论著·公共卫生智库

估计葡萄糖处理率作为非酒精性脂肪性肝病的便捷识别工具:一项基于NHANES的横断面研究揭示其保护性阈值

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［摘要］ **目的** 探讨估计葡萄糖处理率(estimated glucose disposal rate,eGDR)对非酒精性脂肪性肝病(non-alcoholic fatty liver disease,NAFLD)的早期识别价值,为临床精准干预提供简便工具。**方法** 通过横断面分析的方法,从美国国家健康和营养调查数据库中纳入来自2007—2018年共计3 262名具有完整数据的参与者进行分析。采用单因素回归和多元Logistic回归分析探讨估计葡萄糖处理率与非酒精性脂肪肝发病率的相关性,通过亚组分析、限制性三次样条和阈值效应分析探究潜在的因素影响和非线性关系。**结果** 在所有纳入人群中,948例(25.29%)被诊断为NAFLD,并随着估计葡萄糖处理率的增加人数而逐渐减少(P<0.001)。多元logistic回归显示,估计葡萄糖处理率和非酒精性脂肪肝呈负向相关(OR=0.86,95%CI:0.83~0.88,P<0.001),且估计葡萄糖处理率≥10.246时可显著降低非酒精性脂肪肝的发生风险(OR=0.20,95%:0.10~0.39,P<0.001),分层分析进一步证实了这一结果。**结论** 更高的eGDR水平预示着更低的NAFLD患病风险。这提示在临床实践中,通过量化eGDR指标,有助于识别NAFLD的患病风险,从而更早地发现潜在患病人群并实施针对性干预。**对策** 建议有关部门将eGDR这一指标纳入公共卫生防控体系,通过社区筛查构建数据驱动的风险分层管理路径;同时将NAFLD防治整合进现有慢性病管理网络,推动多部门协作制定健康饮食与运动支持政策,并加强疾病监测、药物研发与综合干预,从而实现对高危人群的早期识别与精准管理,全面降低NAFLD的疾病负担。

［关键词］ 估计葡萄糖处理率;非酒精性脂肪肝;NHANES

［中图法分类号］ R181.23;R194.3;R575.5 ［文献标志码］ A

Estimated glucose disposal rate as a practical tool for non-alcoholic fatty liver disease identification: A NHANES-based cross-sectional study uncovering its protective threshold

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［**Abstract**］ **Objective** To explore the early detection value of estimated glucose disposal rate (eGDR) for non-alcoholic fatty liver disease (NAFLD), providing a simple tool for precise clinical intervention. **Methods** A cross-sectional analysis was conducted on totally 3 262 participants with complete data from the National Health and Nutrition Survey Database of the United States from 2007 to 2018. Univariate regression

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and multivariate logistic regression analyses were used to explore the correlation between the estimated glucose treatment rate and the incidence of non-alcoholic fatty liver disease. Subgroup analysis, restricted cubic spline and threshold effect analysis were conducted to investigate the potential factor influences and nonlinear relationships. **Result** Among all the included populations, 948 cases (25.29%) were diagnosed with NAFLD, and the number gradually decreased with the increase of the estimated glucose treatment rate (P<0.001). Multivariate logistic regression showed that the estimated grape processing rate was negatively correlated with non-alcoholic fatty liver disease (OR=0.86, 95%CI: 0.83~0.88, P<0.001), and when the estimated glucose processing rate was ≥10.246, it could significantly reduce the risk of non-alcoholic fatty liver disease (OR=0.20, 95%CI:0.10~0.39, P<0.001), and stratified analysis further confirmed this result. **Conclusion** The eGDR is significantly associated with the incidence risk of NAFLD. A higher eGDR indicates a lower risk of NAFLD. This implies that in clinical practice, the risk of disease detection can be quantified through this indicator, thereby identifying potential patients earlier and initiating intervention. **Countermeasures** As decision-makers, they should strengthen public health education on non-alcoholic fatty liver disease, reduce health risks by promoting healthy diets and lifestyle interventions, and pay attention to the cardiovascular health of high-risk groups for non-alcoholic fatty liver disease. At the same time, promote the research and application of drugs, and dynamically adjust policies through continuous disease monitoring to comprehensively reduce the burden of non-alcoholic fatty liver disease.

