·临床研究·

北京某地区老年人群非酒精性脂肪性肝病的临床特征及影响因素

尹慧君[1],李晓利[1*],徐成[2],田玲[3],李彬[4],胡超[1],王耀辉[1],王晓晴[1],邓玲[4], 李炜[4]
([1]中国人民解放军总医院第二医学中心保健八科,北京 100853;中国人民解放军总医院第八医学中心:[2]重症医学科,[3]体检中心,[4]门诊部,北京 100091)

【摘 要】 目的 探讨老年人群非酒精性脂肪性肝病(NAFLD)的临床特征及影响因素。**方法** 纳入2021年5月至2021年9月北京市海淀区≥60岁的离退休老年人782例。根据是否患有NAFLD,分为NAFLD组200例及非NAFLD组582例。比较2组患者的基线资料。采用SPSS 25.0统计软件进行数据分析。采用多因素logistic回归分析NAFLD的影响因素。建立多指标联合预测模型,采用受试者工作特征(ROC)曲线评价其对NAFLD的临床预测价值。**结果** NAFLD患病率为25.58%(200/782)。与非NAFLD组比较,NAFLD组患者体质量指数(BMI)、糖尿病患病率、丙氨酸氨基转氨酶、天门冬氨酸氨基转移酶、甘油三酯(TG)、空腹血糖(FBG)及尿酸水平均显著升高,年龄、慢性阻塞性肺疾病患病率及高密度脂蛋白胆固醇水平均显著降低,差异均有统计学意义(均$P<0.05$)。多因素logistic回归分析结果显示,NAFLD与女性($OR=1.882$,95%CI 1.142~3.100;$P=0.013$),BMI($OR=1.303$,95%CI 1.219~1.393;$P=0.000$),FBG($OR=1.215$,95%CI 1.076~1.372;$P=0.002$),TG($OR=1.738$,95%CI 1.401~2.154;$P=0.000$)呈正相关,与年龄($OR=0.979$,95%CI 0.964~0.995;$P=0.009$)呈负相关。ROC曲线分析显示,年龄、女性、BMI、FBG及TG多指标联合对老年NAFLD有良好的预测价值,曲线下面积为0.782(95%CI 0.751~0.811)。**结论** 老年NAFLD患病率随年龄的增加而下降。老年NAFLD受多种因素影响,女性、肥胖、糖尿病、血脂异常尤其是TG升高,是老年人NAFLD的危险因素。

【关键词】 老年人;非酒精性脂肪性肝病;危险因素
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Clinical characteristics and influencing factors of non-alcoholic fatty liver disease in the elderly at a district in Beijing

YIN Hui-Jun[1], LI Xiao-Li[1], XU Cheng[2], TIAN Ling[3], LI Bin[4], HU Chao[1], WANG Yao-Hui[1], WANG Xiao-Qing[1], DENG Ling[4], LI Wei[4]
([1]Eighth Department of Healthcare, Second Medical Center, Chinese PLA General Hospital, Beijing 100853, China; [2]Department of Critical Medicine, [3]Physical Examination Center, [4]Outpatient Department, Eighth Medical Center, Chinese PLA General Hospital, Beijing 100091, China)

【Abstract】 Objective To investigate the clinical characteristics and influencing factors of non-alcoholic fatty liver disease (NAFLD) in the elderly. **Methods** A total of 782 retired elderly people aged ≥60 years in Haidian District of Beijing were included during May and September 2021. According to whether they had NAFLD or not, they were divided into NAFLD ($n=200$) and non-NAFLD groups ($n=582$). The baseline data were compared between the 2 groups of patients. SPSS statistics 25.0 was used for data analysis. Multivariate logistic regression analysis was employed to analyze the influencing factors of NAFLD. A multi-index combined prediction model was established, and its clinical predictive value for NAFLD was evaluated by receiver operating characteristic (ROC) curve. **Results** The prevalence of NAFLD was 25.58% (200/782). Compared with the non-NAFLD group, the NAFLD group had significantly higher body mass index (BMI), larger proportion of diabetes, and higher levels of alanine aminotransferase, aspartate aminotransferase, triglyceride (TG), fasting blood glucose (FBG) and uric acid, and obviously younger age, lower prevalence of chronic obstructive pulmonary disease and lower high-density lipoprotein-cholesterol level (all $P<0.05$). Multivariate logistic regression analysis showed that NAFLD was positively correlated with female ($OR=1.882$, 95%CI 1.142-3.100; $P=0.013$), BMI ($OR=1.303$, 95%CI 1.219-1.393; $P=0.000$), FBG ($OR=1.215$, 95%CI 1.076-1.372; $P=0.002$), TG ($OR=1.738$, 95%CI 1.401-2.154; $P=0.000$), and negatively with age ($OR=0.979$, 95%CI 0.964-0.995); $P=0.009$). ROC curve analysis showed that the combination of age, female, BMI, FBG and TG had a good predictive value for elderly NAFLD, with an area under the curve

