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Research article

Clinical characteristics of heavy alcohol consumption in young and middle-aged acute cerebral infarction: A 12-month follow-up study

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ABSTRACT

Objective: To investigate the clinical characteristics and prognosis of heavy alcohol consumption among young and middle-aged patients with acute cerebral infarction (ACI).
Methods: A total of 263 young and middle-aged ACI patients were included in the study from June 2018 to December 2020 and classified into heavy drinkers and non-heavy drinkers. Multivariate logistic regression analysis was conducted to assess the association between ACI and heavy alcohol consumption, considering clinical characteristics and one-year post-discharge prognosis.
Results: Among the patients, 78 were heavy drinkers. Heavy drinkers were more likely to consume alcohol 24 h before ACI onset (OR 4.03, 95 % CI 2.26–7.20), especially in the form of liquor (OR 3.83, 95 % CI 1.59–9.20), and had a higher risk of diastolic blood pressure ≥90 mmHg upon admission (OR 2.02, 95 % CI 1.12–3.64). In the one-year post-discharge prognosis, heavy drinkers had a greater likelihood of poor prognosis at 3 months (OR 2.31, 95 % CI 1.01–5.25), were less likely to quit drinking after discharge (OR 0.36, 95 % CI 0.19–0.66), and had a higher risk of recurrent cerebral infarction (OR 2.79, 95 % CI 1.14–6.84).
Conclusions: Over the 12-month follow-up, young and middle-aged ACI patients with heavy alcohol consumption exhibited worse short-term prognosis. Controlling alcohol consumption levels may improve the prognosis of these patients.

1. Introduction

Acute cerebral infarction (ACI), also referred to as ischemic stroke (IS), arises from reduced or obstructed blood flow within specific cerebral arteries, resulting from stenosis or occlusion. This leads to concurrent cerebral tissue ischemia, hypoxic necrosis, and neurological impairments [1]. ACI comprises approximately 60 %–70 % of all reported stroke cases [2] and stands as the leading cause of mortality and morbidity among Chinese adults. According to statistics provided by the World Stroke Organization (WSO), the most recent Global Burden of Disease (GBD) report in 2019 underscores cerebral infarction as the world's second leading cause of mortality.

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The associated economic burdens constitute approximately 1.12 % of the global Gross Domestic Product (GDP), surpassing 891 billion dollars [3]. In the context of China, cerebral infarction stands as the predominant cause of mortality and disability among adults, manifesting in an annual incidence exceeding 2 million new cases. The overall incidence rate is escalating, evident in the GBD data revealing an increase in China's incidence rate from 1100 per 100,000 in 2010 to 1256 per 100,000 in 2019. The annual mortality rate experienced a notable 12.1 % upswing from 2007 to 2017. Moreover, in 2019, hospitalization costs surged by 37 % compared to 2010, reaching a substantial 54.8 billion yuan [4–6]. Globally, the incidence rate of ACI has markedly risen by 40 % in individuals aged 18–50. In China, the incidence rate of ACI among those aged 40–59 accounts for 56.8 % of all cases, signifying a shift toward a younger demographic. This trend can be attributed to the heightened stroke risk factors observed in young adults [7]. Consequently, it presents a significant challenge to the workforce, primarily composed of young and middle-aged individuals, warranting attention across various sectors of society [8,9].

Presently, the principal treatment modalities for acute cerebral infarction (ACI) encompass intravenous thrombolysis (IVT) and mechanical thrombectomy (MT) [10]. IVT, administered within the effective time window of 3.0–4.5 h, facilitates timely reperfusion, promoting cerebral vessel recanalization and salvaging the ischemic penumbra. MT extends the treatment time window for ACI [11]. Additionally, the combined use of the antiplatelet drug aspirin and the anticoagulant drug clopidogrel represents a conventional therapeutic approach for ACI. Traditional Chinese medicine injections, such as Safflower Yellow Injection, are commonly employed in ACI treatment. Safflower Yellow Injection and associated combination therapies demonstrate notable safety and minimal adverse reactions [12]. However, emphasizing primary and secondary prevention remains paramount in the comprehensive management of stroke-related diseases. Key preventive strategies involve lifestyle modifications, adherence to a healthy diet, and the limitation of alcohol consumption [13].

Alcohol, a well-recognized risk factor for cerebral infarction, assumes a pivotal role in both primary and secondary prevention. It constitutes a prevalent unhealthy lifestyle choice, particularly among the young and middle-aged population [14,15]. The GBD 2020 Alcohol Collaboration study shows that alcohol consumption is the leading risk factor for mortality for men aged 15–49, primarily increasing the risk of ischemic disease. Individuals aged 15–39 years account for 59.1 % of people with harmful drinking habits, with their theoretical minimum risk exposure level ranging from 0 to 0.603 standard drinks per day [16,17]. However, it is imperative to emphasize that there exists no level of alcohol consumption deemed safe. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) delineates heavy drinking as follows: for men, the consumption of more than 4 drinks on any given day or exceeding 14 drinks per week; for women, surpassing 3 drinks on any day or consuming more than 7 drinks per week is categorized as heavy drinking [18]. Numerous studies have delved into the mechanisms that underlie alcohol-induced cerebral infarction. Hypertension [19,20], atrial fibrillation [21], and atherosclerosis [22] have been identified as significant risk factors for cerebral infarction. Additionally, research has elucidated that alcohol can modulate neurotransmitter activity, potentially triggering cerebral infarction [23].

Previous studies have shown that there may be a J-shaped relationship between alcohol consumption and stroke, where modest alcohol consumption may offer protection to cerebral vessels, while moderate to heavy drinking can induce and aggravate stroke [24]. Nonetheless, it is crucial to recognize the heterogeneous associations that exist between heavy alcohol consumption and various stroke subtypes [25]. Presently, clinical investigations pertaining to binge drinking have predominantly centered on mixed-type stroke cohorts encompassing all age groups or have been specific to hemorrhagic stroke. The primary outcome measures have predominantly concentrated on occurrence rates and mortality rates. Regrettably, there remains a noticeable dearth of data dedicated to exploring the clinical attributes and prognostic outcomes among young and middle-aged patients afflicted with ACI [26–29]. Consequently, our study endeavors to scrutinize the clinical characteristics of young and middle-aged ACI patients with a history of heavy drinking. Furthermore, we seek to compare the incidence of hospitalization complications and the resultant prognostic functional outcomes between individuals characterized as heavy drinkers and their non-heavy drinking counterparts. Our aim is to furnish valuable insights for enhancing clinical diagnosis and treatment strategies in this specific patient cohort. Understanding the relationship between heavy drinking and acute cerebral infarction enables the development of targeted drinking intervention strategies through lifestyle modifications, which could reduce the incidence of ACI and improve the functional prognosis of patients, and offer insights for clinical diagnosis and treatment.