[**Key words**] estimated glucose disposal rate; non-alcoholic fatty liver disease; NHANES

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非酒精性脂肪性肝病(non-alcoholic fatty liver disease,NAFLD)是一种以肝脏中脂肪异常积累为特征的慢性疾病,由于超重人群的不断增加,NAFLD已逐渐成为全球范围内成人及儿童肝病的最重要原因[1]。一项荟萃分析表明,目前NAFLD的全球患病率约为30%[2]。在地区分布上,以中东和南美地区最高,且这一增长趋势仍将持续。伴随于此,NAFLD相关肝癌的患病率也在不断增加。值得注意的是,这一疾病往往与酒精、肝炎病毒感染、自身免疫性肝病或药物性肝损伤无关。尽管对NAFLD的发病机制研究不断深入,其具体病因和发生机制尚未完全阐明,通常认为是遗传易感性、宿主代谢异常和环境因素复杂交互作用所致。此外脂质代谢障碍、免疫微环境异常、以及肠道菌群的失调也在疾病发生发展中起重要作用[3]。其中,胰岛素抵抗(insulin resistance, IR)在NAFLD的发生发展中起着关键作用[3]。

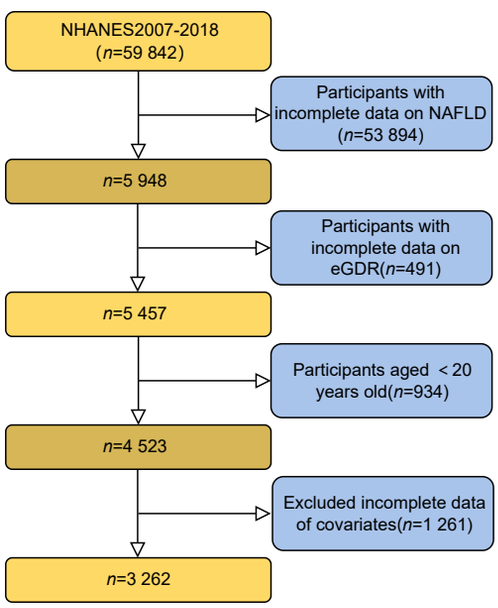
目前用于评估IR的方法有多种,例如胰岛素抵抗稳态模型评估(homeostasis model assessment of insulin resistance,HOMA-IR),但其评估金标准仍为高胰岛素-正常血糖钳夹法。然而,这些方法往往伴随着侵入性、操作复杂性和耗时长的限制,难以用作流行病学研究[4]。估计葡萄糖处理率(estimated glucose disposal rate,eGDR)是一种易获取和评估IR工具,它包含了糖化血红蛋白A1c(hemoglobin a1c,HbA1c)、高血压病史和腰围(waist circumference,WC)3个维度的指标。KATHERINE等[5]的研究证实了eGDR与IR之间的密切联系。此外,既往研究表明,较高的eGDR水平(即更高的胰岛素敏感性)与较低的死亡率相关,且较低的eGDR水平与心血管疾病发病风险增加密切相关[6-7]。然而,目前尚不清楚eGDR评估的IR与NAFLD之间的是否存在非线性关系,既往的研究并未阐明二者之间的相关性,也并未提示eGDR对NAFLD患病率的影响。为了探究这一问题,本研究利用美国国家健康和营养调查(National Health and Nutrition Examination Survey, NHANES)数据,探索eGDR与NAFLD的关联,旨在分析eGDR与NAFLD在普通人群中的关联。本研究结果将有助于深入了解eGDR与NAFLD患病风险之间的关系,为将胰岛素抵抗作为NAFLD预防干预靶点提供科学依据。

1 材料与方法

1.1 数据来源和参与者设计

本研究利用了由美国疾病控制与预防国家健康统计中心主持的美国国家健康和营养检查调查数据库的数据来进行研究。NHANES数据库旨在评估美国本土个体的营养状态和健康状况,收集了包括人口学数据、饮食、实验室数据和体格检查等各个模块的数据。美国国家卫生统计中心伦理审查委员会批准了NHANES研究方案,所有参与者在参与之前提供了书面知情同意书,详细的数据来源和数据检验及身体数据测量可以访问"https://www.cdc.gov/nchs/nhanes/"。本研究数据收集自2007—2018年共计59 842名参与

者,排除了缺少NAFLD诊断信息、eGDR数值、年龄<20岁及其他协变量的人群共计59 842人,最终本研究纳入参与者3 262名,见图1。



NHANES: National Health and Nutrition Examination Survey

图1 2007-2018年NHANES参与者筛选流程图

Figure 1 Flowchart of the participant selection from NHANES 2007—2018

1.2 估计的葡萄糖处置率测量和NAFLD的诊断评估

根据以往研究结果,本研究严格按照以下公式进行了eGDR的计算:eGDR=21.158-(0.09×WC)-(3.407×HT)-(0.551×HbA1c)[WC:腰围(cm),HT(hypertension):高血压(是=1/否=0),HbA1c:糖化血红蛋白百分比][5]。对于非酒精性脂肪肝的定义往往是复杂,需要侵入性,EDDOWES等[8-9]开发了基于非侵入的评分以诊断NAFLD,本研究中定义NAFLD为在没有过度饮酒和病毒性肝炎的情况下,控制衰减参数(controlled attenuation parameter,CAP)得分≥248 dB/m。

