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SWISS HIV COHORT STUDY

The J-curve in HIV: better cardiovascular disease free survival with moderate alcohol intake

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Background

- In HIV-uninfected populations, low to moderate alcohol consumption is associated with a lower cardiovascular morbidity and mortality compared to alcohol abstention[1,2].
- In HIV-infected patients, low or moderate alcohol consumption was associated with a low prevalence of cardiovascular disease in an American cross-sectional study[3] and reduced the risk of major cardiovascular disease events (CADE) in a prospective French cohort[4].
- A detailed analysis of the association between alcohol consumption and CADE free survival and overall mortality from a large nationwide HIV cohort has not yet been performed. Especially, the impact of low and moderate consumption on these outcomes is ill-defined.

1. Ronksley et al. *BMJ* 2011 Feb 22;342:d671.
2. Mukamal et al. *N Engl J Med*. Jan 9 2003;348(2):109-118.
3. Freiberg et al. *J Acquir Immune Defic Syndr.* 2010;53:247–53.
4. Carrieri et al. *BMJ Open*. 2013;2(6).

Objectives

- To study the association between the level of alcohol consumption and CADE free survival in a large, nationwide HIV cohort.
- To evaluate the association between the level of alcohol consumption and secondary endpoints including CADE, heart CADE and overall survival.

Methods

Study population

- All adult individuals enrolled in the Swiss HIV Cohort Study who started antiretroviral therapy and had follow-up time after August 2005 were included.

Definitions

- Self-reported alcohol consumption was categorized into: abstention, low (1-9 g/d), moderate (10-29 g/d in females and 10-39g/d in men) and high alcohol intake.
- CADE included myocardial infarction, coronary angioplasty, coronary artery by-pass grafting, carotid endarterectomy, procedures on other arteries, cerebral infarction and cerebral haemorrhage.

Analyses

- Cox proportional hazards models were used to evaluate the association between time-updated alcohol consumption and cardiovascular disease free survival (combined endpoint) as well as CADE, heart CADE, AIDS and overall survival.
- Baseline demographic and clinical characteristics as well as time-varying risk factors for CADE were included in the models.

Results I: Patient Characteristics And CADE

- Table 1 shows the demographic and clinical characteristics of the patients included.
- Alcohol consumption level during follow-up: 53% abstention, 20% low, 23% moderate and 6% high.
- Among 10,547 individuals included, there were 464 events of CADE and 520 deaths during 52,000 years of follow-up. The incidence of CADE or death (whichever occurred first) was 1.8 events/100 person-years.

Table 1: Baseline characteristics of participants by alcohol consumption level

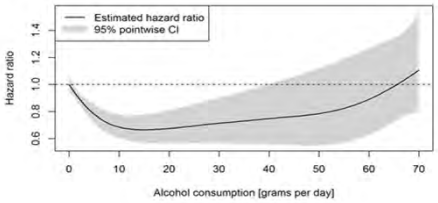
	No N=5006	Low N=1950	Moderate N=2170	High N= 638
Female sex (%)	1970 (39.4)	442 (22.7)	343 (15.8)	135 (21.2)
Median age in years (IQR)	41 (34-47)	41 (35-47)	43 (37-49)	44 (39-49)
Black ethnicity (%)	956 (19.1)	178 (9.1)	183 (8.4)	32 (5.0)
HIV transmission group (%)				
Heterosexual	2232 (46.6)	628 (32.2)	686 (31.6)	233 (36.5)
IDU	911 (18.2)	195 (10.0)	288 (13.3)	180 (28.2)
MSM	1589 (31.7)	1053 (54.0)	1116 (51.4)	209 (32.8)
Other	274 (5.5)	74 (3.8)	80 (3.7)	16 (2.5)
Median CD4 count (IQR)	360 (225-550)	360 (246-535)	375 (247-569)	340 (212-526)
Median log HIV RNA (IQR)	1.7 (0-4.6)	3.0 (0-4.7)	2.6 (0-4.7)	2.8 (0-4.6)
HCV infection (%)	255 (5.1)	85 (4.4)	74 (3.4)	35 (5.5)
CDC stage C (%)	1237 (24.7)	377 (19.3)	436 (20.1)	144 (22.6)
PI-based ART (%)	2509 (50.1)	1003 (51.4)	938 (43.2)	278 (43.6)
ART including ABC (%)	882 (17.6)	326 (16.7)	427 (19.7)	94 (14.7)
Family history (%)	513 (10.5)	215 (11.3)	271 (12.7)	69 (11.1)
Diabetes (%)	174 (3.5)	56 (2.9)	42 (1.9)	13 (2.0)
BMI: Normal (%)	2591 (63.1)	1049 (65.4)	1221 (66.6)	371 (66.7)
Underweight (%)	330 (8.0)	89 (5.5)	89 (4.9)	47 (8.5)
Obese (%)	1185 (28.9)	467 (29.1)	523 (28.5)	138 (24.8)
Arterial hypertension (%)	497 (10.0)	237 (12.2)	256 (11.9)	121 (19.0)
Median pack/d smoking (IQR)	0 (0-0.8)	0 (0-0.8)	0.1 (0-1)	1.0 (0-1)

