



Alcohol—dose question and the weakest link in a chemical interplay

Piotr Hamala^{1*} , Karina Wierzbowska-Drabik^{2*} 

¹I Department and Chair of Cardiology, Medical University of Lodz, Bieganski Hospital, 91-347 Łódź, Poland

²Department of Internal Diseases and Clinical Pharmacology Medical University of Łódź, Bieganski Hospital, 91-347 Łódź, Poland

***Correspondence:** Piotr Hamala, I Department and Chair of Cardiology, Medical University of Łódź, Bieganski Hospital, Kniaziewicz 1/5 street, Poland. piotrhamala@gmail.com; Karina Wierzbowska-Drabik, Department of Internal Diseases and Clinical Pharmacology Medical University of Łódź, Bieganski Hospital, Kniaziewicz 1/5 street, Poland. wierzbowska@ptkardio.pl

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Abstract

The deleterious consequences of alcohol consumption are extensively documented across various dimensions of human health, encompassing somatic disorders such as nervous system impairments, digestive system abnormalities, and circulatory dysfunctions, in addition to socio-psychological aspects. Within the domain of cardiology, a substantial portion of the ongoing scientific discourse centers on elucidating the toxic dose of alcohol. Presented herewith are the findings from a comprehensive review of the latest publications pertinent to this crucial issue.

Keywords

Alcohol, alcohol dose, alcohol cardiomyopathy, toxic cardiomyopathy

Introduction

The harmful effects of alcohol consumption are documented in multiple aspects of human health, starting from somatic disorders such as nervous system damage, digestive system abnormalities, or circulatory dysfunction, going down to socio-psychological aspects. Focusing on the cardiology field, a large part of the ongoing scientific debate is about the toxic alcohol dose [1–4]. Below, a review of the latest publications related to this issue is presented.

Atrial fibrillation

The harmful effect of high alcohol doses on atrial fibrillation (AF) incidence is unquestionable but the scientific data varies according to the risks and benefits of low to moderate alcohol doses. Csengeri D. and co-authors [5] in a cohort study of 107,845 individuals (mean age 47.8, 48.3% men) showed a not-linear but dose-dependent association between alcohol consumption and AF risk. The risk of AF rises in a parallel manner with the rising of alcohol dose, starting with a hazard ratio (HR) 1.01; 95 confidence intervals (CI,



0.99–1.04) for 1 g of pure alcohol per day, through HR 1.16; 95 CI (1.11–1.22) for 12 g of pure alcohol per day, reaching HR 1.61; 95 CI (1.35–1.92) for 60 g/day. The curvilinear relationship of AF risk vs. alcohol dose indicates the rise of the risk immediately when the dose is between 1 g/day to 40 g/day and shows slower further rising (close to plateau) for doses between 41 g/day to 60 g/day. Based on this material, authors did not observe beneficial effect for any doses. The estimated cut-off for the statistically significant increase in AF risk was observed for even 2 g of pure alcohol per day if consumed regularly [5].

Bazal P. and co-authors [6] in the study from PREDIMED registry observed for mean 4.4 years a group with high cardiovascular risk but without previous AF diagnosis [6,077 patients, mean age (year) 66.3 ± 6.1 , 47% women with the presence of over 3 cardiovascular risk factors], who presented a Mediterranean alcohol consumption pattern [mean (standard deviation) low to moderate red wine consumption were 3.4 (4.4) g/day] that this way of drinking was not associated with an increased incidence of AF, but in the heavy alcohol consumption group (> 30 g/day in men and > 15 g/day in women), the authors observed a higher incidence of AF, HR 1.06; 95 CI (0.61–1.85), although still not statistically significant [6].