1.3 协变量设计

根据先前的研究纳入了潜在的协变量。协变量人口学部分包括参与者自我报告的年龄、性别(男/女)、教育程度(高中以下、高中水平、高中以上)、婚姻状况(已婚/单身或离异)、收入比和体质指数(body mass index, BMI)。种族划分为白人、黑人、墨西哥人和其他种族。吸烟状况根据SMQ020、SMQ040,将吸烟数量<100,现在不吸烟参与者定义为否,反之为是。饮酒情况根据ALQ问卷进行判断。其他协变量包括估计肾小球滤过率、慢性肾脏病史(chronic kidney disease, CKD)和心血管疾病史(cardiovascular disease, CVD)。

1.4 统计学方法

使用R studio 4.4.0(包括:survey、rms、dplyr、nhanseA、segmented、do、ggplot2包)和Excel 2021软件进行统计分析。为了有效分析,根据eGDR的四分位数将数据分为4组。连续变量以平均值(95%*CI*)表示,并且对各自的95%*CI*的比例用于分类变量。为了确定4组之间的变化,对连续变量进行了加权方差分析或Kruskal-Wallis检验,而卡方检验则用于分类变量。在*P*值<0.05时考虑统计显着性。进行各种统计分析时,针对人口统计学变量,血液学指标和药物信息进行了调整。接下来,进行了单因素加权无序逻辑回归分析,以检查混杂因素和NAFLD之间的相关性。限制性3次立方样条是用于平滑拟合和建模数据与统计数据的重要工具,可以揭示自变量与因变量潜在的非线性关系。因此,使用加权的逻辑回归分析来研究eGDR与NAFLD之间的关系。为了平衡社会经济因素和人口因素,确保模型结果的稳定,基于阶段式校正构建了3个模型并进行了趋势性检验(趋势性检验*P*<0.05):Model1、Model2和Model3。Model1未进行任何校正,Model2则对年龄、性别、种族的模型进行了调整,Model3对年龄、性别、种族/种族、教育水平、收入比、婚姻情况、饮酒情况、吸烟、eGFR、CVD和CKD进行完全校正。结果以95%可信区间表示为比值比(odd ratio, OR)。使用限制三次立方样条法用于eGDR与NAFLD之间的相关性,使用segmented包进行阈值分析。为了进一步确保结果的可信度,采用了亚组分析以探究亚组水平对二者的关系影响[10]。在对参与者进行倾向性匹配,采用nearest匹配方法,卡钳值为0.25,目标组和对照组的比例为1,随机种子为500并选择*P*<0.05的自变量构建倾向得分模型,经过重新匹配后的数据重新进行趋势性分析,验证模型和相关性的稳定性。

2 结果

2.1 纳入人群的基本特征

本研究共纳入3 262人,年龄集中在20~39岁(39.48%)的区间,其中1 612例(48.77%)为男性,1 650例(51.23%)为女性。BMI在25~30 kg/m^{2}及以上的人群占72.94%,患有高血压或高脂血症的人群分别为1 393(36.86%)、2 192(65.80%)人,随着eGDR分位数的增加人数则逐渐减少,而在非患病人群中呈现着相反的趋势特征(*P*<0.001)。在所有纳入人群中,948例(25.29%)被诊断为NAFLD,随着分位数的增加数量减少(*P*<0.001),见表1。

表1 eGDR四分位数分组的基本特征[$\bar{x}\pm s$,例(%)]

Table 1 Basic characteristics of eGDR quartile groups[$\bar{x}\pm s$,n(%)]

