GENDER-SPECIFIC EFFECTS OF OBESITY ON ALCOHOLIC LIVER DISEASE IN OLDER ADULTS OF DIFFERENT GROUPS AGED 65 AND OVER: A CASE–CONTROL STUDY

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Abstract. Alcoholic liver disease is a common liver disease caused by chronic alcohol consumption and is categorized into fatty liver, alcoholic hepatitis, and alcoholic cirrhosis. This study aimed to examine the relationship between alcoholic liver disease and overweight in older adults, focusing on age and gender differences The study was designed as a retrospective age-matched case-control study using the Chang Gung Research Database (CGRD). The data of this study were collected from January 1, 2018 to December 31, 2022. The subjects were aged over 65 years old with a primary diagnosis of alcoholic liver disease. The experimental group matched gender and age group to conduct a case-control study with a ratio of 1:2 for the control group. The relationship between overweight and alcoholic liver disease was analyzed by logistic regression. The study found that the prevalence of alcoholic liver disease was significantly higher in male than in female. The prevalence of overweight in male with alcoholic liver disease decreased with age distribution. For female, age did not matter much. However, among female aged 65 to 69 years, those who were overweight were more likely to develop alcoholic liver disease than those who were of normal weight. These findings provide guidance for population-specific prevention and treatment strategies and highlight the importance of weight control in aged 65 and over. Particularly in the aging population, attention to weight control and aging, as well as the development of alcoholic liver disease, may improve patient health and quality of life.
Keywords: *alcoholic liver disease, aging society, gender physiological effects, obesity diseases, alcoholism*

Introduction

Alcoholic liver disease is a liver disease caused by chronic alcohol consumption. It is one of the most common liver diseases in the world. Alcoholic liver disease is generally divided into three types: fatty liver, alcoholic hepatitis, and alcoholic cirrhosis (Saberi et al., 2016). Fatty liver is the initial stage, and it is caused by the accumulation of fat as alcohol is metabolized in the liver. Alcoholic hepatitis refers to hepatitis caused by alcohol, which can lead to cirrhosis of the liver if left untreated. Alcoholic cirrhosis means the damage of the liver that leads to hardening and fibrosis of the liver tissue and can lead to liver failure, liver cancer and death (Sivakrishnan and Pharm, 2019; Kamran et al., 2020). In patients who drink heavily for years, about 20 to 25 percent start with steatosis, progress to fibrosis, and eventually cirrhosis (Torruellas et al., 2014). Alcoholic liver disease has a serious impact on individuals and society and therefore requires greater attention and prevention measures.

With the increase of age, the human body's ability to metabolize alcohol will decline, and the function of the liver will gradually decline, making the damage caused by alcohol to the liver more obvious, and long-term alcoholism will gradually accumulate the damage to the body, thus increasing the risk of alcoholic liver disease (Anantharaju et al., 2002; Covarrubias et al., 2021). In particular, female have high levels of oestrogen, a hormone that protects the liver. But after menopause, estrogen

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levels in a female's body drop, which can also increase a female's risk of alcoholic liver disease (Park et al., 2006; An, 2022). Obesity has also been linked to alcoholic liver disease, a condition in which an overweight person has high levels of body fat, which burdens the liver and makes it vulnerable to damage from alcohol and other harmful substances (Abidov et al., 2010). In addition, obesity can cause metabolic syndrome, a syndrome that includes high blood pressure, high blood sugar, triglycerides and low HDL cholesterol, all of which can have an adverse effect on the liver. People with metabolic syndrome are more likely to develop liver diseases such as fatty liver disease and alcoholic liver disease than healthy individuals (Després et al., 2009). However, the studies were inconsistent in age and gender distribution. Previous differences in age distribution may be due to different population registries. The reference growth criteria were different in different subjects, and the association between alcoholic liver disease and BMI in respective age groups was not clear. Therefore, we attempted to investigate age and gender differences in the association between alcoholic liver disease and obesity in aged 65 and over adults by using a population-based database.

