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Editorial

The latest global burden of liver cancer: A past and present threat

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Liver cancer is the fourth most common cause of death globally, accounting for over 800,000 deaths annually.[1,2] Hepatocellular carcinoma represents approximately 90% of primary liver cancers, followed by intrahepatic cholangiocarcinoma and other primary liver malignancies. Approximately 90% of hepatocellular carcinomas are associated with a known underlying cause, most commonly chronic viral hepatitis, heavy alcohol use, and non-alcoholic fatty liver disease.[3] The distribution of these etiologies differs geographically.[4] For instance, East Asia has a higher prevalence of chronic viral hepatitis, while heavy alcohol use is highest in Europe. The incidence and mortality rates of liver cancer also differ regionally.[5]

In this issue of *Clinical and Molecular Hepatology*, Choi et al.[6] analyzed data from the Global Burden of Disease 2019 on primary liver cancer. A Global Burden of Disease report has shown recent trends in liver cancer. Between 1990 and 2019, the crude number of disease-adjusted life years (DALYs) and deaths in 204 countries increased from 11,278,630 to 12,528,422 and from 365,215 to 484,577, respectively. A couple of years ago, Akinyemiju et al.[7] reported on the global burden of liver cancer by 2015 using Global Burden of Disease data. The number of incident liver cancer cases in 2015 was 854,000, whereas the number of deaths and DALYs were 810,000 and 20,578,000, respectively. The number of incident cases increased by 75% between 1990 and 2015, mostly because of changes in population age structures and population growth. Hepatitis B and hepatitis C viruses were responsible for 30% and 21% of liver cancer-related deaths, respectively. As prevention and treatment for risk factors evolve over time, the trend of liver cancer may shift, and we should adapt accordingly. Choi et al.[6] reported that the crude numbers of DALY, mortality, and liver cancer increased during the study period, while the age standardization rates of DALY, mortality, and incidence decreased. The age-standardized rates of DALYs and mortality rates decreased from 258.4 to 151.1 and 8.9 to 5.9, respectively, owing to the aging population structure. This indicates that most liver cancers occur intensively in the oldest age groups. It is believed that it is time to call for a reasonable guideline for the surveillance and treatment strategy for liver cancer in the oldest, most

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vulnerable population with risk factors.

The burden of liver cancer varies worldwide. East Asia had the highest DALYs and death rates. Fortunately, both the DALYs and mortality rates in East Asia have decreased by approximately 60% over the past 20 years. In contrast, the age-standardized DALYs rates in North America and Australasia, regions with lower incidence and mortality, increased by 107% and 94.8%, respectively. In particular, in the high-income Asia-Pacific region, North America, and Australia, the age-standardized DALYs and mortality rates of liver cancer are increasing. Choi et al.[6] meticulously assessed DALYs and mortality rates based on etiology, income level, sex, and age differences. Hepatitis B and C viruses remain the top causes of liver cancer DALYs and mortality, although the rates appear to be declining. This phenomenon might be due to the introduction of hepatitis B virus vaccines and antiviral therapies (nucleos(t)ides and direct-acting agents).[8] Nonetheless, the burden of alcohol consumption and non-alcoholic fatty liver disease is increasing. This trend is evident in North America, Eastern Europe, and other high-income countries. Unlike viral hepatitis, the criteria for the high-risk group of non-alcoholic fatty liver disease/non-alcoholic steatohepatitis (NASH)-related liver cancer have not yet been defined, and there is a lack of social consensus on how to screen, evaluate, and manage the so-called "high-risk group".[9,10] This indicates that some high-income countries require a national strategy or reasonable screening algorithm for non-alcoholic fatty liver disease/non-alcoholic steatohepatitis (NASH)-related liver cancer. Another interesting point is that alcohol-related liver cancer remains an important cause of liver cancer in almost all countries. The crude number of alcohol-related liver cancer cases increased, while the age-standardized incidence rates remained unchanged. Unlike other causes, it is an area of low social attention and pharmaceutical interest in the development of relevant medications and screening strategies for high-risk groups. This seems to be the greatest unmet social need for the future. These results may lead to the development of location-specific prevention and treatment strategies.

However, one important question was left unanswered in the current paper. Choi et al.[6] performed a comparative analysis focusing on age-adjusted DALYs and mortality rates, but crude numbers were rarely presented. Therefore, it is still difficult to answer the question of how to distribute goods, and further economic evaluations are needed.

Over the next 20 years, the burden of primary liver cancer is expected to rise. Rumgay et al.[11] extracted data from the GLOBOCAN 2020 web-based platform, presenting global cancer statistics. They predicted that the incidence of liver cancer would increase by 55.0% and the number of deaths would increase by 56.4% between 2020 and 2040. Therefore, primary liver cancer has always posed a significant threat to global health, both in the past and in the future.

The results of Choi et al.[6] provide an unmet need for social consensus on the surveillance and management of liver cancer in the oldest population. In addition, the necessity of establishing a screening strategy for non-alcoholic fatty liver disease/NASH-related liver cancer, which is leading to an increasing liver cancer incidence in the future, was suggested. Finally, they also suggested a social agenda for the social burden of alcohol-related liver cancer, which has a relatively low social interest.

Authors' contributions

JHO drafted the manuscript. DWJ reviewed and finalized the manuscript.

Conflicts of Interest

The authors have no conflicts to disclose.

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Abbreviations:

DALY, disease-adjusted life year; NASH, non-alcoholic steatohepatitis

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