Tu S. and co-authors [7] using data derived from the United Kingdom (UK) Biobank, including 403,281 individuals, with a mean age 58.2 [interquartile range (IQR) 50.5–63.6] during a mean follow-up 11.4 (IQR 10.7–12.3) years, showed J-shaped relationship between lower risk of AF in individuals consuming < 7 alcoholic units (AU)/week (1 AU is a 10 g of pure ethanol independently about alcohol beverages), with the lowest risk at 5 AU per week (AUW). Moreover, in categorical analysis, consumption of 0–7 AUW was associated with a lower risk of AF than abstinence, HR 0.91; 95 CI (0.86–0.96). Finally, the authors investigated the impact of specific beverage on AF risk and showed beneficial effect of low doses in AF risk reduction for white wine (5 AUW), red wine (7 AUW), and spirits (1 AUW), while beer and cider characterized only harmful effect [7].

Episodes of paroxysmal AF are strongly associated with alcohol consumption. Voskoboinik and co-authors [8], during 6 months observed a group of 140 patients with paroxysmal AF and divided them into two groups. The first group [70 patients, mean age (year) 62 ± 9 , 85% were men], consumed $16.8 \text{ AUW} \pm 7.7 \text{ AUW}$ and after dietary intervention reduced consumption to $2.1 \text{ AUW} \pm 3.7 \text{ AUW}$ (87.5% reduction). Matched control group, consumed $16.4 \text{ AUW} \pm 6.9 \text{ AUW}$ and reduced drinking to $13.2 \text{ AUW} \pm 6.5 \text{ AUW}$ (19.5% reduction). The AF burden after 6 months of follow-up was significantly lower in the first group. The AF recurrences were observed in 37 of 70 patients (53%) in the first group and in 51 of 70 patients (73%) in the control group [8].

Marcus G. et al. [9] studied the electrophysiology data in two matched groups of patients of electrophysiology cath-lab. The first group consisted of 50 persons, 28% female, mean age (year) of 58.8 ± 11.3 , and was exposed to direct intravenous alcohol administration titrated to 0.08% blood alcohol concentration. The second group consisted of 50 matched controls exposed in double-blind manner to placebo solution. The authors analyzed effective refractory periods of the pulmonary veins, an electrophysiologic parameter expressing the inducibility of AF. The alcohol-exposed group showed a significant decrease in pulmonary vein effective refractory periods of 11.61 ms which elevated the risk of AF incidence. No statistically significant change in pulmonary vein effective refractory periods was observed in the placebo group. Moreover, in both groups no AF recurrence was observed and atrial conduction times did not show differences between groups. Thus, based on these data, the authors suggested that the pulmonary vein electrical system is more vulnerable to acute alcohol exposition than the rest of the atrial structures related to their electrophysiology [9]. Accordingly, the European and American cardiac societies have issued AF guidelines advising that avoidance of alcohol excess should be considered for AF prevention, without indicating the exact allowed dose [10, 11].

Arterial hypertension

The alcohol hypertension effect is caused by a few mechanisms: increased renin-angiotensin-aldosterone system activity, sympathetic nervous system activity, cortisol secretion, changed insulin sensitivity, sodium and calcium ion channels related muscle tension, endothelial dysfunction, and reduced nitric oxide production [12].

Recently, a few studies have indicated a new pathological molecular pathway leading to alcohol-induced hypertension. Dakarapu R. and co-authors [13] showed that 20-hydroxy-5,8,11,14-eicosatetraenoic acid (20-HETE) the metabolite of arachidonic acid in cytochrome (CYP450) have a vasoconstrictive effect. In this issue, exposition to alcohol lead to an elevation of 20-HETE concentration through sympathetic system activation and blood pressure elevation [14]. Barden A. and co-authors [15] observed a group of 22 normotensive men (54.1 years old \pm 6.6 years old) after 3 weeks of drinking 41 g of alcohol per day (the kind of alcohol beverage was a red wine), the concentration of 20-HETE was elevated and the blood pressure level increased significantly, mean systolic blood pressure (SBP) elevation achieved 1.4 mmHg \pm 0.5 mmHg with P value = 0.003 and diastolic blood pressure (DBP) elevation was 0.8 mmHg \pm 0.4 mmHg, P = 0.03.

