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在线全文

中老年群体酒精戒断与生物衰老加速的关系：基于英国生物银行数据库的研究*

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【摘要】 目的　探究中老年群体中酒精戒断与生物衰老加速的纵向关联，并探索影响该关联的效应修饰因子。**方法**　基于英国生物银行（UK Biobank，UKB）基线调查与首次重复调查中临床生化数据与人体测量数据，采用Klemera Doubal（KDM）算法构建生物年龄（biological age，BA）并计算BA加速。使用基于多变量线性回归模型的变化分析（change analysis）探究酒精戒断的变化与BA加速的变化之间的关联。将年龄、性别、吸烟、饮茶、喝咖啡和体重指数作为分层因素进行分层分析。**结果**　共纳入5 412名研究对象。与从不饮酒相比，短期戒酒会加速生物衰老〔β=1.00，95%置信区间（confidence interval，*CI*）：0.15～1.86〕，而长期戒酒则未观察到明显生物衰老加速（β=−0.20，95%*CI*：−1.12～0.71）。体重指数可能是潜在的效应修饰因子。**结论**　短期戒酒会加速生物衰老，而随着戒酒时间的延长，该衰老加速作用会逐渐消退。

【关键词】 衰老　生物年龄　酒精戒断　中老年群体　变化分析

Alcohol Abstinence and Accelerated Biological Aging Among Middle-Aged and Older Adults: Evidence From the UK Biobank

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【Abstract】 Objective　To investigate the longitudinal association between alcohol abstinence and accelerated biological aging among middle-aged and older adults and to explore the potential effect modifiers influencing the association. **Methods**　Utilizing the clinico-biochemical and anthropometric data from the baseline and first repeat survey of the UK Biobank (UKB), we employed the Klemera and Doubal method (KDM) to construct the biological age (BA) and calculate BA acceleration. Change analysis based on multivariate linear regression models was employed to explore the association between changes in alcohol abstinence and changes in BA acceleration. Age, sex, smoking status, tea and coffee consumption, and body mass index were considered as the stratification factors for conducting stratified analysis. **Results**　A total of 5 412 participants were included. Short-term alcohol abstinence (β=1.00, 95% confidence interval [*CI*]: 0.15-1.86) was found to accelerate biological aging when compared to consistent never drinking, while long-term abstinence (β=−0.20, 95% *CI*: −1.12-0.71) did not result in a significant acceleration of biological aging. Body mass index may be a potential effect modifier. **Conclusion**　Short-term alcohol abstinence was associated with accelerated biological aging, but the effect gradually diminishes over extended periods of abstinence.

【Key words】 Aging　Biological age　Alcohol abstinence　Middle-aged and older adults　Change analysis

酒精是全球最常消费的饮料之一，至2016年全球饮酒者比例已达43%[1]。鉴于酒精危害，世界卫生组织建议减少饮酒甚至戒酒。然而酒精戒断对于年龄相关疾病影响不一。有研究认为酒精戒断会诱发痴呆[2]。另一些研究则发现酒精戒断会降低心血管疾病[3]、认知障碍[4]和癌症[5]的风险。生物年龄（biological age，BA）是综合多种衰老相关生物标志物的指标，反映机体整体衰老，能够前瞻性预测年龄相关疾病[6]。基因、药物和生活方式等因素可影响BA，这为干预年龄相关疾病提供了独特视角。目前国内外仅一项研究探讨酒精戒断与BA之间的关联[7]。其使用的BA指标是基于DNA甲基化的表观遗传时钟，虽然在反映细胞衰老方面具有优势，却在预测年龄相关疾病方面较为欠缺[6]。此外，该研究仅限于横断面关联，尚缺乏纵向关联证据。另外，该研究的研究对象仅为酒精使用障碍患者，中老年普通人群中酒精戒断与BA之间的关联尚不清楚。我国饮酒者基数大，疾病负担重[8]，目前膳食营养指南仅推荐限酒[9]。基于英国生物银行（UK Biobank，UKB）探索酒精戒断状态的改变与BA的改变之间的关联，可以从行为改变的角度为我国戒酒指南和政

