Reviewer's report

Title: Characterization and prognosis of patients with hepatocellular carcinoma (HCC) in the non-cirrhotic liver

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Reviewer: Marcus-Alexander A Wörns

Reviewer’s report:

Schütte and colleagues report from a retrospective single institution experience of a mixed cohort of patients with hepatocellular carcinoma (HCC) in non-cirrhotic liver (NCL). They compared this entity with a large group of HCC patients with pre-existing liver cirrhosis. They could confirm most of the characteristics of HCC in NCL reported in the literature during the last decades. In addition, they could demonstrate the usefulness of staging systems such as BCLC and CLIP also in HCC patients with NLC. However, they detected a high percentage of patients with advanced HCC (BCLC C, 51.6%) due to high rate of portal vein involvement and extrahepatic spread (EHS). In the univariate analysis (BCLC and CLIP excluded), portal vein thrombosis, EHS, level of AFP, PTT, ASAT, platelets, and ECOG PS were identified as prognostic factors; in multivariate analysis, only EHS and concentration of platelets were confirmed as independent prognostic factors. These results highlight the implementation of surveillance programs to detect HCC in NCL in earlier stages as the major challenge, particularly in patients with signs of NAFLD or NASH.

Despite some limitations (retrospective study, low percentage of available non-tumorous tissue) the results are relevant for clinical practice.

Major Compulsory Revisions:

Abstract: Conclusions have to be shortened and the main topic should be highlighted: implementation of surveillance programs to detect HCC in NCL in earlier stages as the major challenge, particularly in patients with signs of NAFLD or NASH.

Results: Results of Table 6 should be included in the main text, and table 6 should be deleted. The influence of first-line treatment modalities (curative vs. palliative approaches) should be incorporated into the univariate/multivariate analysis. Some of the univariate analyses (Kaplan-Meier curves) should be deleted from figure 2 and 3.

Discussion should be shortened to the most relevant points and subheadings should be deleted.

Level of interest: An article of importance in its field

Quality of written English: Acceptable
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests