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膳食糖摄入量与成年人群中胆石症患病风险的关联性分析

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摘 要

目的：基于美国国家健康与营养检查调查(NHANES)数据库，探讨成年人群胆石症患病风险与膳食糖摄入量的关系。方法：采用NHANES 2017~2020年的数据进行横断面研究。通过24小时饮食回顾评估膳食糖摄入量，胆石症则依据自我报告判定。运用加权Logistic回归模型调整混杂因素分析关联强度，并使用广义相加模型(GAM)探索非线性关系，通过两步递归法计算拐点。结果：共纳入7087名参与者，膳食糖摄入量的中位数为88.00克(IQR：54.45~131.59克)，胆石症的报告率为11.10%。校正混杂因素后，膳食总糖摄入量每增加10克，胆石症患病风险升高4.5% [OR: 1.045 (95% CI: 1.013~1.078), P = 0.011]。GAM提示存在非线性关联，然而对数似然比检验未检测到统计学上显著的阈值效应(P = 0.067)。结论：成年人群中胆石症患病风险与膳食糖摄入量呈连续、非线性的正相关关系，提示较高的膳食糖摄入量与胆石病患病率上升有关。

关键词

胆石症，膳食糖，膳食疗法，横断面研究

Association between Dietary Sugar Intake and the Risk of Gallstone Disease in Adults

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Abstract

Objective: To investigate the association between total dietary sugar intake and the risk of gallstone disease in adults based on the National Health and Nutrition Examination Survey (NHANES). Methods: A cross-sectional study was conducted using NHANES 2017~2020 data. Total dietary sugar intake was assessed by 24-hour dietary recall, and gallstone disease was defined by self-report. Weighted Logistic regression models were used to adjust for potential confounders, and generalized additive models (GAM) were applied to examine non-linear relationships, with the inflection point calculated by a two-step recursive method. Results: Among 7087 participants, the median total sugar intake was 88.00 g (IQR: 54.45~131.59 g), and 11.10% reported gallstone disease. After adjusting for confounders, each 10 g increase in total dietary sugar intake was associated with a 4.5% increase in gallstone disease prevalence [OR = 1.045 (95% CI: 1.013~1.078), P = 0.011]. GAM indicated a non-linear relationship. However, the log-likelihood ratio test did not detect a statistically significant threshold effect (P = 0.067). Conclusion: There is a continuous, non-linear positive correlation between the risk of gallstone disease and total dietary sugar intake in adults, suggesting that higher levels of sugar consumption are associated with increased gallstone disease prevalence.

Keywords

Gallstone Disease, Dietary Sugars, Diet Therapy, Cross-Sectional Study

1. 引言

胆石症以胆道系统内形成结石为特征，全球约 10%~20%的成年人受累[1] [2]。近年来，随着生活水平和饮食结构的改变，其患病率呈显著上升趋势。胆结石的存在与多种共病风险升高相关，其中包括心血管疾病和胆囊癌[3] [4]。胆结石主要分为胆固醇结石与胆色素结石[5]，其中胆固醇结石最为常见，其形成主要与胆汁中胆固醇过饱和、胆囊动力障碍等因素相关，而胆色素结石则源于胆红素代谢异常[1]。多项研究已阐明，代谢综合征、饮食因素、胆囊运动功能减退、胆红素肠肝循环增强，以及各类药物等均是胆结石明确的危险因素[6]-[8]。其中，饮食是胆结石发病机制中一个关键且可干预的因素[9]-[11]。多项流行病学研究表明，某些特定的饮食模式会增加胆结石的患病风险[9] [12] [13]。这些饮食模式通常表现为富含精制碳水化合物、甜食及脂肪，膳食纤维摄入不足、快餐消费频繁等[9]。过量糖摄入是这些高风险饮食模式的一个显著共同特征。然而，关于膳食糖摄入量与胆结石风险之间关系的定量研究仍然有限，二者之间的确切关联亟待深入探究。因此，本研究旨在利用美国国家健康与营养检查调查(NHANES)的全国代表性样本，探究成年人群膳食糖摄入量与胆结石患病率之间的量化关系，阐明膳食糖在胆结石形成过程中的潜在作用，以期为日后制定降低胆结石患病风险的预防策略和饮食建议提供依据。