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策提供理论支持。

本研究基于Klemera and Doubal method(KDM)[10]生物年龄算法和UKB两期临床生化和人体测量数据,在中老年群体中探究酒精戒断状态的改变与生物衰老加速的改变之间的纵向关联,并研究潜在的效应修饰因子。

1 对象与方法

1.1 研究对象

UKB是英国一项著名的前瞻性队列研究,招募超50万名40~69岁参与者[11]。该研究自2006–2010年进行基线调查,并在2012、2014和2019年进行三次重复调查。UKB通过触摸屏电子问卷收集社会人口、生活习惯和自报健康等信息,并开展人体测量、临床生化及基因检测。数据收集前已征得参与者知情同意,且获得英国西北多中心研究伦理委员会伦理批准(编号:11/NW/0382)。考虑到临床生化数据的可及性,本研究只纳入UKB的基线和首次重复调查数据,项目编号为117185。

本研究排除了未参与首次重复调查(482 051人)、缺乏完整两期临床生化和人体测量数据(14 337人)、缺乏酒精戒断状态(5人)、基线调查患有严重疾病(589人)的参与者之后,共纳入5 412名研究对象。

1.2 研究方法

1.2.1 暴露测量

酒精戒断状态的定义基于既往文献[12-13],该变量通过触摸屏电子问卷测量。研究对象回答"您的饮酒频率?"和"您以前饮酒吗?"两个问题,并以此被划分为不饮酒者(从未饮用过任何形式的酒精)、酒精戒断者(曾经饮酒但调查前一年内不饮酒)和当前饮酒者(调查前一年内饮酒)。将酒精戒断状态视为等级变量,根据研究对象两次调查的回答可得到其酒精戒断状态的变化,并再分类为从不饮酒者(保持不饮酒者)、短期戒酒者(酒精戒断状态"减少"者)、长期戒酒者(保持酒精戒断者)、短期饮酒者(酒精戒断状态"增加"者)与长期饮酒者(保持当前饮酒者)[14],分类规则见表1。

表1 酒精戒断状态的变化分类规则

Table 1 Classification rules for changes in alcohol abstinence status

Alcohol abstinence status at baseline survey	Alcohol abstinence status in the first repeat survey	Changes in alcohol abstinence status
Never drinker	Never drinker	Consistent never drinker
Never drinker	Abstainer	
Never drinker	Current drinker	Short-term drinker
Abstainer	Current drinker	
Current drinker	Current drinker	Long-term drinker
Current drinker	Abstainer	
Current drinker	Never drinker	Short-term abstainer
Abstainer	Never drinker	
Abstainer	Abstainer	Long-term abstainer

1.2.2 结局测量

本研究采用基于临床生化和人体测量生物标志物的KDM方法计算BA。该指标预测年龄相关疾病的有效性已在欧洲人群验证[15]。首先收集既往构建BA的生物标志物,再根据UKB中的可及性筛选,初步纳入77个生物标志物。借助Box-Cox转换,对每个生物标志物进行标准化处理。随后,对转换后数据与实足年龄(chronological age, CA)分别进行Pearson相关性分析,保留相关系数绝对值大于0.1且有统计学意义($P<0.05$)的生物标志物。多个反映相同健康信息的生物标志物,根据先验知识仅保留一个。最终纳入18个生物标志物:收缩压(SBP)、腰臀比(WHR)、体脂率(BFP)、1秒用力呼气容积(FEV1)、平均红细胞体积(MCV)、碱性磷酸酶(ALP)、天门冬氨酸氨基转移酶(AST)、C-反应蛋白(CRP)、胱抑素C(CysC)、γ-谷氨酰转肽酶(GGT)、足跟定量超声指数(QUI)、糖化血红蛋白(HBA1C)、胰岛素样生长因子1(IGF-1)、甘油三酯(TG)、尿酸盐、尿素、白蛋白(ALB)和维生素D(VD)[16]。

BA的计算基于已有函数。该算法将CA与m个生物标志物进行回归,并提取m条回归直线的信息以综合计算得到BA[10]。鉴于男性和女性衰老过程的差异,本研究按性别分层并分别计算BA。最后,生物衰老加速(BA加速)定义为BA与CA之差。正值表明该个体在生物学和机体功能上衰老程度更为严重。