Variable	Overall(n=3 262)	Q1(n =816)	Q2(n =815)	Q3(n =815)	Q4(n =816)	P
Age/years						< 0.000 1
20~39	1 118(39.48)	118(18.28)	162(24.48)	330(42.23)	508(65.44)	
40~59	1 103(36.09)	281(40.05)	303(41.57)	291(39.73)	228(25.33)	
≥60	1 041(24.43)	417(41.67)	350(33.95)	194(18.04)	80(9.23)	
Gender						0.004
Male	1 612(48.77)	450(55.06)	404(48.50)	430(54.43)	328(38.65)	
Female	1 650(51.23)	366(44.94)	411(51.50)	385(45.57)	488(61.35)	
Race						0.01
Black	754(10.91)	237(13.41)	209(12.11)	139(8.14)	169(10.56)	
Mexican American	450(9.18)	105(7.57)	97(8.54)	158(12.91)	90(7.49)	
Other Race	922(17.01)	165(12.42)	224(18.22)	251(17.11)	282(19.65)	
White	1 136(62.91)	309(66.60)	285(61.13)	267(61.85)	275(62.30)	
Education						0.1
High school	1 079(33.56)	282(36.74)	273(33.58)	276(35.77)	248(28.95)	
Below high school	211(2.78)	69(3.40)	49(2.73)	63(3.45)	30(1.72)	
Beyond high school	1 970(63.64)	465(59.86)	491(63.69)	476(60.78)	538(69.33)	
Marital Status						<0.001
Married	1 952(61.78)	503(66.59)	484(62.98)	530(67.04)	435(52.10)	
Unmarried /divorced	1 310(38.22)	313(33.41)	331(37.02)	285(32.96)	381(47.90)	
PIR						0.94
<1	470(16.18)	115(10.59)	118(12.14)	118(11.11)	119(12.23)	
1~3	1 236(42.55)	310(32.75)	312(34.42)	325(34.66)	289(32.25)	
>3	1 199(41.27)	297(56.66)	296(53.44)	287(54.23)	319(55.52)	
BMI /(kg/m^2)						<0.000 1
<25	852(26.87)	6(0.72)	202(20.85)	93(8.61)	551(69.68)	
25~<30	1 038(30.38)	138(15.72)	314(34.59)	345(42.15)	241(28.10)	
≥30	1 365(42.56)	670(83.56)	297(44.55)	376(49.24)	22(2.21)	
Alcohol						0.48
Heavy	727(24.63)	165(23.77)	165(23.64)	207(27.01)	190(23.87)	
Moderate	1 474(44.95)	406(47.17)	381(46.10)	348(45.76)	339(41.53)	
Mild	670(22.27)	154(20.68)	154(21.13)	165(20.28)	197(26.26)	
Never	391(8.15)	91(8.39)	115(9.13)	95(6.94)	90(8.33)	
Smoking						0.22
No	2 656(83.22)	683(87.05)	647(81.11)	663(82.26)	663(82.67)	
Yes	606(16.78)	133(12.95)	168(18.89)	152(17.74)	153(17.33)	
Hypertension						<0.000 1
No	1 869(63.14)	38(6.02)	238(33.95)	777(96.76)	816(100.00)	
Yes	1 393(36.86)	778(93.98)	577(66.05)	38(3.24)	0	
Hyperlipidemia						<0.000 1
No	1 070(34.20)	150(17.10)	185(23.75)	253(31.16)	482(58.77)	
Yes	2 192(65.80)	666(82.90)	630(76.25)	562(68.84)	334(41.23)	
CKD						<0.000 1
No	2 691(86.52)	573(74.65)	640(86.86)	721(93.05)	757(95.61)	
Yes	501(11.59)	228(25.35)	158(13.14)	73(6.95)	42(4.39)	
NAFLD						<0.000 1
No	2 314(74.71)	495(65.18)	563(71.40)	549(70.16)	707(89.12)	
Yes	948(25.29)	321(34.82)	252(28.60)	266(29.84)	109(10.88)	
eGFR/(mL/min/1.73m^2)	95.98(0.88)	89.76(1.27)	90.58(1.42)	96.63(1.51)	104.51(0.76)	<0.000 1
Total energy intake/kcal	2 196.82±22.85	2 234.45±54.42	2 186.55±46.64	2 225.62±39.87	2 147.73±47.66	0.5
HbA1c/%	5.62±0.02	6.24±0.08	5.65±0.03	5.48±0.03	5.22±0.02	<0.000 1
ALT/(U/L)	23.96±0.51	28.26±0.99	26.11±1.64	24.66±0.90	18.21±0.66	<0.000 1
AST/(U/L)	22.82±0.43	24.29±1.08	23.95±1.00	22.29±0.44	21.25±0.97	0.22
Uric acid/(mg/dL)	5.39±0.04	5.97±0.08	5.64±0.08	5.43±0.08	4.70±0.06	<0.000 1

PIR: Poverty-to-income ratio; BMI: Body mass index; CKD: Chronic kidney disease; NAFLD: Non-alcoholic fatty liver disease; eGFR: Estimate glomerular filtration rate; HbA1c: hemoglobin A1c; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase

2.2 各类因素对NAFLD患病率的影响

单因素分析结果显示,大多数纳入因素均与NAFLD患病风险显著相关。与60岁以下人群相比,≥60岁人群的NAFLD患病风险显著增高(*OR*=2.98, 95%*CI*: 2.51~3.52, *P*<0.001)。相比之下,男性患NAFLD的风险显著低于女性(*OR*=0.53, 95%*CI*: 0.42~0.67, *P*<0.001)。与既往或当前饮酒者相比,从不饮酒者的NAFLD患病风险更高(*OR*=4.42, 95%*CI*: 2.70~7.22, *P*<0.001),见表2。

