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AGE-RELATED CHANGES IN ALCOHOLIC LIVER CIRRHOSIS: IMPLICATIONS FOR SKELETAL MUSCLE MASS AND OVERALL PROGNOSIS IN OLDER ADULTS

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Abstract. Alcohol use is increasing among adults aged 65 and older, and the size of this population is expanding rapidly. Aging is associated with systemic inflammation, sleep disturbances, cancers, cognitive decline, and increased risk of injury and death from falls and other accidents. Alcohol misuse exacerbates and accelerates these age-related changes. Older drinkers are more sensitive to acute alcohol-induced impairments in memory, coordination, reaction time, and driving performance. Oxidative stress and DNA damage resulting from chronic heavy alcohol consumption contribute to an increased risk of cancer, liver disease, and cardiovascular disease. Medication use increases with age, and many medications prescribed to older adults can negatively interact with alcohol. The rapid expansion of the population aged 65 and older, combined with higher levels of alcohol use and alcohol use disorder (AUD) in the Baby Boomer cohort, could significantly increase the burden of alcohol on the healthcare system. Screening and brief intervention for hazardous alcohol use among older patients, along with education about potential interactions with medications, could substantially reduce the risk of alcohol-related harms, but this approach is currently underutilized.

Keywords: Alcohol use, aging, older adults, alcohol use disorder, healthcare burden, medication interactions, liver aging, liver disease.

Introduction. The number of people aged 65 and older in the United States is increasing rapidly as the Baby Boomer cohort, born between 1946 and 1964, ages. In the decade between 2009 and 2019, the size of the population aged 65+ grew 36% to 54.1 million people, while the population under 65 saw only a 3% increase. By 2030, all individuals in the Baby Boomer cohort will be 65 or older, a demographic shift referred to as the gray (or silver) tsunami (Census Bureau, 2019). By 2040, an estimated 80.8 million people will be aged 65+, more than double the number in 2000.

If the Baby Boomers consumed alcohol at the same levels as the previous generation, the sheer size of the group would lead to a significant increase in alcohol-related harms. In fact, alcohol use levels are higher in this cohort than in the Silent Generation, born between 1928 and 1945. The period of highest per capita alcohol consumption in the United States occurred in the early 1980s when most Baby Boomers were young adults. Subsequently, this cohort, particularly women, maintained a higher total amount and frequency of alcohol consumption than those in preceding or following cohorts (Kerr, Greenfield, Bond, Ye, & Rehm, 2009; Kuerbis, Sacco, Blazer, & Moore, 2014). Thus, the impact of alcohol on health outcomes for older drinkers may significantly increase due to demographic changes and a tendency toward increased alcohol consumption.

Relevance of the Work. According to the results of recent research, the world population is aging, and the incidence of many diseases increases with age, leading to an investigation of cellular senescence and its correlation with age-related diseases. Cellular senescence is characterized by permanent cell cycle arrest, which can be triggered by factors such as DNA damage and oxidative stress. Senescent cells secrete various molecules that affect surrounding cells, potentially serving as markers of senescence and offering therapeutic insights for age-related diseases.

The liver, in particular, is characterized by a slow-aging process that is multifactorial and still insufficiently investigated. It is known that various environmental factors and lifestyles, including

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alcohol consumption and exposure to toxic substances, contribute to the development of chronic liver inflammation. The liver initially reacts to harmful stimuli with the appearance of steatosis, which over time and under the influence of numerous endogenous factors can progress to non-alcoholic fatty liver disease (NAFLD). Studies have shown that the frequency of developing liver cirrhosis in patients with NAFLD increases with age, and patients older than 50 years are at a higher risk for developing severe fibrosis. NAFLD has a tendency to progress to non-alcoholic steatohepatitis (NASH), which is associated with obesity, metabolic syndrome, type 2 diabetes, insulin resistance, and cardiovascular diseases. The frequency of most of these conditions increases with age.

In the case of alcohol abuse, alcoholic steatohepatitis (ASH) occurs, which, if not treated, can lead to progressive fibrosis and the development of liver cirrhosis, similar to NASH. Age is an independent predictor of worse outcomes in patients with ASH. The importance of changes in liver function during aging is also evident in the context of liver transplantation for patients with end-stage liver disease. With the increasing number of patients requiring transplantation, studies have explored the utilization of organs from older donors. Research has shown that the biological and chronological age of the liver can differ, and the liver retains significant regenerative capacity, albeit slower in older individuals. This has implications for donor-recipient matching and the broader management of liver diseases in aging populations.

Purpose. The aim of this study is to investigate the chronological changes in skeletal muscle mass in patients with alcohol-related liver disease (ALD) and viral cirrhosis. We seek to identify key factors influencing rapid muscle loss and assess their impact on the prognosis of patients with liver cirrhosis (LC).

Materials and Methods of Research. This retrospective cohort study included 384 patients with cirrhosis, without hepatocellular carcinoma (HCC) at enrollment, who underwent multiple computed tomography (CT) scans at Gifu University Hospital between March 2004 and June 2021. Clinical characteristics and laboratory results were collected within 1 month of the first CT scan, with follow-ups every 1 to 3 months until death or December 31, 2023. Informed consent was obtained from all participants, and the study protocol conformed to ethical standards.

