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ALCOHOL AND THE HEART: THE ROLE OF ETHANOL IN THE DEVELOPMENT OF CARDIOMYOPATHY AND HEART FAILURE

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ABSTRACT

Objective: Alcoholic cardiomyopathy (ACM) is a dilated cardiomyopathy resulting from chronic excessive alcohol consumption and is a preventable cause of heart failure. While moderate drinking was once thought to reduce cardiovascular risk, recent evidence suggests no safe threshold for ethanol intake. ACM typically develops after prolonged high-dose consumption, often >80 g/day for at least five years, though women may be affected at lower exposure. This review synthesizes epidemiological data, pathophysiology, clinical features, and therapeutic strategies related to ACM.
Methodology: This review synthesizes current evidence on ethanol's cardiac effects and its role in ACM. A narrative synthesis of English-language studies from PubMed and Web of Science was performed, prioritizing systematic reviews, meta-analyses, randomized controlled trials, and large observational studies. Search terms included "alcoholic cardiomyopathy", "cardiomyopathy", "ethanol", "alcohol", and "heart failure". Relevant studies were screened and qualitatively analyzed.
Key findings: Alcohol induces oxidative stress, mitochondrial dysfunction, impaired calcium handling, and disruption of sarcomeric proteins, culminating in progressive ventricular dilation, contractile dysfunction, fibrosis, and arrhythmias. Clinically, ACM progresses from asymptomatic ventricular dilation to overt systolic heart failure. Women are more susceptible, developing ACM at lower cumulative alcohol exposure than men.
Conclusion: ACM represents a preventable cause of heart failure, with early detection and alcohol cessation as critical components for improved outcomes. Public health efforts to reduce harmful drinking remain essential to decreasing ACM incidence and its cardiovascular burden.

KEYWORDS

Ethanol, Alcohol, Alcoholic Cardiomyopathy, Heart Failure

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Introduction:

Alcoholic cardiomyopathy (ACM) is the most common cardiac complication of chronic, high-dose alcohol consumption, typically exceeding 80 g/day for over five years. This review synthesizes epidemiological data, pathophysiology, clinical features, and therapeutic strategies related to ACM. Ethanol exerts direct toxic effects on the myocardium, inducing oxidative stress, acetaldehyde-mediated mitochondrial dysfunction, and disruptions in calcium handling, ion channels, and sarcomeric proteins. These mechanisms lead to progressive ventricular dilation, impaired contractility, fibrosis, and arrhythmias. ACM evolves through a dose-dependent interplay between injury and compensatory remodeling, influenced by individual susceptibility and comorbidities such as hypertension and liver disease. The prognosis hinges on continued alcohol exposure, with abstinence significantly improving cardiac function and survival. While current treatment aligns with standard heart failure management, emerging therapies targeting fibrosis, hypertrophy, and cardiomyocyte regeneration offer new potential. In advanced cases, heart transplantation may be considered, contingent on sustained abstinence. Early detection and management are crucial to improving survival in ACM, emphasizing the role of public health initiatives in limiting harmful alcohol use.

Methodology:

This review discusses the effects of ethanol on the myocardium and its relationship to alcoholic cardiomyopathy and heart failure development. A narrative review was conducted using peer-reviewed studies, meta-analyses, and clinical trials identified in PubMed and Web of Science, restricted to English-language publications. Priority was given to systematic reviews, meta-analyses, randomized controlled trials, and large observational studies. The review followed PRISMA 2020 guidelines. Identifying relevant articles included using combination of keywords such as "alcoholic cardiomyopathy", "cardiomyopathy", "ethanol", "alcohol" and "heart failure". Clinical guidelines and epidemiological data were emphasized to build an evidence-based framework. Titles and abstracts were manually screened for relevance and consistency with the review's objectives, and eligible studies were qualitatively analyzed and summarized to provide and overview of the findings.

1. Epidemiology of alcohol intake

Ethanol, the principal psychoactive component in alcoholic beverages, has been consumed worldwide for centuries. Globally, alcohol consumption is reported by one-third of the population, with 25% of women and 39% of men engaging in drinking. In Europe, up to 50% of adults consume alcohol on a regular basis. On average, women consume 0.73 alcoholic beverages, while men average is 1.7 drinks per day(Rasoul et al., 2023).

