

• 临床研究 •

动脉硬化指数与非酒精性脂肪肝相关性研究

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[摘要] 目的: 分析肝脂肪变性的相关影响因素, 探讨动脉硬化指数(arteriosclerosis index, AI)与非酒精性脂肪肝(non-alcoholic fatty liver disease, NAFLD)之间的关系。方法: 本研究为基于日本村上纪念医院医疗健康检查中心的856例年龄24~84岁的参与者横断面研究公开数据的二次分析。按照是否有NAFLD, 分为NAFLD组($n=209$ 例)和非NAFLD组($n=647$ 例), 比较两组间临床一般资料、实验室指标、AI值和动脉硬化检出率的差异, 采用Logistic回归分析评估NAFLD的相关因素, 构建回归模型评估AI与NAFLD之间的相关性, 并使用受试者工作特征(receiver operating characteristic, ROC)曲线检验AI作为NAFLD风险评估指标的价值。结果: NAFLD组和非NAFLD组男性多于女性, 差异有统计学意义($P < 0.001$)。相比非NAFLD组, NAFLD组具有更高水平的体重指数(body mass index, BMI)、收缩压(systolic blood pressure, SBP)、舒张压(diastolic blood pressure, DBP)、天冬氨酸氨基转移酶(aspartate aminotransferase, AST)、丙氨酸氨基转移酶(alanine aminotransferase, ALT)、 γ -谷氨酰转肽酶(γ -glutamyl transferase, GGT)、空腹血糖(fasting blood glucose, FBG)、尿酸(uric acid)、甘油三酯(triglyceride, TG)、总胆固醇(total cholesterol, TC)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、肱动脉脉搏波速度(arterial pulse wave velocity of brachial artery, baPWV) ($P < 0.001$), 更低水平的高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C) ($P < 0.001$), 并且缺乏规律运动($P=0.001$)。NAFLD组的AI值和动脉硬化检出率高于非NAFLD组($P < 0.001$)。二元多因素Logistic回归分析显示AI、BMI、AST、FBG、baPWV均与NAFLD正相关。在充分调整混杂因素后, 二元多因素Logistic回归分析显示AI与NAFLD呈正相关(OR=1.846, 95%CI: 1.541~2.121, $P < 0.001$), AI最高组的人群与最低组比较, 表现出明显更高的NAFLD倾向(OR=6.169, 95%CI: 3.006~12.661, $P < 0.001$)。在广义相加模型中, AI与NAFLD之间呈直接线性关系(对数似然比检验, $P=0.949$)。AI的ROC曲线下面积(area under the curve, AUC)为0.775(95%CI: 0.739~0.811, $P < 0.001$), 高于baPWV及传统血脂指标[baPWV(AUC=0.616, 95%CI: 0.574~0.659, $P < 0.001$), TC(AUC=0.576, 95%CI: 0.532~0.621, $P=0.001$), TG(AUC=0.735, 95%CI: 0.696~0.774, $P < 0.001$), LDL-C(AUC=0.639, 95%CI=0.597~0.681, $P < 0.001$)。结论: AI、BMI、AST、FBG、baPWV是NAFLD的独立相关因素。尽管AI无法直接作为NAFLD的因果指标, 但其在风险评估中的潜力值得关注, 尤其是结合影像学检查时, 有助于提高NAFLD的早期诊断率。

[关键词] 脂肪变性; 脂肪肝; 血管硬化; 动脉硬化指数**[中图分类号]** R541.4**[文献标志码]** A**[文章编号]** 1007-4368(2025)09-1326-08**doi:** 10.7655/NYDXBNSN241412

Study on the correlation between arteriosclerosis index and non - alcoholic fatty liver disease

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[Abstract] **Objective:** To analyze factors influencing hepatic steatosis and explore the relationship between the arterial sclerosis index (AI) and non-alcoholic fatty liver disease (NAFLD). **Methods:** This study was a secondary analysis based on the public data of a cross-sectional study conducted at the Medical Health Examination Center of Kurosawa Memorial Hospital in Japan, involving 856 participants aged 24 to 84 years. The participants were divided into the NAFLD group ($n=209$) and the non-NAFLD group ($n=647$) according to whether they had NAFLD. The differences in clinical general data, laboratory indicators, AI values, and the detection rate