2.3 eGDR与NAFLD的相关性分析

通过加权二分类逻辑回归探究eGDR与NAFLD的关系,共建立3个多元逻辑回归模型:模型1,未调整;模型2,根据年龄、性别和种族进行调整;模型3,根据表3中列出的所有协变量进行调整。在未校正模型中,eGDR与NAFLD呈现显著的负相关关系(*OR*=0.861,*P*<0.001),在进一步校正其他混杂因素之后这

表2 NAFLD患病率的单因素分析。

Table 2 Univariate analysis of the prevalence of NAFLD

Variable	*OR*(95% *CI*)	*P*	Variable	*OR*(95% *CI*)	*P*
Age/years			BMI/(kg/m^2)		
20~39	ref	ref	<25	ref	ref
40~59	1.81(1.39~2.35)	<0.001	25-30	2.50(1.65~3.78)	<0.001
≥60	2.98(2.51~3.52)	<0.000 1	≥30	3.44(2.27~5.20)	<0.000 1
Gender			Alcohol		
Female	ref	ref	Heavy	ref	ref
Male	0.53(0.42~0.67)	<0.000 1	Moderate	1.21(0.91~1.59)	0.17
Race			Mild	1.32(0.86~2.03)	0.18
White	ref	ref	Never	4.42(2.70~7.22)	<0.000 1
Black	1.02(0.71~1.48)	0.89	Smoking		
Mexican American	1.12(0.75~1.67)	0.55	No	ref	ref
Other Race	0.95(0.70~1.29)	0.74	Yes	0.80(0.64~0.99)	0.04
Education			Hypertension		
Below high school	ref	ref	No	ref	ref
High school	0.89(0.60~1.30)	0.51	Yes	1.62(1.32~1.98)	<0.001
Beyond high school	0.79(0.63~0.98)	0.04	Hyperlipidemia		
Marital. Status			No	ref	ref
Married	ref	ref	Yes	2.00(1.42~2.82)	<0.001
Unmarried/divorced	0.65(0.52~0.83)	0.002	CKD		
PIR			No	ref	ref
<1	ref	ref	Yes	1.51(1.03~2.20)	0.04
1~3	0.77(0.52~1.16)	0.20			
>3	0.75(0.52~1.10)	0.13			

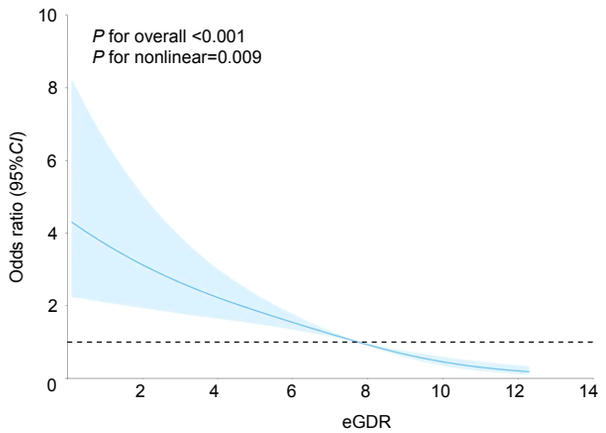
NAFLD: Non-alcoholic fatty liver disease; PIR: Poverty-to-income ratio; BMI: Body mass index; CKD: Chronic kidney disease

表3 eGDR与NAFLD相关性的多因素分析

Table 3 Multivariate logistic analysis of the association between eGDR and NAFLD

Variable	Model 1		Model 2		Model 3	
	OR (95%*CI*)	*P*	*OR* (95%*CI*)	*P*	*OR* (95%*CI*)	*P*
eGDR	0.86 (0.83~0.88)	<0.001	0.87 (0.84~0.89)	<0.001	0.86 (0.83~0.89)	<0.001
eGDR-Quantile						
Q1	1.00		1.00		1.00	
Q2	0.69 (0.56~0.85)	<0.001	0.66 (0.54~0.82)	<0.001	0.65 (0.51~0.82)	<0.001
Q3	0.75 (0.61~0.92)	0.005	0.84 (0.67~1.04)	0.107	0.82 (0.64~1.04)	0.105
Q4	0.24 (0.19~0.30)	<0.001	0.26 (0.20~0.34)	<0.001	0.24 (0.18~0.33)	<0.001

