

## BACKGROUND

Chronic liver disease is currently staged into five METAVIR fibrosis categories F0 to F4 with F0 designating normal and F4 cirrhosis. Fibrosis stage is determined using an invasive biopsy or approximated by non-invasive elastography. However, due to the liver's ability to compensate by generating new functional nodules and increasing blood supply, some F4 patients may live with cirrhosis for years or decades. Other patients may decompensate relatively rapidly and need a transplant for survival.

Current practice for F4 patients is to use blood tests and ultrasound (US) imaging to monitor disease progression and detect hepatocellular carcinoma.

Decompensation is detected when there are clinical manifestations such as ascites, jaundice, variceal bleeding or encephalopathy. Quantitative liver function loss occurs before clinical manifestations are apparent. Such deterioration of quantitative liver function and trend projection can be used for an early indication of impending decompensation.

Liver function is quantified by single photon emission computed tomography (SPECT) after a low dose Technetium 99m sulfur colloid injection which is taken up by the liver, spleen and bone marrow. The distribution of the radioisotope among the organs can be used to determine various indices of liver disease.

The H0 (normal liver function) - H5 (transplant candidate) physiologic liver model captures the disease processes into categories for convenient clinical use.

## METHODS

We hypothesized that cirrhotic patients who have  $PHM \geq 75$  are likely compensated cirrhotics while the rest are decompensated cirrhotics. The hypothesis was tested by analyzing 46 sequential cirrhotic patients who had liver SPECT. Cirrhosis was confirmed using liver biopsies, shear wave velocity, and nodular liver surface by US, CT or MRI. The cirrhosis etiology was MASH (20), hepatitis B and C viruses (5), alcoholic liver disease (3), autoimmune liver disease (9), and cryptogenic cirrhosis (9). The 46 patients were grouped based on abnormal blood tests and clinical manifestations into: Group CC - Compensated Cirrhotics (N=33) and Group DC - Decompensated Cirrhotics (N=13).

Blood tests for these patients were ( $\mu \pm \sigma$ ) Albumin  $3.87 \pm 0.45$ , Bilirubin  $1.45 \pm 1.26$ , INR  $1.14 \pm 0.16$ , Sodium  $138.7 \pm 3.6$ , Creatinine  $1.00 \pm 0.43$ , Platelets  $119.4 \pm 59.8$ , AST  $40.5 \pm 21.9$  and ALT  $31.4 \pm 15.3$ . Each patient's liver SPECT images were processed by the HEPATIQ software (Hepatiq Inc., California, USA) to calculate quantitative liver disease indices PHM  $86.3 \pm 13.4$ , fLV  $8.8 \pm 3.1$  and fSV  $4.5 \pm 2.9$ . Of the 46 cirrhotic patients, 35 had  $PHM \geq 75$  and 11 patients had  $PHM < 75$ .

# SPECT Imaging Identifies Compensated Cirrhotics with Higher Accuracy than Blood Tests

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## RESULTS

The clinically determined CC/DC groupings were considered the "truth" and the PHM and blood tests were compared to that. Of the 35 patients with  $PHM \geq 75$ , 31 were in Group CC (True Positive TP) and 4 were in Group DC (False Positive FP). Of the 11 patients with  $PHM < 75$ , 9 were in Group DC (True Negative TN) and 2 were in Group CC (False Negative FN). Statistics for the ability of PHM to predict compensated cirrhosis were:

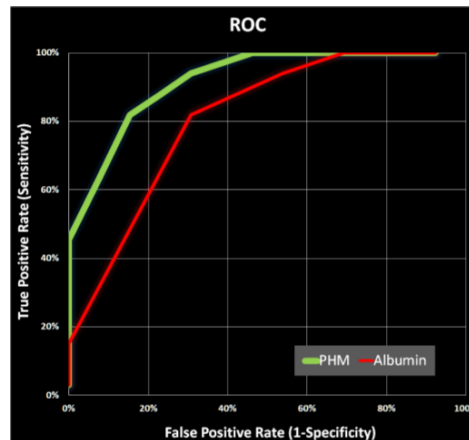
Positive Predictive Value (PPV) = 89%                      Sensitivity  $S_n$  = 94%

Negative Predictive Value (NPV) = 82%                      Specificity  $S_p$  = 69%

Due to the high PPV and high NPV for PHM, the hypothesis is shown to be true.

Cirrhotic patients who have  $PHM \geq 75$  are likely compensated cirrhotics while those with  $PHM < 75$  are likely decompensated cirrhotics.

Performance of blood tests was compared to PHM using the metric Accuracy =  $(TP+TN)/(Patients)$ . PHM was best with Accuracy 87%, followed by Albumin 83%, Bilirubin 76%, INR 74%, Sodium 74% and Creatinine 74%. Other blood test parameters were all worse. ROC curves for PHM and the next best Albumin are shown nearby. It may be noted that of the 35 compensated cirrhotics with  $PHM \geq 75$ , there were 4 patients with normal liver function  $PHM \geq 100$  and 31 patients with reduced liver function  $75 \geq PHM < 100$ . Thus, PHM can spot normal quantitative liver function in cirrhotic patients. These patients generally do well in the long term despite their cirrhosis.



## CONCLUSIONS

- PHM identified compensated cirrhotics with a high PPV of 89% and a high NPV of 82%.
- PHM spotted the patients who will do well despite their cirrhosis due to normal quantitative liver function.
- PHM was more accurate than blood tests such as Albumin, Bilirubin and INR and thus is more useful in setting appropriate monitoring intervals for cirrhotic patients.