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of arterial sclerosis between the two groups were compared. Logistic regression analysis was used to evaluate the related factors of NAFLD, and a regression model was constructed to assess the correlation between AI and NAFLD. The receiver operating characteristic (ROC) curve was used to test the value of AI as an indicator for risk assessment of NAFLD. **Results:** There was a statistically significant difference in the gender composition ratio between the NAFLD group and the non-NAFLD group ($P < 0.001$), with more males in the NAFLD group. Compared with the non-NAFLD group, the NAFLD group had higher levels of body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), γ -glutamyl transferase (GGT), fasting blood glucose, uric acid, triglyceride (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and arterial pulse wave velocity of brachial artery (baPWV) ($P < 0.001$), lower levels of high-density lipoprotein cholesterol (HDL-C) ($P < 0.001$), and less exercise habits ($P=0.001$). The AI values and the detection rate of arterial sclerosis in the NAFLD group were higher than those in the non-NAFLD group ($P < 0.001$). Binary multivariate logistic regression analysis showed that AI, BMI, AST, fasting blood glucose, and baPWV were positively correlated with NAFLD. After fully adjusting for confounding factors, binary multivariate logistic regression analysis showed that AI was positively correlated with NAFLD (OR=1.846, 95% CI: 1.541-2.121, $P < 0.001$), and the population in the highest AI group showed a significantly higher tendency of NAFLD compared to the lowest group (OR=6.169, 95% CI: 3.006-12.661, $P < 0.001$). In the generalized additive model, there is a direct linear relationship between AI and NAFLD (log-likelihood ratio test, $P=0.949$). The area under the ROC curve of AI is 0.775 (95% CI: 0.739-0.811, $P < 0.001$), which is higher than that of baPWV and traditional lipid indicators [baPWV (AUC=0.616, 95% CI: 0.574-0.659, $P < 0.001$), TC (AUC=0.576, 95% CI: 0.532-0.621, $P=0.001$), TG (AUC=0.735, 95% CI: 0.696-0.774, $P < 0.001$), LDL-C (AUC=0.639, 95% CI: 0.597-0.681, $P < 0.001$)]. **Conclusion:** AI, BMI, AST, fasting blood glucose, and baPWV are independent related factors for NAFLD. Although AI cannot directly serve as a causal indicator for NAFLD, its potential in risk assessment is worthy of attention, especially when combined with imaging examinations, which can help improve the early diagnosis rate of NAFLD.

[Key words] steatosis; fatty liver; vascular sclerosis; arteriosclerosis index

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脂肪肝病 (fatty liver disease, FLD) 是以肝脏中过量脂肪积累为特征的临床病理状态^[1], 主要分为酒精性脂肪性肝病 (alcoholic fatty liver disease, AFLD) 和非酒精性脂肪性肝病 (non-alcoholic fatty liver disease, NAFLD)。随着全球肥胖和代谢综合征的流行, NAFLD 已成为最常见的慢性肝病之一。据估计, NAFLD 在西方国家的成年人口中占比高达 20%~30%, 在亚洲某些地区也呈现出类似的流行趋势^[2-3]。NAFLD 不仅与肝脏相关疾病的风险增加有关, 还与心血管疾病、2 型糖尿病等代谢性疾病的发病率和死亡率密切相关^[4-5]。

动脉硬化指数 (arteriosclerosis index, AI) 是一种评估动脉粥样硬化程度的指标, 通常通过计算总胆固醇 (total cholesterol, TC) 与高密度脂蛋白胆固醇 (high-density lipoprotein cholesterol, HDL-C) 的差值与 HDL-C 的比例得出。AI 升高被认为是心血管疾病风险的一个独立预测因子^[6]。

脂肪肝与动脉硬化关系密切, 但两者之间的联系机制尚未明确, 可能涉及胰岛素抵抗 (insulin resistance, IR)、氧化应激、炎症反应、脂代谢紊乱、阻塞性呼吸睡眠暂停和慢性肾脏疾病。近年来, 一些

研究开始关注 AI 与 NAFLD 之间的关联, 但大多数研究集中在西方人群, 且样本量相对较小^[7-8]。此外, AI 在 NAFLD 风险评估中的潜在作用尚未得到充分验证。因此, 本研究旨在通过横断面研究, 利用日本 856 例体检人群数据进行二次分析, 进一步探讨 AI 与 NAFLD 之间的关系及 AI 作为 NAFLD 风险评估指标的有效性和潜在价值。

