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Hepatocellular screening in hepatitis-B infected Asian Americans

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To the Editor:

We thank Dr. Braillon for his comments. Although most evidence in the literature suggest that HCC screening is beneficial [1, 2], we agree that there are limitations to the available data on hepatocellular carcinoma (HCC) screening as indicated in our paper [3]. We also agree that sources of bias such as lead time and length time bias will need to be excluded when assessing the impact of screening modalities. As indicated by Dr. Braillon, practice of evidence-based medicine is of outmost importance; however, as randomized controlled trials (the highest quality evidence) of HCC screening in North America or Europe are unlikely to be feasible or possible [4], current guidelines established by the American [2], European [5] and Asian [6], and other societies recommending HCC screening are based on lesser degrees of evidence.

In our paper, we previously reported that survival was significantly better among patients diagnosed with HCC who had undergone prior screening [3]. This was primarily due to receipt of curative therapy in patients with earlier stage HCC and less severe liver disease. We have now repeated the survival analysis for all-cause mortality and HCC-related mortality in the total study sample ($n = 1870$). Kaplan–Meier curves (Figs 1a, 1b, 2a, and 2b) were computed, and the log-rank test was used to compare survival after HBV diagnosis in those who received HCC screening (having imaging and/or AFP levels at least once yearly) *vs* those who did not. A Cox proportional hazards model was performed to assess the independent effects of factors associated with survival, including HCC screening, age, gender and presence of cirrhosis. Patient characteristics were compared for both screened and unscreened groups using the t-test for continuous variables and chi-squared test for categorical variables. There were a total of 303 patients who had undergone HCC screening and 1567 that were unscreened. There were a total of 86 deaths in the study sample and their characteristics included: mean age at death 56.9 ± 14.1 *vs* 60.8 ± 12.6 years ($P = 0.38$), 16% *vs* 45% female ($P = 0.02$) and 32% *vs* 73% with cirrhosis ($P = 0.009$) in the unscreened *vs* screened groups, respectively. There were 11 deaths from all causes among the screened and 75 deaths among the unscreened groups ($P = 0.021$). There were five HCC-related deaths among screened and 27 deaths among unscreened patients ($P = 0.36$). Among all patients,

screening was associated with longer survival, although HCC-related survival did not reach statistical significance. Among all patients, the unadjusted hazard ratio (HR) for annual screening was 0.48 (95% CI 0.25, 0.91, $P = 0.02$) for all-cause mortality and 0.64 (95% CI 0.24, 1.67, $P = 0.36$) for HCC-related mortality. However, when adjusted for age, gender and presence of cirrhosis, the HR for annual screening was 0.37 (95% CI 0.19, 0.70, $P = 0.002$) for all-cause mortality and 0.37 (95% CI 0.14, 0.97, $P = 0.044$) for HCC-related mortality. These additional analyses indicate that in this study sample of HBV-infected Asian Americans, HCC screening was associated with decreased all-cause mortality and HCC-related mortality independent of age, gender and presence of cirrhosis.

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Fig. 1.

(a) Kaplan–Meier survival curve comparing all-cause mortality in patients screened ($N = 303$) for HCC and unscreened ($N = 1567$) patients. (b) Kaplan–Meier survival curve comparing all-cause mortality in patients screened for HCC and unscreened patients adjusted for mean age, proportion female and proportion with cirrhosis.

Fig. 2.

(a) Kaplan–Meier survival curve comparing HCC-related mortality in patients screened ($N = 303$) for HCC and unscreened ($N = 1567$) patients. (b) Kaplan–Meier survival curve comparing HCC-related mortality in patients screened for HCC and unscreened patients adjusted for mean age, proportion female and proportion with cirrhosis.