Materials and methods

Data sources and study samples

This study used the Chang Gung Research Database (CGRD), the largest multi-institution electronic medical record (EMR) database for de-identifiers, and was designed as a retrospective case-control study with gender and age matching. Overall, CGRD included 21.2% of outpatients and 12.4% of inpatients in Taiwan. The basic architecture of CGRDS contains most of the information for electronic medical records used in healthcare research. Due to its high overall coverage and disease specificity, CGRD provides a good approach for clinical and scientific research with a representative sample. The data of this study were collected from January 1, 2018 to December 31, 2022. The subjects of this study were aged over 65 years old with a primary diagnosis of alcoholic liver disease. The experimental group matched gender and age group to conduct a case-control study with a ratio of 1:2 for the control group. The relationship between overweight and alcoholic liver disease was analyzed by logistic regression. This study was approved by the institutional review board of the Chang Gung Medical Foundation on March 3rd, 2023 (approval No. 202300295B0C601). The data were collected in the form of a review of medical examination reports, without any medical action or treatment for each case. The review committee waived the need for consent.

Patient identification

In this study, patients older than 65 years of age were enrolled using the diagnostic ICD-10 code "K70" for alcoholic liver disease from January 1, 2018 to December 31, 2022, and patients with age, height, weight, and other demographic information were excluded. In the control group, we randomly selected patients who had not been diagnosed with alcoholic liver disease by CGRD and then matched them to patients with alcoholic liver disease by age and gender in a 2:1 ratio. *Figure 1* shows the distribution of the basic demographic variables of the cases in a three-dimensional scatter chart. In addition, subjects were divided into six groups based on the

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following age range: 65-69 years, 70-74 years, 75-79 years, and over 80 years. BMI is calculated by dividing weight in kilograms by height in meters squared and is used to calculate BMI and BMI percentile (adjusted for age and gender). Using the standard age and gender BMI values of Taiwan standard, the old people of different age groups are divided into two individuals, normal weight: $18.5 \leq BMI < 24$, overweight: $BMI \geq 24$.