1 对象和方法

1.1 对象

本研究是基于公共数据的二次分析。数据来自于 Dryad 数据库 (www.Datadryad.org), 源自 Fukuda 等^[9]的原始研究, 该数据库经作者授权, 可以免费下载并且供其他研究者二次分析使用。数据库文件中包含的变量如下: 年龄、体重指数 (body mass index, BMI)、收缩压 (systolic blood pressure, SBP)、舒张压 (diastolic blood pressure, DBP)、天冬氨酸转氨酶 (aspartate aminotransferase, AST)、丙氨酸转氨酶 (alanine aminotransferase, ALT)、 γ -谷氨酰转肽酶 (γ -glutamyl transferase, GGT)、空腹血糖 (fasting blood glucose, FBG)、尿酸、总胆固醇 (total cholesterol,

TC)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol, LDL-C)、肾小球滤过率(glomerular filtration rate, GFR)、肱踝脉搏波传导速度(brachial-ankle pulse wave velocity, baPWV)、性别、吸烟状况、运动、脂肪肝、绝经状况、饮酒、踝关节肱指数(ankle-brachial index, ABI)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol, HDL-C)和甘油三酯(triglyceride, TG)。

Fukuda等^[9]于2004年3月—2012年12月在日本岐阜市村上纪念医院医学健康检查中心进行了横断面研究,探究血清GGT与动脉粥样硬化之间的关联。参与者接受了医疗健康检查计划,包括脉搏波速度和腹部超声检查。根据排除标准,共招募856例受试者。排除标准:①接受激素替代治疗的受试者;②服用口服避孕药的受试者;③乙型肝炎病毒抗原和丙型肝炎病毒抗原阳性;④ABI<0.95;⑤男性每周饮酒量超过140 g和女性每周饮酒量超过70 g的受试者,以满足NAFLD诊断标准^[10]。原始研究依据《赫尔辛基宣言》进行,获得了所有参与者的知情同意。本研究为该横断面研究的二次分析,使用公开授权数据,不涉及新的受试者干预或隐私信息获取,不涉及商业利益,可免除伦理审查。

1.2 方法

资料采集:原始研究脂肪肝的诊断基于腹部超声检查结果,由高年资的技术人员使用Aloka SSD-650CL(Aloka Co公司,日本)进行检查。所有超声图像都以复印件的形式保存,一位消化科专家在不参考任何参与者其他个人数据的情况下通过分析图像并诊断脂肪肝。在已知的4项标准(肝肾回声对比、肝脏亮度、深度衰减和血管模糊)中,需要进行肝肾对比和肝脏亮度检查才能诊断脂肪肝。eGFR使用日本肾脏学会的公式计算^[11]:男性 $eGFR=194\times Cr-1.094\times \text{年龄}-0.287[\text{mL}/\text{min}/1.73\text{ m}^2]$,女性eGFR乘以0.739的校正因子。AI的计算公式是:(TC-HDL-C)/HDL-C^[12]。baPWV及其他协变量的测量和评估在原文中有详细的描述。

1.3 统计学方法

使用SPSS 21.0软件进行统计分析。正态分布的连续变量以均数±标准差($\bar{x}\pm s$)表示,两组间比较采用独立样本 t 检验,偏态分布的连续变量用中位数(四分位数)[$M(P_{25}, P_{75})$]表示,组间比较采用非参数检验,分类变量则以频率(百分比)表示,组间比较采用 χ^2 检验。排除VIF>5的变量后,采用二元多因素Logistic回归分析研究人群发生NAFLD的相