A standard alcoholic beverage typically contains 10 grams of pure ethanol, which is equivalent to 100 mL of wine, 300 mL of beer, or 40 mL of distilled spirits. In clinical and epidemiological literature, alcohol consumption is frequently stratified into mild, moderate, and heavy categories, with thresholds varying by sex (Fernández-Solà, 2020).

Mild alcohol consumption is defined as <20 g/day for men and <10 g/day for women. Moderate consumption ranges from 20 to 60 g/day in men and 10 to 40 g/day in women. Intake exceeding 60 g/day in men or 40 g/day in women is classified as heavy drinking.

2. Dose-dependent effects of alcohol consumption

The adverse effects of alcohol are directly linked to both the quantity of alcohol consumed and the drinking pattern. The risk of harm significantly increases when daily ethanol intake exceeds 10–20 grams. Binge drinking, characterized by episodes of acute intoxication, substantially elevates the risk of accidents, injuries, violence, and cardiovascular disease (Rehm et al., 2009).

Low to moderate alcohol consumption is believed to have a protective role in the prevention of ischemic heart disease and type 2 diabetes mellitus (Howard et al., 2004; Movva & Figueredo, 2013; Ronksley et al., 2011). Moderate alcohol consumption is thought to exert pleiotropic effects that contribute to cardiovascular protection, including increased levels of high-density lipoprotein (HDL) cholesterol, reduced plasma viscosity, lowered fibrinogen concentrations, enhanced fibrinolysis, decreased platelet aggregation and coagulation, and improved endothelial function (Kloner & Rezkalla, 2007). The purported beneficial effects are debated and must be considered in the context of the harmful consequences of alcohol, which contribute to a range of diseases, injuries, accidents, and societal burden (Day & Rudd, 2019).

Recent evidence has questioned earlier claims regarding the cardiovascular benefits of low to moderate alcohol consumption, attributing such findings to methodological biases (Tsai et al., 2023). It is now recognized that individuals consuming light to moderate amounts of alcohol often exhibit healthier lifestyle behaviors, higher socio-economic status, and more robust social and familial engagement, which may confound previously reported benefits (Biddinger et al., 2022).

Nonetheless, the only cardiovascular safe level of ethanol consumption is complete abstinence (Day & Rudd, 2019).

Both acute high-dose ethanol consumption and chronic alcohol dependence can result in toxicological damage to virtually all organ systems and tissues (Addolorato et al., 2011), especially to the liver, central nervous system and cardiovascular system (Addolorato et al., 2016; Fernández-Solà & Porta, 2016).

3. Alcoholic cardiomyopathy

3.1 Impact on heart

Chronic excessive alcohol intake is associated with reduced myocardial contractility, hypertension, cerebrovascular accidents, arrhythmias such as atrial fibrillation, and myocardial infarction, which collectively contribute to the progression of cardiac dysfunction (Piano, 2002). Cumulative lifetime alcohol consumption is believed to be associated with increased left ventricular (LV) mass and a reduction in left ventricular ejection fraction (LVEF) (Urbano-Márquez & Fernández-Solà, 2004). Chronic alcohol consumption is a well-established risk factor for the development of alcoholic cardiomyopathy (ACM) (Urbano-Márquez & Fernández-Solà, 2004), which manifests as dilated cardiomyopathy and may progress to heart failure (HF) (Guzzo-Merello, 2014; Piano, 2002).

3.2 Epidemiology of ACM

The reported prevalence of alcoholic cardiomyopathy ranges from 21% to 32% of dilated cardiomyopathies in studies conducted at referral centers. However, these figures may be higher in patient cohorts with a higher incidence of alcohol use disorder (Regan, n.d.). Some studies propose that alcohol is responsible for at least 50% of all cases of dilated cardiomyopathy (Segel et al., 1984). Although, approximately 3.8% of all cardiomyopathy cases are attributable to alcoholic cardiomyopathy (Piano, 2002).