OR: Odd Ratio; CI: Confidence interval; eGDR:estimated glucose disposal rate; Model 1: Unadjusted; Model 2: Adjust: Gender, Race, Race; Model 3: Adjust: Age, gender, race, PIR, education, alcohol, CKD, smoking, CVD, Marital, eGFR; PIR: Poverty-to-income ratio; CKD: Chronic Kidney Disease; CVD: Cardiovascular disease; eGFR: Estimated glomerular filtration rate



eGDR: Estimated glucose disposal rate

图2 限制性三次样条分析探究 eGDR 与 NAFLD 的关联

Figure 2 Restrictive cubic spline analysis of the association between eGDR and NAFLD

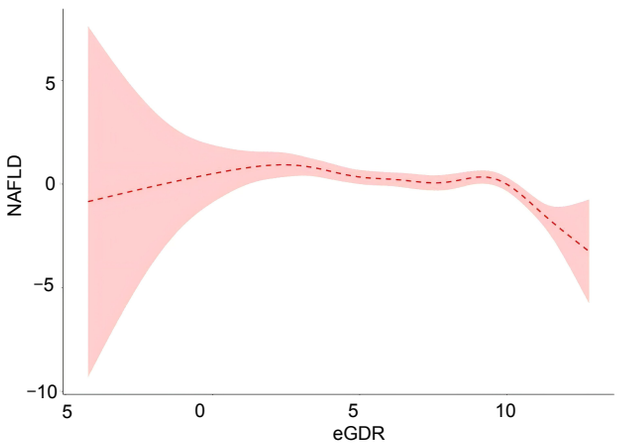


图3 平滑曲线拟合和阈值效应分析

Figure 3 Smooth curve fitting and threshold effect analysis

种关系仍然稳定。在eGDR的四分位数分组中,观察到最强的负相关关系出现在Q4组(*OR*=0.24,95%*CI*:0.19~0.30,*P*<0.001),继续校正其他因素后结果仍然稳定。限制性3次样条分析也显示二者存在显著的负相关关系(图2)。

如表4所示,阈值效应分析表明eGDR与NAFLD的关联存在显著的阈值效应(似然比检验*P*<0.001)。总体而言,eGDR与NAFLD呈负相关(*OR*=0.84,95%*CI*:0.82~0.87,*P*<0.001)。根据图3所示的限制性立方样条曲线,识别出拐点为10.246。分段回归分析显示,当eGDR水平低于10.246时,eGDR与NAFLD风险呈负相关(*OR*=0.91,95%*CI*:0.88~0.95);当eGDR水平高于10.246时,二者仍呈负相关,但关联强度显著增强(*OR*=0.20,95%*CI*:0.10~0.39,*P*<0.001)。

2.4 亚组分析与敏感性分析

进一步对eGDR与NAFLD的关系进行了分层分析和相互作用检验(表5)。校正混杂因素后,eGDR的影响大小在亚组中几乎一致,包括种族、婚姻、教育水平、收入比、吸烟情况、高血压和CKD(相互作用*P*≥0.05)。但在年龄、性别、饮酒情况、高脂血症和体质指数则表现出不一样的结果,这可能提示在这些人口学特征人群中的结果存在差异。在敏感性分析中进一步探究这些因素中模型的稳定情况,结果仍提示两者之间为显著的负相关性(表6)。

3 讨论

本研究利用了NHANES数据库提供的优质数据样本探究了eGDR和NAFLD患病率之间的关系,研究结果显示出eGDR对NAFLD之间提示潜在的保护因素,这种负相关关系在eGDR四分位分组中的Q4组中最为显著(*P*<0.05)。在部分或完全校正了混杂因素之后这种关系仍然显著。此外限制性三次立方样条分析揭示了eGDR与NAFLD之间存在非线性关系,进一步通过阈值效应分析,也验证了NAFLD与eGDR负相关的关系,这种关系在亚组分析和敏感性检验中得到了进一步证实。尽管在亚组分析中,CKD和吸烟分组中的人群结果与其他分组并不一致,这与本研究纳入人群数量较少,患病人群与正常人群数量差距较大,导致在一些人数差异较大的分组中,没有观察到稳定的关系。

表4 eGDR与NAFLD的阈值效应分析

Table 4 Threshold effect analysis between eGDR与NAFLD

Result	*OR*(95%*CI*)	*P*
Model 1	0.84(0.82~0.87)	<0.001
Model 2 (Two-segment linear regression fitting model)	10.246	
<10.246	0.91(0.88~0.95)	<0.001
≥10.246	0.20(0.10~0.39)	<0.001
Likelihood ratio *P*		<0.001