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通信作者:李晓利;E-mail:lixiaoli1@aliyun.com

of 0.782 (95%*CI* 0.751-0.811). **Conclusion** The prevalence of NAFLD in the elderly is decreased with age. NAFLD in the elderly is affected by many factors. Female, obesity, diabetes and dyslipidemia, especially TG elevation, are the risk factors of NAFLD in the elderly.

【**Key words**】 aged; non-alcoholic fatty liver disease; risk factors

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Corresponding author: *LI Xiao-Li*, *E-mail*: *lixiaoli1@aliyun.com*

非酒精性脂肪性肝病(non-alcoholic fatty liver disease,NAFLD)包括非酒精性肝脂肪变性、非酒精性脂肪性肝炎(non-alcoholic steatohepatitis,NASH)、肝硬化和肝细胞癌[1]。目前,全球 NAFLD 患病率约为 25%,在我国则达到 29.2%,已取代病毒性肝炎成为我国第一大慢性肝病。NAFLD 除了增加老年人肝病死亡风险,还显著增加动脉硬化性心血管疾病和多种恶性肿瘤的发病风险[2,3]。NAFLD 作为一种常见的慢性疾病,在老年人群中的研究相对较少。因此,本研究以≥60 岁的离退休老年人为研究对象,探讨其发生 NAFLD 的临床特点及相关影响因素。

1 对象与方法

1.1 研究对象

纳入 2021 年 5 月至 2021 年 9 月北京市海淀区年龄≥60 岁的离退休老年人 782 例。根据是否患有 NALFD,分为 NAFLD 组 200 例及非 NAFLD 组 582 例。排除标准:有过量饮酒史和其他可以导致脂肪肝的特定疾病[1]。本研究经中国人民解放军总医院科学和伦理审查委员会批准,所有入选者均签署知情同意书。

1.2 方法

(1)问卷调查:主要内容包括社会学特征、生活方式、疾病状况及用药情况。(2)实验室检验指标:丙氨酸氨基转氨酶(alanine aminotransferase,ALT)、天门冬氨酸氨基转移酶(aspartate aminotransferase,AST)、甘油三酯(triglyceride,TG)、总胆固醇(total cholesterol,TC)、高密度脂蛋白胆固醇(high-density lipoprotein cholesterol,HDL-C)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol,LDL-C)、空腹血糖(fasting blood glucose, FBG)及尿酸(uric acid, UA)。(3)超声检查:受检者空腹行腹部彩色多普勒超声检查。

1.3 诊断标准

NAFLD 的诊断:有弥漫性肝细胞脂肪变性的影像学或组织学证据,并且排除酒精滥用等可以导致肝脂肪变的其他病因[1]。本研究应用传统超声进行 NAFLD 的影像学诊断。糖尿病的诊断:有糖尿病病史或随机血糖≥11.1 mmol/L,FBG≥7.0 mmol/L,糖化血红蛋白≥6.5%。高血压、冠心病、高脂血症、缺血性脑卒中及慢性阻塞性肺疾病(chronic obstructive pulmonary disease,COPD)均依据病史诊断。

1.4 统计学处理

采用 SPSS 25.0 统计软件进行数据分析。符合正态分布的计量资料以均数±标准差($\bar{x}\pm s$)表示,组间比较采用 t 检验。计数资料以例数(百分率)表示,组间比较采用 χ^2 检验。采用多因素 logistic 回归分析发生 NAFLD 的影响因素。建立多指标联合预测模型,绘制受试者工作特征(receiver operating characteristic,ROC)曲线评价其对 NAFLD 的临床预测价值。$P<0.05$ 为差异有统计学意义。