2. Methods

A retrospective observational study was conducted at the First Affiliated Hospital of Chongqing Medical University, utilizing data from all patients admitted to the hospital with a diagnosis of acute cerebral infarction (ACI), as included in the Sino-data for Stroke Survivors (SSS).

2.1. Participant

A total of 2628 ACI cases were documented between June 2018 and December 2020. Inclusion criteria: 1. Age within the range of 18–60 years old; 2. Acute onset of symptoms; 3. Presence of focal neurological deficits, such as weakness or numbness on one side of the face or limbs, language disorders, etc., with a subset experiencing comprehensive neurological deficits; 4. Imaging confirmation of responsible lesions or symptoms/signs persisting for more than 24 h; 5. Exclusion of cerebral hemorrhage determined by computed tomography (CT) scan or magnetic resonance imaging (MRI); 6. The primary admission diagnosis must be acute cerebral infarction (ACI). Exclusion criteria encompassed patients who had ceased alcohol consumption before admission, those with incomplete alcohol consumption records, individuals who abstained from alcohol, patients transferred or discharged within 24 h of admission, and those with severe cardiac, renal, or hepatic dysfunction. In this investigation, patients were classified into two groups: heavy drinkers and

non-heavy drinkers, based on their alcohol consumption levels. This study received approval from the Ethics Committee of the First Affiliated Hospital of Chongqing Medical University (Approved Protocol Number: 2022-201; Date of Approval: September 14, 2022). The information utilized in the study was sourced from the SSS, and written informed consent was obtained from all participating patients.

2.2. Demographic characteristics and medical history

Demographic data, including age, gender, comorbidities, and vascular risk factors, were retrieved from the hospital's electronic medical record system. This encompassed the history of hypertension, diabetes, hyperlipidemia. Within the initial 24 h of hospitalization, the patients' functional independence levels were assessed employing the Modified Rankin Scale (mRS) [30]. Those individuals exhibiting an mRS score exceeding 2 were classified as functionally dependent [31]. Additionally, the National Institutes of Health Stroke Scale (NIHSS) was employed to gauge the severity of neurological deficits upon admission.

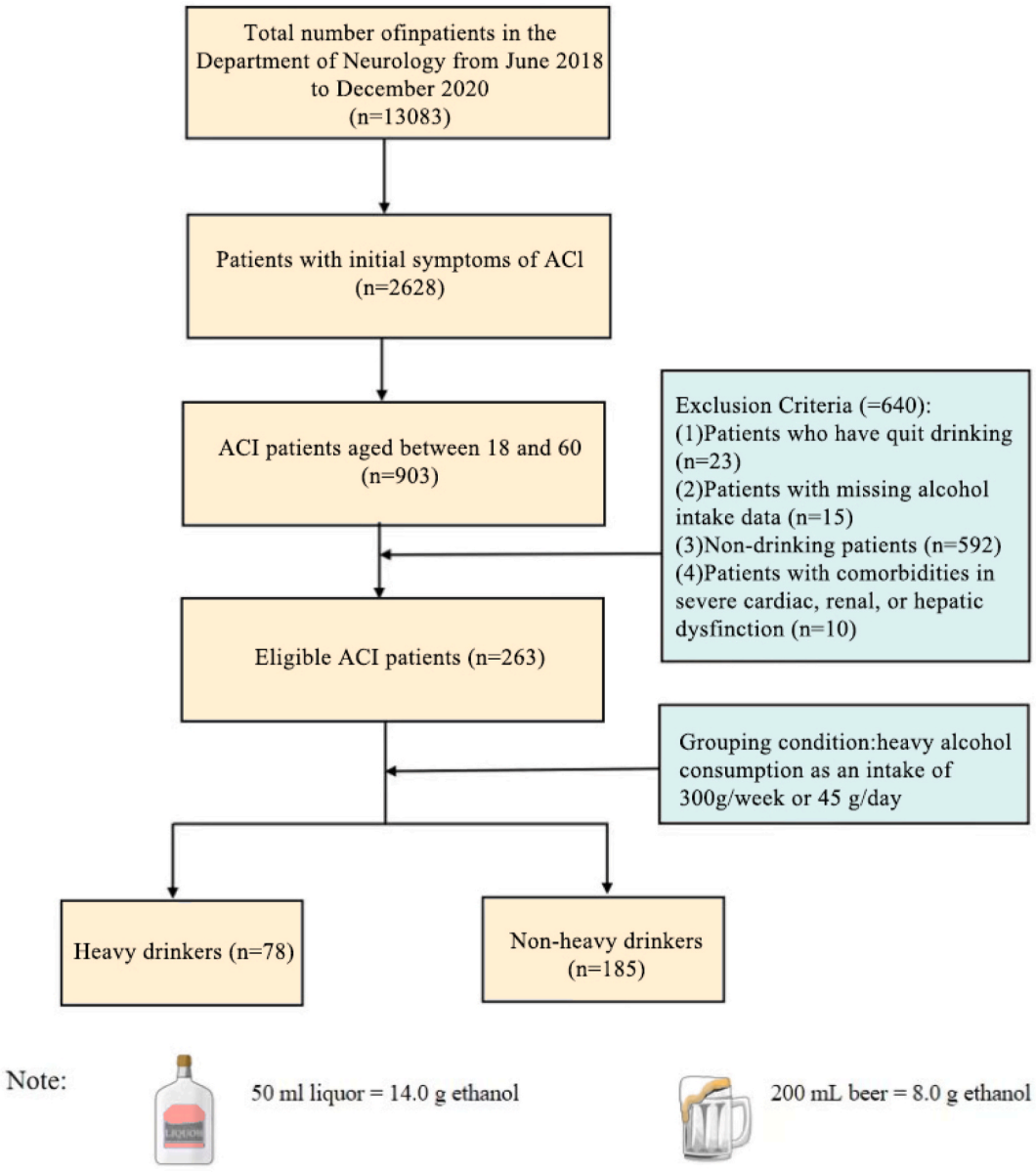

Fig. 1. Flow chart of the selection procedure.

2.3. Alcohol consumption

In this study, patient alcohol consumption characteristics retrieved from the electronic medical record system were documented. This encompassed details such as the duration and frequency of alcohol consumption, the type of alcoholic beverage consumed, the volume of alcohol ingested, and whether alcohol had been consumed within the 24 h preceding the onset of ACI. Daily alcohol consumption was quantified in grams of ethanol, with specific conversions applied: 200 mL of beer containing 8.0 g of ethanol, 100 mL of wine containing 10.0 g of ethanol, and 50 mL of liquor containing 14.0 g of ethanol. The daily alcohol intake (in grams) was determined by aggregating the ethanol quantities [32]. For the purpose of this study, heavy alcohol consumption was defined as a regular intake of alcohol equal to or exceeding 300 g per week or 45 g per day [33]. The study excluded the following categories of patients: nondrinkers (n = 602), individuals with indeterminate drinking patterns (n = 15), and those who had ceased drinking before admission (n = 23) (Fig. 1).