Evidence suggests that the majority of individuals with alcohol use disorder may exhibit preclinical myocardial dysfunction. Autopsy findings have shown cardiac enlargement and other characteristics of cardiomyopathy in alcoholics who did not present with overt symptoms of heart disease (Davidson, n.d.).

The development of alcoholic cardiomyopathy is associated with the volume of daily ethanol intake and the duration of alcohol abuse. However, the exact thresholds of consumption and duration needed to induce cardiac dysfunction remain unclear. Chronic alcohol consumption exceeding 80 grams per day for at least five years significantly heightens the risk of ACM development (Fernández-Solà et al., 2000; Guzzo-Merello, 2014). However, not all individuals with chronic excessive alcohol consumption develop dilated cardiomyopathy.

3.3 Male and female differences

The prevalence of alcoholic cardiomyopathy is comparable between male and female populations (Ferná Ndez-Solà et al., n.d.). Nonetheless one study demonstrated a pronounced gender disparity in hospital admissions for alcoholic cardiomyopathy, with men outnumbering women by a ratio of 9 to 1 (Ram et al., n.d.). Despite higher alcohol intake and a greater incidence of alcohol use disorders observed in males, females exhibit increased vulnerability to ethanol-induced organ damage. This heightened susceptibility is attributed to lower total body water volume and diminished hepatic and gastric alcohol dehydrogenase activity, resulting in elevated blood alcohol concentrations in females compared to males (Addolorato et al., 1999). Thus, women may experience the onset of alcoholic cardiomyopathy at an earlier stage and with a lower cumulative lifetime ethanol intake (approximately 40% less) compared to men (Urbano-Márquez & Fernández-Solà, 2004).

4. Pathophysiology of ACM

The pathogenesis of alcoholic cardiomyopathy entails a multifactorial process, including the direct cytotoxic effects of ethanol on myocardial tissue, heightened oxidative stress, mitochondrial impairment, and underlying genetic predisposition.

4.1 Direct ethanol toxic effect

Ethanol contributes to myocardial oxidative stress by facilitating the generation of reactive oxygen species (ROS) and activating secondary pathways, including the renin–angiotensin system (RAS) (Wang & Ren, 2018).

Ethanol and its metabolites are considered toxic to the myocyte sarcoplasmic reticulum and mitochondria (Schoppet & Maisch, 2001). Heavy alcohol consumption directly impairs myocardial function by disrupting calcium homeostasis, mitochondrial function, and the structure and function of contractile proteins (Mirijello et al., 2017). Ethanol induces early structural alterations in the sarcomeric complex, characterized by a reduction in titin protein levels, which plays a crucial role in maintaining sarcomere compliance and left ventricular diastolic function (Fernández-Solà, 2020). Moreover, ethanol impacts contractile sarcomeric proteins, including myosin, actin, and

troponin, resulting in a gradual decline in myocardial contractility, which contributes to the progression toward heart failure (Patell et al., 1995; Urbano-Márquez & Fernández-Solà, 2005). Ethanol decreases the calcium sensitivity of myofilaments by altering the calcium-binding properties of regulatory proteins, leading to impaired myocardial contractility (Ren & Wold, 2008).

Animal models have shown a significant increase in myocyte loss through apoptosis in hearts exposed to high levels of ethanol (Capasso et al., n.d.; Haunstetter & Izumo, 1998). In an in vivo study, the authors concluded that inflammation and oxidative stress are the underlying mechanisms responsible for the detrimental effects of ethanol on the heart (Shirpoor et al., 2015).

Findings indicate that cardiomyocyte apoptosis is a crucial factor in the pathogenesis of alcoholic cardiomyopathy, contributing significantly to the progression of heart failure (Fernández-Solà et al., 2006).

4.2 Inflammatory biomarkers of damage

Association studies have unequivocally demonstrated variable levels of inflammatory biomarkers in alcoholic cardiomyopathy. Specifically, increased concentrations of interleukins (IL-6, IL-8, IL-12), tumor necrosis factor-alpha (TNF-α), and its receptors (TNF-R) were found in patients with ACM, with the severity of cardiomyopathy correlating with elevated levels of these inflammatory mediators (Obad et al., 2018). In particular, TNF-α has been recognized as having a pivotal role in ethanol-induced heart failure (Meldrum et al., 1998).