1.2.3 统计学方法

本研究按照酒精戒断状态的变化将研究对象分组,并描述基线特征。连续变量表示为中位数(P_{25}, P_{75}),分类变量表示为频数和构成比。时变变量的变化也依据酒精戒断状态的变化分组描述,连续变量的变化通过两波个体数据相减得到,分类变量的变化则综合两波个体数据

再分类得到。

为探究酒精戒断的变化与BA加速的变化的关联，本研究基于多变量线性回归模型进行变化分析（change analysis）。该方法通过扣除个体内部非时变特征（如遗传特征）来估计暴露的变化与结局的变化的关联，有效控制未测非时变混杂因素[17]。最终模型以BA加速的变化为因变量，酒精戒断状态的变化为自变量（从不饮酒者作为参照组），并控制时变协变量的变化。协变量选择基于既往文献[7]构建有向无环图，包括年龄、女性月经、吸烟、被动吸烟、体力活动、失眠、焦虑、抑郁、膳食评分、喝咖啡、饮茶、体重指数（body mass index, BMI）、自报高血压和自报糖尿病。上述分析中对缺失的协变量进行多重填补，估算五次并按Rubin规则[18]合并效应估计值，以确保结果的稳健和全面。为探究潜在的效应修饰因子，本研究将年龄、性别、吸烟、饮茶、喝咖啡和BMI作为分层因素进行分层分析。

为评估结果稳健性，本研究进行了敏感性分析。首先使用包含基线调查严重疾病患者的数据集重复分析。其次剔除因健康原因戒酒的短期戒酒者。再者，使用未填补数据分析。最后计算E值以评估未测混杂，E值没有公认界值但一般认为越大越好[19]。

