Liver Disease: Developments in the Understanding and Assessment of Liver Fibrosis

According to recent statistics [1] deaths from liver disease have risen by 40% between 2001 and 2012 and the disease is the only major disease group in which annual deaths are on the rise. With this in mind it becomes increasingly important to measure liver fibrosis, the scarring process that represents the liver's response to injury or disease. Liver fibrosis is the final common pathway of all chronic liver disease (CLD), and most of these liver diseases are asymptomatic and the patient is unaware of the symptoms until it is often too late.

Substantial work has gone into developing new treatments for the major causes of liver disease which are alcohol abuse, viral hepatitis B and C infections and non-alcoholic fatty liver disease (NALFD). If detected early enough, most causes of liver diseases are treatable. It is therefore important that changes are put in place to diagnose and treat those with early signs of the condition.

Professor William Rosenberg, FRCP, Peter Scheuer Chair of Liver Diseases at University College London, recently shared his thoughts on why it is so important to measure liver fibrosis. "Once a diagnosis of liver disease has been made, clinicians need to determine the extent of the liver damage. A lot of work has gone in to developing new treatments for the major causes of liver disease, yet they are often very costly and have side effects, making it increasingly important for the clinician to decide how bad the liver disease is from the outset. Once treatment has been determined, clinicians then have an on-going need for a biomarker that can tell them accurately whether or not the treatment is working."

Standards in Diagnosing Liver Fibrosis

The current standard of care to assess liver fibrosis is an invasive liver biopsy. Numerous problems with obtaining and interpreting liver biopsies have fuelled the search for additional methods for assessing liver fibrosis severity. Direct serum biomarkers of liver fibrosis are proving increasingly attractive for liver fibrosis assessment because they are minimally invasive and can be run on fully-automated testing platforms.

Professor Rosenberg explains the range of tests currently available. "The test we have traditionally had at our hands has been liver biopsy. This has been the only established reference test to quantify liver fibrosis, but it is an uncomfortable, daunting experience for the patient and an expensive process for the healthcare system due to the sheer number of specialists and staff required to obtain, prepare, and process a biopsy. In effect, the biopsy represents 1/50,000 of the "best organ in the body". Others have also compared the process to removing a single brick from a house in order to determine which colour you've painted your hall."

A number of non-invasive tests exist, and extensive work has gone into the development of techniques such as imaging, ultrasound tests and elastography. These solutions all have their limitations, particularly when dealing with the large number of cases of obesity-related liver disease. The community has therefore been looking towards alternatives, such as blood tests, which can be used consistently across multiple patient groups.

Professor William Rosenberg, FRCP, Peter Scheuer Chair of Liver Diseases, University College London outlines the importance of measuring liver fibrosis at a recent Siemens Healthcare Diagnostics seminar

Working Towards the Enhanced Liver Fibrosis (ELF™) Test

The European Association for the Study of the Liver (EASL) approves use of non-invasive methods instead of liver biopsy to assess the degree of liver fibrosis in hepatitis C patients. The recently-introduced ADVIA Centaur ELF test [2] from Siemens Healthcare Diagnostics is a simple, standardised and routine blood test that measures the severity of liver fibrosis and is clinically validated in viral hepatitis, NAFLD and alcoholic patient groups.

The ELF score combines three serum biomarkers: hyaluronic acid (HA), procollagen III N-terminal peptide (PIIINP) and tissue inhibitor of matrix metalloproteinase 1 (TIMP-1). Each ELF test component is standardised to ensure reproducible analytical and clinical quality, and is designed and validated for the sole purpose of liver fibrosis assessment.

Positive Outcomes in Sight for the Future

Professor Rosenberg further explains, "The discovery of the ELF markers represents a significant step forward in the diagnosis of patients with liver disease; it has potential to save tens of thousands of lives if adopted across England. We have found the test to perform particularly well in alcoholic liver disease and fatty liver disease, with much better prognostic abilities than a liver biopsy. When looking at patients who had undergone a liver transplant for hepatitis C, studies comparing non-invasive tests to liver biopsies and vascular resistance of liver fibrosis showed the ELF test to perform the best."

He concludes, "The test is currently being evaluated by certain Clinical Commissioning Groups (CCGs) but a real lack of awareness within the market means the test is not yet widely used. Clinicians must not only prepare for wider use of the test, but proactively find out where it sits locally and educate colleagues on the benefits."

The All-Party Parliamentary Hepatology Group (APPHG) recently recommended [1] that liver function tests should become part of standard medical assessments alongside blood pressure and urine tests. This came alongside statistics that more than 30 people a day are dying of liver disease, most of which is preventable and treatable.

We are at a time when the spotlight is on liver disease due to the rising numbers of patients suffering from this disease. More discussion and research is inevitable as liver disease is treated as a priority area by the Department of Health. The evolution of simple and effective non-invasive tests will continue, and it is hoped that they will be adopted across the UK as standard clinical practice with the emergence of more evidence on how they save time, money and improve outcomes compared to traditional invasive methods. We all wait for results of the current evaluations to start the ball rolling.

1. Liver Disease: Today's complacency, tomorrow's catastrophe, The All-Party Parliamentary Hepatology Group (APPHG), March 2014, http://appghep.org.uk.dedi452.your-server.de/download/report/APPHG%20Inquiry%20into%20Outcomes%20in%20Liver%20Disease,%20March%202014.pdf

2. The ADVIA Centaur ELF test from Siemens Healthcare Diagnostics, http://www.healthcare.siemens.co.uk/clinical-specialities/liver-disease/elf-test-now-avail#