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Severe liver disease outcomes and mortality among patients with chronic hepatitis B who completed an in-depth health and behavior survey in 2012

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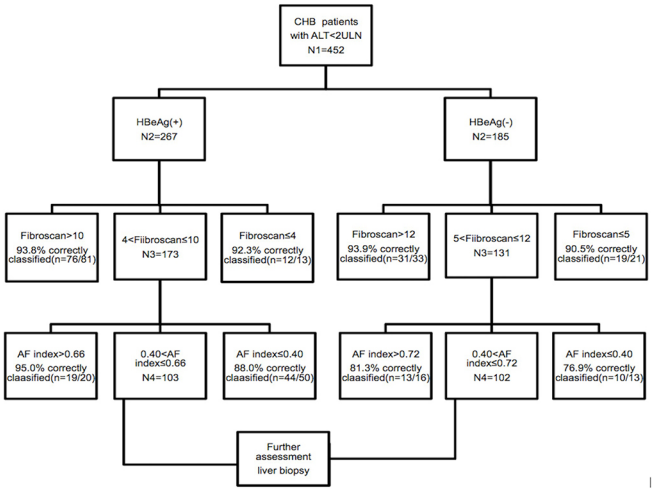
diagnostic efficiency for moderate inflammation or significant fibrosis among CHB patients with ALT<2ULN, regardless of HBeAg status. AF index, which is combined Fibroscan and AST, is a more reliable non-invasive predictor.



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2123

Risk of Hepatitis Flare in Patients with Chronic Hepatitis B Increases Even in Short Course of High-Dose Corticosteroid Therapy – a Study of 85,763 Subjects

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Background: Hepatitis B virus reactivation during chemotherapy or immunosuppressive therapy is a major concern in HBV-endemic areas, as the mortality can be high if reactivation is complicated by fulminant hepatic failure. We studied the impact of duration and peak dose of corticosteroid on the risk of hepatitis flare in patients with chronic hepatitis B (CHB). **Methods:** All patients received corticosteroid from January 2001 to December 2004 (when oral antiviral therapy was not available in public sector) were retrieved from the Clinical Data Analysis and Reporting System of the Hospital Authority, Hong Kong. Three strata of daily dose prednisolone equivalents (<20mg, 20-40mg, >40mg) and durations (1-7; 8-27; ≥28 days) were set. Main analysis was carried out on CHB patients while non-CHB patients served as a control group. Primary endpoint was hepatitis flare (alanine aminotransferase [ALT] >2x upper limit of normal [ULN], *i.e.* 80 IU/L) at one year. **Results:** We identified 224,939 subjects prescribed with corticosteroid; 85,763 fulfilled the inclusion criteria (5,254 CHB, 80,509 non-CHB). CHB patients had higher risk of hepatitis flare (470/5,254 [8.9%]) than those without CHB (3,191/80,509 [4.0%]; p<0.001 by log-rank test). Among CHB patients, peak daily dose > 40mg prednisolone equivalents (adjusted hazard ratio [aHR] 1.64, 95% CI 1.26–2.14; p<0.001), but not prolonged duration of corticosteroid, was an independent risk factor of hepatitis flare. After combining these two factors together, patients received corticosteroid of peak daily dose > 40mg prednisolone equivalents for 7-28 days and >28 days had highest risk of hepatitis flare (aHR 1.90 and 1.64 respectively, both p<0.001). Nonetheless the risk started to increase in those received corticosteroid of peak daily dose > 40mg prednisolone equivalents <7 days (aHR 1.55, p=0.026). **Conclusion:** High peak daily dose of corticosteroid >40mg prednisolone equivalents is more important than prolonged duration as the risk factor for hepatitis flare in CHB patients. The risk starts to increase even in short course of high dose steroid for <7 days.

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2124

Severe Liver Disease Outcomes and Mortality Among Patients with Chronic Hepatitis B Who Completed an in-Depth Health and Behavior Survey in 2012

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Background: Understanding factors associated with liver disease progression among patients with chronic hepatitis B (CHB) is vital for clinical decision-making. We examined liver related outcomes and mortality among CHB patients using clinical and laboratory data, supplemented by an in-depth health and behavior survey conducted in 2011-2012. **Methods:** CHB patients at four large U.S. healthcare systems completed a cross-sectional survey of demographic characteristics, smoking history, drug/alcohol use, coffee intake, and physical and psychosocial functioning. We reviewed survey responses and electronic medical records (EMRs) to examine clinical outcomes, including death, and determined patient characteristics at the time of survey associated with progression to decompensated cirrhosis [DCC] or hepatocellular carcinoma [HCC]) through the end of 2016, using a Cox model adjusted for age, sex, CHB diagnosis date, cirrhosis status, treatment history, diabetes mellitus, and alanine aminotransferase level. **Results:** Among 996 eligible CHB respondents, median age was 49 years, 51% were male, 34% were US-born, 55% were Asian-born, 69% were employed, 72% had a college or graduate education, 70% had private insurance, 38% were ever smokers (11% were current), 10% consumed alcohol >2 times per week, and 2% reported a history of injection drug use. At the time of survey,