2　结果

2.1　研究对象特征描述

研究对象基线特征见表2。与从不饮酒者中男性（35.3%）、吸烟者（0.7%）和喝咖啡者（58.3%）相比，短期与

表 2　研究对象的基线特征

Table 2　Baseline characteristics of study participants

Characteristic	Overall (*n*=5 412)	Consistent never drinker (*n*=139)	Short-term drinker (*n*=40)	Long-term drinker (*n*=5 013)	Short-term abstainer (*n*=123)	Long-term abstainer (*n*=97)
BA acceleration/yr., median (P_{25}, P_{75})	−1.72 (−5.34, 2.14)	0.29 (−3.44, 4.66)	−1.57 (−5.74, 2.49)	−1.83 (−5.37, 2.04)	−0.27 (−5.76, 2.82)	−0.77 (−4.26, 2.99)
Age/yr, median (P_{25}, P_{75})	58.33 (51.58, 62.83)	59.17 (52.12, 62.83)	58.04 (54.56, 62.08)	58.33 (51.58, 62.83)	58.25 (50.62, 63.33)	57.00 (52.25, 61.83)
Sex/case (%)						
Male	2 820 (52.1)	49 (35.3)	20 (50.0)	2 640 (52.7)	56 (45.5)	55 (56.7)
Female	2 592 (47.9)	90 (64.7)	20 (50.0)	2 373 (47.3)	67 (54.5)	42 (43.3)
Ethnicity/case (%)						
White	5 272 (97.6)	110 (80.3)	35 (87.5)	4 916 (98.2)	115 (94.3)	96 (99.0)
Other	132 (2.4)	27 (19.7)	5 (12.5)	92 (1.8)	7 (5.7)	1 (1.0)
Education attainment/case (%)						
Less than high school	455 (8.4)	12 (8.7)	8 (21.1)	416 (8.3)	11 (8.9)	8 (8.2)
High school or equivalent	2 582 (47.9)	70 (50.7)	17 (44.7)	2 371 (47.5)	73 (59.3)	51 (52.6)
College or above	2 350 (43.6)	56 (40.6)	13 (34.2)	2 204 (44.2)	39 (31.7)	38 (39.2)
Occupation/case (%)						
Employed	2 023 (37.6)	57 (41.6)	18 (45.0)	1 865 (37.4)	51 (41.5)	32 (33.3)
Unemployed or retired	3 355 (62.4)	80 (58.4)	22 (55.0)	3 117 (62.6)	72 (58.5)	64 (66.7)
Current smoking/case (%)						
No	5 071 (93.8)	138 (99.3)	39 (97.5)	4 695 (93.8)	112 (91.1)	87 (89.7)
Yes	334 (6.2)	1 (0.7)	1 (2.5)	311 (6.2)	11 (8.9)	10 (10.3)
Physical activity/(MET-hours/week), median (P_{25}, P_{75})	29.55 (13.30, 57.90)	23.30 (10.60, 66.20)	25.18 (8.70, 40.55)	29.83 (13.55, 57.57)	29.55 (12.03, 68.73)	30.69 (16.54, 59.63)
BMI/(kg/m^2), median (P_{25}, P_{75})	26.08 (23.73, 28.87)	25.31 (23.42, 29.48)	26.52 (22.05, 28.17)	26.08 (23.76, 28.85)	25.23 (23.43, 29.16)	27.46 (23.85, 30.45)
Insomnia symptom/case (%)						
No	1 404 (25.9)	34 (24.5)	12 (30.0)	1 301 (26.0)	32 (26.0)	25 (25.8)
Yes	4 008 (74.1)	105 (75.5)	28 (70.0)	3 712 (74.0)	91 (74.0)	72 (74.2)
Anxiety symptom/case (%)						
No	5 095 (96.8)	124 (94.7)	33 (89.2)	4 734 (97.0)	115 (95.8)	89 (92.7)
Yes	171 (3.2)	7 (5.3)	4 (10.8)	148 (3.0)	5 (4.2)	7 (7.3)
Depression symptom/case (%)						
No	4 998 (96.8)	120 (93.0)	33 (100.0)	4 648 (96.9)	109 (98.2)	88 (95.7)
Yes	165 (3.2)	9 (7.0)	0 (0.0)	150 (3.1)	2 (1.8)	4 (4.3)
Coffee consumption/case (%)						
No	1 089 (20.1)	58 (41.7)	15 (38.5)	949 (18.9)	33 (26.8)	34 (35.1)
Yes	4 317 (79.9)	81 (58.3)	24 (61.5)	4 059 (81.1)	90 (73.2)	63 (64.9)
Tea consumption/case (%)						
No	779 (14.4)	24 (17.3)	8 (20.0)	701 (14.0)	17 (13.8)	29 (29.9)
Yes	4 628 (85.6)	115 (82.7)	32 (80.0)	4 307 (86.0)	106 (86.2)	68 (70.1)

长期戒酒者中男性(45.5%和56.7%)、吸烟者(8.9%和10.3%)和喝咖啡者(73.2%和64.9%)占比更高。时变特征的变化见表3。生物衰老加速方面,相较于从不饮酒者〔−0.62(−3.34, 1.51)〕,短期戒酒者〔0.22(−2.39, 3.01)〕BA加速更大,长期戒酒者BA加速〔−1.05(−3.39, 1.08)〕则更小。协变量方面,与从不饮酒者中保持吸烟者(0.7%)和保持喝咖啡者(54.7%)占比相比,短期和长期戒酒者中保持吸烟者(4.1%和6.2%)和保持喝咖啡者(65.0%和60.8%)占比更高。

2.2 酒精戒断状态的变化与BA加速的变化的关系

如图1A,与从不饮酒者相比,短期戒酒者〔β= 1.00, 95%置信区间(confidence interval, *CI*): 0.15 ~ 1.86〕的BA加速更大,甚至超过短期饮酒者(β= 0.33, 95%*CI*: −0.91 ~ 1.57)和长期饮酒者(β= 0.49, 95%*CI*: −0.10 ~ 1.09)的BA加速。而长期戒酒者(β= −0.20, 95%*CI*: −1.12 ~ 0.71)BA加速更小。

2.3 分层分析结果

如图2,在短期戒酒者中, BMI≥25 kg/m^{2}者(β= 1.76, 95%*CI*: 0.61 ~ 2.92)比BMI< 25 kg/m^{2}者(β= 0.19, 95%*CI*: −1.10 ~ 1.48)BA加速更大。尽管两组间的BA加速差异接近显著(I^2= 68.5%, *P*= 0.075),但未达统计学意义,这提示BMI可能是潜在的效应修饰因子但需要更多证据验证。未观察到其他人群特征的效应修饰作用。