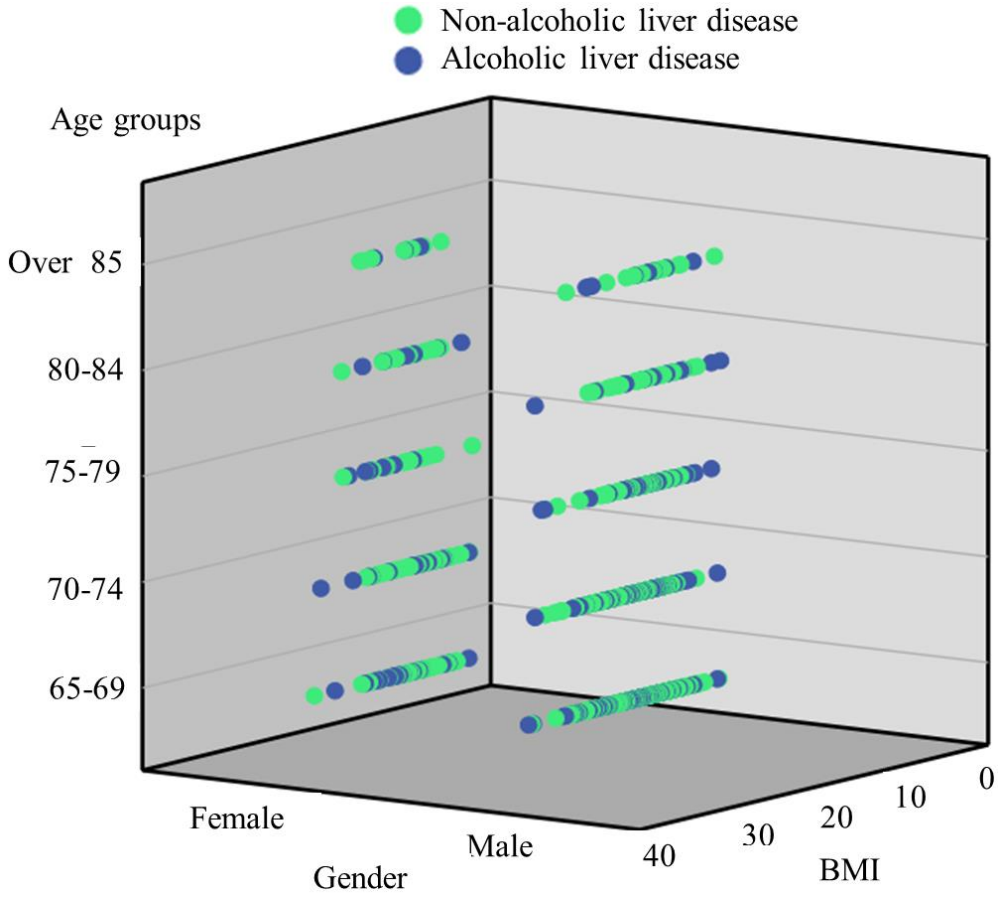

Figure 1. *Stereoscopic comparison of gender, body mass index (BMI) and age between case group and control group*

Statistical analysis

In this study, IBM SPSS statistics version 28 was used for data collation and data analysis. Firstly, descriptive statistics are carried out to describe the value distribution of each variable from the two aspects of frequency distribution and percentage of data. Baseline patient characteristics included age, gender, and BMI. In this study, categorical variables were reported as counts and percentages. Continuous variables are expressed as median and quartile ranges (IQR). To compare the differences between the two groups in the alcoholic liver disease population, the Chi-square test was used for categorical variables, and the independent sample t test was used for continuous variables and baseline patient characteristics. logistic regression analysis was used to determine the relationship between obesity and alcoholic liver disease. $p < 0.05$ was considered statistically significant.

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Results

Basic characteristics of the study samples

A total of 297 older adults with alcoholic liver disease and 594 age-matched controls were enrolled in the study from January 1, 2018 to December 31, 2022, based on the ICD diagnostic code. Among the 297 cases, there were 238 males (80.1%) and 59 females (19.9%), and 476 males and 118 females in the control group, indicating that most of the elderly patients were males. The mean age of the overall sample was 71.52 years, and the standard deviation was 6.04 years. In terms of age groups, 137 cases were aged 65 to 69 years (46.1%), followed by 87 cases aged 70 to 74 years (29.3%) and 24.6% over 75 years. In terms of BMI classification, 138 cases (46.5%) were classified as normal and 159 cases (53.5%) were classified as overweight. There were 298 people (50.2%) in the normal group and 296 people (49.8%) in the overweight group compared with the control group. The BMI distribution of the whole sample accounted for half. In terms of BMI distribution, the median BMI of the case group was 25.3 kg/m^2, and that of Q1-Q3 was 23.1 kg/m^2 to 28.2 kg/m^2. The median BMI in the control group was 25.0 kg/m^2, and Q1-Q3 was 22.9 kg/m^2 to 27.8 kg/m^2. The data collation is shown in *Table 1*. Gender distribution was observed across all subjects. There were 714 males (80.1%) and 177 females (19.9%), age group and BMI as shown in *Table 2*.

Table 1. *Demographic narrative statistics of the study sample*

Characteristic	Alcoholic liver disease	Control
Gender, n (%)		
Female	59 (19.9)	118 (19.9)
Male	238 (80.1)	476 (80.1)
Age, years		
Mean ± SD	71.52 ± 6.04	71.52 ± 6.04
Age group, n (%)		
65-69	137 (46.1)	274 (46.1)
70-74	87 (29.3)	174 (29.3)
75-79	38 (12.8)	76 (12.8)
Over 80	35 (11.8)	70 (11.8)
BMI classification, n (%)		
Normal (18.5 ≤ BMI < 24)	138 (46.5)	298 (50.2)
Overweight (BMI ≥ 24)	159 (53.5)	296 (49.8)
BMI, median (Q1–Q3)	25.3 (23.1-28.2)	25.0 (22.9-27.8)

