· 营养与食品卫生 ·

宏量营养素供能比例组合与非酒精性脂肪性肝病的关联

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摘要:目的　探讨不同宏量营养素供能比例组合与非酒精性脂肪性肝病(NAFLD)之间的关联。**方法**　基于 1999—2018 年美国国家健康与营养调查数据库成年参与者数据,计算脂肪、碳水化合物和蛋白质供能比,采用三维营养素空间逐步划分法构建营养集群。运用加权逻辑回归分析集群与 NAFLD 的关联,并进行交互和亚组分析,使用 K - means 聚类作为敏感性分析。**结果**　与最常见供能比例(集群 1:中等脂肪、中高碳水化合物、中等蛋白质)相比,以中高脂肪、中/中低碳水化合物和中等蛋白质为特征的集群(集群 3 和 4)显著增加 NAFLD 风险。在完全调整模型中,集群 3(*OR* = 1.367,95% *CI*:1.142 ~ 1.636)和集群 4(*OR* = 1.462,95% *CI*:1.137 ~ 1.879)均显示风险升高。交互作用分析均未发现显著交互作用($P > 0.05$)。敏感性分析结果与主要发现一致。**结论**　宏量营养素比例组合与 NAFLD 风险密切相关,中高脂肪搭配中/低碳水化合物、中等蛋白模式风险更高,提示应重视膳食结构调控以指导 NAFLD 防治。

关键词:非酒精性脂肪性肝病;宏量营养素;NHANES

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Association of macronutrient energy proportion combinations with Non - Alcoholic Fatty Liver Disease

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Abstract: Objective　To investigate the association between different macronutrient energy supply proportion combinations and non - alcoholic fatty liver disease (NAFLD). **Methods**　Using data from adult participants in the National Health and Nutrition Examination Survey (NHANES) 1999—2018, the energy supply proportions of fat, carbohydrate, and protein were calculated. Nutrient clusters were constructed using a three - dimensional nutrient space sequential partitioning method. Weighted logistic regression was employed to analyze the association between clusters and NAFLD, along with interaction and subgroup analyses. K - means clustering was used as a sensitivity analysis. **Results**　Compared with the most common energy supply pattern (Cluster 1: moderate fat, medium - high carbohydrate, moderate protein), clusters characterized by medium - high fat, medium/low - medium carbohydrate, and moderate protein (Cluster 3 and 4) were significantly associated with an increased risk of NAFLD. In the fully adjusted model, both Cluster 3 (*OR* = 1.367, 95% *CI*: 1.142 - 1.636) and Cluster 4 (*OR* = 1.462, 95% *CI*:1.137 - 1.879) showed elevated risks. Interaction analysis indicated a borderline significant interaction with hypertension ($P = 0.053$), while no significant interactions were found for other covariates ($P > 0.05$). Sensitivity analysis results were consistent with the main findings. **Conclusion**　Macronutrient proportion combinations are significantly associated with NAFLD risk. A dietary pattern of medium - high fat paired with medium/low carbohydrate is associated with higher risk, highlighting the importance of dietary structure regulation for guiding NAFLD prevention and management.

Keywords: Nonalcoholic fatty liver disease; Macronutrients; NHANES

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非酒精性脂肪性肝病(Nonalcoholic Fatty Liver Disease, NAFLD)已是全球最常见的慢性肝病,成人患病率约 32%[1-2]。该病与肥胖[3]、2 型糖尿病[4]及代谢综合征[5]密切相关,并显著心血管疾病、慢性肾病风险[6-7],带来重大公共卫生负担。

营养干预是 NAFLD 防治的基石,宏量营养素(脂肪、碳水化合物和蛋白质)的摄入比例对代谢健康具有重要影响。研究表明,过量摄入果糖可通过促进肝脏脂肪新生和内质网应激等途径驱动肝脂肪变性与炎症[8];高饱和脂肪酸能经 TLR4/MyD88 通路激活胰岛 β 细胞炎症反应[9];而多不饱和脂肪酸则可抑制 NLRP3 炎症小体激活,并通过 FFAR4 介导的肠肝轴改善 NAFLD[10-11]。

然而,饮食行为涉及多种营养素的复杂组合,研究重点已从单一营养素转向整体膳食模式。例如,高热量、低营养密度的西方饮食可加速肝脂肪变性和炎症[12];富含不饱和脂肪酸和膳食纤维的地中海饮食则有助改善炎症与氧化应激[13]。此外研究表明碳水化合物亚型、不同脂肪酸类型与 NAFLD 的关系,强调高脂、高糖及总能量过剩的关键作用[14-15]。横断面研究进一步分析了各类糖、脂肪酸与蛋白质来源与 NAFLD 的关联,并借助营养素替代探讨其相互影响[16-17]。这些研究深化了对多重营养素与 NAFLD 关系的理解,但对三大宏量营养素供能比例组合进行系统评估的研究仍较为缺乏。

为此,本研究利用 NHANES 数据库,结合营养几何学方法,系统评估不同宏量营养素供能比例组合与 NAFLD 风险的关系,旨在为膳食指导和公共卫生策略提供依据。

1 材料与方法

1.1 *数据来源* 研究数据基于 1999—2018 周期的 NHANES,已获得美国国家卫生统计中心伦理审查委员会的批准,所有参与者获得了知情同意。

研究参与者的筛选流程如下:从初始 101 316 名 NHANES 参与者,排除年龄 < 18 岁的个体(n = 42 112)、乙型或丙型肝炎感染者(n = 906)、孕妇(n = 1 548)、过量饮酒者(n = 23 575)、缺乏膳食摄入数据、NAFLD 诊断信息的参与者(n = 10 253)以及总能量摄入值异常(<400 千卡/天)或营养素供能比异常(偏离平均值 > 3 个标准差)的个体。最终共 22 922 名成人纳入分析(图 1)。

1.2 *三维营养素空间构建* 研究采用三维立方体法,以脂肪、碳水化合物和蛋白质的供能百分比分别作为坐标轴,构建三维营养素空间[18]。将每位参与者的膳食数据映射为三维空间中的一个点。通过以 50%、25% 和 12.5% 为阈值划分各营养素的坐标轴,利用坐标轴不同区间的组合成多个立方体单元,每个单元即为一个营养素集群(Cluster),通过列举所有立方体以识别宏量营养素供能比例组合(见图 2A)。

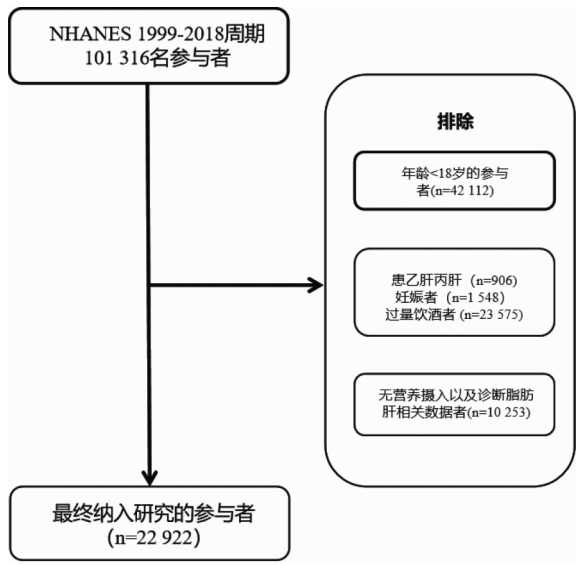


图 1 研究者筛选流程图

Fig. 1 Flowchart of participant selection

首先,以 50% 阈值将三条坐标轴各自划分为两段,形成 8 个立方体。分布显示,集群 1(脂肪 0% ~ 50%,碳水化合物 0% ~ 50%,蛋白质 0% ~ 50%)占 54.85%,集群 2(脂肪 0% ~ 50%,碳水化合物 50% ~ 100%,蛋白质 0% ~ 50%)占 43.16%,其余集群占 1.99%(图 2B)。将两个主要立方体按 25% 阈值细分,得到 16 个集群,其中三个主要集群分别占总体的 50.35%、33.81% 和 8.63%。最后,对这 3 个集群以 12.5% 阈值进行划分,得到 24 个子集群,选取样本量较大的 8 个(共 18 932 人)用于分析。为提升结果的可读性与可比性,本研究将每种营养素供能水平按不同百分比分为:低、中低、中等、中高、高五个等级(见图 3)。

1.3 *肝脂肪变性评估* 依据周期不同采用两种方法。1999—2016 周期采用脂肪肝指数(Fatty Liver Index, FLI),以 FLI ≥ 60 为肝脂肪变性的判定标准[19],

$$FLI = [e^{0.953\times\ln(TG)+0.139\times BMI+0.718\times\ln(GGT)+0.053\times WC-15.745}]/[1+e^{0.953\times\ln(TG)+0.139\times BMI+0.718\times\ln(GGT)+0.053\times WC-15.745}]\times 100,$$

其中 TG 为甘油三酯(Triglycerides, TG),GGT 为 γ-谷氨酰转移酶(Gamma glutamyl transferase, GGT),WC 为腰围(Waist Circumference, WC),其中 TG 以 mg/dL 为单位,GGT 以 U/L 为单位,WC 以厘米为单位。2017—2018 周期采用瞬时弹性成像获取受控衰

减参数(Controlled Attenuation Parameter, CAP),当 CAP 值≥274 dB/m,则定义为肝脂肪变性[20]。

1.4 协变量的选择　协变量包括年龄、性别、种族、教育程度、婚姻状况、贫困收入比(Poverty Income Ratio, Pir),吸烟状况,糖尿病和高血压以及总能量摄入。种族/民族分为:墨西哥裔美国人、非西班牙裔白人、非西班牙裔黑人及其他种族。教育程度分为:高中以下学历、高中或同等学历以及高中以上学历。Pir 分为低水平(Pir < 1.30)、中等水平(Pir:1.30 ~ 3.50)和高水平(Pir > 3.50)[21]。婚姻状况分为已婚/与伴侣同居、离婚/分居/丧偶、从未结婚。吸烟状况分为从不吸烟(吸烟 < 100 支)、既往吸烟(≥100 支且已戒)和当前吸烟(≥100 支且仍在吸)[22]。过量饮酒定义为:男性每天 > 3 杯,女性每天 > 2 杯[23]。

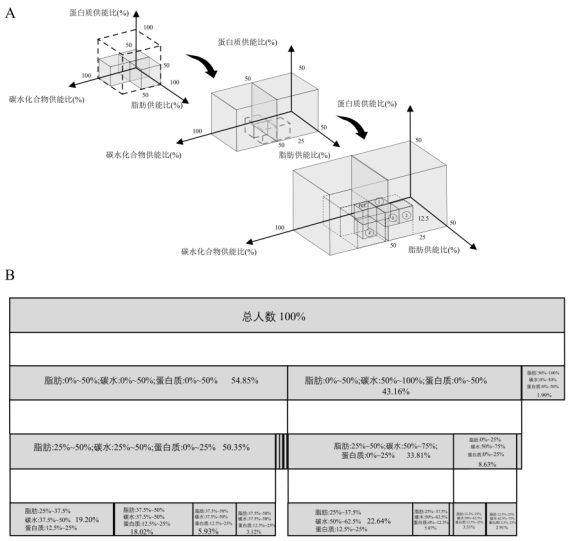


图 2　常量营养素三维空间构建的坐标系图(A)和群体划分比例流程图(B)

Fig. 2　Coordinate system diagram for three - dimensional macronutrient space construction (A) and group allocation proportion flowchart (B)

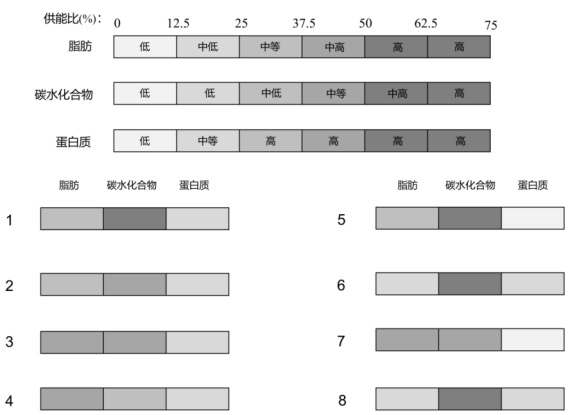


图 3　各集群比例及等级划分图

Fig. 3　Proportion and classification of each cluster

1.5 统计学方法　所有统计分析均考虑 NHANES 复杂抽样设计,并纳入抽样权重。数据清理与分析采用 R 软件(版本 4.4.1)及决策链软件(版本 1.0 版本,https://www.statsape.com/)。