2 结 果

2.1 2 组患者一般资料比较

本研究纳入的 782 例老年人中,60~69 岁 283 例,70~79 岁 72 例,80~89 岁 240 例,≥90 岁 187 例。男性 655 例(83.76%),女性 127 例(16.24%),年龄 60~101(78.43±12.17)岁。NAFLD 组患者 BMI、糖尿病患病率、ALT、AST、TG、FBG 及 UA 显著高于非 NAFLD 组,年龄、COPD 患病率及 HDL-C 显著低于非 NAFLD 组,差异均有统计学意义(均 $P<0.05$;表 1)。

2.2 多因素 logistic 回归分析 NAFLD 的影响因素

以 NAFLD 作为因变量,将单因素分析中 $P<0.1$ 的参数:年龄、性别、BMI、糖尿病、高血压、COPD、ALT、AST、TG、HDL-C、LDL-C、FBG 以及 UA 作为自变量,采用多因素 logistic 回归模型的逐步后退法筛查 NAFLD 的影响因素,结果显示 NAFLD 与女性、BMI、FBG 及 TG 呈正相关,与年龄呈负相关(均 $P<0.05$;表 2)。

2.3 多指标联合预测 NAFLD 的诊断价值

根据多因素 logistic 回归方程,建立联合预测模型。ROC 曲线分析结果显示,年龄、女性、BMI、FBG 及 TG 联合预测老年 NAFLD 的曲线下面积为 0.782 (95%*CI* 0.751~0.811),灵敏度为 76.02%,特异度为 66.26%(图 1)。

3 讨 论

NAFLD 以肝脏内脂肪组织沉积为主要表现,而长期的脂质负荷过重,会导致肝脏向肝脂肪变性、肝炎、肝纤维化、肝硬化、甚至是肝癌演变。在老年人群中,NAFLD 不仅会增加肝内并发症发病率,还会

增加肝外疾病(糖尿病、心血管疾病、慢性肾脏病及肝外肿瘤)的发病风险,加速病程进展[4,5]。老年人常合并多种慢性疾病,其NAFLD发病特征及影响因素必然有自身的特征。因此,本研究积极探索老年人群NAFLD的影响因素,为临床NAFLD的精准干预及老年病综合诊治提供研究基础。

首先,本研究结果表明,老年人NAFLD患病率随年龄增加而下降。Eguchi等[6]与Wang等[7]的研究发现,NAFLD患病率在男性40~49岁、女性60~69岁后开始逐渐下降。Hartleb等[8]研究也发现,NAFLD患病率与增龄呈反向相关。分析原因可能与以下3种因素相关。一是存在"生存偏差"。由NAFLD引起严重并发症的老年人可能更早死亡,会出现高龄期NAFLD患病率较高龄期前下降的结果[5]。Golabi等[9]的研究发现,60~74岁老年人5年和10年全因死亡率与NAFLD相关,而在≥74岁老年人中,NAFLD与全因或心血管死亡率无关。二是由于NAFLD病程向肝纤维化进展,部分患者会由单纯性肝脏脂肪变性/NASH发展为严重的肝损害。若衰老与长期代谢异常因素并存,会导致脂毒性脂质的形成,促使细胞应激(即氧化应激和内质网应激)、炎症体激活和凋亡细胞死亡,进而加速非酒精性肝脂肪变性向NASH的演变,出现进展性肝纤维化,肝细胞内脂质下降甚至消失,最终发展为肝硬化