IDU: injection drug users; MSM: men who have sex with men; HCV: hepatitis C virus; PI: protease inhibitor; ART antiretroviral therapy; ABC: abacavir; BMI: body mass index; IQR: interquartile range

Results II: Combined End-point: CADE or Death

- Compared to alcohol abstention, low (Hazard Ratio (HR) 0.73 (95% Confidence Interval (95% CI) 0.60-0.88), p=0.001) and moderate alcohol intake (HR 0.67 (0.56-0-80), p<0.001) were associated with a lower incidence of the combined endpoint, whereas for high intake no association was detected (HR 0.9 (0.70-1.14), p=0.40). Figure 1 shows a fitted curve of daily alcohol consumption level with the HR of the combined endpoint.
- All classical cardiovascular risk-factors, including family history, diabetes, smoking, obesity and arterial hypertension, as well as low CD4 cell count were significantly associated with a higher hazard of CADE or death.

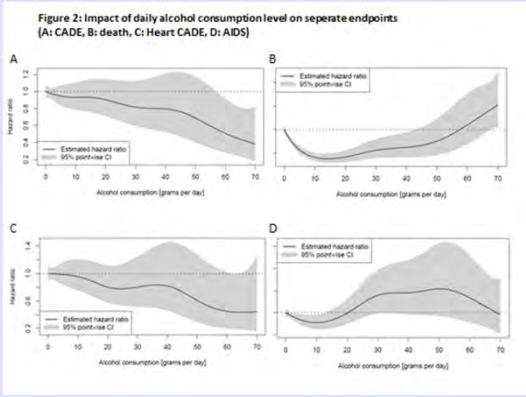
Figure 1: Impact of daily alcohol consumption level on the combined endpoint (CADE or death)



Results III: Treatment Outcomes

- Alcohol consumption showed a monotonic inverse association with CADE incidence: HR 0.91 (95% CI 0.85-0.97, p= 0.01) per 10 g increase of daily alcohol intake.
- A J-curve similar to the one for the combined end-point was found for overall survival (Fig. 2).

Figure 2: Impact of daily alcohol consumption level on seperate endpoints (A: CADE, B: death, C: Heart CADE, D: AIDS)



Discussion and Conclusions

- Compared to abstention, low and moderate alcohol intake were associated with a better CADE free survival and overall survival in participants of the Swiss HIV Cohort Study on antiretroviral therapy.
- However, the incidence of CADE and, to a lesser extent, heart CADE, seemed to be lower with increasing alcohol consumption, possibly due to competing risks in heavy drinkers.
- The reasons for the alcohol J-shaped curve for CADE-free survival need to be explored further, including the roles of drinking patterns and types of alcohol consumed ("French paradox").

Acknowledgements And Conflict of Interest

This study has been financed within the framework of the Swiss HIV Cohort Study, supported by the Swiss National Science Foundation (grant # 134277). The data are gathered by the Five Swiss University Hospitals, two Cantonal Hospitals, 15 affiliated hospitals and 36 private physicians (listed in http://www.shcs.ch/31-health-care-providers). The members of the Swiss HIV Cohort Study are: Aubert V, Barth J, Battegay M, Bernasconi E, Böni J, Bucher HC, Burton-Jeangros C, Calmy A, Cavassini M, Egger M, Elzi L, Fehr J, Fellay J, Furrer H (Chairman of the Clinical and Laboratory Committee), Fux CA, Gorgievski M, Günthard H (President of the SHCS), Haerry D (deputy of "Positive Council"), Hasse B, Hirsch HH, Hösli I, Kahlert C, Kaiser L, Keiser O, Klimkait T, Kouyos R, Kovari H, Ledergerber B, Martinetti G, Martinez de Tejada B, Metzner K, Müller N, Nadal D, Pantaleo G, Rauch A (Chairman of the Scientific Board), Regenass S, Rickenbach M (Head of Data Center), Rudin C (Chairman of the Mother & Child Substudy), Schöni-Affolter F, Schmid P, Schultze D, Schüpbach J, Speck R, Staehelin C, Tarr P, Telenti A, Trkola A, Vernazza P, Weber R, Yerly S.

Conflict of interest: HF grew up in a farm in Zurich "Wyland", which included a vineyard. His brother produces and sells his own red wine.