连续型变量,若变量满足正态性与方差齐性,使用独立样本 t 检验进行组间比较,结果以 $\bar{x} \pm s$ 表示;若不满足正态分布或方差齐性,采用 Wilcoxon 秩和检验,结果以[$M(P_{25}, P_{75})$]表示。分类变量的组间比较采用 χ^2 检验,若理论频数小于 5 则使用 Fisher 精确检验,统计结果以例数(n)和百分比(%)表示。

采用多因素逻辑回归模型分析营养素组合模式与 NAFLD 风险的关联;并通过交互作用与亚组分析探讨不同人群特征的效应修饰。敏感性分析中,基于三种宏量营养素供能比进行 Kmeans 数据驱动聚类并重复回归;此外,基于 2015—2018 周期数据,采用代谢相关脂肪肝病(Metabolic Associated Fatty Liver Disease, MAFLD)的诊断标准验证结果的稳健性。

2　结　果

2.1 不同营养素组合集群特征　基于三维营养素空间划分最终得到 8 个集群,Cluster 1 以中等脂肪(25% ~ 37.5%)、中高碳水(50% ~ 62.5%)和中等蛋白质(12.5% ~ 25%)为主要特征,是最常见的集群;Cluster 3 与 Cluster 4 具有较高脂肪供能比例(37.5% ~ 50%),但碳水分别处于中等(37.5% ~ 50%)、中低(25% ~ 37.5%),表现为"中高脂 + 中或中低碳水"结构。其余集群(Cluster 2、Cluster 5 ~ 8)表现为低脂或低碳水等特征(见表 1)。

表 1　营养素组合集群的各营养素供能特征

Table 1　Macronutrient energy contribution profiles across nutrient combination clusters

集群	脂肪供能占比(%)	碳水化合物供能占比(%)	蛋白质供能占比(%)	样本量
1	25.0 ~ 37.5	50.0 ~ 62.5	12.5 ~ 25.0	5 190.00
2	25.0 ~ 37.5	37.5 ~ 50.0	12.5 ~ 25.0	4 401.00
3	37.5 ~ 50.0	37.5 ~ 50.0	12.5 ~ 25.0	4 137.00
4	37.5 ~ 50.0	25.0 ~ 37.5	12.5 ~ 25.0	1 356.00
5	25.0 ~ 37.5	50.0 ~ 62.5	0.0 ~ 12.5	1 662.00
6	12.5 ~ 25.0	50.0 ~ 62.5	12.5 ~ 25.0	804.00
7	37.5 ~ 50.0	37.5 ~ 50.0	0.0 ~ 12.5	715.00
8	12.5 ~ 25.0	62.5 ~ 75.0	12.5 ~ 25.0	667.00

2.2 研究人群的基线特征　最终分析共纳入 18 932

名参与者,其中 NAFLD 患者 8 430 例。NAFLD 人群年龄较大(48.88vs. 53.41 岁),男性比例更高(70.93% vs. 60.17%)。非西班牙裔白人比例更高、脂肪供能比更高(35.06% vs. 33.98%)、蛋白质供能比略高(16.13% vs. 15.93%),糖尿病和高血压更为常见,碳水供能比更低(48.17% vs. 49.43%)。

经三维空间构建纳入的 8 个集群(Clusters)显示,Cluster 1(脂肪:25% ~37.5%,碳水化合物:50% ~62.5%,蛋白质:12.5% ~25%)在 NAFLD 和 non - NAFLD 人群中均占较大比例,是最常见的组合。NAFLD 患者较非 NAFLD 的 Cluster 3(脂肪:37.5% ~50%,碳水化合物:37.5% ~50 %,蛋白质:12.5% ~25%)与 Cluster 4(脂肪:37.5% ~50%,碳水化合物:25% ~37.5%,蛋白质:12.5% ~25%)的分布比例更高(见表 2)。