2.4 敏感性分析结果

如图1B,纳入基线调查严重疾病患者后,样本量略有增加但结果仍稳健。如图1C,排除因健康原因戒酒的短期戒酒者后,该组样本量略有下降但结果仍稳健。如图1D,使用未填补数据后,样本量均显著减少,短期戒酒

表 3 研究对象时变特征从基线调查到首次随访调查的变化

Table 3 Changes in time-varying characteristics from baseline survey to first repeated survey

Changes in time-varying characteristic	Overall (*n*=5 412)	Consistent never drinker (*n*=139)	Short-term drinker (*n*=40)	Long-term drinker (*n*=5 013)	Short-term abstainer (*n*=123)	Long-term abstainer (*n*=97)
Outcome						
BA acceleration/yr, median (P_{25}, P_{75})	−0.33 (−2.77, 2.27)	−0.62 (−3.34, 1.51)	0.06 (−2.40, 2.47)	−0.32 (−2.75, 2.27)	0.22 (−2.39, 3.01)	−1.05 (−3.39, 1.08)
Covariates						
Age/yr, median (P_{25}, P_{75})	4.50 (3.92, 5.00)	4.58 (4.08, 5.17)	4.79 (4.17, 5.33)	4.50 (3.92, 5.00)	4.67 (4.00, 5.12)	4.50 (3.92, 5.08)
Physical activity/(MET-hours/week), median (P_{25}, P_{75})	0.20 (−15.20, 15.25)	0.35 (−19.15, 14.66)	−0.75 (−14.11, 15.70)	0.33 (−15.07, 15.30)	−3.62 (−27.09, 11.04)	−2.14 (−16.43, 11.10)
Current smoking/case (%)						
Always no	5 038 (93.4)	137 (99.3)	39 (97.5)	4 663 (93.3)	112 (91.1)	87 (89.7)
Changing from no to yes	22 (0.4)	0 (0.0)	0 (0.0)	22 (0.4)	0 (0.0)	0 (0.0)
Changing from yes to no	125 (2.3)	0 (0.0)	1 (2.5)	114 (2.3)	6 (4.9)	4 (4.1)
Always yes	209 (3.9)	1 (0.7)	0 (0.0)	197 (3.9)	5 (4.1)	6 (6.2)
Insomnia symptom/case (%)						
Always no	3 459 (63.9)	83 (59.7)	31 (77.5)	3 206 (64.0)	81 (65.9)	58 (59.8)
Changing from no to yes	613 (11.3)	18 (12.9)	3 (7.5)	570 (11.4)	15 (12.2)	7 (7.2)
Changing from yes to no	486 (9.0)	14 (10.1)	3 (7.5)	447 (8.9)	13 (10.6)	9 (9.3)
Always yes	852 (15.7)	24 (17.3)	3 (7.5)	788 (15.7)	14 (11.4)	23 (23.7)
Anxiety symptom/case (%)						
Always no	4 921 (95.3)	116 (92.1)	31 (91.2)	4 576 (95.5)	112 (94.1)	86 (91.5)
Changing from no to yes	80 (1.5)	4 (3.2)	0 (0.0)	73 (1.5)	2 (1.7)	1 (1.1)
Changin from yes to no	114 (2.2)	2 (1.6)	3 (8.8)	104 (2.2)	2 (1.7)	3 (3.2)
Always yes	50 (1.0)	4 (3.2)	0 (0.0)	39 (0.8)	3 (2.5)	4 (4.3)
Depression symptom/case (%)						
Always no	4 755 (94.9)	109 (90.1)	32 (100.0)	4 431 (95.1)	102 (94.4)	81 (92.0)
Changing from no to yes	97 (1.9)	5 (4.1)	0 (0.0)	84 (1.8)	4 (3.7)	4 (4.5)
Changin from yes to no	114 (2.3)	4 (3.3)	0 (0.0)	107 (2.3)	1 (0.9)	2 (2.3)
Always yes	43 (0.9)	3 (2.5)	0 (0.0)	38 (0.8)	1 (0.9)	1 (1.1)
Tea consumption/case (%)						
Always no	603 (11.2)	22 (15.8)	6 (15.0)	538 (10.7)	12 (9.8)	25 (25.8)
Changing from no to yes	176 (3.3)	2 (1.4)	2 (5.0)	163 (3.3)	5 (4.1)	4 (4.1)
Changin from yes to no	155 (2.9)	6 (4.3)	1 (2.5)	143 (2.9)	3 (2.4)	2 (2.1)
Always yes	4 472 (82.7)	109 (78.4)	31 (77.5)	4 163 (83.1)	103 (83.7)	66 (68.0)
Coffee consumption/case (%)						
Always no	772 (14.3)	46 (33.1)	12 (30.8)	659 (13.2)	27 (22.0)	28 (28.9)
Changing from no to yes	317 (5.9)	12 (8.6)	3 (7.7)	290 (5.8)	6 (4.9)	6 (6.2)
Changin from yes to no	238 (4.4)	5 (3.6)	2 (5.1)	217 (4.3)	10 (8.1)	4 (4.1)
Always yes	4 078 (75.4)	76 (54.7)	22 (56.4)	3 841 (76.7)	80 (65.0)	59 (60.8)
BMI/(kg/m^2), median (P_{25}, P_{75})	0.10 (−0.72, 0.93)	0.06 (−1.01, 0.61)	0.69 (−0.23, 1.74)	0.11 (−0.70, 0.93)	0.07 (−0.67, 1.33)	−0.19 (−1.14, 0.89)