Coelho J. and co-authors [16] investigated 3,990 participants [mean age (year) 49.3 \pm 8.4, 43% women] with and without arterial hypertension and compared the alcohol dose to the level of hypertension at baseline and after 4 years of follow-up. In the men, in individuals who reduce the alcohol dose (Δ = -10.4 g/day \pm 14.4 g/day) the increase of SBP levels was lower (1.1 mmHg \pm 10.4 mmHg) than in the groups who maintained (Δ = 0 g/day, SBP = 2.4 mmHg \pm 9.2 mmHg) or increase (Δ = 11.4 g/day \pm 15.9 g/day, SBP = 2.3 mmHg \pm 10.7 mmHg) the alcohol consumption. DBP showed a significant rise in patients who increased daily alcohol dose (Δ = 11.4 g/day \pm 15.9 g/day, DBP = 2.2 mmHg \pm 7.1 mmHg). It was particularly interesting that at this level of alcohol doses in the women group, changes in alcohol consumption were not associated with changes in blood pressure levels. Multivariate analysis showed a higher risk of developing hypertension in men group drinking 16.5 g/day \pm 17.9 g/day, odds ratio (OR) 1.62, 95 CI (1.14–2.29) in comparison with men drinking solely 0.8 g/day \pm 2.1 g/day.

Phillips A. and co-authors [17] performed a study to investigate a potential indirect role of a sedentary lifestyle, improper diet, smoking, and poor medication taking in the association between alcohol consumption level and blood pressure. They investigated the group of 1,835 participants with hypertension, mean age (year) 45.5 \pm 3.6, mean SBP 128.7 mmHg \pm 15.5 mmHg, and mean DBP of 83.2 mmHg \pm 10.1 mmHg. The increase of every single alcohol drink per day was related to blood pressure elevation, for SBP (β = 0.71 mmHg, 95 CI, 0.398–1.028) and for DBP (β = 0.39 mmHg, 95 CI, 0.160–0.55). In addition, the episodes of binge drinking did not significantly alternate this relationship and the other investigated risk factors did not influence the dose-dependent blood pressure elevation, maintaining a relatively strict and constant dose-dependent effect of alcohol taking.

S. van Oort and co-authors [18] using genomic data from UK Biobank and FinnGen registry have investigated the impact of common risk factors coded in genes on hypertension. Based on special statistical analysis (Mendelian randomization), they evaluated the prevalence of genetically predicted risk factors and the relationship between specific genes and hypertension. The authors confirmed the relationship of some genes promoting alcohol dependence with the risk of hypertension development, the respective OR for arterial hypertension assessed in UK Biobank was 1.31 (1.08–1.60) and in FinnGen 1.16 (0.8–1.69).

Cardiomyopathy

Heart failure, in general, consists of many phenotypes related to an etiology and left ventricle ejection fraction preservation, and similarly, the impact of alcohol on heart is non-equal and depends on the alcohol dose, individual vulnerability, and the duration time of alcoholism [19]. In the last study, published in 2022 and coming from Italy, the authors investigated 43 patients (36 males) taking part in an outpatient program of alcohol dependence treatment. At baseline, when compared to age-matched control group, thickness of the heart muscle and left ventricle diastolic diameter were higher and ejection fraction (EF) was lower, in the observed patients, with P value = 0.009. E/A ratio, deceleration time of E wave, and LA diameter were in normal range but the baseline E/e' ratio was significantly higher in the study group (P < 0.001). The authors observed a significant positive correlation between the alcohol dose before baseline assessment and E/e' ratio (P = 0.028). Moreover, after 6 months of follow-up, a reduction in E/e' ratio was observed in the abstainers as compared to the control group (P = 0.041) [20]. Thus, the authors postulate E/e' ratio as a predictor of a very early stage of alcohol-related heart dysfunction, and this observation was confirmed in a similar study performed by Rosa G. et al. [21].

