EJMO

DOI: 10.14744/ejmo.2022.77974
EJMO 2022;6(2):190–191

Letter to the Editor

Prevalence of MAFLD-Related Hepatocellular Carcinoma

Yu-Xian Teng,[1] Hao-Tian Liu,[1] Zhu-Jian Deng,[1] Jia-Yong Su,[1] Yi-Hua Lu,[1] Jian-Hong Zhong[1,2]

1Department of Hepatobiliary Surgery, Guangxi Liver Cancer Diagnosis and Treatment Engineering and Technology Research Center, Guangxi Medical University Cancer Hospital, Nanning, China
[2]Key Laboratory of Early Prevention and Treatment for Regional High Frequency Tumor (Guangxi Medical University), Ministry of Education; Guangxi Key Laboratory of Early Prevention and Treatment for Regional High Frequency Tumor

Cite This Article: *Teng YX, Liu HT, Deng ZJ, Su JY, Lu YH, Zhong JH. Prevalence of MAFLD-Related Hepatocellular Carcinoma. EJMO 2022;6(2):190–191.*

We read with great interest the article by Vitale et al.,[1] who examined 6882 patients with hepatocellular carcinoma (HCC) in Italy to estimate the prevalence of metabolic-associated fatty liver disease (MAFLD).[1] They found the prevalence of MAFLD to be increasing rapidly among such patients in Italy. They also found that patients with MAFLD-related HCC were at a lower risk of HCC-related death than patients with other HCC subtypes. We applaud the investigators for providing important insights into the prevalence of MAFLD-related HCC. However, we wish to draw attention to some points to place their findings in perspective.

Vitale et al. reported that they diagnosed patients with MAFLD if they were overweight or obese, defined as a body mass index > 25 kg/m^2, or had type 2 diabetes mellitus, or showed evidence of metabolic disorders.[1] This is not entirely consistent with international consensus guidelines, according to which MAFLD should be diagnosed based on the presence of fatty liver as well as one of the following: overweight/obesity, type 2 diabetes mellitus, or lean/normal weight with evidence of metabolic disorders.[2] In addition, Vitale et al. apparently did not assess waist circumference, insulin resistance, or levels of C-reactive protein, which should also be taken into account when diagnosing MAFLD.

Even if the prevalence reported by Vitale et al. can be taken to reflect bona fide MAFLD, we are concerned about whether it can be extrapolated to the larger population of HCC patients in Italy or elsewhere. Among the 6882 patients whom Vitale et al. enrolled consecutively from January 2002 to December 2019, 17.1% had single-etiology MAFLD and 51.2% had mixed-etiology MAFLD, while 31.6% did not have MAFLD. These proportions differed significantly from the corresponding proportions of 10.9%, 30.1%, and 59.0% from another sample of Italian HCC patients[3] ($p<0.001$, Fig. 1a) despite the fact that the enrollment window of the second sample lay within that of the sample of Vitale et al., and some patients in both samples came from the same medical center.

Vitale et al. combined the prevalences of single- and mixed-etiology MAFLD to give an overall prevalence of MAFLD-related HCC of 68.3%,[1] which is significantly higher than the 12.8%[4] or 19.8%[5] in Mainland China or 38.8% in Taiwan[6] (both $p<0.001$, Fig. 1a). The latter two prevalences seem more reasonable to us given recent estimates of the global prevalence of MAFLD as 39.2% in the general

The first two authors contributed equally to this work.

Address for correspondence: Jian-Hong Zhong, MD. Guangxi Medical University Cancer Hospital, He Di Rd. #71, Nanning 530021, P.R. China
Phone: +86-771-5330855 **E-mail:** zhongjianhong@gxmu.edu.cn

Submitted Date: May 20, 2022 **Accepted Date:** June 02, 2022 **Available Online Date:** June 06, 2022