2. 资料与方法

2.1. 研究资料

本研究数据来自 2017~2020 年 NHANES，最初纳入 15,560 名受试者。其中，6328 例因年龄在 20 岁以下被排除，88 例因妊娠数据缺失被排除，21 例因缺乏胆结石疾病信息被排除，1506 例因缺少饮食总糖

摄入量的数据被排除，530 例因相关协变量值缺失被排除，最终 7087 名受试者被纳入分析。该项目获得了美国国家卫生统计中心伦理审查委员会的批准，所有参与者均提供了书面知情同意书。

2.2. 调查内容

收集人口学特征、生活方式和合并症等数据。我们采用 NHANES 的 24 小时饮食回顾数据[14] [15]，通过与美国农业部(USDA)的食物与营养素数据库系统(FNDDS)和食物模式等效数据库(FPED)进行匹配，以计算总能量和糖摄入量[16]。24 小时饮食回顾数据的收集分两次进行：首次回顾在移动体检中心进行面对面访谈，第二次回顾在 3~10 天后通过电话完成，两次评估均采用相同评估方法以保证数据一致性[17]。本研究采用首次 24 小时回顾数据，并以克/天为单位对膳食糖摄入量进行量化。膳食糖摄入量定义为六种特定单糖与双糖的总和，包括：葡萄糖、果糖、半乳糖、蔗糖、乳糖和麦芽糖[18] [19]。胆结石疾病通过 NHANES 访谈过程中自我报告数据进行评估[20] [21]。人口学特征包括年龄、性别、种族(非西班牙裔白人、非西班牙裔黑人、西班牙裔和其他)和贫困收入比(PIR，衡量社会经济地位的指标)。生活方式因素包括吸烟状况(当前、既往或从不吸烟)和饮酒状况(根据摄入的频率和量分类)。身体质量指数(BMI)根据测量的身高和体重计算，并根据世卫组织指南进行分类。我们还评估了三种主要合并症：高血压、高脂血症和糖尿病。高血压的定义依据 2017 年美国心脏病学会和美国心脏协会指南，综合考虑降压药使用情况和血压读书[22]。高脂血症依据血脂谱异常或降脂药物使用情况判定[23]。糖尿病是通过自我报告的医师诊断、药物使用情况和实验室指标(包括空腹血糖、口服葡萄糖耐量试验结果和糖化血红蛋白水平)相结合来确定的。

2.3. 统计学方法

本研究基于 NHANES 的复杂抽样设计，应用调查权重、分层和聚类变量进行统计分析。连续变量以均数 ± 标准差表示，分类变量以例数(百分比)描述。应用加权逻辑回归模型探讨膳食糖摄入量与胆石病的关系；使用广义相加模型探讨二者之间的非线性关联，并通过递归算法确定拐点。所有分析使用 R 软件(4.2.0 版)和 EmpowerStats 完成，$P < 0.05$ 视为差异有统计学意义。

3. 结果

不同膳食糖摄入组临床特征比较各组间年龄、性别、种族分布差异均有统计学意义(均 $P < 0.001$)。生活方式方面，吸烟与饮酒状况在不同分组间亦存在显著差异($P < 0.001$, $P = 0.004$)。值得注意的是，糖尿病患病率随糖摄入增加呈下降趋势(Q1 组 25.11%至 Q4 组 16.42%，$P < 0.001$)，而胆结石患病率在各组间差异无统计学意义(10.50%~12.48%, $P = 0.197$)。见表 1。

Table 1. Baseline characteristics of study participants by quartiles of dietary sugar intake
表 1. 按膳食糖摄入量四等分组的研究对象基线特征