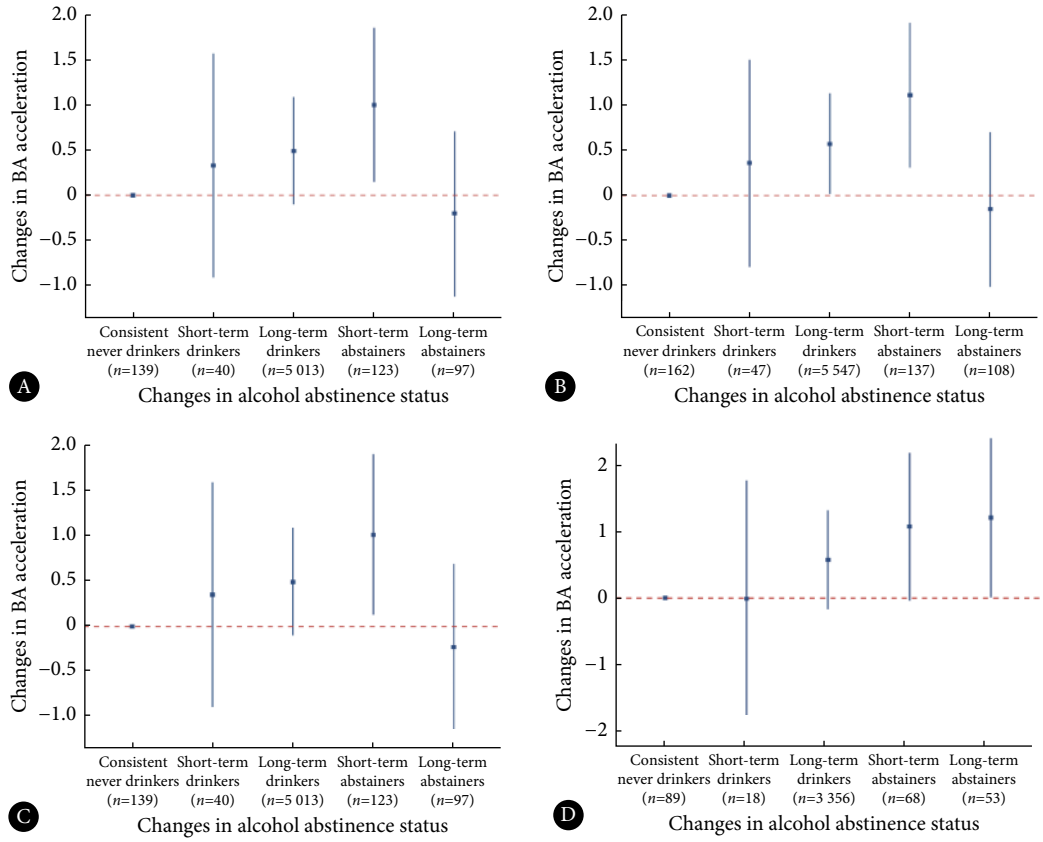

图 1 酒精戒断状态的变化与BA加速的变化的关联结果

Fig 1 Results of associations between changes in alcohol abstinence and changes in BA acceleration

A, Main results; B, results after inclusion of participants with serious illness at baseline; C, results after exclusion of short-term abstainers from alcohol for health reasons; D, results without multiple imputations.