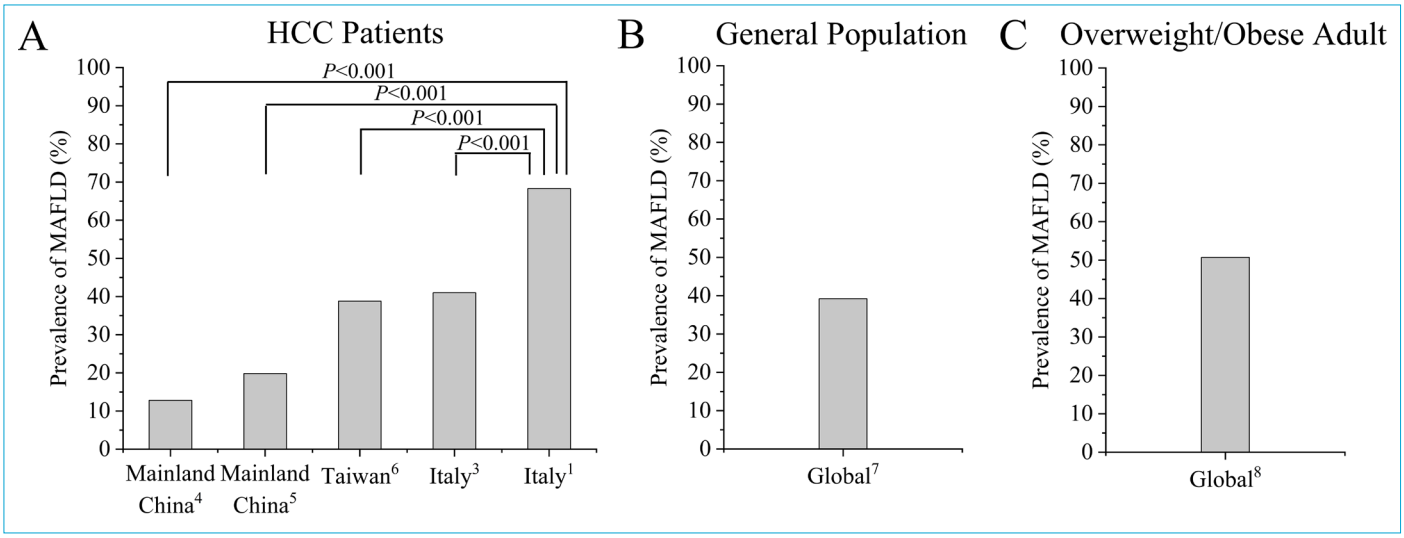

Figure 1. Prevalence of metabolic-associated fatty liver disease in **(a)** patients with HCC, **(b)** the general population, and **(c)** overweight/obese adults.

population (based on data from 379 801 adults)[7] or 50.7% among overweight/obese adults (based on data from more than 2.6 million such adults).[8] We consider it unlikely that MAFLD should be much more prevalent among HCC patients than among overweight/obese adults or in the general adult population (Fig. 1b and c).

We think that it would be more accurate to describe the study of Vitale et al.[1] as an analysis of metabolic disease-related HCC, rather than MAFLD-related HCC. Adherence to an accepted definition of MAFLD is important for ensuring proper interpretation of results and for effective health policymaking,[9] and we concur that MAFLD should include evidence of fatty liver disease.[10] We urge clinicians and researchers to adhere to the consensus definition of MAFLD and to differentiate clearly between MAFLD and, more broadly, metabolic disease. This may lead to a clearer and deeper understanding of MAFLD-related HCC, including its prevalence, pathogenic mechanisms, and treatment.

Disclosures

Financial Support and Sponsorship: This work was supported by the Specific Research Project of Guangxi for Research Bases and Talents (GuiKe AD22035057), the Natural Science Foundation of Guangxi Province (2020GXNSFAA159022), and Guangxi Undergraduate Training Program for Innovation and Entrepreneurship (X202210598347).

Conflict of Interest: There are no conflicts of interest.

Authorship Contributions: Concept – J.-H.Z; Design – J.-H.Z; Supervision – J.-H.Z; Materials – Y.-X.T., J.-H.Z; Data collection &/or processing – Y.-X.T., J.-H.Z; Analysis and/or interpretation – Y.T., H.L., Z.D., J.S., J.-H.Z.; Literature search – J.-H.Z; Writing – Y.-X.T., J.-H.Z; Critical review – J.-H.Z

References

1. Vitale A, Svegliati-Baroni G, Ortolani A, et al. Epidemiological trends and trajectories of MAFLD-associated hepatocellular carcinoma 2002-2033: the ITA.LI.CA database. Gut. 2021 Dec 21. doi: 10.1136/gutjnl-2021-324915. [Epub ahead of print].
2. Eslam M, Sanyal AJ, George J. MAFLD: A consensus-driven proposed nomenclature for metabolic associated fatty liver disease. Gastroenterology 2020;158:1999–2014.e1. [CrossRef]
3. Conci S, Cipriani F, Donadon M, Marchitelli I, Ardito F, Famularo S, et al; He.RC.O.Le.S Group. Hepatectomy for Metabolic Associated Fatty Liver Disease (MAFLD) related HCC: Propensity case-matched analysis with viral- and alcohol-related HCC. Eur J Surg Oncol 2022;48:103–12. [CrossRef]
4. Liu L, Xie S, Teng YX, Deng ZJ, Chen K, Liu HT, et al. Outcomes of liver resection for metabolic dysfunction-associated fatty liver disease or chronic hepatitis B-related HCC. Front Oncol 2022;11:783339.
5. Xiong KG, Ke KY, Chen LF, Kong JF, Ling TS, Lin QB, et al. The impact of metabolic dysfunction-associated fatty liver disease on the prognosis of patients with hepatocellular carcinoma after radical resection. Hepatobiliary Pancreat Dis Int. 2022 Apr 6. doi: 10.1016/j.hbpd.2022.1004.1001. [Epub ahead of print].
6. Lin YP, Lin SH, Wang CC, Lin CC, Chen DW, Chuang CH, et al. Impact of MAFLD on HBV-Related Stage 0/A Hepatocellular Carcinoma after Curative Resection. J Pers Med 2021;11:684.
7. Lim GEH, Tang A, Ng CH, Chin YH, Lim WH, Tan DJH, et al. An observational data meta-analysis on the differences in prevalence and risk factors between MAFLD vs NAFLD. Clin Gastroenterol Hepatol 2021:S1542–3565. [CrossRef]
8. Liu J, Ayada I, Zhang X, Wang L, Li Y, Wen T, et al. Estimating global prevalence of metabolic dysfunction-associated fatty liver disease in overweight or obese adults. Clin Gastroenterol Hepatol 2022;20:573–82. [CrossRef]
9. Shiha G, Korenjak M, Eskridge W, Casanovas T, Velez-Moller P, Högström S, et al. Redefining fatty liver disease: an international patient perspective. Lancet Gastroenterol Hepatol 2021;6:73–9.
10. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol 2020;73:202–9. [CrossRef]