Table 2. *Demographic characteristics of patients gender*

Characteristic	Male	Female
Gender, n (%)	714 (80.1)	177 (19.9)
Age group, n (%)		
65-69	342 (38.4)	69 (7.7)
70-74	213 (23.9)	48 (5.4)
75-79	90 (10.1)	24 (2.7)
Over 80	69 (7.7)	36 (4.0)
BMI classification, n (%)		
Normal (18.5 ≤ BMI < 24)	358 (40.2)	78 (8.8)
Overweight (BMI ≥ 24)	356 (40.0)	99 (11.1)

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Cross analysis between alcoholic liver disease and body mass index (BMI) for gender and age

The study then carried out a separate crossover analysis of male and female in different age groups. *Table 3* summarizes the distribution of older adults with and without alcoholic liver disease in terms of age and gender. Among elderly male with alcoholic liver disease, 71 patients were in the age range of 70 to 74 years, and this proportion decreased with age. The results also showed that the median BMI of elderly male with alcoholic liver disease was significantly lower than that of those without alcoholic liver disease, all in the overweight status ($p = 0.031$). In addition, among elderly female with alcoholic liver disease, 23 patients were in the 65 to 69 years old and 8 patients were in the 75 to 79 years old. Although the number proportion decreased with age, the BMI gradually increased and all were in the overweight status ($p = 0.025$; $p = 0.043$). In particular, the median BMI of elderly female with alcoholic liver disease between the ages of 75 and 79 was as high as 28.8 kg/m^2 and the Q3 percentile was as high as 31.3 kg/m^2.

Table 3. *The association between alcoholic liver disease and body mass index (BMI) by gender and age*

Age	Alcoholic liver disease	Male			Female		
		Cases	BMI, median (Q1–Q3)	P-value	Cases	BMI, median (Q1–Q3)	P-value
65-69	Yes	114	25.6 (23.4-28.2)	0.075	23	27.4 (25.1-29.4)	0.025
	No	228	25.1 (22.8-27.7)		46	24.6 (22.9-26.7)	
70-74	Yes	71	24.7 (22.7-28.3)	0.031	16	25.0 (22.0-29.9)	0.298
	No	142	25.8 (23.9-28.5)		32	25.2 (22.2-28.2)	
75-79	Yes	30	23.9 (21.3-26.5)	0.185	8	28.8 (27.6-31.1)	0.043
	No	60	24.5 (22.5-26.7)		16	26.1 (23.9-28.9)	
Over 80	Yes	23	23.7 (20.4-26.7)	0.422	12	26.1 (24.3-28.5)	0.474
	No	46	23.6 (21.7-25.8)		24	25.1 (22.9-28.0)	

Figure 2 showed the BMI distribution of elderly male with alcoholic liver disease in four age groups (65-69 years, 70-74 years, 75-79 years, and over 80 years). The results showed that the distribution of BMI in all age groups was similar, and there were a few cases of BMI up to 40, but with the increase of age, the BMI tended to decrease slightly. *Figure 3* showed the BMI distribution of elderly female with alcoholic liver disease across four age groups. The results showed that the distribution of BMI was similar in all age groups, and there were fewer cases with an outlier of up to 40 compared with male. In contrast, elderly female without alcoholic liver disease had a more inconsistent distribution of BMI, such as in the 75-79 age group, which was relatively concentrated in overweight.

Logistic regression analysis of the alcoholic liver disease and overweight by gender and age

Logistic regression was used to analyze the relationship between alcoholic liver disease and BMI. First, in terms of descriptive statistics, the prevalence of overweight in male with alcoholic liver disease decreased with the age distribution. For female, age did not matter much. The effects of alcohol consumption on the liver and revealed clear gender differences in susceptibility to alcoholic liver disease. But among female aged

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65 to 69, those who were overweight were more likely to develop alcoholic liver disease than those who were of normal weight, with an even higher risk of developing it by up to five times. (odds ratio [OR]: 5.12, 95% confidence interval [CI]: 1.62-16.18). Among elderly female aged 75 to 79 years, there were 8 samples with alcoholic liver disease, all of whom were overweight. Although there was no direct correlation between being overweight and developing alcoholic liver disease in this age group, there tended to be a significant difference, with overweight individuals being more likely to develop alcoholic liver disease. However, there was a tendency for significant differences in the fact that overweight individuals were likely to be more likely to develop alcoholic liver disease. The analysis results are summarized in *Table 4*.