2.4. Evaluation of clinical and biological characteristics upon admission

This study documented various clinical and biochemical indicators upon admission. These encompassed mean arterial blood pressure, body mass index (BMI), platelet count, prothrombin time ratio, activated partial thromboplastin time, fibrinogen levels, high-density lipoprotein cholesterol (HDLC), total cholesterol, fasting blood glucose (FBG) at admission.

2.5. Follow-up

This study encompassed an assessment of several parameters during the follow-up period. These included the duration of hospital stays, treatment modalities administered, and in-hospital complications, which comprised endotracheal intubation, a history of ICU admission, intravenous thrombolysis, occurrences of infection, electrolyte imbalances, anemia, gastrointestinal bleeding, and lower-limb venous thrombosis. Prior to patient discharge, their functional status and neurological deficits were evaluated utilizing the mRS and NIHSS scales, respectively. Subsequently, at the 3-month and 12-month intervals post-discharge, medical personnel responsible for the follow-up conducted assessments. These assessments encompassed patient mortality rates, abstinence rates from alcohol, revisit rates to healthcare facilities, recurrence rates of cerebral infarction, the occurrence of adverse events (such as falls), and the degree of functional recovery. These assessments were performed through telephone interviews.

2.6. Data collection

To prevent bias in the data collection process, this study provided training to data collectors and follow-up personnel on data collection procedures and questionnaire items. If patients had questions during the follow-up, follow-up personnel provided uniform explanations and cross-checked the drinking information in the electronic medical record system at admission to ensure accuracy and

Table 1
Baseline demographics of the study group.

	Heavy drinkers (n = 78)	Non-heavy drinkers (n = 185)	*P-value*
Sex, male	76 (97.4)	178 (96.2)	0.619
Age	51.40 ± 5.95	52.39 ± 5.92	0.214
SBP on admission ≥140 mmHg	57 (73.1)	117 (63.2)	0.080
DBP on admission ≥90 mmHg	51 (65.4)	93 (50.3)	0.017
BMI	25.18 ± 2.73	25.05 ± 2.75	0.724
Previous history			
History of hypertension	49 (62.8)	85 (45.9)	0.012
History of diabetes	14 (17.9)	47 (25.4)	0.191
History of hyperlipidemia	19 (24.4)	40 (21.6)	0.627
Life-history			
Smoking status			0.372
No	10 (12.8)	25 (13.5)	
Had quit smoking	3 (3.9)	16 (8.6)	
Yes	65 (83.3)	144 (77.9)	
Type of alcoholic beverage consumed			0.002
Liquor	71 (91.4)	136 (65.4)	
Beer	7 (8.6)	49 (34.6)	
History of alcohol consumption within 24 h before the onset	50 (64.1)	60 (32.4)	<0.0001
Years of drinking	25.41 ± 10.97	25.57 ± 10.15	0.908
mRS on admission	2.46 ± 1.15	2.09 ± 1.16	0.017
NIHSS on admission	3.00 (1.75–5.25)	2.00 (1.00–4.00)	0.077

Note: Data are represented as mean ± SD, n (%) or median (interquartile range).
Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index, [weight(kg)/height(m)^2]; SD, standard deviation; TIA, transient ischemic attack; mRS, modified rankin scale (scoring from 0 to 6, lower scores indicate better neurological recovery); NIHSS, National Institutes of Health stroke scale (scoring from 0 to 42, higher scores indicate worse neurological damage); IQR, interquartile range.

consistency. After the completion of the follow-up data collection of each study participant, the data collector and follow-up personnel conducted on-site verification, examining the original data for anomalies, inconsistencies, missing values, etc, to ensure the authenticity and reliability of the data and collect the data again if necessary.

2.7. Statistical analysis

The statistical analysis was carried out utilizing SPSS 25.0 software. Normally distributed measurement data were presented as mean ± standard deviation ($\overline{X}$ ±s) and analyzed using the *t*-test. Count data were presented as cases (%) and intergroup characteristics were compared using the chi-square test or Fisher's exact probability method. Non-normally distributed measurement data were expressed as median and interquartile range (M [P25, P75]) and assessed with the Wilcoxon rank-sum test. Indicators that exhibited statistical significance in the univariate analysis were incorporated as covariates in the multivariate logistic regression analyses. Here, heavy alcohol consumption served as the independent variable, while the 1-year follow-up outcome was the dependent variable. A multivariate logistic regression model was established to compare the prognosis between heavy drinkers and non-heavy drinkers at the 1-year post-discharge mark. Variable screening employed the Forward LR method.

The challenge of unbalanced sample sizes was primarily addressed through strategic subject sampling, ensuring a more equitable distribution of data across different categories. Concurrently, the algorithm underwent optimization, factoring in the varying costs associated with different misclassification scenarios. The dataset in this study is notably comprehensive, devoid of any instances of missing data. To prevent the oversight of potentially significant variables, the threshold for *P*-values was extended to 0.07 for single factors demonstrating statistical significance. Additionally, consideration was extended to single factors that, while lacking statistical significance, hold clinical relevance, have been reported as significant in prior research, or are integral to the focus of this study.

3. Results

3.1. Baseline characteristics

Table 1 presents an overview of the demographic characteristics of cerebral infarction patients in this study. A total of 263 patients were included, comprising 254 men (96.6 %), with a median age of 53 years (IQR: 48–56). Among these, 78 patients (29.7 %) were diagnosed with heavy alcohol consumption (29.9 % in men and 22.2 % in women). The majority of heavy drinkers were men (76 cases [97.4 %] vs. 2 cases [2.6 %]), with an average age of 51.40 years, while the average age for non-heavy drinkers was 52.39 years. Significant differences were observed between heavy drinkers and non-heavy drinkers in terms of the history of hypertension (62.8 % vs. 45.9 %, P = 0.012), liquor consumption rate (91.4 % vs. 65.4 %, P = 0.002), alcohol consumption within 24 h before ACI (64.1 % vs. 32.4 %, P < 0.001), and the proportion of individuals with diastolic blood pressure ≥90 mmHg upon admission (65.4 % vs. 50.3 %, P = 0.017). Heavy drinkers also exhibited a significantly lower average mRS functional level upon admission compared to non-heavy drinkers (2.46 vs. 2.09, mRS range: 0–6, P = 0.017). However, no statistically significant differences were found in terms of sex, age, history of diabetes, hyperlipidemia, smoking status, years of drinking, or median NIHSS score upon admission between the two groups (P > 0.05) (Table 1, Fig. 2).

A series of variables were included and screened via multivariate logistic regression analysis. These variables encompassed the history of hypertension, the type of alcoholic beverage consumed, whether alcohol was consumed within 24 h before the onset of ACI, diastolic blood pressure upon admission, HDLC levels, and mRS scores upon admission (Table 2).