表 2 研究对象基线特征表

Table 2 Baseline characteristics of participants

变量	总人数 (n = 18 932)	Non - Nafld (n = 10 502)	Nafld (n = 8 430)	统计量	P 值
年龄(岁,$\bar{x} \pm s$)	50.90 ± 17.46	48.88 ± 18.26	53.41 ± 16.06	7.747	<0.001
性别[n(%)]				237.195	<0.001
男性	12 298.00(64.96)	6 319.00(60.17)	5 979.00(70.93)		
女性	6 634.00(35.04)	4 183.00(39.83)	2 451.00(29.07)		
种族[n(%)]				114.962	<0.001
墨西哥裔美国人	2 442.00(12.90)	1 153.00(10.98)	1 289.00(15.29)		
非西班牙裔黑人	3 556.00(18.78)	2 003.00(19.07)	1 553.00(18.42)		
非西班牙裔白人	10 082.00(53.25)	5 583.00(53.16)	4 499.00(53.37)		
其他种族	2 852.00(15.06)	1 763.00(16.79)	1 089.00(12.92)		
教育水平[n(%)]				83.575	<0.001
低于高中学历	3 039.00(16.05)	1 556.00(14.82)	1 483.00(17.59)		
高中或等同高中学历	3 922.00(20.72)	2 004.00(19.08)	1 918.00(22.75)		
高中以上学历	11 971.00(63.23)	6 942.00(66.10)	5 029.00(59.66)		
婚姻状况[n(%)]				157.225	<0.001
已婚/同居	12 835.00(67.80)	6 901.00(65.71)	5 934.00(70.39)		
离婚/丧偶/分居	3 342.00(17.65)	1 771.00(16.86)	1 571.00(18.64)		
从未结婚	2 755.00(14.55)	1 830.00(17.43)	925.00(10.97)		
贫困收入比[n(%)]				16.619	<0.001
<1.5	3 638.00(19.22)	1 976.00(18.82)	1 662.00(19.72)		
1.5 ~3.5	6 991.00(36.93)	3 782.00(36.01)	3 209.00(38.07)		
>3.5	8 303.00(43.86)	4 744.00(45.17)	3 559.00(42.22)		
卡路里($\bar{x} \pm s$)	2 173.54 ±811.32	2 160.23 ±802.23	2 190.12 ±822.25	8.667	0.004
脂肪供能比	34.46 ±6.79	33.98 ±6.73	35.06 ±6.83	1.923	<0.001
碳水供能比	48.87 ±7.98	49.43 ±7.91	48.17 ±8.00	2.320	<0.001
蛋白质供能比	16.02 ±3.29	15.93 ±3.32	16.13 ±3.26	5.363	<0.001
集群[n(%)]				133.965	<0.001
1	5 190.00(27.41)	3 039.00(28.94)	2 151.00(25.52)		
2	4 401.00(23.25)	2 463.00(23.45)	1 938.00(22.99)		
3	4 137.00(21.85)	2 076.00(19.77)	2 061.00(24.45)		
4	1 356.00(7.16)	639.00(6.08)	717.00(8.51)		
5	1 662.00(8.78)	1 003.00(9.55)	659.00(7.82)		
6	804.00(4.25)	481.00(4.58)	323.00(3.83)		
7	715.00(3.78)	399.00(3.80)	316.00(3.75)		
8	667.00(3.52)	402.00(3.83)	265.00(3.14)		
糖尿病				963.298	<0.001
否	16 239.00(85.78)	9 750.00(92.84)	6 489.00(76.98)		
是	2 693.00(14.22)	752.00(7.16)	1 941.00(23.02)		
高血压				965.326	<0.001
否	10 076.00(53.22)	6 650.00(63.32)	3 426.00(40.64)		
是	8 856.00(46.78)	3 852.00(36.68)	5 004.00(59.36)		