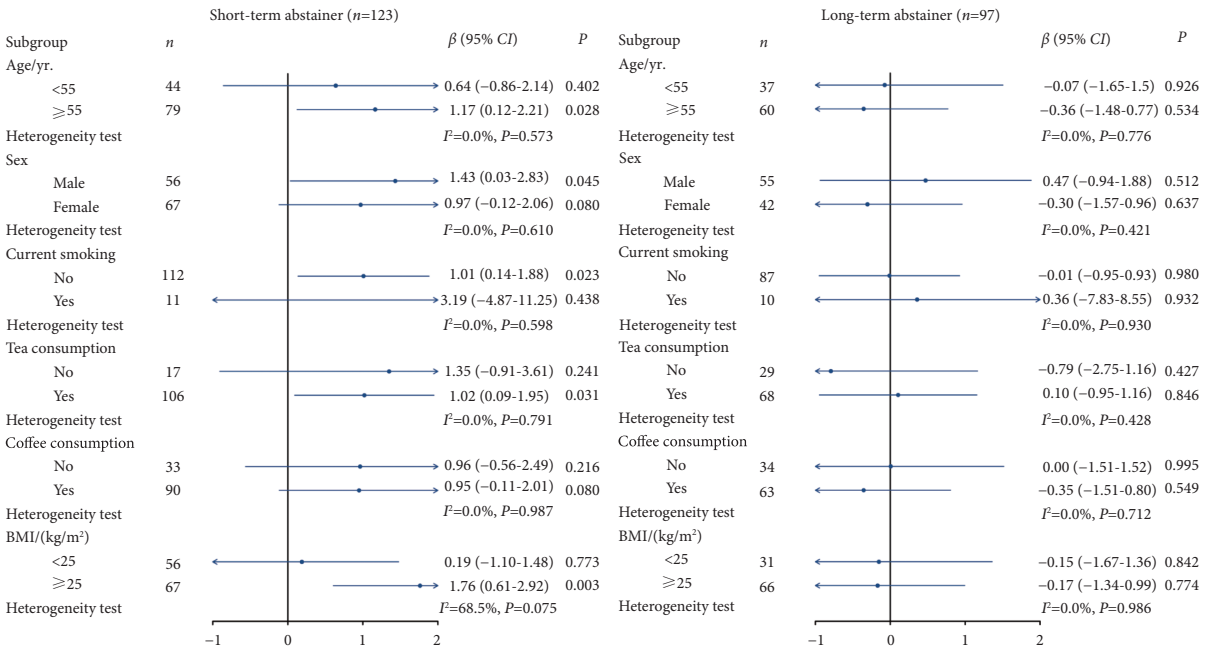

图 2 短期戒酒者与长期戒酒者中分层分析结果

Fig 2 Stratified analysis results of short-term abstainers and long-term abstainers

者仍表现出加速衰老但长期戒酒者也出现加速衰老。主分析结果中短期和长期戒酒者的β值和95%*CI*的E值分别为4.42和1.56、1.70和1.00。以短期戒酒者的β值为例，其E值表示至少需要4.42倍的现有未测混杂才能使该β值不具有统计学意义，提示未测混杂对短期戒酒者的点估计值影响较小。

3 讨论

本研究探究了酒精戒断的变化与生物衰老加速的关联，并探索了潜在的效应修饰因子。衰老是涉及多器官系统的复杂过程。本研究结果不仅验证短期酒精戒断对机体单方面的影响[20-21]，而且进一步证实短期酒精戒断加速整体衰老过程。以往研究使用表观遗传时钟评估酒精戒断与生物衰老关联[7]，而本研究采用已被证实更好预测年龄相关疾病的BA[6]，强化了短期酒精戒断与加速衰老的关联。总之，虽然使用不同衰老指标，本研究与以往研究均为短期酒精戒断加速生物衰老提供了有力的证据。

