Alcohol 61 (2017) 9–15

Contents lists available at ScienceDirect

Alcohol

journal homepage: http://www.alcoholjournal.org/

Quantifying the contribution of alcohol to cardiomyopathy: A systematic review

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ARTICLE INFO

Article history:
Received 26 November 2016
Received in revised form
21 December 2016
Accepted 20 January 2017

Keywords:
Cardiomyopathy
Alcohol
Patterns of drinking
Dose-response
Population
Attributable fraction

ABSTRACT

Alcohol has a direct toxic impact on the heart, and while there is an ICD code for alcoholic cardiomyopathy, the burden of alcohol-attributable cardiomyopathy is not clear. For the usual estimation of this burden via population-attributable fractions, one would need to determine the risk relationships, i.e., average risk associated with different dimensions of alcohol exposure. The most important among these risk relationships is the dose-response relationship with different levels of average alcohol consumption. To establish risk relationships, we systematically searched for all studies on dose-response relationships, directly and indirectly, via reviews. The results did not permit computation of pooled estimates through meta-analyses. There were clear indications that heavy drinking (≥80 g per day) over several years was linked to high risk of cardiomyopathy, with greater lifetime exposure of alcohol linked to higher risks. Some studies indicated potential effects of patterns of drinking as well. As such, the global quantification of alcohol-attributable cardiomyopathy will have to rely on other methods than those used conventionally.

Background

Alcohol consumption is a major risk factor for non-communicable diseases (Parry, Patra, & Rehm, 2011; World Health Organization, 2014a, 2014b), with causal impacts on cancer, cardiovascular disease, and diabetes. The relationship between alcohol consumption and cardiovascular disease outcomes is complex, as different dimensions of consumption play a role for different outcomes (Klatsky, 2015a; O'Keefe, Bhatti, Bajwa, DiNicolantonio, & Lavie, 2014; Puddey, Rakic, Dimmitt, & Beilin, 1999; Roerecke & Rehm, 2012a). Heavy drinking, both irregular and chronic, is detrimental, whereas light to moderate drinking without any heavy drinking occasions can be beneficial. (For the detrimental effect of chronic heavy drinking on hypertensive disease, see Briasoulis, Agarwal, & Messerli, 2012; and Taylor et al., 2009; on ischemic heart disease see Roerecke & Rehm, 2014b; on atrial fibrillation and flutter see Kodama et al., 2011; on all types of stroke see Patra et al., 2010; for the detrimental effect of irregular heavy drinking on ischemic heart disease see Leong et al., 2014; and Roerecke & Rehm, 2010, 2014a; on stroke see Guiraud, Amor, Mas, & Touzé, 2010; O'Donnell et al., 2016; for the beneficial effect on ischemic disease see Roerecke & Rehm, 2012b; and Ronksley, Brien, Turner, Mukamal, & Ghali, 2011.)

This complex relationship may lead to substantial alcohol-attributable cardiovascular health burden in some countries, where alcohol is consumed often in heavy drinking occasions, such as Russia (Zaridze et al., 2009, 2014), and to almost no or even positive net cardiovascular health burden in other countries, where alcohol is mainly consumed in a way avoiding heavy drinking (see Shield, Rylett, & Rehm, 2016a, 2016b for the comparison of alcohol-attributable burden in more than 50 countries over the previous 25 years). However, in most burden of disease studies, the effect of

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http://dx.doi.org/10.1016/j.alcohol.2017.01.011
0741-8329/

Abbreviations

AUD	alcohol-use disorders
ACM	alcoholic cardiomyopathy
AAF	alcohol-attributable fractions
CI	confidence interval
CM	cardiomyopathy
ICD-10	International Statistical Classification of Diseases

alcohol consumption on cardiomyopathy (CM) is not included. To include this effect, population-attributable fractions need to be estimated, combining the distribution of alcohol exposure with information on risk (dose-response) relations (Rehm et al., 2010b). However, to date, there have been no meta-analyses on risk relations between alcohol consumption and this disease category (Rehm et al., 2010a, 2017). While there is a disease category of alcoholic cardiomyopathy (ACM) in ICD-10 (I 42.6; World Health Organization, 2016), which is fully attributable to alcohol by definition and could be used alternatively, this category is rarely used in comparative risk assessments, as it is too small a category to be estimated for or listed in global mortality statistics and is not available in countries without a detailed vital registration system (Rehm & Imtiaz, 2016).