关因素。通过建模进一步检验AI与NAFLD的关系。模型1为初始模型;模型2调整年龄、性别;模型3增加对BMI、AST、FBG进行的调整;模型4进一步调整了吸烟情况和运动状态。为了研究AI与NAFLD之间是否存在非线性关系,使用了平滑曲线。采用受试者工作特征(receiver operating characteristic, ROC)曲线分析评估AI作为NAFLD风险评估指标的价值,曲线下面积(area under the curve, AUC)是评估模型整体性能的一个重要指标,AUC值越接近1表明其预测价值越好。对于不同指标AUC的差异比较,使用R语言(4.3.0版本)通过安装并加载pROC包,并通过roc.test函数进行DeLong检验。该检验方法可直接评估各指标(如AI与baPWV、TC、TG、LDL-C)ROC曲线AUC之间的差异是否具有统计学意义,从而进一步支持评估结果的稳健性。所有统计检验均采用双侧检验, $P<0.05$ 为差异有统计学意义。

2 结果

2.1 两组间临床和实验室特征比较

856例参与者中NAFLD发生率为24.42%,NAFLD组和非NAFLD组的临床和实验室特征见表1。结果显示NAFLD组男性比例显著高于女性($P<0.001$)。NAFLD组的BMI、SBP、DBP、AST、ALT、GGT、FBG、血尿酸、TG、TC、LDL-C、baPWV水平显著高于非NAFLD组($P<0.001$),而HDL-C水平显著低于非NAFLD组($P<0.001$),运动状态方面存在显著差异($P=0.001$),eGFR值低于非NAFLD组($P<0.05$),有吸烟习惯或曾经吸烟的占比高于非NAFLD组($P<0.05$),而在年龄、eGFR、吸烟情况、饮酒情况方面两组间差异无统计学意义($P>0.05$,表1)。

2.2 两组间AI值和血管硬化率的比较

与正常对照组比较,NAFLD组的AI值显著升高($P<0.001$),且基于baPWV值评估动脉硬化率显著高于非NAFLD组,差异均有统计学意义($P=0.001$,表1)。

2.3 NAFLD相关影响因素的二元多因素Logistic回归分析

排除VIF>5的变量后,以是否为NAFLD为因变量(赋值:否=0,是=1),以性别(赋值:男性=1,女性=2)以及单因素分析中 $P<0.1$ 的因素(赋值:无规律运动=0,每周至少1次运动=1;体重正常=0,超重=1,肥胖=2)作为自变量进行二元多因素Logistic回归

表1 NAFLD组与非NAFLD组体检人群组间资料比较

Table 1 Comparison of physical examination data between the NAFLD group and the non-NAFLD group

Variable	NAFLD(n=209)	Non-NAFLD(n=647)	$\chi^2/t/Z$	P
Sex[n(%)]			38.667 ^a	<0.001
Male	170(81.3)	372(57.5)		
Female	39(18.7)	275(42.5)		
Age(years, $\bar{x} \pm s$)	50.2 ± 9.8	51.5 ± 9.6	1.684 ^b	0.092
BMI(kg/m ² , $\bar{x} \pm s$)	25.7 ± 3.3	22.1 ± 2.4	-16.882 ^b	<0.001
SBP(mmHg, $\bar{x} \pm s$)	126.2 ± 13.8	117.5 ± 14.6	-7.646 ^b	<0.001
DBP(mmHg, $\bar{x} \pm s$)	80.2 ± 8.7	74.2 ± 9.8	-7.881 ^b	<0.001
AST[U/L, M(P ₂₅ , P ₇₅)]	22(18, 27)	18(16, 22)	-7.942	<0.001
ALT[U/L, M(P ₂₅ , P ₇₅)]	28(20, 41)	16(13, 21)	-13.875	<0.001
GGT[U/L, M(P ₂₅ , P ₇₅)]	22(17, 30)	22(17, 30)	-7.577	<0.001
FBG(mmol/L, $\bar{x} \pm s$)	5.8 ± 1.2	5.3 ± 0.5	-8.697 ^b	<0.001
Uric acid(μmol/L, $\bar{x} \pm s$)	350.4 ± 80.2	295.3 ± 77.2	-8.893 ^b	<0.001
TC(mmol/L, $\bar{x} \pm s$)	5.6 ± 1.0	5.4 ± 0.9	-3.669 ^b	<0.001
TG[mmol/L, M(P ₂₅ , P ₇₅)]	1.3(0.9, 2.0)	0.8(0.5, 1.2)	-10.222	<0.001
HDL-C(mmol/L, $\bar{x} \pm s$)	1.2 ± 0.3	1.5 ± 0.4	10.943 ^b	<0.001
LDL-C(mmol/L, $\bar{x} \pm s$)	3.6 ± 0.8	3.2 ± 0.8	-6.351 ^b	<0.001
eGFR[mL/(min·1.73 m ²), $\bar{x} \pm s$]	69.4 ± 12.1	70.9 ± 12.1	1.565 ^b	0.118
baPWV(cm/s, $\bar{x} \pm s$)	1 480.4 ± 256.4	1 388.5 ± 238.1	-4.760 ^b	<0.001
AI($\bar{x} \pm s$)	4.1 ± 1.3	2.9 ± 1.1	-13.745 ^b	<0.001
Atherosclerosis[n(%)]			12.386 ^a	0.001
Yes	112(53.6)	257(39.7)		
No	97(46.4)	390(60.3)		
Smoking status[n(%)]			1.517 ^a	0.240
None or past	159(76.1)	518(80.1)		
Current	50(23.9)	129(19.9)		
Regular exercise[n(%)]			10.087 ^a	0.001
≥1 time/week	26(12.4)	146(22.6)		
<1 time/week	183(87.6)	501(77.4)		
Body weight condition[n(%)]			206.198 ^a	<0.001
Normal weight	66(31.6)	525(81.1)		
Over weight	107(51.2)	115(17.8)		
Obesity	36(17.2)	7(1.1)		