4.3 Acetaldehyde damage

Chronic excessive alcohol consumption is associated with metabolic alterations in cardiomyocytes, such as a reduction in the activity of respiratory enzymes and lactate dehydrogenase, diminished β-oxidation of fatty acids, and an upregulation of alcohol dehydrogenase activity. This cascade may lead to the accumulation of acetaldehyde and impaired protein synthesis, culminating in myocardial injury (Guo et al., 2012).

Ethanol and its primary metabolite, acetaldehyde, directly damage the heart by decreasing the synthesis of structural proteins, reducing myocardial contractility, and increasing oxidative and metabolic stress, which leads to autophagy (Ren & Wold, 2008). In experimental studies, acetaldehyde directly impairs myocardial contractility, disrupts excitation-contraction coupling in the heart, and promotes oxidative injury and lipid peroxidation (Ii & Ren, 2003; Ren & Wold, 2008). Furthermore, acetaldehyde can bind to proteins, forming protein adducts that are highly reactive and may contribute to further inflammatory and immune-mediated myocardial injury (Leibing & Meyer, 2016).

This damage leads to the onset of diastolic dysfunction, initially subclinical, but later becoming clinically manifest (Fernández-Solà et al., 2000).

4.4 Heart adaptations

Cardiac remodeling is a comprehensive physiological response of the myocardium, characterized by structural and functional adaptations to various pathological stress factors (Hill et al., 2008). Cardiac myocytes demonstrate relative resistance to ethanol toxicity by initiating compensatory functional and structural adaptations that reduce or repair ethanol-induced damage (Iacovoni et al., 2010). Progressive myocytolysis impairs the sarcomeric contractile framework, resulting in ventricular hypertrophy and compensatory dilation. Cardiac output progressively diminishes in a dose-dependent manner, correlating with the total cumulative alcohol intake over a lifetime (Urbano-Márquez & Fernández-Solà, 2004). Although the regenerative response following myocyte apoptosis and necrosis is limited, compensatory mechanisms such as hypertrophy of surviving cardiomyocytes can initially mitigate the effects of myocyte loss (Fernández-Solà, 2015). However, decreased myofibrillar protein levels, in conjunction with the expression of various myosin isoforms, result in diminished myocardial contractile function (Mirijello et al., 2017). These alterations ultimately contribute to increased left ventricular dilation and mass, myocardial atrophy, and left ventricular systolic dysfunction (George & Figueredo, 2010).

The ultimate outcome is determined by the balance between the extent of myocardial damage and the heart's reparative capacity in each individual (Guzzo-Merello et al., 2015).

5. Clinical manifests:

The clinical manifestations and age of onset in patients with idiopathic dilated cardiomyopathy (IDCM) are analogous to those observed in individuals with alcoholic cardiomyopathy (Fauchier et al., 2000). Both idiopathic dilated cardiomyopathy and alcoholic cardiomyopathy patients demonstrated similar distributions in terms of New York Heart Association (NYHA) functional classes I-II and III-IV. Additionally, echocardiographic and hemodynamic parameters were indistinguishable between the two groups (Gavazzi et al., 2000).

The clinical presentation reflects a reduction in cardiac output, with symptoms consistent with chronic heart failure of any etiology, including exertional dyspnea, bilateral pitting edema, fatigue, cognitive dysfunction, oliguria, and nocturia. Physical examination may reveal elevated jugular venous pressure, a third and/or fourth heart sound, systolic murmurs, and potentially tachyarrhythmias, such as atrial fibrillation (Klatsky, 2015; Laonigro et al., 2009).

These patients may also exhibit symptoms of liver disease, malnutrition, peripheral neuropathy, and other neurological conditions, such as Wernicke-Korsakoff syndrome, commonly associated with alcohol use disorder (Addolorato et al., 2016).

6. Diagnosis

Diagnosis is based on a comprehensive history of chronic alcohol consumption and the exclusion of other underlying causes of dilated cardiomyopathy.