表5 亚组分析

Table 5 Subgroup analysis

Variable	*n*(%)	*OR*(95%*CI*)	*P*	*P* for interaction
Age/years				0.761
20~39	1 118(34.27)	0.86(0.75~1.00)	0.054	
40~59	1 103(33.81)	0.77(0.67~0.88)	<0.001	
≥60	1 041(31.91)	0.75(0.65~0.87)	<0.001	
Gender				0.027
Female	1 650(50.58)	0.75(0.68~0.84)	<0.001	
Male	1 612(49.42)	0.87(0.76~1.00)	0.045	
Race				0.193
White	1 136(34.83)	0.83(0.73~0.95)	0.005	
Mexican American	450(13.80)	0.78(0.61~0.99)	0.045	
Black	754(23.11)	0.79(0.68~0.92)	0.002	
Other race	922(28.26)	0.80(0.67~0.96)	0.015	
Marital Status				0.173
Married	1 952(59.84)	0.79(0.71~0.88)	<0.001	
Unmarried/divorced	1 310(40.16)	0.80(0.71~0.91)	<.001	
PIR				0.669
<1	470(16.18)	0.81(0.67~0.99)	0.037	
1~3	1 236(42.55)	0.75(0.66~0.84)	<0.001	
>3	1 199(41.27)	0.83(0.73~0.94)	0.005	
Education				0.779
Below high school	211(6.47)	0.77(0.46~1.29)	0.321	
High school	1 079(33.10)	0.79(0.68~0.90)	<0.001	
Beyond high school	1 970(60.43)	0.80(0.72~0.88)	<0.001	
Alcohol				0.041
Mild	670(20.54)	0.72(0.60~0.86)	<0.001	
Moderate	1 474(45.19)	0.80(0.71~0.90)	<0.001	
Heavy	727(22.29)	0.91(0.76~1.08)	0.286	
Never	391(11.99)	0.59(0.43~0.82)	0.001	
Smoking				0.323
No	2 656(81.42)	0.78(0.71~0.85)	<0.001	
Yes	606(18.58)	0.85(0.70~1.04)	0.115	
CKD				0.232
No	2 691(84.30)	0.77(0.70~0.84)	<0.001	
Yes	501(15.70)	0.87(0.73~1.03)	0.108	
Hyperlipidemia				<0.001
No	1 070(32.80)	0.78(0.65~0.92)	0.003	
Yes	2 192(67.20)	0.80(0.73~0.88)	<0.001	
Hypertension				0.599
No	1 869(57.30)	0.80(0.71~0.90)	<0.001	
Yes	1 393(42.70)	0.79(0.71~0.88)	<0.001	
BMI/(kg/m^2)				<0.001
<25	852(26.18)	0.47(0.34~0.64)	<0.001	
25~<30	1 038(31.89)	0.77(0.63~0.94)	0.009	
≥30	1 365(41.94)	0.86(0.78~0.95)	0.002	

OR: Odd Ratio; CI: Confidence interval; PIR: Poverty-to-income ratio; BMI: Body mass Index; CKD: Chronic kidney disease

表6 敏感性分析

Table 6 Sensitivity analysis

Variable	Model 1		Model 2		Model 3	
	OR (95%*CI*)	*P*	*OR* (95%*CI*)	*P*	*OR* (95%*CI*)	*P*
eGDR	0.87 (0.84~0.91)	<0.001	0.84 (0.80~0.88)	<0.001	0.84 (0.80~0.88)	<0.001
eGDR-Quantile						
Q1	1.00		1.00		1.00	
Q2	0.67 (0.50~0.89)	0.006	0.63 (0.47~0.84)	0.002	0.62 (0.47~0.84)	0.002
Q3	1.00 (0.75~1.35)	0.974	0.86 (0.63~1.18)	0.353	0.86 (0.62~1.17)	0.331
Q4	0.28 (0.20~0.39)	<0.001	0.23 (0.16~0.32)	<0.001	0.22 (0.16~0.32)	<0.001

OR: Odd Ratio; CI: Confidence interval; eGDR: estimated glucose disposal rate; Model 1: Unadjusted; Model 2: Adjust: Gender, Race; Model 3: Adjust: Age, gender, race, PIR, education, alcohol, CKD, smoking, CVD, Marital, eGFR; PIR: Poverty-to-income ratio; CKD: Chronic Kidney Disease; CVD: Cardiovascular disease; eGFR: Estimated glomerular filtration rate