a: χ^2 ; b: t value; The residual statistic was Z-value; AI=(TC-HDL-C)/HDL-C; Obesity: BMI≥28 kg/m²; Over weight: 24 kg/m²≤BMI<28 kg/m²; Normal weight: BMI<24 kg/m²; Atherosclerosis: baPWV≥1 400 cm/s.

分析, 结果显示 AI、BMI、AST、FBG、baPWV 是 NAFLD 的影响因素, 均与 NAFLD 呈正相关。该模型 $R^2=0.366$, Nagelkerke $R^2=0.546$ (表 2)。

2.4 不同模型中 AI 与 NAFLD 相关关系的多因素 Logistic 回归分析

在对混杂变量进行全面调整后, 二元多因素 Logistic 回归分析揭示了较高 AI 水平与 NAFLD 增加之间的显著关联(OR=1.846, 95%CI=1.541~2.121, $P < 0.001$, 表 3)。值得注意的是, 在仔细调整多个因素后, AI 最高组的人群与最低组相比, 表现出明

显更高的 NAFLD 倾向(OR=6.169, 95%CI=3.006~12.661, $P < 0.001$)。此外, 通过使用广义相加混合模型曲线拟合, 图 1 直观地展示了 AI 与 NAFLD 之间呈现直接线性关系, 而不是非线性关系(对数似然比检验, $P=0.949$)。

2.5 AI 与 baPWV 及传统血脂指标作为 NAFLD 风险评估指标的 ROC 曲线分析

AI 的 AUC 为 0.775 (95%CI=0.739~0.811, $P < 0.001$), 高于同为血管硬化指标的 baPWV (AUC=0.616, 95%CI=0.574~0.659, $P < 0.001$; DeLong 检验,

表2 NAFLD相关影响因素的二元多因素Logistic回归分析

Table 2 Multifactorial logistic regression analysis of NAFLD-related influencing factors

Index	B	SE	Wald χ^2	P	OR(95%CI)
AI	0.743	0.141	27.701	<0.001	2.103(1.595-2.774)
Sex					
Male					1.000(Ref.)
Female	-0.035	0.317	0.012	0.913	0.966(0.519-1.797)
Age	-0.025	0.015	2.850	0.091	0.975(0.947-1.004)
BMI	0.356	0.090	15.674	<0.001	1.428(1.197-1.703)
SBP	0.001	0.009	0.016	0.899	1.001(0.983-1.020)
AST	0.071	0.016	19.987	<0.001	1.073(1.041-1.107)
FBG	0.783	0.186	17.665	<0.001	2.188(1.519-3.152)
Uric acid	0.003	0.002	2.617	0.106	1.003(0.999-1.007)
TG	-0.055	0.035	2.549	0.110	0.946(0.884-1.013)
LDL-C	-0.070	0.079	0.775	0.379	0.932(0.798-1.090)
baPWV	0.001	0.001	6.323	0.012	1.001(1.000-1.003)
eGFR	0.019	0.011	2.760	0.097	1.019(0.997-1.042)
Frequency of regular exercise					
<1 time/week					1.000(Ref.)
\geq 1 time/week	-0.492	0.307	2.566	0.109	0.611(0.335-1.116)
Body weight condition					
Normal weight			1.334	0.513	1.000(Ref.)
Over weight	0.399	0.370	1.164	0.281	1.490(0.722-3.077)
Obesity	0.370	0.817	0.206	0.650	1.448(0.292-7.177)