Table 4. *Odds ratios (OR) between alcoholic liver disease and overweight by gender and age*

Age	Over weight	Male					Female				
		Alcoholic liver disease cases (%)	Control cases (%)	OR	95% CI	P-value	Alcoholic liver disease cases (%)	Control cases (%)	OR	95% CI	P-value
65-69	Yes	64 (56.1)	115 (50.4)	1.26	0.80-1.98	0.320	5 (21.7)	19 (41.3)	5.12	1.62-16.18	0.005
	No	50 (43.9)	113 (49.6)				18 (78.3)	27 (58.7)			
70-74	Yes	34 (47.9)	84 (59.2)	0.63	0.36-1.13	0.120	8 (50.0)	16 (50.0)	1.04	0.90-1.21	0.588
	No	37 (52.1)	58 (40.8)				8 (50.0)	16 (50.0)			
75-79	Yes	12 (40.0)	23 (38.3)	0.88	0.44-2.63	1.071	8 (100.0)	11 (68.8)	1.29	0.95-1.76	0.099
	No	18 (60.0)	37 (61.7)				0 (0.0)	5 (31.3)			
Over 80	Yes	8 (34.8)	16 (34.8)	1.01	0.90-1.13	0.840	7 (58.3)	12 (50.0)	1.40	0.35-5.67	0.637
	No	15 (65.2)	30 (65.2)				5 (41.7)	12 (50.0)			

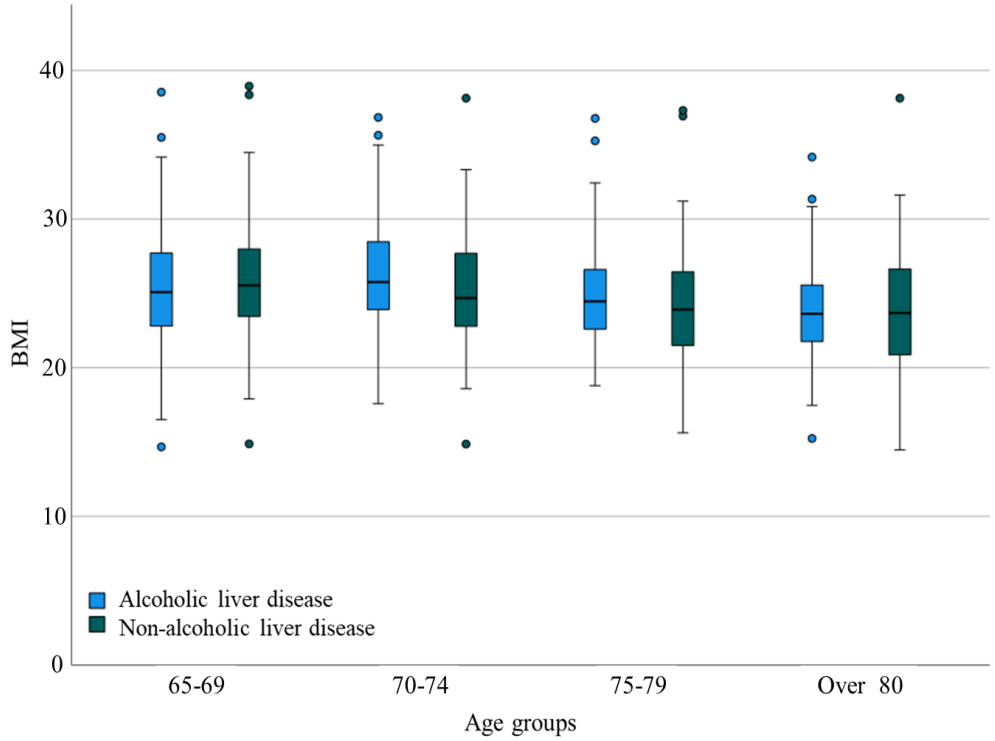

Figure 2. *Comparison of body mass index (BMI) between male between case group and control group*