肝脏的脂肪变性或脂肪变性肝炎是常见的组织学病变,其特征往往是肝细胞中的脂质积聚。而NAFLD的发生往往与饮酒、肝炎病毒、自身免疫抗体无关,据估计NAFLD的患病率为每1 000人年46.9例并仍在快速增加,估计患病率为29.8%,这给公共医疗系统带来沉重负担[11]。研究指出男性患病率较女性更高,但本研究尚未体现这一趋势,这可能与抽样误差和缺失值删除有关[12]。尽管对NAFLD的病因研究不断深入,但病因的研究仍尚未清晰,随着经济全球化的发展引起的饮食习惯改变造成的精制碳水、精制糖、动物蛋白的消费增加都将助长NAFLD的发展。这种饮食模式带来的能量不平衡将导致胰岛素抵抗和肥胖的增加,而这二者都将促进NAFLD的发展[13, 14]。这可能是因为胰岛素抵抗带来的高血糖、高胰岛素水平、低胰岛素敏感性,同时阻碍了胰岛素的抗脂肪分解作用,引起了游离脂肪酸的增加[15]。这也进一步导致了脂肪酸氧化受阻,并促进了肝脏脂肪酸的摄取和脂质的形成,导致NAFLD患者伴随着高脂血症、高血压等其他代谢疾病[16]。一项研究指出大约50%的高脂血症患者的超声检查都提示着NAFLD[17],而根据一项对22 090名韩国男性的前瞻性研究,NAFLD患者比起非NAFLD患者有更高的高血压患病率,且患病率与超声诊断NAFLD的严重程度相关[18]。

通过腰围、高血压、糖化血红蛋白测算的eGDR作为易于得到的指标,且能够显著的提示骨骼肌的胰岛素抵抗,这对于辅助诊断NAFLD具有重要意义[19]。越低的eGDR提示着越严重的胰岛素抵抗,而越严重的胰岛素抵抗往往与更严重的NAFLD相关。这与本研究中的观察结果一致,随着eGDR的分位数增加,高血压病和高脂血症的患病人群出现显著的下降,在已经患病的人群中属于eGDR低分位数组的人数也更多。这种情况也同样表现在CKD人群中,更低的eGDR分组CKD的患病人数更多。一项基于韩国人群的横断面研究提示NAFLD是CKD的独立危险因素,患有NAFLD的人群罹患晚期CKD的风险较普通人群高出约1.45倍[20-21],这可能与免疫浸润、炎症反应及程序性细胞死亡机制相关[22]。这些结果都强烈提示着eGDR与NAFLD的相关性,进一步使用了限制性三次样条和预支效应分析。结果显示在eGDR为10.246及更高水平时,表现出显著的负相关并遵循着非线性的关系。而10.246位于Q4分位数区间中,这提示着高水平的eGDR带来的保护作用,降低80%的患病风险,这种效应在敏感性分析得到了进一步验证。而更高水平的eGDR往往与更低的脑卒中、心血管疾病风险有关[23, 24]。尽管精确的胰岛素抵抗依赖着葡萄糖钳夹法,但eGDR的简易且与NAFLD高度的相关性,这可能意味着保持高水平的eGDR将对降低患病风险有着直接的作用。本研究的优势在于数据来源于公共数据库,数据质量稳定且具有完备有效的系统性抽样,给研究数据采集和分析带来了极大便利。但本研究也存在一定的局限性:①本研究仅仅为横断面研究,并未建立有效的队列研究,因此无法得出确切的结论;②此外考虑到其他未被纳入的因素影响,不能排除这些混杂因素对结果的潜在影响;③本研究纳入的人群较少,缺少其他队列数据的研究验证,降低了研究结论的可靠性。

本研究通过横断面分析,详细地阐述了eGDR与NAFLD之间的显著关系,这对公共卫生专家和社区级别的卫生政策决策者具有潜在的帮助。首要的是,NAFLD作为众多慢性病的高危因素并可进展至伴随着纤维化、肝硬化等更为严重的病变,因此加强疾病健康宣教和提高公众对NAFLD的认识至关重要,这是

进行后续干预和政策影响的重要前提。由疾病史、化验指标和体质测量指标构成的eGDR,意味着通过这一指标评估的高危人群,可以通过改善饮食结构,鼓励地中海饮食、限制热量摄入饮食等健康膳食,实现降低腰围、糖化血红蛋白和血压的目标。其次,我们仍需要警惕NAFLD与冠心病、脑卒中的高度相关,因此对这一疾病的预防和管理,还需要关注患者和高危人群的心血管健康状况,及时采取必要的生活方式干预和药物干预,全面降低健康风险。此外,鼓励新型药物的研发与临床应用也有助于改善NAFLD目前药物控制的窘况,如FDA已经批准使用的瑞美替隆,可以改善中晚期肝纤维化和肝脏损伤生物标志物。但仍需警惕的是,随着疾病负担的进一步加重,政策干预的滞后性始终会影响着这一卫生难题的解决,只有通过持续地追踪才能始终保持政策的准确性。

综上所述,本研究揭示了eGDR与NAFLD存在负向相关性,越高的eGDR水平伴随着越低的NAFLD发病风险,这种关系并不受人口学的差异性影响,但其因果关系和机制还需进行进一步研究。

利益冲突 本文所有作者声明不存在利益冲突

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