表3 不同模型中AI与NAFLD相关关系的二元多因素Logistic回归分析

Table 3 Multifactorial logistic regression analysis of the association between AI and NAFLD in different models

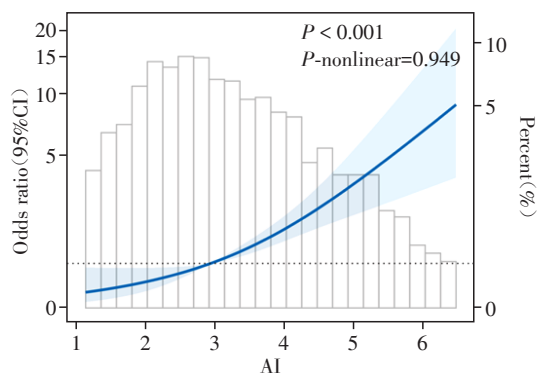
Index	Model 1		Model 2		Model 3		Model 4	
	OR(95%CI)	P	OR(95%CI)	P	OR(95%CI)	P	OR(95%CI)	P
AI	2.335(2.009-2.713)	<0.001	2.216(1.899-2.586)	<0.001	1.850(1.548-2.210)	<0.001	1.846(1.541-2.121)	<0.001
AI(quantile)								
Q1	Ref.		Ref.		Ref.		Ref.	
Q2	2.304(1.158-4.580)	0.017	2.150(1.073-4.308)	0.031	1.385(0.637-3.013)	0.411	1.449(0.662-3.171)	0.353
Q3	5.453(2.880-10.325)	<0.001	4.775(2.949-9.144)	<0.001	2.296(1.103-4.777)	0.026	2.294(1.097-4.795)	0.027
Q4	16.893(9.071-31.460)	<0.001	13.860(7.313-26.270)	<0.001	6.180(3.035-12.584)	<0.001	6.169(3.006-12.661)	<0.001
P	<0.001		<0.001		<0.001		<0.001	

Model 1 did not adjust for confounding factors; Model 2 adjusted for age and gender; Model 3 adjusted for age, gender, BMI, AST, and fasting blood glucose; Model 4 adjusted for age, gender, BMI, AST, fasting blood glucose, smoking status, and exercise status. The arterial sclerosis index(AI) was divided into four equal groups: the first group(Q1, AI \leq 2.23, n=213), the second group(Q2, AI \leq 2.24-2.93, n=215), the third group(Q3, AI \leq 2.94-3.90, n=214), and the fourth group(Q4, AI \geq 3.91, n=214).

$P < 0.001$),也高于传统血脂指标TC(AUC=0.576, 95% CI=0.532~0.621, $P=0.001$; DeLong 检验, $P < 0.001$)、TG(AUC=0.735, 95% CI=0.696~0.774, $P < 0.001$; DeLong 检验, $P=0.013$)、LDL-C(AUC=0.639, 95% CI=0.597~0.681, $P < 0.001$; DeLong 检验, $P < 0.001$),提示AI具有更优异的预测能力(图2)。

3 讨论

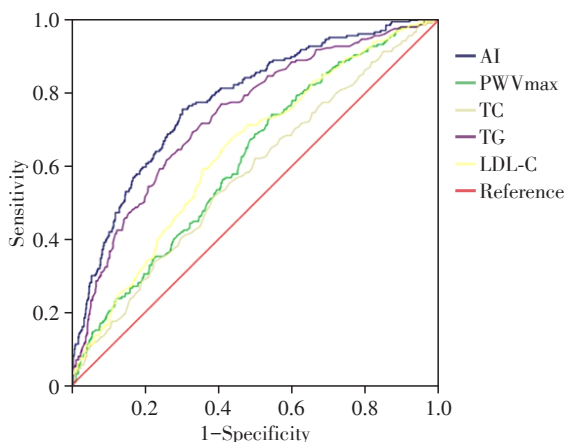
本研究的856例日本体检人群发生脂肪肝209例, NAFLD的发生率为24.42%,体重正常、超重和肥胖者NAFLD患病率分别为11.17%、48.20%和83.72%, BMI与NAFLD呈正相关,这与现有的研究一致。窦紫



After adjusting for age, gender, BMI, AST, fasting blood glucose, smoking status, and physical activity (log-likelihood ratio test, $P=0.949$), a linear relationship was observed between AI and the probability of NAFLD.

