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The Impact of Alcohol Consumption on the Risk of Stroke - A Systematic Review

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Abstract:

Introduction: Both ischemic and hemorrhagic stroke are currently among the leading causes of death and disability worldwide. The causes of stroke are diverse and often involve several interconnected factors. Although alcohol consumption is harmful, it remains widespread among people, leading to many negative consequences for the body. Its impact on the risk of stroke varies depending on the amount and frequency of alcohol intake.

Aim of the Study: The aim of this article is to highlight the relationship between alcohol consumption and the occurrence of stroke, emphasizing the multifaceted nature of this phenomenon by considering the amount and frequency of intake, the type of alcohol consumed, and drawing attention to the controversies surrounding this topic.

Materials and Methods: A comprehensive literature review was conducted using the PubMed, Google Scholar, with particular focus on studies examining both the short- and long-term effects of alcohol consumption on the risk of stroke, considering both direct and indirect impacts arising from various mechanisms.

Results and Conclusions: Alcohol consumption affects the risk of developing stroke. High and very high levels of intake are associated with an increased risk, while data regarding low and moderate consumption remain inconclusive, indicating the need for further research on this topic.

Keywords: Stroke; ischaemic stroke; intracerebral haemorrhage; alcohol; alcohol consumption;

Introduction

Stroke, both hemorrhagic and ischemic, currently constitutes the second leading cause of death worldwide and the third leading cause of disability [1]. Between 1990 and 2021, a significant seventy percent increase in new stroke cases was recorded. Of particular concern is the noticeable rise among young individuals, which represents a substantial social burden, leading to a reduction in life expectancy during the most productive years, as well as long-term complications [1, 3, 4]. Recent observations indicate that in high income countries, there is a decrease in age adjusted incidence rates, whereas in low and middle income countries, an

increase in stroke frequency has been noted [7]. In every age group, ischemic strokes constitute the largest proportion, followed by intracerebral and subarachnoid haemorrhages [1].

Risk factors for stroke can be divided into modifiable and non-modifiable. Among the non-modifiable factors are age, where the risk increases with age, sex with a higher risk observed in males, and race, particularly black and Hispanic populations [5]. Genetic factors also play a role. Studies have shown that monozygotic twins have a higher concordance rate for stroke occurrence at 17%, compared to dizygotic twins, who show a concordance rate of 3.6% [5, 6]. Furthermore, a positive family history among parents is known to be a strong risk factor for their children [5].

The second group comprises modifiable factors, among which the most important are hypertension, cardiovascular diseases (especially atrial fibrillation), dyslipidemia, diabetes, coagulation disorders, low physical activity, trauma, smoking, alcohol consumption, obesity, oral contraceptives and hormone replacement therapy [5, 1].

Alcohol is one of the most commonly used addictive substances worldwide, consumed for various reasons due to its brain function suppressing, intoxicating, and calming effects. Although the first indications of its harmfulness appeared as early as antiquity, excessive alcohol consumption has only been recognized as a disease for about the last hundred years. Currently, as many as 1 in 3 people globally are alcohol consumers, which accounts for 43% of the population aged over 15 years [7]. WHO data indicate that over the years, the prevalence of alcohol consumption decreased from 47.6% in 2000 to 43.2% in 2016; however, this does not reflect the trend observed in the change of total alcohol per capita consumption (APC), which increased from 5.7 liters in 2000 to 6.4 liters in 2016. Creating an accurate database on alcohol consumption is very challenging, as unrecorded consumption constitutes up to 26% of the global alcohol intake [7]. From a global perspective, the highest alcohol consumption is observed in European countries, whereas the lowest is in the Eastern Mediterranean Region [7, 8].

