

The Impact of Alcohol Consumption in NAFLD

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Disclosures

- Abbvie
- Allergan
- Bio-Rad
- Diafir
- Echosens
- Gilead
- Intercept
- MSD
- Siemens

Hey Doc, is there any chance that my alcohol consumption could be benefit for my health ?



Alcohol consumption and mortality

- Meta-analysis of 34 prospective studies
- 1 015 835 subjects
- 94 533 deaths during the follow-up
- Protection apparent up to 3 drinks per day in men and up to 2 drinks per day in women



Alcohol consumption and cardiovascular outcomes

Meta-analysis of 84 studies, mean follow-up: 11 ± 6 years



Alcohol consumption and mortality



- 694 data sources
- 28 millions individuals
- 649 000 registered cases (23 outcomes)

GBD 2016 Alcohol Collaborators, Lancet 2018

Alcohol consumption and mortality from ischemic heart disease



GBD 2016 Alcohol Collaborators, Lancet 2018

Moderate alcohol consumption and mortality in NAFLD

- 4 568 NAFLD patients from the NHANES 1988-2010
- Alcohol consumption ≤ 3 drinks per day (men) or ≤ 2 drinks per day (women)



Subgroup	0.5-1.4 drink/day	≥1.5 drink/day
All (fully adjusted)	0.64 (0.42-0.97)	1.45 (1.01-2.10)
Men	0.64 (0.42-0.97)	1.29 (0.91-1.84)
Women	0.40 (0.16-0.98)	1.47 (0.63-3.41)
≥65 years	0.43 (0.26-0.71)	0.92 (0.56-1.52)
<65 years	0.69 (0.40-1.19)	1.62 (1.03-2.54)
FIB4 <1.79	0.46 (0.26-0.81)	1.42 (0.92-2.18)
FIB4 ≥1.79	0.64 (0.29-1.35)	1.08 (0.51-2.28)
Noncardiovascular death	0.59 (0.36-0.96)	1.45 (0.96-2.21)

Hajifathalian, Hepatology 2018

Hey Doc, would moderate alcohol consumption reduce my risk of cardiovascular disease despite NAFLD ?



Alcohol and CVD in NAFLD

- 2 280 consecutive men ≥30 years old with NAFLD, single center (Korea)
- Daily alcohol intake <20 g/day, no history of CVD



Alcohol and CVD in NAFLD

- 570 NAFLD patients
- 25 years follow-up in the CARDIA study (USA)
- Alcohol ≤14 drinks /week (women), ≤21 drinks /week (men)
- Association between alcohol use (yes/no) and CVD risk
- Adjustment on 15
 parameters

		B (SE) / OR (95% Cl)	р
Measures of cardiac structure	LV mass index	0,75 (1,1)	0,51
	LV end diastolic volume	-2,1	0,44
	Left atrial volume index	0,93 (0,81)	0,25
Measures of cardiac function	Absolute GLS	-0,24 (0,25)	0,33
	E/A ratio	-0,04 (0,03)	0,22
	E/e ratio	0,20 (0,23)	0,38
Hemodynamics	Cardiac output	-57,3 (152,7)	0,71
Markers of diastolic dysfunction	Abnormal LV relaxation	1,2 (0,77-1,8)	0,44
	Higher LV filling pressures	1,2 (0,75-1,88)	0,45
CAC >0		1,46 (0,94-2,28)	0,09

Hey Doc, what is the worth for my liver : alcohol or metabolic syndrom ?

Interaction between Alcohol and Obesity

- 9 959 participants of the Midspan ٠ prospective cohorts (Scotland)
- 29 years median follow-up ٠
- 80 deaths related to liver disease ٠





Hart. BMJ 2010

Interaction between Alcohol and Obesity



Hart, BMJ 2010

Interaction between Alcohol and Metabolic Syndrome

- 6 366 subjects from the Health 2000 Study (Finland)
- 11.4 years median follow-up (range: 0-13 years)
- Bindge drinking: ≥5 alcohol drinks per occasion
- 84 liver decompensation events





Adberg, Liver Int 2017

Hey Doc, would a moderate alcohol consumption reduce my risk of cirrhosis ?