CM denotes a disease of the heart muscle, reducing its ability to pump blood to the rest of the body (Heart & Stroke Foundation, 2011). There are different forms of CM, with different etiologies, and chronic heavy alcohol is linked to dilated CM by ethanol acting as a toxin to weaken the heart muscle directly (Dancy, Bland, Leech, Gaitonde, & Maxwell, 1985; Fernández-Solà, 2015; Rubin, 1979; Sander, von Heymann, Spies, & Braun, 2005; Urbano-Márquez et al., 1989; Urbano-Márquez & Fernández-Solà, 2004; for experimental demonstrations of the toxic effect of alcohol on muscles and cardiac indicators see; Kozlovskij, 2007; Song & Rubin, 1972). The phenomenon had been discovered already in the 19th century and was described in several medical books (e.g., Wood, 1855; for a summary of historical accounts see; Massumi et al., 1965). There was also the description of what we now call ACM by a Munich pathologist, who labeled the phenomenon the Münchner Bierherz (the Munich beer heart), a disease characterized by cardiac dilatation and hypertrophy ascribed to heavy consumption of beer over time (Bollinger, 1884). Actually, the effect is caused by both ethanol (pure alcohol) and acetaldehyde, the first metabolite of ethanol, and it can be worsened by interaction with other toxins, such as heavy metals or by lack of proper nutrition (Klatsky, 2015a, 2015b; Maisch, 2016; Sliwa, Damasceno, & Mayosi, 2005). Moreover, cardiomyopathies are associated with liver disease even though there has been anecdotal evidence to the contrary (Estruch et al., 1995; Gautam, Ghimire, Subramanyam, & Guruprasad, 2013). However, there may be an additional category of cirrhotic CM caused by non-alcoholic liver cirrhosis (Ruiz-del-Árbol & Serradilla, 2015; but see Pellicori et al., 2013).

To quantify the relationship between alcohol consumption and CM for future comparative risk assessments, we searched the literature either to find a relevant meta-analysis or to find epidemiological studies, which could be used to conduct a meta-analysis.

Materials and methods

Search strategy

Based on the PRISMA guidelines (Moher, Liberati, Tetzlaff, Altman, & The Prisma Group, 2009), a systematic literature search was done in OVID, Medline, and Embase databases to identify reviews for CM attributable to alcohol consumption, or individual studies that could be used to quantify the effect of alcohol on CM. Therefore, the search strategy used a combination of the keywords “literature review”, “systematic review”, “meta-analysis”, “alcohol”, “cardiomyopathy” and “dose response”. These database searches were supplemented by hand searches of reference lists from the included studies (see Web Appendix 1 for the PRISMA chart). No language restrictions were applied and publications between January 2007 and November 2016 were screened.

Inclusion and exclusion

For a first selection, we included all studies with dose-response information on alcohol consumption and CM or ACM (both meta-analyses and individual studies), and any general review for screening for further studies containing these dose-response relationships. Web Appendix 2 provides a list of all studies included.

We excluded reviews on animal studies, reviews with no specific information on CM or ACM (e.g., reviews on atrial fibrillation or other cardiovascular topics; or general reviews on cardiovascular disease without any specific larger section on alcohol, CM, or ACM; or reviews on CM without any mention of alcohol), reviews on clinical management, and reviews on genetics/genomics and specific pathological mechanisms only without any information that would allow the quantification of the relationship between alcohol and CM or ACM.

Terminology

All alcohol levels were converted into grams of pure alcohol/day from the measures used in the original articles. We used the term “alcohol-use disorder” or “people with alcohol-use disorders”, whereas in the original articles different terms were used such as “alcoholics” or “dependence”.

Results

Systematic searches

Two types of reviews could be identified (see Web Appendix 2 for a listing of all reviews): firstly, reviews focusing on ACM only (Adam, Nicholson, & Owens, 2008; Awtry & Philippides, 2010; Correale, Laonigro, Altomare, & Di Biase, 2008; George & Figueredo, 2011; Guzzo-Merello, Cobo-Marcos, Gallego-Delgado, & Garcia-Pavia, 2014; Iacovoni, De Maria, & Gavazzi, 2010; Maisch, 2016; Piano & Phillips, 2014; Rosenberg & Frey, 2010); and secondly, reviews with at least one specific point on alcohol and CM or ACM (Charlet & Heinz, 2016; Correale, Laonigro, Altomare, & Di Biase, 2009; Djoussé & Gaziano, 2008; Fernández-Solà, 2015; Klatsky, 2009, 2015a; Laonigro, Correale, Di Biase, & Altomare, 2009; Matsumoto, Miedema, Ofman, Gaziano, & Sesso, 2014; O'Keefe et al., 2014; Skotzko, Vrinceanu, Krueger, & Freudenberger, 2009). However, no meta-analyses on the dose-response relations between ACM and levels of alcohol consumption, or any other dimension of alcohol, were found. Each review was used to search for specific studies on dose-response relationships between dimensions of alcohol and the incidence and/or mortality of CM or ACM.

Dose-response relationships between level of alcohol consumption and cardiomyopathy or alcoholic cardiomyopathy

While few classic epidemiological studies on the relationship between dose of alcohol and incidence of CM or ACM could be