Other interesting observations were delivered from a novel echocardiographic parameter analysis, longitudinal strain assessed with speckle tracking in the respective endocardial and epicardial layers of the heart muscle. The authors evaluated a group of 65 patients, 77% men, with mean (IQR) age 44 (38–51) years, and compared them with a matched control group. The mean (IQR) alcohol consumption was 30 (12–51) AUW in the study group and 0 (0–0) in the controls. The strain rate in cardiac muscle layers, endocardial and epicardial, showed systolic dysfunction. The endocardial strain was –14% (9–18%) vs. –24% (21–27%) in controls, the epicardial strain was –19% (12–23%) vs. –19% (16–20%) in controls, P for both = 0.007. Moreover, both layer strains with estimated cut-off absolute values for epicardial strain < 15% and endocardial strain < 19% offered a significant prognostic value indicating worse outcomes in mid-term follow-up [22].

Dilated cardiomyopathy (DCM) forms another alcohol-related phenotype of heart dysfunction. Fernández-Solà and co-authors [23] showed higher prevalence of DCM among patients consuming alcohol in comparison with general population reaching 0.43% in males [pure alcohol consumption assessed for all life was 30 kg/kg \pm 7 kg/kg body mass during mean age (year) 29 \pm 6], and among women 0.25% [pure alcohol consumption assessed for all life was 17 kg/kg \pm 7 kg/kg body mass during mean age (year) 23 \pm 7], whereas in general population DCM prevalence is 1:2,500 (0.4‰).

Magnetic resonance comprehensive insight into alcohol cardiomyopathy was presented in Artico J. et al. [24] study in 2021. A group of 52 patients was diagnosed with alcohol DCM based on alcohol overuse history (> 80 g of alcohol per day for more than 5 years) and the lack of other causes of cardiomyopathy, mean age (year) 52 \pm 11, 90% men. Control group consisted of 62 patients diagnosed with DCM, mean age (year) 49 \pm 14, 64% males. Mean ejection fraction was 31% \pm 12% in the study group vs. 38% \pm 11% in the control group. Late gadolinium enhancement (LGE) was observed in 22 patients (43%) in the study group vs. 26 (47%) in the control group. It was interesting that the distribution of LGE was significantly different in both groups. In alcohol cardiomyopathy, a predominating septal LGE localization was observed (87% of patients). Whereas, in control group, the predominating LGE localization affected the lateral wall (50% of patients). The follow-up time reached 42 months. The presence of LGE was related to a higher rate of adverse outcomes and a higher rate of arrhythmic events during follow-up but only in controls. The study group showed only a trend for higher rate of arrhythmic events related to the LGE presence. In another study, similar observations were obtained by Haliday and co-authors [25]. In the group of 853 DCM patients (11.1% alcohol etiology) the localization of LGE in septum was related to HR 3.13; 95 CI (1.68–5.81); P < 0.001 of sudden cardiac death in comparison to DCM patients without LGE. The abstinence syndrome has an influence on corrected QT interval (QTc). In 62 patients [52 of them were male, mean age (year) 43.7], admitted to the hospital with a diagnosed alcohol abstinence syndrome mean QTc interval during admission to the hospital was 439 ms \pm 32 ms and after alcohol cessation, QTc was shorter 417 ms \pm 26 ms, P < 0.001. This observation can explain a potential reason of ventricular arrhythmia in alcohol abuse patients [26]. Further studies are needed to explain the complex cardiac recovery phenomenon. Unfortunately, to our best knowledge, the literature is still pure according to this issue [26].