Echocardiography is essential for the diagnosis of alcoholic cardiomyopathy and for excluding alternative etiologies of heart failure. It typically demonstrates biventricular dilation, along with impairments in both systolic and diastolic function.(Day & Rudd, 2019) In asymptomatic male individuals with alcohol use disorder, the primary early finding is left ventricular dilation accompanied by an increase in LV mass. Diastolic dysfunction is typically observed early in the disease process; however, both diastolic and systolic dysfunctions may be present in affected patients (Laonigro et al., 2009). In alcoholic patients, the observed changes include prolonged relaxation time, reduced peak early diastolic velocity, slower early flow acceleration, and an elevated atrial-to-early peak velocity ratio, indicating a primary defect in left ventricular relaxation (Kupari et al., n.d.).

Cardiac magnetic resonance imaging (MRI) may be necessary to confirm the diagnosis, particularly when echocardiographic images are suboptimal. Additionally, coronary angiography is frequently employed to rule out the presence of coronary artery disease as a contributing factor (Day & Rudd, 2019).

Electrocardiographic (ECG) abnormalities, including alterations in the ST-T wave and QT interval, are commonly observed in individuals with chronic alcohol consumption. Long-term excessive alcohol intake is associated with significantly increased dispersion of both QTc and JTc intervals. Furthermore, these individuals exhibit a notably higher relative risk for prolonged QTc intervals and increased QTc dispersion, which in turn contributes to a higher risk of arrhythmogenic events compared to controls (Čorović et al., 2006).

Chest radiography may reveal findings consistent with advanced cardiac dysfunction, including cardiomegaly, pulmonary venous congestion, and pleural effusions, the presence and extent of which are indicative of the severity of the underlying cardiomyopathy (Mirijello et al., 2017).

The diagnosis of alcoholic cardiomyopathy is determined by the improvement in cardiac function after the cessation of alcohol intake (Nicolá et al., 2002).

7. Treatment

7.1 Management of alcohol use disorder

Absolute cessation of ethanol intake is the most effective strategy for managing the progression of alcoholic cardiomyopathy. In fact, individuals with ACM who refrain from alcohol demonstrate a more favorable long-term prognosis compared to those with idiopathic dilated cardiomyopathy. Psychosocial interventions have demonstrated clinical efficacy in the management of alcohol use disorder and represent the cornerstone of therapeutic strategies (Drummond et al., 2011). Therapeutic programs centered on harm reduction aim to promote self-directed controlled alcohol use, often functioning as a transitional strategy toward sustained abstinence (Mann et al., 2017). Evidence indicates that interventions targeting a reduction in total alcohol intake and modification of drinking patterns yield favorable outcomes among individuals with hazardous, harmful, or alcohol-dependent consumption patterns (Charlet & Heinz, 2017).

7.2 Pharmacological interventions targeting alcohol dependence

Acamprosate and naltrexone, when administered alongside psychosocial interventions, have been shown to significantly reduce the risk of relapse in individuals with alcohol use disorder. Importantly, both pharmacologic agents are not associated with contraindications related to cardiac function (Day & Rudd, 2019).

Disulfiram acts by inhibiting aldehyde dehydrogenase, causing acetaldehyde accumulation following alcohol consumption, which induces adverse effects such as flushing, nausea, dizziness, and chest discomfort. Its use may improve treatment adherence when administered under supervision (Jørgensen et al., 2011). Disulfiram can provoke significant cardiovascular reactions—including QT interval prolongation, hypotension, and hypertension. Given the risk of potentially fatal cardiac events, particularly in those with underlying heart disease, its use is generally avoided in this population (Chick, n.d.).

7.3 Treatment for heart failure

Treatment of patients with ACM should align with established guidelines for heart failure with reduced ejection fraction (HFrEF). Standard pharmacotherapy includes beta-adrenergic blockers, angiotensin receptor–neprilysin inhibitors (ARNIs), ACE inhibitors or angiotensin II receptor blockers (ARBs), mineralocorticoid receptor antagonists, and sodium–glucose cotransporter-2 (SGLT2) inhibitors. Diuretics are used as needed to control fluid retention (McDonagh et al., 2021).