2.3 不同营养素比例组合与 NAFLD 的关联 以样本量最大、最常见的集群 1 作为参考组,以获得稳定的风险估计,并直观解释其他集群相对于常见集群的差异。未调整模型 1 中,以 Cluster 1 为参考,Cluster 3

($P<0.001$)与 Cluster 4 ($P<0.001$)的 NAFLD 风险显著升高;在调整年龄、性别、种族、教育水平、婚姻状况、Pir、总能量摄入等全部变量的模型 3 中,关联仍然稳健:Cluster 3 的 *OR* 值 = 1.367($P<0.001$),Cluster 4 的 *OR* 值 = 1.462($P=0.003$)。其余集群(Cluster 2、5 ~ 8)未见与 NAFLD 风险的显著关联(见表 3)。

表 3　不同营养比例组合集群与 NAFLD 的回归分析

Table 3　Regression analysis of different nutritional ratio combination clusters and NAFLD

变量	模型 1		模型 2		模型 3	
	OR(95% *CI*)	*P* 值	*OR*(95% *CI*)	*P* 值	*OR*(95% *CI*)	*P* 值
集群 1	参考		参考		参考	
集群 2	1.007(0.852 ~ 1.191)	0.935	0.993(0.841 ~ 1.173)	0.937	0.973(0.827 ~ 1.145)	0.740
集群 3	1.396(1.176 ~ 1.657)	<0.001	1.382(1.160 ~ 1.646)	<0.001	1.367(1.142 ~ 1.636)	<0.001
集群 4	1.628(1.265 ~ 2.093)	<0.001	1.618(1.259 ~ 2.079)	<0.001	1.462(1.137 ~ 1.879)	0.003
集群 5	0.954(0.739 ~ 1.231)	0.714	0.994(0.761 ~ 1.298)	0.964	1.028(0.790 ~ 1.339)	0.834
集群 6	0.870(0.672 ~ 1.127)	0.290	0.853(0.648 ~ 1.124)	0.256	0.918(0.707 ~ 1.192)	0.517
集群 7	1.167(0.897 ~ 1.519)	0.248	1.211(0.908 ~ 1.614)	0.191	1.227(0.889 ~ 1.693)	0.212
集群 8	0.742(0.550 ~ 1.001)	0.051	0.744(0.549 ~ 1.007)	0.056	0.772(0.560 ~ 1.063)	0.112

2.4　交互与亚组分析　交互作用分析显示,性别、种族、教育水平等协变量与营养集群间均无显著交互作用(所有 $P_{交互}>0.05$)(见表 4)。亚组分析中,高血压在多数集群中与 NAFLD 风险呈正向关联,但部分集群(如 Cluster 7)置信区间跨越 1,结果解读需谨慎(见表 5)。

表 4　各协变量与营养集群的交互作用分析

Table 4　Interaction analysis between covriates and nutrient clusters

自变量	协变量	$P_{交互}$
集群	性别	0.269
	种族	0.093
	教育程度	0.140
	婚姻状况	0.729
	贫困收入比	0.300
	糖尿病	0.328
	吸烟状况	0.498
	高血压	0.053

表 5　高血压在不同营养集群中的交互作用及亚组分析

Table 5　Interaction and subgroup analyses of hypertension across different nutrient clusters

变量		*OR*(95% *CI*)	$P_{交互}$
集群	高血压(ref:否)		0.053
1	是	3.759(3.021 ~ 4.679)	
2	是	3.053(2.478 ~ 3.762)	
3	是	2.554(2.025 ~ 3.221)	
4	是	2.080(1.367 ~ 3.160)	
5	是	2.427(1.753 ~ 3.359)	
6	是	3.967(2.360 ~ 6.670)	
7	是	1.853(0.974 ~ 3.528)	
8	是	3.023(1.643 ~ 5.563)	