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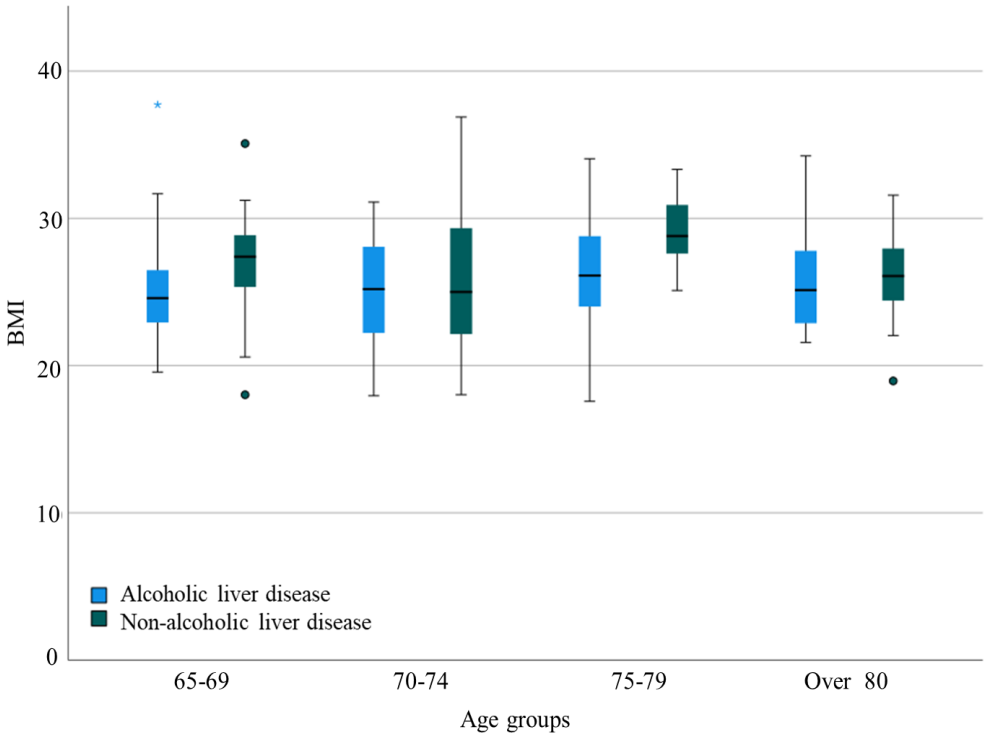

Figure 3. *Comparison of body mass index (BMI) between female between case group and control group*

Discussion

This study aimed to examine the relationship between alcoholic liver disease and overweight in older adults, focusing on age and gender differences. Alcoholic liver disease is a liver disease caused by chronic alcohol consumption, and this study found a significantly higher prevalence in male than in female. This can be attributed to differences in the metabolism of alcohol in male, who typically have higher alcohol consumption and more frequent alcohol abuse behaviors. This is consistent with a previous study by Zhou et al. (2007). In addition, male's liver function may also be more susceptible to damage from alcohol than female's (Agabio et al., 2017). However, female are also at increased risk of developing alcoholic liver disease after menopause because the protective effect on the liver is diminished when estrogen levels decline (Ezhilarasan, 2020). Thus, gender plays an important role in the development and progression of alcoholic liver disease, and more research is needed to gain insight into the mechanisms and prevention strategies.

Elderly patients with alcoholic liver disease usually present with overweight or obesity, which is consistent with past research findings and can be explained in several ways (Dyson et al., 2014). First, alcohol itself is a high-calorie beverage, long-term alcohol consumption will increase caloric intake, easily leading to weight gain (French et al., 2010). Second, alcohol intake will produce direct damage to the liver, affecting its normal metabolic function, which in turn affects the metabolism and decomposition of fat. This may lead to the accumulation of fat in the liver, the formation of fatty liver (Ding et al., 2018). Fatty liver and obesity have a close relationship, the two often affect each other. In addition, alcohol intake may also lead to poor diet and nutritional imbalance, further exacerbating overweight or obesity (Johnson et al., 2013; Stanhope, 2016).