The results revealed that whether alcohol was consumed within 24 h before the onset of ACI, the type of alcoholic beverage consumed, and diastolic blood pressure emerged as independent risk factors for alcohol-related ACI. As presented in Table 2,

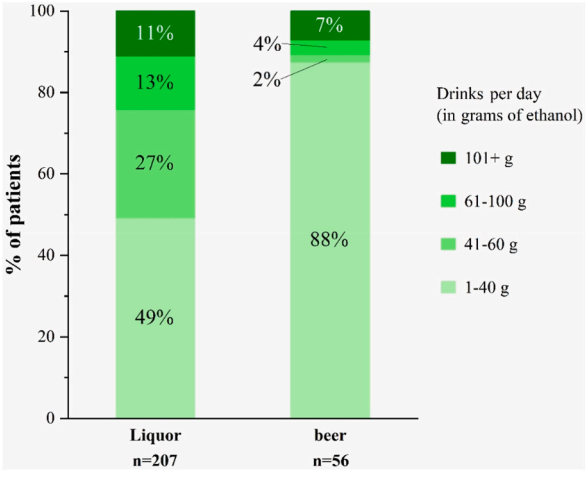

Fig. 2. The distribution of alcohol consumption among the study population.

Table 2
The covariates included in the LR model.

No.	Covariate
1	History of hypertension
2	Type of alcohol consumption
3	Alcohol consumption within 24 h prior to stroke onset
4	Diastolic blood pressure at admission (≥90 mmHg)
5	High-density lipoprotein cholesterol
6	mRS scores at admission

individuals who had consumed alcohol within 24 h prior to the onset exhibited a 4.03-fold increased risk of developing alcohol-related ACI in comparison to those who had not consumed alcohol within the 24-h window (OR 4.03, 95 % CI 2.26–7.20, p < 0.001). Furthermore, patients with a daily consumption of liquor were 3.83 times more likely to develop alcohol-related ACI than those who primarily consumed beer (OR 3.83, 95 % CI 1.59–9.20, P = 0.003). Additionally, patients presenting with diastolic blood pressure levels ≥90 mmHg upon admission exhibited a 2.02-fold increased risk of developing alcohol-related ACI (OR 2.02, 95 % CI 1.12–3.64, P = 0.020) (Fig. 3) (Table 3).

3.2. Clinical and biological assessment associated with heavy alcohol consumption

Table 3 presents a comparative analysis of clinical and biological indicators between heavy drinkers and non-heavy drinkers. While the concentration of high-density lipoprotein cholesterol (HDLC) in heavy drinkers fell within the normal range, it was notably lower compared to non-heavy drinkers (1.00 ± 0.25 vs. 1.09 ± 0.27, P = 0.017). However, no statistically significant differences were observed in terms of platelet count, prothrombin time ratio, activated partial thromboplastin time, fibrinogen levels, total cholesterol, and at-admission fasting blood glucose (FBG) between the two groups (Table 4).

3.3. The effect of heavy alcohol consumption on in-hospital complications

Table 4 delineates the impact of heavy alcohol consumption on in-hospital complications. Notably, heavy drinkers exhibited a higher incidence of nosocomial infection (10.3 %) compared to non-heavy drinkers (3.2 %), and this difference was statistically significant (P = 0.044). However, no statistically significant differences were observed in the incidence of other complications, including the need for endotracheal intubation or intravenous thrombolysis, a history of ICU admission, electrolyte imbalances, anemia, gastrointestinal bleeding, and venous thrombosis between the two groups. The median length of hospital stay was 10 days for heavy drinkers (IQR: 8–14) and 11 days for non-heavy drinkers (IQR: 8–14). There was no significant difference in the length of hospital stay between the two groups (P = 0.427) (Table 5).

3.4 The effect of alcohol consumption on functional outcome at 3 months and 12 months after discharge

At the time of discharge, heavy drinkers and non-heavy drinkers exhibited median mRS scores of 1.00 (IQR: 1.00–2.25) and 1.00 (IQR: 0.00–2.00), respectively, with a statistically significant difference (P = 0.037). Subsequently, after 3 months, heavy drinkers displayed a notably higher proportion of functional dependence in comparison to non-heavy drinkers (26.9 % vs. 12.4 %). This disparity in functional dependence persisted at the 12-month mark, with heavy drinkers still exhibiting a significantly higher proportion of functional dependence (16.7 % vs. 7.6 %). During the 12-month follow-up period, more than half of the patients had discontinued alcohol consumption, and the abstinence rate among non-heavy drinkers was significantly higher than that among heavy drinkers (38.5 % vs. 64.3 %). Furthermore, heavy drinkers exhibited a significantly higher recurrence rate of cerebral infarction in the advanced stage compared to non-heavy drinkers (16.7 % vs. 5.9 %). The mortality rate among heavy drinkers was higher than that

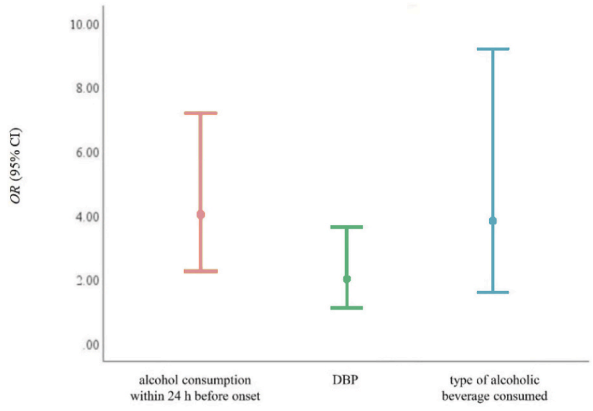

Fig. 3. Forest plot of independent risk factors in ACI patients with heavy alcohol consumption.

Table 3
Independent risk factors in ACI patients with heavy alcohol consumption.

	B	SE	Wald	*P-value*	*OR* (95 % CI)
Alcohol consumption within 24 h before the onset	1.395	0.296	22.232	<0.0001	4.03 (2.26–7.20)
Type of alcoholic beverage consumed					
Beer	Ref				
Liquor	1.342	0.447	8.999	0.003	3.83 (1.59–9.20)
DBP on admission	0.703	0.301	5.453	0.020	2.02 (1.12–3.64)
Constant	−3.064	0.503	37.063	<0.0001	0.047

Abbreviations: DBP, diastolic blood pressure; Ref, reference; SE, standard error; OR, odds ratio; CI, confidence interval.

Table 4
Clinical characteristics of enrolled subjects.

	Heavy drinkers (n = 78)	Non-heavy drinkers (n = 185)	*P-value*
Platelet count	217.12 ± 65.47	219.24 ± 65.25	0.809
Prothrombin time ratio	0.97 ± 0.09	0.96 ± 0.07	0.658
Activated partial thromboplastin	25.78 ± 4.29	25.37 ± 3.79	0.440
Fibrinogen	3.16 ± 0.99	3.02 ± 0.90	0.264
High density lipoprotein cholesterol	1.00 ± 0.25	1.09 ± 0.27	0.017
Total cholesterol	4.54 ± 1.34	4.43 ± 1.18	0.437
Fasting blood glucose upon admission	6.86 ± 2.87	6.80 ± 2.26	0.841

Note: Data are represented as mean ± SD or median (interquartile range).
Abbreviations: SD, standard deviation; IQR, interquartile range.