2.5　敏感分析

2.5.1　基于 K - means 聚类方法的验证　采用 K - means 聚类法对三种宏量营养素供能进行分析,将参与者划分为 8 类,各集群分布差异明显(表 6)。以“中等脂肪、中高碳水化合物、中等蛋白质”为特征的 Cluster 1(聚类中心值:脂肪 33.54%、碳水 53.36%、蛋白 13.49%)为参照,Cluster 4(中高脂肪、中等碳水化合物、中等蛋白质)和 Cluster 8(中高脂肪、中低碳水化合物、中等蛋白质)的 NAFLD 风险显著增加,Cluster 4($P<0.001$)、Cluster 8($P=0.003$)(见表 7)。此外,将聚类数设置为 5 时,其结果与 8 类模型及主分析一致(附表 1、2),进一步支持结论的稳健性。

表 6　基于 K 均值聚类的各集群营养素特征

Table 6　Cluster - level nutrient profiles based on K - means clustering

集群	脂肪供能聚类中心值(%)	蛋白质供能聚类中心值(%)	碳水供能聚类中心值(%)	集群样本量
1	33.54	53.36	13.49	4 143
2	37.40	46.61	15.29	4 965
3	27.04	59.13	14.14	3 285
4	43.48	40.11	15.82	3 212
5	27.52	49.30	19.42	2 676
6	33.33	37.77	20.75	2 240
7	19.97	68.13	13.28	1 230
8	48.17	29.13	19.89	1 171

2.5.2　基于 MAFLD 为定义的验证　为检验在 MAFLD 的适用,基于 2015—2018 周期数据,依据最新标准重新定义 MAFLD 病例,并在相应人群(n = 2 575)中复现三维营养素空间构建流程,最终形成与主分析结构一致的 7 个营养素集群,构建多因素逻辑回归模型。结果显示,与参照组(Cluster 1:中等脂肪、中高碳水化合物、中等蛋白质)相比,Cluster 4(中高脂肪、中低碳水化合物、中等蛋白质)与 MAFLD 风险显著相关($P=0.039$)(见表 8),高风险营养素组合的情况与主分析一致。

表 7 K – means 聚类划分的营养组合模式与 NAFLD 风险的关联

Table 7 Association between dietary pattern clusters identified by K – means clustering and risk of NAFLD

变量	模型 1		模型 2		模型 3	
	OR(95% *CI*)	*P* 值	*OR*(95% *CI*)	*P* 值	*OR*(95% *CI*)	*P* 值
集群 1	参考		参考		参考	
集群 2	1.070(0.915 ~ 1.251)	0.396	1.042(0.889 ~ 1.223)	0.608	1.056(0.896 ~ 1.244)	0.516
集群 3	0.930(0.773 ~ 1.120)	0.441	0.912(0.753 ~ 1.102)	0.338	0.971(0.800 ~ 1.179)	0.764
集群 4	1.495(1.244 ~ 1.797)	<0.001	1.446(1.194 ~ 1.750)	<0.001	1.416(1.157 ~ 1.734)	<0.001
集群 5	0.902(0.769 ~ 1.057)	0.201	0.883(0.749 ~ 1.040)	0.135	0.902(0.770 ~ 1.056)	0.196
集群 6	1.308(1.075 ~ 1.591)	0.008	1.235(1.009 ~ 1.512)	0.041	1.200(0.972 ~ 1.483)	0.090
集群 7	0.802(0.623 ~ 1.031)	0.085	0.825(0.635 ~ 1.072)	0.149	0.876(0.660 ~ 1.162)	0.356
集群 8	1.627(1.295 ~ 2.045)	<0.001	1.583(1.255 ~ 1.996)	<0.001	1.459(1.143 ~ 1.863)	0.003

表 8 不同营养比例组合集群与 MAFLD 的回归分析

Table 8 Regression analysis of different nutritional ratio combination clusters and MAFLD