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Conversely, the results are also synchronized to show a slight decrease in BMI with increasing age in older male. The inference is that older male with alcoholic liver disease may face changes in body composition, including a decrease in muscle mass and an increase in adipose tissue, which may lead to a relative decrease in body weight (Ebadi et al., 2020; Shida et al., 2018). In addition, older male may face decreased appetite and reduced digestive and absorption functions, which may also lead to weight loss (Ahmed and Haboubi, 2010). Thus, it may be due to a decrease in metabolic rate, changes in body composition, and other physiological changes associated with aging. For male with alcoholic liver disease, a trend that may reflect the fact that male are more likely to experience weight loss or muscle loss in older age, which in turn reduces the chance of being overweight or obese (Nielson et al., 2012). However, further research is needed to determine this association and possible mechanisms. In contrast, the prevalence of overweight in female with alcoholic liver disease did not vary significantly by age. However, among female aged 65 to 69 years, overweight individuals were more likely to develop alcoholic liver disease than those of normal weight. This finding may be related to the specific physiological and metabolic changes that female face at this age. For example, after menopause, female's estrogen levels decline, which may increase the risk of liver damage from alcohol, as the protective effect on the liver is diminished (Ezhilarasan, 2020). In addition, alcohol use, dietary habits, and other lifestyle factors may also play a role in the association between overweight and alcoholic liver disease in this age group (Zhou et al., 2007). These findings suggest that gender and age may differ between male and female with alcoholic liver disease in terms of overweight and disease risk. Further research will help provide insight into the mechanisms underlying these differences and provide population-specific prevention and intervention strategies. In addition, given that overweight female aged 65 to 69 years are more likely to develop alcoholic liver disease, health management and education for this population is particularly important.

Our study had some limitations. First of all, since this study is a retrospective study, there was no special evaluation due to the possible influence of other physiological factors. In this study, it can be seen that the elderly are the main subjects. But in fact, there are many people who are diagnosed with alcoholic liver disease at a young age. Although this is not in the research purpose of this study, it also leads to the reason that the sample of this study is less than expected. In addition, the data of hospitals in the national Chang Gung system was analyzed in this study, but it is possible that due to regional and individual differences, the results may not be able to fully infer the national alcoholic liver disease patients. Finally, in the absence of an analysis of addiction in this study, we cannot know whether there is a difference in the rate of alcohol addiction between male and female. Therefore, it is suggested that future studies can include addictive factors or use questionnaires to analyze addictive behaviors.

Conclusions

This study investigated the age and gender differences between alcoholic liver disease and overweight in older adults using a population-based database. The results showed significant differences in the occurrence of alcoholic liver disease between male and female. The study found that the condition was significantly more prevalent in male, and revealed the potential influence of biological and behavioral factors that may contribute to the observed differences in disease prevalence between the sexes. Further

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research in this area could help to develop targeted prevention and intervention strategies to effectively address this health problem in both sexes. The findings suggest an interaction between these variables, which may be informative for public health departments and clinicians. In particular, in an aging population, attention to weight control and aging, as well as the occurrence of alcoholic liver disease, may improve the health status and quality of life of patients. However, for female, age did not significantly affect the prevalence of overweight. However, in female aged 65 to 69 years, overweight individuals are more likely to develop alcoholic liver disease than normal weight individuals. This may be related to specific physiological and metabolic changes that female face at this age, such as postmenopausal declines in estrogen levels and reduced hepatic protection. These results highlight the possible differences between gender and age in the risk of overweight and disease in patients with alcoholic liver disease. This has important implications for health care professionals and policy makers. The findings provide guidance for population-specific prevention and treatment strategies and emphasize the importance of weight control and health in older adults.

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