图1 AI与NAFLD发生概率之间的关系

Figure 1 The relationship between AI and the probability of NAFLD occurrence



The area under the ROC curve for AI was 0.775 (95% CI: 0.739-0.811, $P < 0.001$), which was higher than that for baPWV and traditional lipid indicators.

图2 AI与baPWV及传统血脂指标作为NAFLD风险评估指标的ROC曲线分析

Figure 2 ROC curve analysis of AI, baPWV and traditional lipid indicators as risk assessment indicators for NAFLD

岩等^[13]研究2018—2021年北京市体检人群,发现NAFLD检出率为33.31% (108 512/325 726),其中,轻、中、重度NAFLD检出率分别为68.25%、30.67%、1.08%,男性检出率高于女性,BMI是NAFLD的独立危险因素,超重/肥胖是NAFLD的重要风险因素,尤其是内脏脂肪含量与NAFLD呈现明显的正相关^[14-15]。值得注意的是,虽然BMI正常人群NAFLD的患病率明显低于超重/肥胖群体,但其发生代谢综合征、心血管疾病、肝外并发症的风险更高,预后更差^[16]。

究其原因,可能与BMI不仅受脂肪量的影响,还受肌肉量和骨量等因素的影响,不能衡量实际脂肪分布情况有关。另外BMI正常的NAFLD患者可能在其生活习惯、饮食结构、遗传基因方面与超重/肥胖的NAFLD患者存在差异。

本研究中FBG和AST是NAFLD的相关影响因素,提示葡萄糖代谢、脂肪代谢与脂肪肝之间的复杂关系,众多研究逐渐揭示了一系列代谢紊乱与IR之间的密切联系。IR是一个复杂的病理生理现象,涉及多种因素的相互作用。当机体摄入过多的能量时,会导致糖代谢失衡,未被利用的糖分转化为脂肪,并通过血液运输,最终储存在皮下组织、骨骼肌以及肝脏和大网膜等内脏器官,形成内脏脂肪^[17]。这种内脏脂肪的积累通过氧化应激、炎症反应、免疫调节等多种机制,干扰了细胞对胰岛素的正常反应,从而导致IR^[18]。IR不仅减少了靶细胞对胰岛素的敏感性,还进一步加剧了糖代谢和脂质代谢的紊乱。长期的IR状态可导致多种慢性疾病的发生,包括但不限于糖尿病、血脂异常、NAFLD、动脉粥样硬化,以及某些类型的癌症,如乳腺癌和结直肠癌。对于单独个体来说,NAFLD可能是IR的结果,也可能是IR的原因。

AI和baPWV作为血管硬化相关指标,在脂肪肝组中也显著升高,提示NAFLD患者可能伴有早期动脉硬化的现象。在充分调整混杂因素后,高AI值始终是NAFLD的独立相关因素。脂肪肝和心血管疾病之间存在密切关联,Xin等^[19]针对上海某中老年社区的前瞻性研究表明,动脉硬化指标baPWV与NAFLD发生风险增加和纤维化可能性增加独立相关。许天旗等^[20]通过颈动脉CT血管成像技术探讨非NAFLD与颈动脉高危斑块之间的关系,在调整性别、年龄、糖尿病、高血压等协变量后,NAFLD与颈动脉高危斑块仍显示独立相关($OR=4.847$, $95\%CI=1.771\sim 13.280$, $P=0.002$)。有研究者以B超检测的颈动脉硬化斑块和颈动脉内膜中层厚度作为动脉硬化的指标,对各项混杂因素调整后,并未发现动脉硬化和NAFLD独立相关。这些研究结果的差异可能与研究对象的选择及动脉硬化相关指标的选择不同有关。但较为一致的结论是,亚临床动脉粥样硬化和NAFLD的进展具有重叠的病理生理决定因素和发病机制,炎症、脂肪因子失衡和胰岛素抵抗被认为在NAFLD和动脉粥样硬化的发病和进展中起着至关重要的作用^[21]。炎症在NAFLD和动脉粥样硬化的发展中扮演了核心角色。它不仅促进了