膳食糖摄入量(g/d)	Q1 (0~54.83)	Q2 (54.85~88.18)	Q3 (88.21~131.42)	Q4 (131.54~600.79)	P 值
年龄(岁)	51.59 ± 17.56	52.49 ± 17.23	51.33 ± 17.37	49.82 ± 17.04	<0.001
贫困收入比	2.65 ± 1.64	2.69 ± 1.66	2.70 ± 1.63	2.55 ± 1.59	0.027
总能量摄入量(kcal/d)	1496.41 ± 598.94	1798.25 ± 609.86	2136.34 ± 646.48	2637.20 ± 683.08	<0.001
性别[例(%)]					<0.001
女性	1053 (59.42%)	1020 (57.59%)	895 (50.51%)	734 (41.42%)	
男性	719 (40.58%)	751 (42.41%)	877 (49.49%)	1038 (58.58%)	

续表

种族[例(%)]					<0.001
非西班牙裔白人	602 (33.97%)	618 (34.90%)	645 (36.40%)	694 (39.16%)	
非西班牙裔黑人	553 (31.21%)	479 (27.05%)	443 (25.00%)	378 (21.33%)	
墨西哥裔美国人	194 (10.95%)	213 (12.03%)	211 (11.91%)	191 (10.78%)	
其他	423 (23.87%)	461 (26.03%)	473 (26.69%)	509 (28.72%)	
BMI [kg/m^2，例(%)]					0.270
≤25	467 (26.81%)	419 (23.92%)	450 (25.70%)	449 (25.55%)	
>25	1275 (73.19%)	1333 (76.08%)	1301 (74.30%)	1308 (74.45%)	
饮酒状况[例(%)]					0.004
从不	164 (9.26%)	173 (9.77%)	153 (8.63%)	129 (7.28%)	
低	603 (34.03%)	656 (37.04%)	670 (37.81%)	600 (33.86%)	
中	302 (17.04%)	279 (15.75%)	299 (16.87%)	286 (16.14%)	
高	326 (18.40%)	277 (15.64%)	267 (15.07%)	322 (18.17%)	
不明	377 (21.28%)	386 (21.80%)	383 (21.61%)	435 (24.55%)	
吸烟状况[例(%)]					<0.001
从不	1050 (59.26%)	1072 (60.53%)	1063 (59.99%)	935 (52.77%)	
既往	430 (24.27%)	450 (25.41%)	424 (23.93%)	423 (23.87%)	
当前	292 (16.48%)	249 (14.06%)	285 (16.08%)	414 (23.36%)	
糖尿病[例(%)]					<0.001
否	1327 (74.89%)	1358 (76.68%)	1438 (81.15%)	1481 (83.58%)	
是	445 (25.11%)	413 (23.32%)	334 (18.85%)	291 (16.42%)	
高脂血症[例(%)]					0.561
否	576 (32.51%)	588 (33.20%)	581 (32.79%)	613 (34.59%)	
是	1196 (67.49%)	1183 (66.80%)	1191 (67.21%)	1159 (65.41%)	
高血压[例(%)]					0.293
否	915 (51.64%)	937 (52.91%)	964 (54.40%)	963 (54.35%)	
是	857 (48.36%)	834 (47.09%)	808 (45.60%)	809 (45.65%)	
胆结石[例(%)]					0.197
否	1579 (89.11%)	1550 (87.52%)	1585 (89.45%)	1586 (89.50%)	
是	193 (10.89%)	221 (12.48%)	187 (10.55%)	186 (10.50%)	

注：BMI 为体重指数；数据以均数 ± 标准差或例数(百分比)表示。

表 2 显示了不同调整模型下膳食糖摄入量与胆石病的关联。将膳食糖作为连续变量分析时，其在所有调整模型中均与胆结石风险显著相关。在完全调整模型(模型 3)中，糖摄入每增加 10 g，胆结石患病风险增加 4.5% (OR = 1.045, 95% CI: 1.013~1.078, P = 0.011)。然而，当以四分位数分组进行分析时，与最低分位组(Q1)相比，中等至较高糖摄入组(Q2~Q4)的胆结石患病风险均无统计学差异(均 P > 0.05)。