Table 5
Differences in medical complications of the study groups.

	Heavy drinkers (n = 78)	Non-heavy drinkers (n = 185)	*P-value*
Infection	8 (10.3)	6 (3.2)	0.044
Electrolyte disturbance	4 (4.9)	11 (6.3)	1.000
Anemia	2 (2.6)	3 (1.6)	0.987
Gastrointestinal bleeding	3 (3.8)	3 (1.6)	0.515
Lower extremity venous thrombosis	1 (1.3)	3 (1.6)	1.000
Tracheal intubation	4 (5.1)	6 (3.2)	0.706
Intravenous thrombolysis	1 (1.3)	7 (3.8)	0.493
History of intensive care unit	13 (19.8)	31 (14.2)	0.986

Note: Data are represented as n (%).

among non-heavy drinkers after 3 months (2.50 % vs. 1.1 %) and 12 months (3.7 % vs. 3.1 %) of follow-up; however, no statistically significant differences were observed (Table 6).

Additionally, the prognosis of heavy drinkers was notably worse than that of non-heavy drinkers at 3 months after discharge (OR 2.31, 95 % CI 1.01–5.25, P = 0.046). The odds of abstinence after discharge were lower among heavy drinkers (OR 0.36, 95 % CI 0.19–0.66, P = 0.001). Furthermore, heavy drinkers faced an increased risk of recurrent cerebral infarction (OR 2.79, 95 % CI 1.14–6.84, P = 0.024) (Table 6).

4. Discussion

In this study, a cohort of 263 patients was examined, comprising 78 heavy drinkers (97.4 % men and 2.6 % women), with a median age of 52 years (IQR: 47–56 years), and 185 non-heavy drinkers (96.2 % men and 3.8 % women), with a median age of 54 years (IQR: 49–57 years). Our findings revealed several significant associations. Firstly, heavy drinkers demonstrated a heightened likelihood of alcohol consumption within 24 h preceding the onset of symptoms, with an odds ratio (OR) of 4.03 (95 % CI 2.26–7.20). Furthermore, they exhibited a preference for liquor consumption, with an OR of 3.83 (95 % CI 1.59–9.20). Importantly, heavy drinkers had an elevated risk of presenting with diastolic blood pressure levels ≥90 mmHg upon admission, with an OR of 2.02 (95 % CI 1.21–3.64). Regarding post-discharge outcomes, heavy alcohol drinkers were more likely to experience a poor prognosis at the 3-month follow-up, with an OR of 2.31 (95 % CI 1.01–5.25). Additionally, they were less inclined to discontinue alcohol consumption after discharge, with an OR of 0.36 (95 % CI 0.19–0.66). Furthermore, heavy drinkers faced a substantially increased risk of recurrent cerebral infarction, with an OR of 2.79 (95 % CI 1.14–6.84). These findings underscore the intricate relationship between heavy alcohol consumption and acute cerebral infarction, highlighting the importance of considering alcohol consumption patterns in clinical assessment and intervention strategies.

This study constitutes a single-center retrospective observational investigation focusing on assessing the impact of heavy alcohol consumption on the prognosis of young and middle-aged patients with acute cerebral infarction (ACI). A comprehensive evaluation of

Table 6
Outcomes according to alcohol consumption in ACI patients.

	Heavy drinkers (n = 78)	Non-heavy drinkers (n = 185)	*P-value* (unadjusted)	*OR* (95 % CI)	*P -value* (adjusted)[a]	*OR* (95 % CI)
mRS at discharge	19 (24.4)	29 (15.7)	0.103	1.73 (0.90–3.22)	0.832	0.91 (0.38–2.20)
NIHSS at discharge	12 (15.4)	21 (11.4)	0.393	1.71 (0.76–3.85)	0.484	1.45 (0.53–4.00)
mRS after 3 months	21 (26.9)	23 (12.4)	0.008	2.74 (1.40–5.35)	0.202	2.11 (0.49–7.53)
mRS after 12 months	13 (16.7)	14 (7.6)	0.044	2.55 (1.14–5.74)	0.545	1.56 (0.59–4.13)
Death after 3 months + functional dependence	23 (29.5)	25 (13.5)	0.003	2.68 (1.41–5.10)	**0.046**	2.31 (1.01–5.25)
Death after 12 months + functional dependence	18 (23.1)	20 (10.8)	0.012	2.48 (1.23–4.99)	0.311	1.53 (0.68–3.47)
Alcohol withdrawal	30 (38.5)	119 (64.3)	0.000	0.35 (0.20–0.60)	**0.001**	0.36 (0.19–0.66)
Recurrent cerebral infarction	13 (16.7)	11 (5.9)	0.008	3.16 (1.35–7.42)	**0.024**	2.79 (1.14–6.84)
Revisit rate	47 (60.3)	104 (56.2)	0.544	1.18 (0.69–2.02)	0.976	0.99 (0.55–1.79)
Adverse event	11 (14.1)	34 (18.4)	0.393	0.73 (0.35–1.53)	0.181	0.58 (0.26–1.31)

Note: Data are represented as n (%). *P*-values below 0.05 are presented in bold.
Abbreviations: mRS, modified rankin scale; NIHSS, National Institutes of Health stroke scale; functional dependence = mRs>2; OR, odds ratio; CI, confidence interval; Adverse events include but not limited to falls, bed falls, infections, aspiration, pressure sores, deep vein thrombosis, burns.
[a] Adjusted by DBP on admission ≥90 mmHg, history of hypertension, type of alcoholic beverage consumed, history of alcohol consumption within 24 h before the onset, mRS on admission, high density lipoprotein cholesterol, infection.