34% were currently receiving or had taken antiviral treatment in the past, 75% had FIB4 values ≤2.0, and 15 (1.5%) had received a liver transplant. Median EMR follow-up after survey among respondents was 4.6 years. As of December 31, 2016, 50 (5%) patients had died (including 11 [22%] liver-related deaths). After exclusion of 43 patients with a history of DCC, HCC, or liver transplant at the time of survey, 29 of 953 (3%) patients developed DCC (n=19) or HCC (n=7) or both (n=3) during follow-up; median time to DCC or HCC was 2.3 years. Characteristics at time of survey associated with development of DCC or HCC included age ≥65 years (adjusted Hazard Ratio [aHR] 3.3, vs. age <45 years), FIB4 >3.0 (aHR 16.2, vs. FIB4 <1.0), CHB diagnosis <10 years pre-survey (aHR 2.8, vs. >20 years), and antiviral treatment initiation <5 years pre-survey (aHR 2.3, vs. >10 years). Country of birth, insurance status, smoking, alcohol and drug use, and coffee intake were not associated with development of DCC or HCC after the survey. **Conclusion:** After approximately five years of follow-up post-survey, liver-related deaths and incident HCC and DCC were uncommon. The association of incident DCC and HCC with recent CHB diagnosis and treatment initiation highlights the importance of earlier diagnosis of CHB and appropriate surveillance and care to prevent severe health outcomes.

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2125
High Predictive Value of Meld for Short-Term Mortality in Severe Acute Flares of Chronic Hepatitis B

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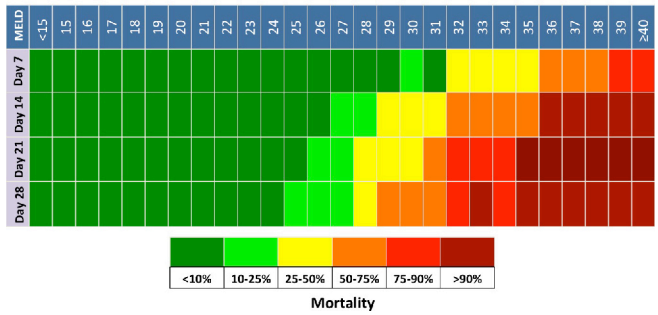
Background: In patients with severe acute flares of chronic hepatitis B (AFOCHB), the prognosis is often unclear, especially with respect to full recovery or the need for liver transplantation. The current study aims to establish the predictive value using the Model for End Stage Liver Disease (MELD) score for short-term mortality for patients with severe AFOCHB. **Methods:** Patients admitted with severe AFOCHB with bilirubin >50 umol/l, ALT >10x upper limit of normal, and INR >1.5 were included. All patients were commenced on entecavir and/or tenofovir. Longitudinal blood results from each patient were recorded. The laboratory results and MELD scores were pooled to calculate the mortality rate at four time points (day 7, 14, 21, and 28) from the time of MELD calculation. **Results:** A total of 111 severe AFOCHB patients were included with a median age of 53 years (range, 21-81), of which 86% were male. On admission, the median bilirubin, ALT, creatinine, INR, MELD and log HBV DNA was 220 umol/L (range, 52-719), 2042 U/L (range, 505-11443), 73 umol/L (range, 36-355), 1.9 (range, 1.5-8.0), 24 (range, 15-41), and log 7.33 U/mL (range, 2.35-10.06) respectively. Using the pooled results from 1,978 tests, the AUROC using the MELD score for predicting 7, 14, 21, and 28 day-mortality was 0.953, 0.946, 0.927, and 0.911 respectively. This was superior to bilirubin (0.765, 0.800, 0.807, and 0.800 respectively), ALT (0.407, 0.474, 0.492, and 0.507 respectively), creatinine (0.844, 0.750, 0.709. 0.693 respectively) and INR (0.881, 0.890, 0.870, and 0.850 respectively). The optimal MELD cut-off for predicting day 7, 14, 21, and 28 day mortality was 32, 28, 28, and 28 respectively, with a sensitivity of 0.89, 0.91, 0.84, and 0.80 respectively, and specificity of 0.88, 0.84, 0.88, and 0.90 respectively. A MELD of ≤24 at any time point was associated with mortality <10% at 28 days. A MELD-based mortality risk for the 4 time points was derived (figure 1), allowing day-to-day risk stratification based on the MELD score. **Conclusion:** The MELD score was highly accurate in predicting short-term mortality at different time points in severe AFOCHB patients, allowing for risk stratification and early liver transplantation for those with high mortality risk.

Figure 1. MELD-based Predictor of Short-Term Mortality in Severe Acute Flares of Chronic Hepatitis B



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Red Cell Distribution Width As an Useful Index for Predicting the Severity and Prognosis of Chronic Hepatitis B-Related Liver Diseases

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Background: Red cell distribution width (RDW) was reported as a potential indictor for the severity of liver disease. We aimed to investigate the association between RDW and severity of chronic hepatitis B (CHB)-related liver diseases and the prognostic values of RDW for CHB related liver cirrhosis (CHB-LC) in a large cohort of CHB patients. **Methods:** Patients were enrolled from two medical centers (2011-2017). 1482 patients with treatment-naïve CHB and 485 patients with CHB-LC were enrolled. 325 healthy individuals were included as controls (HC). CHB patients were classified into immune tolerance phase (IT, n = 139), immune clearance phase (IC, n = 375), low replicative phase (LR, n = 762) and HBeAg-negative hepatitis phase (ENH, n = 206). Patients with CHB-LC were