Results and Discussion. The primary aim of this study was to assess the rate of skeletal muscle loss in patients with ALD, hepatitis B virus (HBV) cirrhosis, or hepatitis C virus (HCV) cirrhosis. We found that the rate of skeletal muscle loss in ALD cirrhosis is faster than that in viral cirrhosis, suggesting a strong association between ALD and rapid muscle loss, which predicts mortality in patients with LC. However, further prospective studies on larger patient populations with various underlying etiologies are needed to validate these findings.

The liver's regenerative capacity, though age-related, plays a critical role in the progression of liver diseases. Research conducted on animal models has shown that complete hepatic restoration in older individuals is slower than in younger ones, highlighting the importance of age as a factor in liver disease outcomes. This underscores the need for tailored interventions for older adults, particularly those with a history of alcohol misuse, to mitigate the accelerated progression of liver damage and its associated complications.

Conclusion. The prevalence of certain liver diseases increases with aging, leading to a higher incidence of advanced liver diseases in older patients. The term “age-related liver disease” has gained popularity, referring to several liver disorders that result in impaired liver function and increased mortality risk. Given the demographic shifts and increased alcohol consumption among older adults, it is crucial to implement interventions to address the rising burden of alcohol-related health issues in

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this population. Screening for hazardous alcohol use, educating patients about medication interactions, and promoting liver health through lifestyle modifications are essential strategies to reduce the impact of alcohol on aging populations.

References

1. Campisi, J. Aging, Cellular Senescence, and Cancer. Annu. Rev. Physiol. 2013, 75, 685–705. https://doi.org/10.1146/annurev-physiol-030212-183653

2. d'Adda di Fagagna, F. Living on a Break: Cellular Senescence as a DNA-Damage Response. Nat. Rev. Cancer 2008, 8, 512–522. https://doi.org/10.1038/nrc2440

3. Georgieva, M.; Xenodochidis, C.; Krasteva, N. Old Age as a Risk Factor for Liver Diseases: Modern Therapeutic Approaches. Institute of Molecular Biology "Acad. Roumen Tsanev", Bulgarian Academy of Sciences, 1113 Sofia, Bulgaria, 25 November 2023.

4. Hanai, T.; Nishimura, K.; Unome, S.; Miwa, T.; Nakahata, Y.; Imai, K.; Suetsugu, A.; Takai, K.; Shimizu, M. Alcohol-Associated Liver Disease Increases the Risk of Muscle Loss and Mortality in Patients with Cirrhosis. J Gastroenterol 2024, 59, 932–940. https://doi.org/10.1007/s00535-024-02137-4

5. Kumari, R.; Jat, P. Mechanisms of Cellular Senescence: Cell Cycle Arrest and Senescence Associated Secretory Phenotype. Front. Cell Dev. Biol. 2021, 9, 645593. https://doi.org/10.3389/fcell.2021.645593

6. McHugh, D.; Gil, J. Senescence and Aging: Causes, Consequences, and Therapeutic Avenues. J. Cell Biol. 2018, 217, 65–77. https://doi.org/10.1083/jcb.201708092

7. Ogrodnik, M. Cellular Aging beyond Cellular Senescence: Markers of Senescence Prior to Cell Cycle Arrest in Vitro and in Vivo. Aging Cell 2021, 20, e13338. https://doi.org/10.1111/acel.13338

8. Radonjić, T.; Dukić, M.; Jovanović, I.; Zdravković, M.; Mandić, O.; Popović, M.; Nikolić, N.; Klašnja, S.; Branković, M.; Divac, A.; Todorović, Z. Aging of Liver in Its Different Diseases. University Hospital Medical Center Bežanijska Kosa, Belgrade, Serbia, 28 October 2022.

9. Salama, R.; Sadaie, M.; Hoare, M.; Narita, M. Cellular Senescence and Its Effector Programs. Genes Dev. 2014, 28, 99–114. https://doi.org/10.1101/gad.235184.113

10. Shmulevich, R.; Krizhanovsky, V. Cell Senescence, DNA Damage, and Metabolism. Antioxid. Redox Signal. 2021, 34, 324–334. https://doi.org/10.1089/ars.2020.8043

11. Sikora, E.; Bielak-Zmijewska, A.; Mosieniak, G. A Common Signature of Cellular Senescence; Does It Exist? Ageing Res. Rev. 2021, 71, 101458. https://doi.org/10.1016/j.arr.2021.101458

12. Tchkonia, T.; Zhu, Y.; van Deursen, J.; Campisi, J.; Kirkland, J.L. Cellular Senescence and the Senescent Secretory Phenotype: Therapeutic Opportunities. J. Clin. Investig. 2013, 123, 966–972. https://doi.org/10.1172/JCI64098

13. White, A.M.; Orosz, A.; Powell, P.A.; Koob, G.F. Alcohol and Aging – An Area of Increasing Concern. Volume 107, March 2023, Pages 19-27.

14. Yoshiji, H.; Nagoshi, S.; Akahane, T.; et al. Evidence-Based Clinical Practice Guidelines for Liver Cirrhosis 2020. J Gastroenterol. 2021, 56, 593–619.

15. Yoshiji, H.; Nagoshi, S.; Akahane, T.; et al. Evidence-Based Clinical Practice Guidelines for Liver Cirrhosis 2020. Hepatol Res. 2021, 51, 725–749.