PLoS One, 2013. In press*

UNIVERSITY OF GOTHENBURG

On the assessment and impact of liver fibrosis in patients with chronic Hepatitis C

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Abstract:
Hepatitis C virus (HCV) infection is associated with increased risk of severe liver damage, cirrhosis, and hepatocellular carcinoma (HCC). Despite pending highly efficacious HCV treatment, assessment of liver damage will remain important for prognostication, treatment decisions, and indication for HCC surveillance. The aims of this thesis was to evaluate (i) which patients benefit from look-back screening for HCV, (ii) factors impacting on survival in the HCV-associated liver transplant setting, (iii) non-invasive diagnostic markers of HCV-associated cirrhosis and (iv) host genetic factors impacting on HCV-associated fibrosis.

In **paper I**, we identified chronic HCV infection in 113 out of 13,573 subjects (0.8%) screened for HCV following blood transfusion prior to 1992. The majority of those individuals were eligible for therapeutic intervention. Additionally, 73% of the identified subjects were women, often infected following transfusions during childbirth. Thus, screening for HCV among recipients of blood transfusions prior to 1992 is meaningful.

In **paper II** we evaluated survival among 84 patients who underwent liver transplantation for HCV-related liver disease from 1992 to 2006. We found that portal inflammation and fibrosis in the donor liver may deleteriously affect both patient and graft survival. Thus, pre-transplant evaluation of donor histopathology may be of value in the selection of donors for transplantation of HCV positive individuals, especially among older donors.

In **paper III**, we created a new model for prediction of liver cirrhosis in a cohort of 278 patients comprising age, body mass index (BMI), platelet count, prothrombin-INR and D7-lathosterol. The model was validated in an independent set of 83 patients and could confidently predict cirrhosis using the novel index, referred to as the Nordic Liver Index (NoLI).

In **paper IV**, we noted an association between CC carriage at *rs12979860* and more pronounced liver damage among HCV genotype 3 infected patients in a cohort of 771 patients with HCV infection which suggest that *IL28B* may differentially regulate the course of HCV infection across genotypes.

Keywords: Hepatitis C virus; blood transfusion; liver fibrosis; cirrhosis; histopathology; liver transplantation; survival; Index; Biochemical markers; Non-invasive; AUROC; Genotype 1; Genotype 3; IL28B; Liver stiffness measurement; Transient Elastography; Liver Histology

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