From the histopathological point of view, there are no specific symptoms of alcoholic cardiomyopathy. Observed elements are myofibrils atrophy, mitochondriopathy (the differentiation of mitochondria in size and forms due to chronic exposition to toxins including ethanol and its metabolic products and the presence of megamitochondria), cardiomyocyte necrosis and fibrosis, similar to other etiologies of dilated cardiomyopathies. Some typical differences were documented however in molecular biology. The excessive production of type I collagen is a result of the activation of fibroblasts and myocardial muscle exposition to alcohol in extracellular matrix [27]. Moreover, in fibroblast, alcohol triggers the molecular tracks of pro-inflammatory signals (the MAPK protein kinase group, the transcription factor STAT3 and the nuclear factor NF- κ B) releasing the pro-inflammatory cytokines from the fibroblast (such as: IL-6, TNF- α , IL-1 β , IL-33) and causing cardiomyocytes dysfunction. The final consequence is a lower expression of genes coding contractile proteins like Acta1, Actc1 (encoding actin), and Myh7 (encoding the myosin heavy chain). Additionally, through the track mediated by TNF- α , alcohol, can influence cardiomyocytes directly without fibroblast as a reaction mediator, intensifying the decrease of fibers contractility [28]. Even though

the molecular pathophysiology is still not fully understood and it needs to be further investigated. In the last study performed by de Araújo Melo L and co-authors [29], the diagnostic role of microRNA (post-transcriptional gene regulators) in alcohol cardiotoxicity has been evaluated. As mentioned above, alcohol exposition impairs protein synthesis and this can influence microRNA expression. Authors collect the study group consisted of patients who reported drinking alcohol for at least 5 years with an average of 80 g/day for men and 40 g/day for women who revealed diffuse hypokinesia and dilatation of the left ventricle in echocardiography. Patients with another type of cardiomyopathy were excluded from the study. The control group consisted of 20 age-, sex-, comorbidities- and even echocardiography parameters-matched patients. The microRNA (miR-133b and miR-138) levels were assessed and compared with echocardiography findings. In the study group, the downregulation of the miR-133b was observed and an increase in the miR-138 expression was correlated with an increased EF and left atrium diameter normalization [29].

The myocardial metabolism was investigated with the use of nuclear medicine imaging in a study performed by Shi X. et al. [30]. In this study, a group of 37 male subjects were examined. The group consisted of 8 moderate-drinking patients who consumed 2–5 alcohol units per day, 20 heavy-drinking patients who consumed over 5 AU/day, 5 patients with diagnosed alcohol cardiomyopathy (the respective criteria were: 8 AU/day during at least 5 years, left ventricular diastolic diameter over 58 mm \pm 4 mm, EF below 50%, and a normal imaging of coronary arteries) and 13 healthy abstainers. Mean age (year) was consecutively 48.1 (35–67), 47.9 (41–59), 47.2 (38–61), and 50.3 (31–65). The groups were age-, body mass index (BMI)-, comorbidities- matched. All patients had echocardiography examination and ^{11}C -Acetate positron emission tomography (PET) imaging performed on the same day. Alcohol cardiomyopathy group showed higher-end diastolic left ventricle volume (220.4 mL \pm 75.1 mL) in comparison to healthy controls (97.1 mL \pm 18.6 mL), moderate drinking group (90.0 mL \pm 19.4 mL) or even heavy drinking group (90.9 mL \pm 15.9 mL, $P < 0.05$). A similar observation was obtained for end-systolic left ventricle volume (154.4 mL \pm 80.2 mL, 33.5 mL \pm 8.6 mL, 30.1 mL \pm 7.3 mL, and 31.8 mL \pm 7.6 mL, respectively; P for all < 0.05). The EF in alcohol cardiomyopathy group was (33.6% \pm 9.0%) and was lower in comparison to healthy controls, moderate drinking group, and heavy drinking group (65.2% \pm 6.6%, 66.2% \pm 6.4%, and 65.1% \pm 5.5%, respectively, P for all < 0.05). Myocardial external efficiency, which expresses the level of kinetic energy related to myocardial work and the amount of oxygen consumed by left ventricle, and represents the parameter obtained with nuclear imaging was lower in alcohol cardiomyopathy patients (13.0% \pm 4.3%) than in healthy controls (22.4% \pm 4.6%), moderate drinking group (20.1% \pm 4.5%), and high drinking group (22.3% \pm 4.5%, P for all < 0.05). Myocardial oxygen consumption was significantly reduced in the high drinking group (0.121 mL/min \pm 0.018 mL/min) and alcohol cardiomyopathy group (0.111 mL/min \pm 0.017 mL/min) when compared with healthy controls (0.144 mL/min \pm 0.023 mL/min) and moderate drinking group (0.146 mL/min \pm 0.027 mL/min, P for all < 0.05). Work metabolic index, which represents the oxidative metabolism of myocardium, did not show the differences among investigated groups (3.958 mL/mmHg \pm 1.187 mL/mmHg to 4.710 mL/mmHg \pm 1.445 mL/mmHg; P for all < 0.05). In conclusion, authors postulate that the impairment of cardiac work and the oxygen consumption expressed by myocardial external efficiency observed in alcohol cardiomyopathy group is a marker of toxic alcohol-related heart muscle damage [30].