The impact of alcohol on the human body depends on two factors: the pattern of its use and the total amount of alcohol consumption [7]. Harmful alcohol consumption is associated with the risk of developing as many as 200 diseases and injuries [7, 9]. These include, among others, cardiovascular diseases such as hypertension, heart failure, cardiac arrhythmias, alcoholic cardiomyopathy as well as liver diseases, cancers, infectious diseases, violence, suicides,

neuropsychiatric disorders, and strokes [7, 8, 10]. Additionally, alcohol is a cause of many accidents due to its effects on sensory and motor functions [7, 11]. This means that alcohol can influence the risk of stroke through various mechanisms, such as increased blood pressure, development of inflammation, induction of atrial fibrillation, reduction of fibrinogen levels, changes in endothelial function, or alterations in cholesterol levels [12]. Moreover, over the years, many studies have indicated that small amounts of alcohol may have a protective effect against the risk of stroke [13].

Low to Moderate Alcohol Consumption and Ischemic Stroke

Determining the impact of alcohol on the risk of stroke is not straightforward due to difficulties in creating homogeneous study designs, defining standard amounts of alcohol consumption, and the presence of many potential **coexisting factors** [14]. There is growing evidence that consumption of small amounts of ethanol, estimated at around 20–30 g per day, may reduce the risk of stroke [5]. A meta-analysis including cohort studies from 1966 to 2002 showed that daily consumption of less than 12 g of alcohol, equivalent to one drink, led to about a 20% reduction in the risk of ischemic stroke [14, 15]. Another meta-analysis confirmed earlier data on the reduced risk of ischemic stroke with light to moderate alcohol consumption, defined as up to two drinks per day, with a risk estimate of 1.08 (approximately 12 g of alcohol) for one drink per day, and a risk of 1.08 for 1–2 drinks per day, with an overall ischemic stroke risk of 0.90 (95% CI) [13].

A meta-analysis was conducted to separate morbidity and mortality rates. A curvilinear relationship was demonstrated, once again showing a protective effect of alcohol on the risk of ischemic stroke at low to moderate consumption levels, and an increased risk at high consumption levels. Regarding mortality, the protective effect in men was observed at alcohol consumption below 35 g per day, which corresponds to less than 3 drinks per day (using the US standard), with the curve's minimum at 12 g per day, approximately 1 drink. For women, the protective effect was seen at consumption below 44 g per day (almost 4 drinks), with the curve's minimum also at 12 g (1 drink). Similar results were obtained for ischemic stroke incidence data, where the protective effect was observed up to 37 g per day (around 3 drinks) for men and 46 g (4 drinks per day) for women [17].

It is also worth noting the types of alcohol consumed. It has been observed that wine consumption is associated with a significantly lower risk of ischemic stroke [12], which is linked to its effects on lipid metabolism and the coagulation system [5]. However, preferences for types of alcohol vary depending on many factors; for instance, wine is more frequently chosen by women, older individuals, those with higher income, and those with higher education levels. For this reason, it is not entirely clear whether the stronger protective effect of wine compared to other alcoholic beverages is due to its beneficial impact on the cardiovascular system or because it is consumed by a completely different social group [12, 16].

The protective effect of low to moderate alcohol consumption may result from its influence on fibrinolytic activity, as it leads to a reduction in plasma levels of C-reactive protein and fibrinogen [19, 20]. Furthermore, it affects inflammation, which is primarily related to wine consumption, especially red wine, due to the polyphenols it contains [19, 21]. Moderate amounts of alcohol may also positively impact lipid profiles, adipokine activity, and tissue insulin sensitivity [19].

However, data regarding the protective effect of low to moderate alcohol consumption remain controversial and are not always confirmed in studies. A study conducted on participants of the ARIC (Atherosclerosis Risk in Communities) Study, which was a long-term analysis based on self-reported alcohol consumption among middle-aged individuals (between 45 and 64 years old), ultimately did not show a reduced risk of ischemic stroke among middle-aged patients who consumed small or moderate amounts of alcohol [18, 23]. Similar conclusions were drawn from the INTERSTROKE study, where no reduction in stroke risk was observed with low alcohol consumption compared to non-drinkers [12].