missing data was performed to ensure robust statistical analyses. The study identified missing data in several key variables, including mRS score on admission (n = 1), NIHSS score on admission (n = 2), NIHSS at discharge (n = 4), platelet count (n = 18), prothrombin time ratio (n = 15), activated partial thromboplastin (n = 15), γ-glutamyl transferase (n = 8), fibrinogen (n = 15), high-density lipoprotein cholesterol (HDLC) (n = 18), total cholesterol (n = 18). To address the challenge of missing data, a rigorous approach was adopted. The multivariate imputation by chained equations (MICE) package was employed to perform multiple imputations, thereby mitigating the impact of missing data on the overall sample size and statistical outcomes. This approach enhances the stability of the statistical results while minimizing inflated standard errors [34]. The study systematically collected fundamental data pertaining to alcohol consumption patterns. This encompassed information such as the frequency and duration of drinking, the type of alcoholic beverage consumed, the volume of alcohol ingested, and whether alcohol intake occurred within 24 h before the onset of ACI. It is worth noting that the alcohol consumption data in the medical records were reliant on self-reporting by patients upon admission, introducing a potential source of recall bias [35]. It is pertinent to note that a consensus on standardized levels of alcohol consumption remains elusive, with varying definitions of a "standard drink" prevailing across different countries. Consequently, to ensure optimal comparability within this study, the preferred approach was to quantify alcohol consumption in terms of volume or grams of pure alcohol consumed [36]. The criteria utilized for classifying heavy alcohol consumption within this study were established in accordance with existing guidelines and pertinent research findings, designating heavy alcohol consumption as an intake of 300 g/week or 45 g/day [14,33,37]. To enhance homogeneity and mitigate potential biases between the two groups under examination, this study intentionally excluded both non-drinkers and abstainers from the analysis. Furthermore, it is important to clarify that the laboratory indicators considered in this study were derived from the initial examinations conducted upon patients' admission, with the majority of data collection occurring within 48 h following admission. This approach ensures that the data accurately reflects the baseline clinical status of the patients at the onset of their medical care.

Heavy alcohol consumption stands as a prominent risk factor contributing to the global disease burden, responsible for approximately 10 % of deaths among young and middle-aged individuals worldwide [38]. The results gleaned from this study have shed light on a noteworthy observation. Among heavy drinkers, the average age of acute cerebral infarction (ACI) onset was 51.40 years, signifying a difference of 1 year when compared to non-heavy drinkers. This finding aligns with the outcomes of a prior prospective study conducted in Japan, which similarly documented that heavy drinkers, within the population of young and middle-aged individuals afflicted by stroke, experienced stroke onset at a younger age compared to their non-heavy drinking counterparts [25]. Several previous investigations have illuminated the role of alcohol-related hypertension as a potential causal pathway leading to stroke [39]. Mechanisms implicated in this context encompass alcohol-induced vascular constriction and oxidative stress. Heavy alcohol consumption has the capacity to induce hypertension by inhibiting the vagus nerve while simultaneously activating the sympathetic nerve [40]. Notably, within this study, 62.8 % of patients with heavy alcohol consumption exhibited pre-existing hypertension before their admission. Furthermore, the average diastolic blood pressure upon admission was significantly higher in heavy drinkers in comparison to their non-heavy drinking counterparts (96.17 ± 15.89 vs. 91.98 ± 14.17). An additional aspect meriting consideration is the correlation between alcohol and high-density lipoprotein cholesterol (HDLC), which hints at a potential mechanism involving the induction of atherosclerosis [41]. This study identified a significant reduction in HDLC levels among heavy

drinkers in comparison to non-heavy drinkers, despite both groups falling within the normal range. It is pertinent to highlight the regional prevalence of alcohol consumption patterns, particularly in China, where liquor and beer are commonly consumed by residents [42]. These regional nuances can contribute to variations in the type of alcoholic beverages consumed, which may also differ between men and women [43]. Within this study, liquor consumption accounted for 74.9 % of the total study population. Notably, individuals who consumed liquor exhibited 3.828 times higher odds of developing severe alcohol-induced ACI when contrasted with those who favored beer consumption. A prospective cohort study has previously demonstrated that individuals who frequently consumed liquor faced a heightened risk of cardiovascular events and mortality, followed by consumers of red wine and beer/cider, a pattern that resonates with the findings of this study [44]. In this study, only nine women were included, consistent with previous epidemiological reports of chronically higher alcohol consumption among men compared to women [38,45]. Additionally, previous studies have shown that women usually consume less alcohol than men, so there may also be gender differences in drinking criteria [46]. As the population of this study was almost exclusively male with limited female participation, this study may have overestimated the average alcohol consumption, which affects the generalizability of the findings to a broader population. Future studies with larger sample sizes are needed to explore the impact of alcohol consumption on female patients with stroke.

ACI exhibits the capacity for classification into distinct subtypes based on etiology and infarct site, and it is plausible that alcohol consumption exerts differing effects on each of these subtypes [28]. A recent meta-analysis, encompassing a diverse array of prospective studies with varying geographic locations and age distributions, discerned a correlation between heavy alcohol consumption and an elevated risk of ACI. However, the meta-analysis encountered limitations due to the scarcity of studies delving into the subtypes of ACI. Consequently, it did not undertake a specific analysis to assess the impact of alcohol consumption based on ACI subtype, whether delineated by potential etiology or infarct site. Prior research has hinted at nuanced correlations between alcohol consumption levels and ACI subtypes. Specifically, it has suggested a positive correlation between moderate to heavy alcohol consumption and cardioembolism, alongside a negative correlation between low to moderate alcohol consumption and small artery occlusion [25]. In the context of our study, heavy drinkers exhibited a notably higher prevalence of large artery atherosclerosis, cardioembolism, and small artery occlusion when compared to their non-heavy drinking counterparts, although these differences did not achieve statistical significance. It is imperative to acknowledge that the relatively small sample size of our study may have contributed to these non-significant results. Consequently, further investigations featuring larger sample sizes are warranted to elucidate the intricate relationship between alcohol consumption and ACI subtypes more comprehensively.

Within our study, after meticulous control for variables exhibiting significant disparities in univariate analysis, a noteworthy trend emerged: patients characterized by heavy alcohol consumption experienced notably poorer outcomes. While heavy alcohol consumption didn't correlate with increased mortality within the first year, it did confer a statistically significant elevation in the likelihood of experiencing comprehensive disability and mortality three months following discharge (OR 2.31, 95 % CI 1.01–5.25). This phenomenon may be attributed to the detrimental effects of excessive alcohol intake on cerebellar function, leading to motor incoordination and balance disorders [47]. Previous research has detected a comparable pattern in patients with cerebral hemorrhage, where heavy alcohol consumption heightened the risk of adverse outcomes at both the 3-month and 12-month post-discharge junctures [34], aligning with our study's findings. It is crucial to acknowledge that the non-significant difference observed at the 12-month mark in our study might be attributable to the relatively lower short-term mortality rates typically encountered in patients with acute cerebral infarction (ACI). Additionally, when assessing functional prognosis, it's vital to recognize that ACI patients frequently exhibit more favorable prognostic outcomes in comparison to their cerebral hemorrhage counterparts [48]. Heavy alcohol consumption may yield varying effects across different subtypes of cerebral infarction [49]. Our study concentrated on the young and middle-aged demographic, a selection that might introduce variations in prognosis and outcome tendencies among distinct cerebral infarction subtypes. This warrants further clinical research to dissect these variations comprehensively. Another intriguing observation emerged from our study, revealing that patients characterized by severe alcohol consumption demonstrated a diminished likelihood of ceasing alcohol use after discharge (OR 0.36, 95 % CI 0.19–0.66). This phenomenon can be partly attributed to the heightened dependency on alcohol exhibited by individuals with severe alcohol consumption [50]. The relationship between alcohol consumption and the risk of stroke recurrence remains a multifaceted area. Our study suggested a potential upward trajectory in the risk of recurrent cerebral infarction among patients with moderate to severe alcohol consumption (OR 2.79, 95 % CI 1.14–6.84). While some prior studies have illuminated a correlation between stroke recurrence and alcohol consumption [51,52], there exists a scarcity of research that probes the recurrence rate of stroke as a comprehensive outcome indicator. Moreover, the recurrence rate may exhibit variations within each subtype of stroke. Thus, further clinical investigations are imperative to scrutinize these findings with greater precision. In addition, previous studies have shown that heavy drinking tends to be more prevalent in higher-income and upper-middle-income countries [18]. The study population was selected from a grade A tertiary hospital in Chongqing, China. Differences in socioeconomic, regional culture and racial or ethnic groups may affect the drinking patterns and levels of alcohol consumption among the study participants. Moreover, the standard of healthcare may also impact the socioeconomic health of patients with acute cerebral infarction [38]. Therefore, future studies with large sample sizes across diverse regions are needed to explore the relationship between socio-economic factors and drinking culture.