Atherosclerosis

The cardiovascular risk related to alcohol consumption was comprehensively evaluated in the study based on data derived from 3 registries in 19 countries (UK Biobank, the Emerging Risk Factors Collaboration, EPIC-CVD). The study cohort consisted of 599,912 current drinkers without previous cardiovascular disease. Authors characterized associations between alcohol dose and cardiovascular risk. HR was adjusted for age, sex, smoking, and presence of diabetes. Higher cardiovascular risk with higher alcohol consumption was observed for stroke HR 1.14; 95 CI (1.10–1.17), coronary disease excluding myocardial infarction HR 1.06; 95 CI (1.00–1.11), fatal coronary disease excluding myocardial infarction HR 1.11; 95 CI (1.04–1.18) and sudden cardiac death HR 1.12; 95 CI (0.90–1.41). Contrary, the myocardial infarction (fatal and

non-fatal) was negatively related to alcohol consumption HR 0.94; 95 CI (0.91–0.97). Moreover, the authors show that the threshold for the lowest risk of all-cause mortality, was about 100 g/week (10 AUW) [31]. Kaul S. and co-authors [32] investigated a group of 45 individuals, 40 years \pm 10 years, 50% female, with ischemic coronary disease probability < 1% in search for microvascular circulation changes according to alcohol consumption. They assigned 12 patients to the vodka group, 11 persons to the wine group, alcohol groups consumed 2 AU daily per week during 2 consecutive weeks, the third group 22 persons were abstainers. Myocardial blood flow reserve was measured at baseline and after 2 weeks using myocardial contrast echocardiography and no difference was observed between the two examinations [32]. This clinical observation has pathophysiological explanation. In the histological study performed by Mall and co-authors, in electron microscopy structural changes in the endothelium of the capillaries of male rabbits exposed to ethanol (10 mL of 20% solution per day) for 3 weeks were documented. The density of endothelial cells was increased which can be a marker of the proliferation of endothelial cells as the result of chronic alcohol-induced hypoxia [33]. Moreover, alcohol exposition is related to higher serum level of vascular endothelial growth factor (VEGF) which confirms previous observation [34]. This can be a potential reason for pro-angiogenic cardio-protective effects of moderate ethanol doses which improve microvascular reactivity, function of endothelium, and myocardial perfusion [35].