肝脏的脂肪沉积和损伤,还加剧了血管内皮的功能障碍,为动脉粥样硬化的形成创造了条件。此外,脂肪因子的失衡,如脂联素水平的降低和抵抗素水平的升高,也与NAFLD和动脉粥样硬化的病理过程密切相关。这些脂肪因子直接或间接地影响了血管壁的炎症反应和脂质沉积。IR是联系NAFLD和动脉粥样硬化的另一个重要环节。它不仅增加了肝脏的脂肪酸合成和储存,还减弱了胰岛素对血管内皮的保护作用,从而促进了动脉粥样硬化的发展。因此,动脉硬化相关指标对NAFLD人群长期预后提示作用。

鉴于有小部分肝脂肪变性患者会发展为非酒精性脂肪性肝炎(non-alcoholic steatohepatitis, NASH)、肝硬化或肝细胞癌,因此评估脂肪变性程度并预估其炎症、纤维化程度对于识别哪些患者会出现疾病进展显得尤为重要。根据亚太肝病研究学会(the Asia-Pacific Association for the Study of the Liver, APASL)指南的建议,NASH诊断的金标准是组织学活检,但手术费用昂贵且有创性操作导致发生并发症风险增加。而磁共振成像技术,例如磁共振质子密度脂肪分数(magnetic resonance imaging-proton density fat fraction, MRI-PDFF)和质子磁共振波谱(hydrogen proton magnetic resonance spectroscopy, 1H-MRS),被认为是量化肝脏脂肪的金标准,但这在常规临床实践中并未得到常规应用。而肝脏超声检查一般能检测出肝脏脂肪变性,但它不能量化脂肪变性的程度,也不能排除肝脏脂肪变性。本研究通过绘制ROC曲线,比较AI和传统血脂指标以及baPWV对NAFLD的风险评估价值,结果显示AI的AUC为0.775,优于baPWV(0.616)、TC(0.576)、TG(0.735)和LDL-C(0.639),这一结果表明,对于AI值较高的个体,尽早开展影像学检查能够有效提高NAFLD的早期诊断率,这不仅有助于对高危人群进行精准筛查,还能为临床初步诊断提供有力支持,并在治疗后的随访观察中发挥重要作用。

本项研究在执行过程中存在一些局限性:①本研究是一项针对公开数据二次分析的横断面研究,因此在暴露与结果之间提供的证据很弱,难以区分因果关系。②由于研究人群仅包含日本人,可能无法推广到其他地区和种族。③由于原始数据的限制,不能分析饮食习惯、睡眠状况等生活方式以及其他检测指标与NAFLD之间可能的相关性。

综上所述,本研究人群中NAFLD发生率与全球患病率相近^[2],且多伴有代谢综合征,包括肥胖、高

血糖、高血脂、高血压等。该结果对同样作为东亚人种的我们有很好的提示作用,相比肥胖率更高的西方人群,东亚人群NAFLD的患病率并未明显降低,这值得进一步研究。另外,本研究结果提示AI、BMI、AST、FBG、baPWV是NAFLD的独立相关因素。尽管AI无法直接作为NAFLD的因果指标,但在风险评估中的潜力值得关注,尤其是结合影像学检查时,有助于提高NAFLD的早期诊断率。

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冯晓棠负责研究数据的收集、整理、统计分析和论文撰写;张丽俐负责提出研究方向,提供论文修订建议;肖利斌负责复核统计数据,核对图表;刘建军负责论文的质量控制与审查、最终版本修订,对论文负责。

Author's Contributions:

FENG Xiaotang was responsible for the collection, organization, statistical analysis, and writing of the research data; ZHANG Lili was responsible for proposing research directions and providing suggestions for paper revision; XIAO Libin was responsible for reviewing statistical data and checking charts; LIU Junjun was responsible for the quality control and review of the paper, final version revision, and was accountable for the paper.

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