This study concentrated primarily on young and middle-aged individuals diagnosed with ACI. A striking contrast emerged when comparing ACI patients with heavy alcohol consumption to their non-heavy drinking counterparts, revealing distinctive clinical characteristics. It is crucial to note that despite initial similarities in clinical severity and in-hospital complication rates between the two groups, heavy drinkers appeared to exhibit a poorer prognosis concerning recurrent cerebral infarction and an elevated incidence of alcohol withdrawal at the three-month post-discharge juncture.

This study aims to investigate the correlation between heavy drinking and acute cerebral infarction. The objective is to promote the assessment of drinking behavior, highlight the adverse association between drinking and disease prognosis, encourage patients to

reduce alcohol consumption, develop appropriate intervention strategies through advocating lifestyle changes to improve the prognosis of patients with stroke, and provide reference for advancing primary and secondary prevention of stroke.

4.1. Limitations of the study

Despite the valuable insights garnered from this research, several limitations should be acknowledged. Firstly, it is important to note that the drinking data retrieved from the electronic medical record system may be subject to inaccuracy, given its reliance on patient self-reporting. This inherent limitation introduces the possibility of recall bias. Secondly, the study's relatively small sample size hinders the comprehensive analysis of the relationship between heavy drinking and the risk associated with distinct subtypes of cerebral infarction as categorized by the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification. This study is a single-center study, which may limit the generalizability of findings in other settings or populations. Furthermore, this study lacks longitudinal data to monitor changes in drinking habits over time and their impact on ACI risk and prognosis. At present, there is an international lack of consensus on alcohol intake standards, leading to varying definitions of "heavy drinking." US dietary guidelines suggest women consume up to 1 drink a day and men up to 2 drinks a day (1 drink = 14.0 g of ethanol) [36], while Australian alcohol guidelines recommend healthy adults to limit alcohol intake to 10 drinks a week (1 drink = 10.0 g of ethanol) [53]. These differing standards complicate the comparability of drinking data. In this study, gender differences were large, and future studies with larger sample sizes are needed to explore the impact of alcohol consumption on female patients with stroke. These limitations underscore the need for future research endeavors to address these constraints and yield a more nuanced understanding of the complex interplay between heavy alcohol consumption and cerebral infarction subtypes.

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Data availability

The datasets used and analyzed during the current study are not publicly available due to the authors do not have permission to share data, but are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Jia Liao: Writing – original draft, Methodology, Data curation, Conceptualization. **Xin Li:** Writing – review & editing, Investigation, Data curation. **Ling Wang:** Writing – review & editing, Investigation, Data curation. **Mingfen Chen:** Writing – review & editing, Investigation. **Fengying Quan:** Writing – review & editing, Supervision. **Zhiqin Xi:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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References

[1] K. Walter, What is acute ischemic stroke? JAMA, J. Am. Med. Assoc. 327 (2022) 885.
[2] S. Wu, et al., Stroke in China: advances and challenges in epidemiology, prevention, and management, Lancet Neurol. 18 (2019) 394–405.
[3] V.L. Feigin, M. Brainin, B. Norrving, World Stroke Organization (WSO): global stroke fact sheet 2022, Int. J. Stroke 17 (2022) 18–29.
[4] W.J. Tu, L.D. Wang, China stroke surveillance report 2021, Military Med. Res. 10 (2023) 33.
[5] C.W. Tsao, et al., Heart disease and stroke statistics-2022 update: a report from the American Heart Association, Circulation 145 (2022) E153–E639.
[6] W.J. Tu, et al., Estimated burden of stroke in China in 2020, JAMA Netw. Open 6 (2023) e231455.
[7] G.A. Roth, et al., Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: a systematic analysis for the Global Burden of Disease Study 2017, Lancet 392 (2018) 1736–1788.
[8] M.S. Ekker, et al., Epidemiology, aetiology, and management of ischaemic stroke in young adults, Lancet Neurol. 17 (2018) 790–801.
[9] R. Zhang, et al., Global burden of ischemic stroke in young adults in 204 countries and territories, Neurology 100 (2023) E422–E434.
[10] F. Herpich, F. Rincon, Management of acute ischemic stroke, Crit. Care Med. 48 (2020) 1654–1663.
[11] V. Saini, L. Guada, D.R. Yavagal, Global epidemiology of stroke and access to acute ischemic stroke interventions, Neurology 97 (2021) S6–S16.
[12] Y. Li, et al., Safflower yellow pigment and Sanqi Panax notoginseng in the treatment of acute cerebral infarction: a systematic review, meta-analysis, and cost-effectiveness analysis, Ann. Transl. Med. 9 (2021) 1407.
[13] S.J. Mendelson, S. Prabhakaran, Diagnosis and management of transient ischemic attack and acute ischemic stroke: a review, JAMA, J. Am. Med. Assoc. 325 (2021) 1088–1098.
[14] M. Han, et al., Habitual alcohol intake and risk of atrial fibrillation in young adults in Korea, JAMA Netw. Open 5 (2022) e2229799.