变量	模型 1		模型 2		模型 3	
	OR(95% *CI*)	*P* 值	*OR*(95% *CI*)	*P* 值	*OR*(95% *CI*)	*P* 值
集群 1	参考		参考		参考	
集群 2	0.911(0.569 ~ 1.461)	0.688	0.946(0.572 ~ 1.567)	0.817	0.981(0.568 ~ 1.697)	0.939
集群 3	1.114(0.802 ~ 1.546)	0.505	1.124(0.803 ~ 1.573)	0.467	1.124(0.761 ~ 1.659)	0.510
集群 4	1.551(1.093 ~ 2.201)	0.016	1.651(1.152 ~ 2.367)	0.010	1.608(1.031 ~ 2.507)	0.039
集群 5	1.173(0.665 ~ 2.070)	0.568	1.257(0.686 ~ 2.304)	0.430	1.429(0.713 ~ 2.863)	0.270
集群 6	1.004(0.416 ~ 2.423)	0.994	1.097(0.402 ~ 2.992)	0.846	1.207(0.411 ~ 3.543)	0.698
集群 7	1.682(0.922 ~ 3.070)	0.087	1.848(0.975 ~ 3.505)	0.059	2.127(1.019 ~ 4.441)	0.046

3 讨 论

本研究基于 NHANES 数据,系统评估了宏量营养素比例组合与 NAFLD 风险的关联。结果显示,较于最常见的饮食模式(Cluster 1:中等脂肪、中高碳水化合物、中等蛋白质),以中高脂肪配合中/中低碳水化合物及中等蛋白质为特征的饮食模式(Cluster 3 和 4)显著增加了 NAFLD 风险,该关联在敏感性分析中保持稳健。

在现实饮食结构中,即使碳水摄入比例适度降低,若脂肪供能比显著升高,仍会增加 NAFLD 风险,多项研究证实过量脂肪摄入对肝脏具有显著危害。如,西方饮食模式(高糖饮料、加工肉类等)短期内即可促进肝脂肪变性[26],在每日额外摄入1 000 kcal 脂肪酸的条件下,摄入高饱和脂肪酸的人群甘油三酯含量比摄入多不饱和脂肪酸者高出 40%[27],显著提升 NAFLD 风险。动物研究证据也证实,过量高脂饮食不仅导致肝脏脂质沉积,还会引发胰岛素抵抗与全身性炎症[28-29]。

中高脂肪搭配中/中低碳水化合物的饮食模式可能通过多途径促进 NAFLD 发展。脂毒性是核心因素:游离胆固醇和脂肪酸在肝细胞内蓄积,触发内质网应激、线粒体功能障碍、氧化应激及炎症小体激活,共同导致肝细胞损伤、炎症与纤维[30-31]。脂肪酸过载超过线粒体氧化能力,引发活性氧爆发并导致脂质过氧化与细胞凋亡;同时 β – 氧化上调伴氧化磷酸化偶联受损,进一步增加活性氧生成[32-33]。长链饱和脂肪酸激活 TLR4/NF – κB 通路,诱导 TNF – α、IL – 6 等促炎因子表达[34];脂质过载产生的活性氧和胆固醇晶体还可激活 NLRP3 炎症小体,引起 Caspase – 1 依赖的肝细胞焦亡,放大炎症反应[35]。此外,高脂饮食破坏肠道菌群结构,增加 NAFLD 相关致病菌的丰度,加剧代谢紊乱、胰岛素抵抗[36-37],例如,高脂摄入(即使碳水摄入降低)仍可增强肝脏 JNK 与 C/EBP 同源蛋白的磷酸化水平,提高肠道厚壁菌门的相对丰度[38]。菌群多样性降低与肠屏障完整性受损增加肠道通透性,促进内毒素进入门脉系统,内毒素通过 TLR4 – NF – κB 信号通路激活 Kupffer 细胞,促使 TNF – α、IL – 1β 等释放,推动 NAFLD 的进展[39-40]。

本研究存在以下局限性。首先,依赖 24 小时膳食回顾法,数据可能受回忆偏倚影响;其次,横断面设计难以推断因果关系;第三,本研究基于美国人群数据,考虑到中美在膳食结构(如碳水化合物来源与脂肪类型)及 NAFLD 患病特征的差异,研究结果在中国的适用性(外推性)需谨慎解读。第四,未区分脂肪类型和蛋白质来源,未充分反映膳食质量的影响。最后,不同聚类方法所得集群结构存在差异。未来需在中国开展前瞻性队列研究,并深入分析营养素质量,以提供更高级别的证据。

利益冲突声明 本研究不存在任何利益冲突

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