Table 2. Weighted Logistic regression analysis of the association between dietary sugar intake and the risk of gallstone disease
表 2. 膳食糖摄入量与胆结石风险关系的加权 Logistic 回归分析

	未调整模型	模型 1	模型 2	模型 3
膳食糖摄入量 (每 10 g)	1.004 (0.988, 1.020) 0.637	1.029 (1.010, 1.049) 0.007	1.027 (1.006, 1.048) 0.026	1.045 (1.013, 1.078) 0.011
膳食糖摄入量分类				
Q1	1.0	1.0	1.0	1.0
Q2	0.892 (0.648, 1.228) 0.492	0.903 (0.646, 1.262) 0.558	0.862 (0.632, 1.176) 0.373	0.909 (0.588, 1.405) 0.570
Q3	0.954 (0.670, 1.357) 0.794	1.132 (0.744, 1.724) 0.570	1.100 (0.701, 1.728) 0.686	1.202 (0.668, 2.164) 0.425
Q4	0.823 (0.626, 1.082) 0.176	1.128 (0.845, 1.506) 0.425	1.043(0.768, 1.418) 0.793	1.164 (0.713, 1.901) 0.429

注：未调整模型未调整任何变量；模型 1 调整了年龄、性别、种族；模型 2 在模型 1 的基础上调整了贫困收入比、吸烟状况、饮酒状况；模型 3 在模型 2 的基础上调整了总能量摄入量、高血压、糖尿病、高脂血症。

膳食糖摄入量与胆石病的非线性关系：为进一步探讨膳食糖摄入量与胆结石风险的关系，本研究采用广义相加模型进行拟合，发现膳食糖摄入量与胆结石风险呈非线性关联，高风险主要集中于摄入量较高区间(图 1)。然而，进一步的阈值效应分析未发现统计学上显著的拐点(P = 0.066) (表 3)。