[15] Centers for Disease Control and Prevention, Postneonatal mortality among Alaska Native infants-Alaska, 1989-2009, MMWR-Morb, Mortal. Wkly. Rep. 61 (2012) 1–5.
[16] J. Manthey, K. Shield, J. Rehm, Alcohol and health, Lancet 400 (10365) (2022) 1764–1765.
[17] D. Bryazka, M.B. Reitsma, M.G. Griswold, et al., Population-level risks of alcohol consumption by amount, geography, age, sex, and year: a systematic analysis for the Global Burden of Disease Study 2020, Lancet 400 (10347) (2022) 185–235.
[18] A.F. Carvalho, M. Heilig, A. Perez, C. Probst, J. Rehm, Alcohol use disorders, Lancet 394 (2019) 781–792.
[19] M. Roerecke, et al., The effect of a reduction in alcohol consumption on blood pressure: a systematic review and meta-analysis, Lancet Public Health 2 (2017) E108–E120.
[20] P.D. Arkwright, L.J. Beilin, I. Rouse, B.K. Armstrong, R. Vandongen, Alcohol: effect on blood pressure and predisposition to hypertension, Clin. Sci. 61 (1981) 373s–375s.
[21] S. Brunner, et al., Alcohol consumption, sinus tachycardia, and cardiac arrhythmias at the Munich Octoberfest: results from the Munich beer related electrocardiogram workup study (MunichBREW), Eur. Heart J. 38 (2017) 2100–2106.
[22] E.L. O'Keefe, J.J. DiNicolantonio, J.H. O'Keefe, et al., Alcohol and CV health: Jekyll and Hyde J-curves, Prog. Cardiovasc. Dis. 61 (1) (2018) 68–75.
[23] K.H. Cho, H.S. Nam, D.J. Kang, M.H. Park, J.H. Kim, Long-term alcohol consumption caused a significant decrease in serum high-density lipoprotein (hdl)-cholesterol and apolipoprotein a-i with the atherogenic changes of hdl in middle-aged Korean women, Int. J. Mol. Sci. 23 (2022) 8623.
[24] E.V. Sullivan, Q. Zhao, K.M. Pohl, N.M. Zahr, A. Pfefferbaum, Attenuated cerebral blood flow in frontolimbic and insular cortices in alcohol use disorder: relation to working memory, J. Psychiatr. Res. 136 (2021) 140–148.
[25] H. Iso, et al., Alcohol consumption and risk of stroke among middle-aged men: the JPHC Study Cohort I, Stroke 35 (2004) 1124–1129.
[26] S. Ikehara, et al., Alcohol consumption and risk of stroke and coronary heart disease among Japanese women: the Japan Public Health Center-based prospective study, Prev. Med. 57 (2013) 505–510.
[27] C. Gentile, L. Stein, M.S. Dhamoon, Alcohol-related hospital encounters trigger thrombotic and hemorrhagic vascular events, J. Stroke Cerebrovasc. Dis. 28 (2019) 104395.
[28] S.C. Larsson, A. Wallin, A. Wolk, H.S. Markus, Differing association of alcohol consumption with different stroke types: a systematic review and meta-analysis, BMC Med. 14 (2016) 178.
[29] D. Spiegelman, et al., The Moderate Alcohol and Cardiovascular Health Trial (MACH15): design and methods for a randomized trial of moderate alcohol consumption and cardiometabolic risk, Eur. J. Prev. Cardiol. 27 (2020) 1967–1982.
[30] S.E. Kasner, Clinical interpretation and use of stroke scales, Lancet Neurol. 5 (2006) 603–612.
[31] T.J. Quinn, J. Dawson, M.R. Walters, K.R. Lees, Functional outcome measures in contemporary stroke trials, Int. J. Stroke 4 (2009) 200–205.
[32] R. Vliegenthart, et al., Alcohol consumption and risk of peripheral arterial disease: the Rotterdam study, Am. J. Epidemiol. 155 (2002) 332–338.
[33] B. Casolla, et al., Heavy alcohol intake and intracerebral hemorrhage: characteristics and effect on outcome, Neurology 79 (2012) 1109–1115.
[34] Z. Zhang, Multiple imputation with multivariate imputation by chained equation (MICE) package, Ann. Transl. Med. 4 (2016) 30.
[35] M. Cox, B. Chaney, L. McDonald, M.B. Miller, Assessing alcohol use in situ: correlates of self-report vs. objective alcohol consumption, Addict. Behav. 129 (2022) 107278.
[36] H. Hendriks, Alcohol and human health: what is the evidence? Annu. Rev. Food Sci. Technol. 11 (2020) 1–21.
[37] C. Avellaneda-Gómez, et al., Alcohol overuse and intracerebral hemorrhage: characteristics and long-term outcome, Eur. J. Neurol. 25 (2018) 1358–1364.
[38] M.G. Griswold, et al., Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016, Lancet 392 (2018) 1015–1035.
[39] I.B. Puddey, T.A. Mori, A.E. Barden, L.J. Beilin, Alcohol and hypertension-new insights and lingering controversies, Curr. Hypertens. Rep. 21 (2019) 79.
[40] F.D. Fuchs, S.C. Fuchs, The effect of alcohol on blood pressure and hypertension, Curr. Hypertens. Rep. 23 (2021) 42.
[41] E.L. O'Keefe, J.J. DiNicolantonio, J.H. O'Keefe, C.J. Lavie, Alcohol and CV health: Jekyll and Hyde J-curves, Prog. Cardiovasc. Dis. 61 (2018) 68–75.
[42] A.F. Di Castelnuovo, S. Costanzo, G. de Gaetano, Alcohol and the global burden of disease, Lancet 393 (10189) (2019) 2389.
[43] A. Kalinowski, K. Humphreys, Governmental standard drink definitions and low-risk alcohol consumption guidelines in 37 countries, Addiction 111 (7) (2016) 1293–1298.
[44] F. Huang, et al., Public health response to drinking behavior and control of harmful drinking among Chinese residents, Chin. J. Prev. Contr. Chron. Dis. 28 (2020) 861–865.
[45] L. Chen, et al., Analysis on the trend of drinking behavior in a healthy physical examination group in urban area of Beijing from 2008 to 2018, Chin. J. Dis. Contr. Prev 25 (2021) 284–288.
[46] B.D. Jani, et al., Association between patterns of alcohol consumption (beverage type, frequency and consumption with food) and risk of adverse health outcomes: a prospective cohort study, BMC Med. 19 (2021) 8.
[47] R. Rao, A. Topiwala, Alcohol use disorders and the brain, Addiction 115 (2020) 1580–1589.
[48] K. Toyoda, et al., Twenty-year change in severity and outcome of ischemic and hemorrhagic strokes, JAMA Neurol. 79 (2022) 61–69.
[49] A.M. Russo, Alcohol intake and risk of stroke in atrial fibrillation: the lesser the better, but this is not enough, Eur. Heart J. 42 (2021) 4769–4771.
[50] J.A. Rosansky, H. Rosenberg, A systematic review of reasons for abstinence from alcohol reported by lifelong abstainers, current abstainers and former problem-drinkers, Drug Alcohol Rev. 39 (2020) 960–974.
[51] J. Han, et al., Rate and determinants of recurrence at 1 year and 5 years after stroke in a low-income population in rural China, Front. Neurol. 11 (2020) 2.
[52] K. Aarnio, et al., Long-term mortality after first-ever and recurrent stroke in young adults, Stroke 45 (2014) 2670–2676.
[53] K.M. Conigrave, R.L. Ali, R. Armstrong, et al., Revision of the Australian guidelines to reduce health risks from drinking alcohol, Med. J. Aust. 215 (11) (2021) 518–524.