Moderate alcohol consumption and NAFLD

	Context	Effect of moderate alcohol use
Dunn 2012	NAFLD (n=582)	OR 0.52 for NASH presence OR 0.56 for one-unit increase in fibrosis stage
Kwon, 2014	NAFLD (n=77)	OR 0.26 for F3/4 fibrosis presence in patients with lifetime ≥24 gram-years of alcohol
Dixon 2011	Morbidly obese (n=108)	NS for NASH presence after adjustement for insulin resistance
Coltrim 2009	Morbidly obese (n=132)	OR 2.69 for NASH presence
Ekstedt 2009	NAFLD (n=71)	OR 7.1 for fibrosis progression for heavy episodic drinkers
Ascha 2010	Cirrhotic NASH (n=195)	HR 3.8 for HCC occurence

Lack of standardized alcohol questionnaires

Lack on adjustment for:

- Pattern of alcohol use
- Past heavy alcohol use
- Race
- Sex
- Obesity
- Other chronic illnesses
- Socioeconomic status
- Education
- Physical activity Ajmera, Hepatology 2017

Moderate alcohol consumption and NAFLD

58 927 NAFLD patients with low probability of advanced fibrosis (NFS <-1.455, FIB4 <1.30)



Chang, Hepatology 2018

Hey Doc, what is the effect of moderate alcohol consumption on NAFLD regression?



Alcohol and NAFLD regression

- 285 NAFLD patients (placebo groups of FLINT & PIVENS trials, NASH CRN repository)
- Inclusion of: « non drinkers » (never drink) and « modest drinkers (1-2 drink on a typical day)
- Paired liver biopsies, mean duration between biopsies : 47 ± 26 months



Hey Doc, would a moderate alcohol consumption reduce my risk of diabetes ?



Moderate alcohol consumption and diabetes

- Meta-analysis of 26 prospective observationnal studies (706 716 patients, 31 621 T2DM cases)
- Follow-up: 3.0 to 19.8 years
- Alcohol consumption: interviews (3 studies), self-reports (2), questionnaires (21)



Moderate alcohol consumption and diabetes



Li, Am J Clin Nutr 2016

Alcohol and diabetes



GBD 2016 Alcohol Collaborators, Lancet 2018

Hey Doc, could I undergo bariatric surgery even if I continue to drink alcohol?



- 11 115 patients who underwent a bariatric surgery in Sweden (1980 2006)
- Comparison after 4 161 gastric bypass vs 6 954 restrictive surgery (gastric banding, vertical banded gastroplasty)



2003 patients from the Longitudinal Assessment of Bariatric Surgery-2 cohort (US)



King, Surg Obes Relat Dis 2017



• Baseline factors associated with incident alcohol use disorders: male sex, younger age, smoking, any or regular alcohol consumption, lower social support, RYGB procedure

King, Surg Obes Relat Dis 2017

Hypotheses

- After GBS, an important source of alcohol dehydrogenase, the stomach, is by-passed, resulting in less alcohol being degraded before it enters the intestine
- Laparoscopic adjustable gastric band (LAGB), is associated with higher peak blood alcohol concentration, which is reached more quickly compared with presurgery status or nonsurgical controls
- Rapid emptying of liquids from the gastric pouch enables rapid absorption of alcohol into the jejunum
- Men have higher alcohol dehydrogenase activity in the liver than do women
- Addiction transfer
- Rodent models suggest that RYGB increases alcohol reward sensitivity via a neurobiological mechanism, independent of changes in alcohol absorption. Hypothesized pathways include changes to the ghrelin system and altered genetic expression in regions of the brain associated with reward circuitry