High and Very High Alcohol Consumption and Ischemic Stroke

In a large international study, INTERSTROKE, attempts were made to assess risk factors for stroke occurrence [22]. Based on this study, an analysis of stroke risk in relation to alcohol consumption, considering other coexisting factors, was conducted. One aspect of this study involved self-reported alcohol consumption by participants, who were then divided into groups: low consumption defined as 1–7 drinks per week; moderate consumption defined as 7–14 drinks per week for women and 7–21 drinks per week for men; and high consumption, defined as more than 14 drinks per week for women and more than 21 drinks per week for men.

Additionally, heavy episodic drinking (HED) was defined as consuming more than 5 drinks on at least one day per month [12, 22]. Participants were also categorized as current drinkers (25.0%), former drinkers (16.7%), and never drinkers (58.3%). Analysis of the data showed that current alcohol consumption was associated with an overall increased risk of stroke (OR 1.14; 95% CI 1.04–1.26) and haemorrhagic stroke (ICH) (OR 1.50; 95% CI 1.21–1.84), but not with ischemic stroke (OR 1.06; 95% CI 0.95–1.19). Both HED patterns and high alcohol consumption were linked to an increased risk of all types of stroke. These patterns may vary depending on the region of the world, sex, and age; however, the overall risk pattern was consistent regardless of these differences. Additionally, no association was found between former drinkers and stroke [12].

A meta-analysis was conducted, reviewing 27 prospective studies. To standardize the data on alcohol consumption, one standard drink was defined as 12 grams of alcohol. The participants were divided into four groups, in which high consumption was defined as 2–4 drinks per day, and very high consumption as more than 4 drinks per day. The analysis concluded that both high and very high alcohol intake were associated with an increased risk of ischemic stroke. The overall risk was 0.90 (95% CI, 0.85–0.95), with a risk of 1.08 (95% CI, 1.01–1.15) for high consumption and 1.14 (95% CI, 1.02–1.28) for very high consumption. As in previous analyses, it was noted that drinking patterns and types of alcohol consumed may vary between populations; however, after conducting analyses across different geographic regions, similar conclusions were reached consistently across regions [13].

In the aforementioned study conducted among participants of the ARIC (Atherosclerosis Risk in Communities) study, 24% of respondents reported consuming 4–17 drinks per week, while 5% consumed more. This was associated with a 31% increased risk of ischemic stroke compared to abstainers. However, the researchers noted that this study has several limitations, as the data were based on self-reported alcohol consumption, which may have led to underreporting, and the findings may not be representative of the general population outside the ARIC cohort [18, 23].

Risk of Ischemic Stroke Right After Alcohol Consumption

Most studies examine the impact of long-term alcohol consumption on the risk of developing a stroke. In the Stroke Onset Study, researchers investigated the time between alcohol consumption and the onset of the first stroke symptoms, as well as whether the risk varied

depending on the type of alcohol consumed. The study involved collecting medical histories from patients, on average 3 days (ranging from 0 to 14 days) after the stroke occurred. In this study, one alcoholic drink was defined as 350 ml of beer, 120 ml of wine, or 50 ml of drink with a high alcohol content. It was found that within one hour of alcohol consumption, the risk of stroke increased 2.3 times compared to periods when no alcohol was consumed. This risk declined over the following three hours and was lowest after 24 hours. When comparing different types of alcohol, the highest risk was observed for drink with a high alcohol content and the lowest for wine, although this difference was not statistically significant [19]. The exact causes of this association are not fully understood, although several potential mechanisms have been proposed, such as the effects of alcohol on heart rhythm, blood pressure, the development of a hyperkinetic circulation, or spontaneous Valsalva maneuvers, which can occur during severe alcohol intoxication [24]. Other possible explanations include changes in platelet function, coagulation systems, or alcohol-induced cerebral vasospasm [25]. It is also worth noting the numerous accidents that can occur during intoxication, which may lead to, for example, traumatic arterial dissection [24].