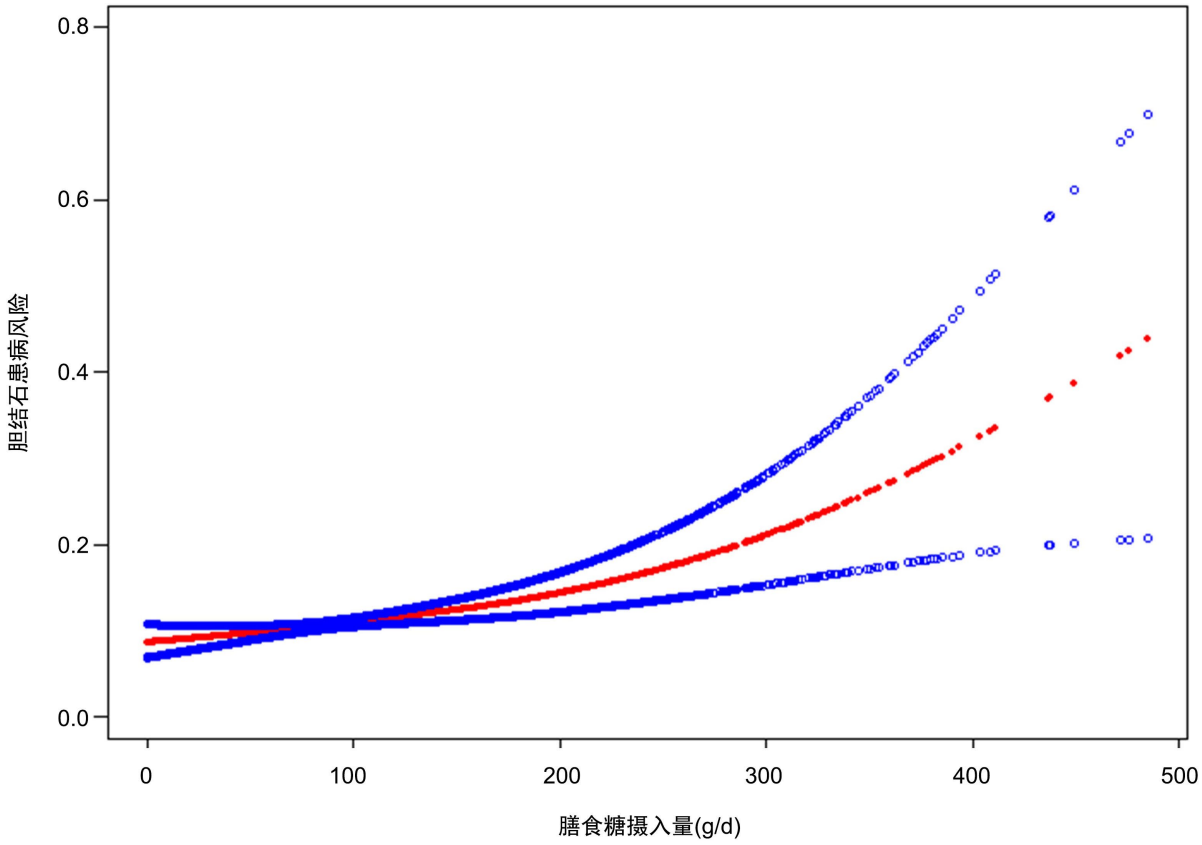

Figure 1. Non-linear relationship diagram between dietary sugar intake and the risk of gallstone disease
图 1. 膳食糖摄入量与胆结石患病风险的非线性关系图

Table 3. Piecewise linear regression analysis of the association between dietary sugar intake and the risk of gallstone disease
表 3. 膳食糖摄入量与胆结石风险的分段线性回归分析

	OR 值(95% CI)	P 值
标准线性模型	1.029 (1.012, 1.046)	<0.001
两段式线性模型		
拐点(g/d)	189	
<189	1.015 (0.993, 1.037)	0.176
>189	1.061 (1.024, 1.098)	<0.001
对数似然比检验		0.066

注：暴露因素为膳食糖摄入量(每升高 10 g)；结局因素为胆结石风险；OR 为比值比；CI 为置信区间；调整的协变量有年龄、性别、种族、贫困收入比、吸烟状况、饮酒状况、总能量摄入量、高血压、糖尿病、高脂血症。

4. 讨论

本横断面研究显示，在美国成年人群中，膳食糖摄入量与胆结石患病率之间存在显著的正向关联，且该关联呈现非线性特征。随着每日膳食糖摄入量水平的升高，胆结石患病风险会逐渐增加。

本研究的结果补充并拓展了饮食因素与胆结石风险的现有证据。以往研究多聚焦于宏观膳食模式或特定宏量营养素的作用。例如，Tsai 等[24]报告了高碳水化合物摄入与胆囊切除风险增加相关。而近期研究则强调了超加工食品对胆结石风险的潜在影响[25]。在此基础上，本研究通过聚焦膳食糖摄入量，为该领域提供了新的视角。膳食糖作为碳水化合物和超加工食品中的关键组分，有效衔接了宏观饮食模式与微观营养素研究，为今后制定更具针对性的胆结石饮食预防策略提供了理论依据。

关于膳食糖影响胆结石形成的分子机制，目前尚未完全阐明。我们推测，高糖摄入可刺激胰岛素分泌增加并诱发胰岛素抵抗[26] [27]，而后者已被证实可通过多种途径参与胆结石形成[21] [28]。此外，高糖摄入也可能导致肝脏脂代谢紊乱，增加胆固醇合成与分泌[29] [30]，从而提升胆汁中胆固醇饱和度——此为胆固醇性结石形成的关键环节[31]-[33]。

本研究也存在一定的局限性。首先，作为一项横断面研究，本研究无法推断糖摄入与胆结石之间的因果关系。其次，膳食数据的收集采用 24 小时饮食回顾法，可能引入回忆偏倚及报告误差。此外，尽管已对多种潜在混杂因素进行校正，但仍无法完全排除残余混杂的影响。未来研究可进一步纳入遗传背景、体力活动等变量，并借助前瞻性研究设计或膳食生物标志物以增强因果推断力度。

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