Associations of Liver Biochemistry on Long-Term Blood Pressure Control and Mortality in Hypertensive Patients

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Introduction There is evidence for an inverse relationship with mortality for ALT and Bilirubin, even though higher, not low, ALT is also considered a marker for Non-Alcoholic Fatty Liver Disease. In addition, there are complex associations between liver biochemistry and aging, environmental factors like smoking, alcohol intake which can confound associations. We sought to study the association between liver indices and mortality and blood pressure control in a large cohort of treated hypertensive patients.

Methods: We analysed baseline liver enzymes and bilirubin in 12,000 hypertensive individuals followed up for a maximum of 35 years. Cox proportional hazards model and generalized estimating equations were used to assess their associations with cause-specific mortality and longitudinal BP control. The Harrel C-statistic, net reclassification index (NRI), and integrated discrimination index (IDI) were calculated to determine if any of the liver tests singly or in combination provided additive prognostic value beyond both traditional risk factors.

Results: The study population was middle aged (mean age=50.82$\pm$14.63 years), predominantly female (53%) and overweight (BMI=27.63$\pm$5.79). The total time at risk was 173,806 person years (p-y). Higher ALT and bilirubin levels (up to 4 SD from mean) were associated with lower mortality and lower follow-up BP; while higher GGT and ALP levels were associated with higher mortality risk and higher follow-up BP. Inclusion of all liver tests, albumin+GGT+bilirubin classified cardiovascular mortality better than the basic model with traditional risk factors (C-statistic improvement 1.26% and 1.51%; NRI +10.7% and +5.2%; IDI 0 p<0.0001). Longitudinal BP was higher with each unit increase in ALP or GGT, but lower with each unit increase in bilirubin or ALT (figure).

Conclusions: We show in a hypertensive cohort liver enzymes and bilirubin up to about 4SD from the mean show specific effects on mortality and BP control. Bilirubin and ALT levels show a direct association with longitudinal BP control indicating that these indices may influence the pharmacokinetics of antihypertensive drugs.