本研究还发现短期戒酒加速生物衰老，但长期戒酒后衰老加速会减缓。酒精戒断影响机体衰老是一个复杂而长期的过程。戒酒初期1个月内，个体会经历酒精戒断综合征，表现为运动和认知障碍，从而加速衰老[22]。戒酒5年内，血压等指标可能逐渐趋于正常[3]，但大脑[23]等器官尚未恢复甚至出现进一步衰老加速和病理改变。戒酒5年后，机体自我修复更加彻底，全身衰老速率趋于正常[23]。本研究发现短期戒酒加速衰老和长期戒酒衰老恢复正常，与既往研究一致，验证了酒精戒断影响机体衰老的进程。

既往机制学证据支持本研究结果。短期戒酒时血浆食欲素A增高，加剧酒精戒断症状和对酒精的渴求，从而加速衰老[24]。短期戒酒还影响额叶代谢从而加速衰老[25]。而随着戒断时间增长，大脑结构功能会逐渐恢复[26]。长期酒精戒断还会降低酒精导致的氧化应激，延缓细胞的加速衰老[27]。

本研究结果提示BMI可能是酒精戒断和衰老加速关联的效应修饰因子。BMI高者可能因为超重或肥胖会影响中枢神经系统的中央杏仁核功能[28]，加重酒精依赖[29]。因此该类人群戒酒时认知损害更显著且恢复更慢，从而表现更大衰老加速。因此针对超重肥胖者的戒酒指南应更精准。

本研究有以下优势：首先，据笔者所知本研究是第一篇探究酒精戒断与生物衰老加速之间纵向关联的研究；其次，本研究生物年龄的构建基于两期临床生化数据，该类型数据在以往的研究中极为稀缺；最后，本研究还进行了多个敏感性分析以测试结果的稳健性。本研究也存在局限：首先，酒精戒断状态的测量基于自填问卷，无法估计研究对象的具体戒酒时间与戒酒持续状态；其次，由于两期数据的稀缺性，短期戒酒者和长期戒酒者样本量不大，导致一些结果出现较宽的置信区间；最后，尽管本研究控制了许多协变量，仍有可能存在未测混杂，这对结果及结论外推均会产生影响。

综上所述，本研究探究了中老年人群中酒精戒断与生物衰老加速之间的纵向关联，并探索了潜在的效应修饰因子。结果发现，相较于从不饮酒者，短期戒酒会加速生物衰老，而随着戒酒时间的延长，这种衰老加速作用会逐渐消退。

* * *

作者贡献声明 陈鸿祥负责论文构思、数据审编、正式分析、调查研究、研究方法、可视化、初稿写作和审读与编辑写作，蔡佳洁负责数据审编和软件，魏君负责数据审编和验证，张红梅负责验证，向毅负责调查研究和审读与编辑写作，黄子桐负责审读与编辑写作，徐浩和赵星负责经费获取、研究项目管理、提供资源和监督指导，肖雄负责论文构思、经费获取、研究项目管理、提供资源和监督指导。所有作者已经同意将文章提交给本刊，且对将要发表的版本进行最终定稿，并同意对工作的所有方面负责。

Author Contribution CHEN Hongxiang is responsible for conceptualization, data curation, formal analysis, investigation, methodology, visualization, writing--original draft, and writing--review and editing. CAI Jiajie is responsible for data curation and software. WEI Jun is responsible for data curation and validation. ZHANG Hongmei is responsible for validation. XIANG Yi is responsible for investigation and writing--review and editing. HUANG Zitong is responsible for writing--review and editing. XU Hao and ZHAO Xing are responsible for funding acquisition, project administration, resources, and supervision. XIAO Xiong is responsible for conceptualization, funding acquisition, project administration, resources, and supervision. All authors consented to the submission of the article to the Journal. All authors approved the final version to be published and agreed to take responsibility for all aspects of the work.

利益冲突 所有作者均声明不存在利益冲突

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