In cases of end-stage alcoholic cardiomyopathy (LVEF <15%), cardiac transplantation may be the only therapeutic option. However, most transplant protocols require a sustained period of alcohol abstinence, typically at least three months, prior to eligibility. In one cohort, only 15% of chronic alcoholics with ACM individuals underwent cardiac transplantation (Guzzo-Merello et al., 2015).

7.4 Therapeutic approach to extracardiac conditions

The management of extracardiac complications such as hepatic cirrhosis, malnutrition, vitamin and electrolyte disturbances requires targeted intervention by relevant clinical specialists. Moreover, comprehensive control of prevalent cardiovascular comorbidities, including arterial hypertension, diabetes mellitus, dyslipidaemia, and tobacco use, is essential. Optimisation of these systemic and metabolic factors contributes to improved clinical outcomes and long-term prognosis in this patient population (Fernández-Solà, 2020).

7.5 Prospective therapies based on pathogenic mechanisms

Novel therapeutic approaches for alcoholic cardiomyopathy are being developed using animal models, targeting mechanisms such as oxidative stress, cardiac fibrosis, and apoptosis. Activation of ALDH2 with Alda-1 enhances acetaldehyde clearance and protects against alcohol-induced myocardial injury (Münzel & Daiber, 2018). Inhibition of soluble epoxide hydrolase reduces fibrosis by restoring autophagic balance (Zhou et al., 2018).

CaMKII, implicated in ethanol-induced apoptosis and arrhythmias, has emerged as a promising target. Orally available inhibitors like RA306 and RA608 improve cardiac function and reduce arrhythmia in preclinical studies (Beauverger et al., 2020). Additionally, ranolazine prevents alcohol-induced atrial arrhythmias through late sodium current inhibition, though its impact on ventricular function in ACM is still under investigation (Mustroph et al., 2023).

8. Discussion

This review underscores the dose-dependent cardiotoxicity of alcohol, refuting earlier beliefs of cardiovascular benefits from moderate drinking. The multifactorial pathogenesis of ACM involves direct myocardial toxicity from ethanol and acetaldehyde, oxidative stress, inflammation, and maladaptive remodeling. Women's increased vulnerability highlights the need for sex-specific risk assessment. Early detection and sustained abstinence are critical, as cessation can improve cardiac function and prognosis. While current management follows heart failure guidelines, novel therapies targeting molecular pathways offer hope for better outcomes. Public health initiatives remain essential to reduce harmful drinking and prevent ACM. Future research should clarify precise pathogenic mechanisms and optimize personalized treatment strategies.

9. Conclusion

While low to moderate alcohol intake has been associated with reduced risk of ischaemic heart disease, higher levels of consumption markedly increase cardiovascular risk and overall mortality. Episodic binge drinking negates any potential benefits of light drinking. Chronic excessive alcohol intake is also linked to hypertension, cardiac arrhythmias, cardiomyopathy and eventually heart failure. ACM typically evolves from an asymptomatic phase marked by LV dilation, increased LV mass, and early diastolic dysfunction, to a symptomatic phase characterized by progressive LV dilation, wall thinning, systolic dysfunction, and overt signs of HF. The pathogenesis of ACM is multifactorial, involving disruptions in mitochondrial integrity, calcium regulation, contractile proteins, and sarcoplasmic reticulum function. However, the precise mechanisms underlying myocyte dysfunction remain incompletely defined. Management of ACM should include complete abstinence from alcohol, which remains the cornerstone of treatment. In symptomatic patients, guideline-directed heart failure therapies should be implemented to improve clinical outcomes.

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Disclosure:

Authors' contribution

Conceptualization: MB, PK
Methodology: MM, AN
Software: KD, JK
Check: JM, JZ
Formal analysis: KM, JZ
Investigation: Resources: MB, JK
Data curation: GŁ, KM
Writing- rough preparation MB
Writing - review and editing: MB, PK, KD
Visualization: GŁ, MM
Supervision: AN, JM
Project administration: MB

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