Conclusion

The effect of alcohol consumption on cardiovascular diseases is the issue of a constant scientific discussion. In a recent article, published in 2022, Krittanawong Ch. et al. [36] tried to organize and sum up the results of published studies by performing a systematic review of peer-reviewed publications searched within group of databases, e.g., MEDLINE, Ovid Embase, Ovid Cochrane Database, Scopus, and Web of Science. Starting from 1986, 56 studies mentioning alcohol's impact on cardiovascular system and reporting alcohol dose were collected. The analyzed cohort consisted of 1,579,435 patients, individuals with liver disease were excluded. Authors emphasize the inability to perform typical meta-analysis due to significant heterogeneity of investigated population. Nevertheless, a few conclusions have been done. The low to moderate dose of alcohol (1–4 AU of red wine per week) may be beneficial to cardiovascular system but increasing alcohol consumption can be harmful expressed as J-shape curve. In conclusion, authors emphasized that the presence of many confounding factors such as physical activity, diet, genetics, social relations, or environment can significantly alter the alcohol effect on cardiovascular system. Guzzo-Merello and co-authors [37], observed 94 patients with alcohol cardiomyopathy mean alcohol consumption was 136 g/day \pm 64 g/day for 23 years \pm 12 years before enrolment, in the follow-up, 63% reported abstinence and in 37% EF improved, controversially alcohol cessation in this group was not established as a prognostic factor of left ventricle function recovery in statistical analysis, this suggests the presence of another prognosis modifying co-factors [37]. Thus, Amor-Salamanca and co-authors [38] observed a group of 101 alcohol cardiomyopathy patients during a mean follow-up period of 82 months. In this group, 42 patients showed recovery after alcohol cessation defined as EF increase over 10% to a final value of \geq 40%. Authors suggested a QRS < 120 ms, beta-blocker therapy, and the absence of diuretics therapy as predictors of EF improvement [38]. Alcohol withdrawal effect have been investigated in the study performed on rats. Animals were exposed to ethanol and in the time points (6 hours, 1, 3, and 7 days) after alcohol cessation, the histological changes and creatine phosphokinase activity have been evaluated. During the time of alcohol discontinuation, dystrophic changes in the subcellular structures and formation of foci containing disintegrating myocytes with contractures have been observed. Moreover, creatine phosphokinase activity increased and the contractile function was impaired in the isolated heart. Interestingly, reported pathologies were most severe during 3 days after ethanol discontinuation and disappeared after 7 days [39]. In the latest study based on 408,712 participants from UK Biobank, the alcohol dose wasn't related to the rate of ventricular tachycardia but the authors observed J-shaped relation with alcohol dose and risk of sudden cardiac death. The lowest risk of sudden cardiac death was at the dose 7 AUW and consecutively rise up over 26 AUW [40]. The alcohol-drinking behavior (depending on the dose, the kind of beverages, and the severity of consumption) can be an expression of a specific lifestyle and can impede proper

alcohol-related outcome evaluation. Further studies, as well as more detailed retrospective analyses on this issue, are needed taking into account that the prospective studies are significantly limited due to the ethical restriction [36]. The summary of scientific societies' recommendations for alcohol-related disease prevention is displayed in Table 1.

Table 1. Safety alcohol dose recommendation summary

The year of publication	Document	Safety dose	
		Men	Women
2023	Canada’s guidance on alcohol and health [41]	0 g/week is safe, 10–20 g/week is a low risk (1:1,000 for premature death)	0 g/week is safe, 10–20 g/week is a low risk (1:1,000 for premature death)
2021	ESC guidelines on cardiovascular disease prevention in clinical practice [42]	100 g/week	100 g/week
2021	New Australian guidelines for the treatment of alcohol problems: an overview of recommendations [43]	80 g/week and no more than 40 g on any one day	80 g/week and no more than 40 g on any one day
2019	ACC/AHA guideline on the primary prevention of cardiovascular disease [44]	≤ 28 g/day	≤ 14 g/day
2018	ACG clinical guideline: alcoholic liver disease [45]	> 30 g/day for > 5 years	> 20 g/day for > 5 years
2018	ESC guidelines on hypertension management [46]	≤ 20 g/day	≤ 11.5 g/day

Abbreviations

- AF: atrial fibrillation
- AU: alcoholic unit
- AUW: alcoholic unit per week
- CI: confidence interval
- DBP: diastolic blood pressure
- DCM: dilated cardiomyopathy
- EF: ejection fraction
- HR: hazard ratio
- IQR: interquartile range
- LGE: Late gadolinium enhancement
- QTc: corrected QT interval

Declarations

Author contributions

PH: Resources, Software, Writing—original draft. KWD: Conceptuation, Resources, Supervision, Validation, Writing—original draft, Project administration.

Ethical approval

Not applicable.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Consent to participate

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