Alcohol Consumption and the Risk of Haemorrhagic Stroke

Data on the impact of alcohol consumption on the risk of haemorrhagic stroke remain inconclusive. Particularly inconsistent are the findings regarding low and moderate consumption. The Ethnic/Racial Variations of Intracerebral Haemorrhage (ERICH) study, which included a multiethnic population, showed that rare (<1 drink per month) and moderate (≥1 drink per month and ≤2 per day) consumption was associated with a lower risk of haemorrhagic stroke [26]. However, this contradicts most of the currently available data. Some studies did not demonstrate a protective effect of alcohol consumption on the risk of haemorrhagic stroke [13,26], while others found such an effect but only in women consuming up to 36 g of pure alcohol (approximately 3 drinks per day), with the lowest risk observed at less than 1 drink per day [17]. Other studies indicate that the relationship between alcohol consumption and haemorrhagic stroke risk is linear, meaning that even low doses are associated with increased risk [12,16].

Also noteworthy are reports concerning mortality, where one of the main causes in cases of intracerebral haemorrhage is secondary brain injury (SBI). This results from the compression of brain tissue and the toxic effects of blood components that induce edema, necrosis, apoptosis,

blood-brain barrier disruption, and a strong inflammatory response. It has been shown that moderate alcohol consumption (up to 1 drink per day for women and 2 drinks for men, with one drink containing approximately 10g of pure alcohol) may have a protective effect by reducing oxidative stress and inflammation, which could contribute to decreased mortality related to these mechanisms [27, 28, 29].

Regarding the impact of high and very high alcohol consumption on the risk of haemorrhagic stroke, studies are consistent and show a significant increase of risk [12, 13, 18, 26, 30, 31]. The challenge remains in defining alcohol intake levels, as these varied across different studies. The WHO suggests that a standard drink contains 10g of pure ethanol [29]. The National Institute on Alcohol Abuse and Alcoholism (NIAAA) classifies heavy drinking as more than 4 drinks per day or 14 per week for men, and more than 3 drinks per day or 7 per week for women; binge drinking is defined as 5 or more drinks for men, and 4 or more drinks for women within a 2-hour period; moderate drinking is up to 2 drinks per day for men and up to 1 drink per day for women [29]. Some studies have shown that even moderate consumption can increase this risk [18].

Alcohol consumption and risk factors for stroke

Alcohol is also a risk factor for diseases that may ultimately lead to the development of stroke. One such condition is atrial fibrillation, which increases the risk of stroke by up to five times [32]. Most meta-analyses have shown a linear relationship between alcohol consumption and the risk of atrial fibrillation; however, based on current knowledge, it is not possible to establish a completely safe dose in this regard [33]. Another important factor is hypertension, which increases the risk of both ischemic and haemorrhagic stroke up to fourfold [5, 34]. There is no doubt that high doses of alcohol elevate blood pressure values, and meta-analyses show that this risk increases even at alcohol consumption levels lower than generally recommended (2 units per day, equivalent to 20-28g) [35,36]. Another risk factor is dyslipidemia, especially high levels of low-density lipoprotein cholesterol (LDL-C), which increase the risk of stroke [37]. It has been shown that alcohol consumption, particularly regular use, worsens the lipid profile, especially in individuals with comorbidities such as hypertension and diabetes [38]. Undoubtedly, there are many more indirect risk factors linked to alcohol's impact on the entire body, which require further research and analysis.

Conclusions

It is not possible to determine the impact of alcohol consumption on the risk of stroke in a completely unambiguous way. In the case of low and moderate intake, alcohol may have a protective effect against both ischemic and haemorrhagic strokes; however, studies in this area often present conflicting data. There is no doubt, that high and very high levels of alcohol consumption are consistently associated with an increased risk. Thorough investigation of this phenomenon appears to be very difficult, if not impossible, due to challenges in assembling an appropriate study population. Most studies rely on self-reported data, where participants estimate their own alcohol intake, which is often subject to misinformation or underreporting. Additionally, in long-term observations, the amount and type of alcohol consumed frequently change, making it difficult to obtain consistent results. Alcohol affects the human body on multiple levels and may ultimately contribute to stroke through a variety of mechanisms, which underscores the need for further research. It should also be emphasized that this paper does not promote the consumption of alcohol in any amount.

Disclosure

Authors contribution

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