表1 2组患者一般资料比较

Table 1 Comparison of baseline data between two groups

Item	NAFLD group(n=200)	Non-NAFLD group(n=582)	t/χ^2	P value
Age(years, $\bar{x}\pm s$)	77.95±12.12	78.62±12.20	10.014	0.002
Gender[n(%)]			2.792	0.095
Male	160(80.0)	495(85.1)		
Female	40(20.0)	87(14.9)		
Physical exercise[n(%)]	166(83.0)	475(81.6)	0.193	0.660
BMI(kg/m^2, $\bar{x}\pm s$)	25.95±2.83	23.51±3.00	99.484	0.000
Alcohol drinking[n(%)]	70(35.0)	190(32.6)	0.372	0.542
Smoking[n(%)]	30(15.0)	90(15.5)	0.025	0.875
Comorbidity[n(%)]				
Hypertension	130(65.0)	335(57.6)	3.418	0.064
Coronary heart disease	78(39.0)	208(35.7)	0.682	0.409
Diabetes mellitus	75(37.5)	165(28.4)	5.858	0.016
Stroke	24(12.0)	68(11.7)	0.014	0.905
COPD	14(7.0)	72(12.4)	4.387	0.036
Medication[n(%)]				
Hypoglycemic drugs	23(11.5)	60(10.3)	0.222	0.637
Statins	66(33.0)	171(29.4)	0.923	0.337
Biochemical parameters				
ALT(U/L, $\bar{x}\pm s$)	23.78±15.59	17.53±13.59	29.117	0.000
AST(U/L, $\bar{x}\pm s$)	24.81±7.94	23.05±8.19	6.997	0.008
TG(mmol/L, $\bar{x}\pm s$)	1.80±0.95	1.28±0.75	61.369	0.000
TC(mmol/L, $\bar{x}\pm s$)	4.43±1.08	4.35±1.14	0.666	0.415
HDL-C(mmol/L, $\bar{x}\pm s$)	1.20±0.27	1.33±0.32	24.796	0.000
LDL-C(mmol/L, $\bar{x}\pm s$)	2.87±0.75	2.75±0.80	3.454	0.063
FBG(mmol/L, $\bar{x}\pm s$)	6.22±1.44	5.80±1.37	13.623	0.000
UA(umol/L, $\bar{x}\pm s$)	368.07±85.82	347.90±84.09	8.469	0.004

NAFLD: non-alcoholic fatty liver disease; BMI: boby mass index; COPD: chronic obstructive pulmonary disease; ALT: alanine aminotransferase; AST: aspartate aminotransferase; TG: triglyceride; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose; UA: uric acid.

表2 影响NAFLD的多因素logistic回归分析

Table 2 Multivariate logistic regression analysis of influencing factors of NAFLD

Variable	B	OR	95%CI	χ^2	P value
Age	−0.021	0.979	0.964−0.995	6.758	0.009
Female	0.632	1.882	1.142−3.100	6.164	0.013
BMI	0.265	1.303	1.219−1.393	60.261	0.000
COPD	−0.583	0.558	0.282−1.103	2.813	0.093
FBG	0.195	1.215	1.076−1.372	9.913	0.002
TG	0.552	1.738	1.401−2.154	25.361	0.000
HDL-C	−0.637	0.529	0.259−1.080	3.061	0.080

NAFLD: non-alcoholic fatty liver disease; BMI: boby mass index; COPD: chronic obstructive pulmonary disease; FBG: fasting blood glucose; TG: triglyceride; HDL-C: high-density lipoprotein cholesterol.

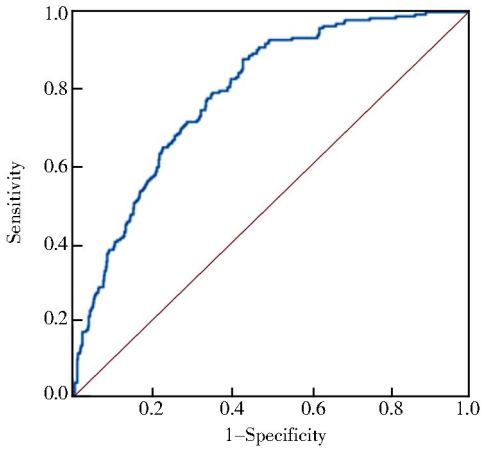

图 1 多指标联合预测 NAFLD 的 ROC 曲线

Figure 1 ROC curve of multi-index combined prediction of NAFLD

NAFLD: non-alcoholic fatty liver disease; ROC: receiver operating characteristic.

甚至肝细胞癌[10]。既往报道也证实年龄与进展性肝纤维化呈正相关[9,11]。近期 Loomba 等[12]的研究表明,随着年龄增长,单纯性肝脏脂肪变性/NASH 1 年后进展为更严重的肝病(肝硬化、肝移植或肝细胞癌)的比例为 9%,第 8 年则达到 39%。三是 NAFLD 病程的自然消退。NALFD 属于可逆性疾病,TG 增加是其重要的危险因素之一(OR = 1.738),而老年人随着年龄增加,TG 水平呈下降趋势[11]。

同样,本研究发现女性、BMI、FBG 及 TG 是老年 NAFLD 的危险因素。女性绝经后雌激素水平下降,从而使脂肪分解代谢减少,这可能是老年女性 NAFLD 的发病机制。高甘油三酯血症、肥胖、高血糖是代谢综合征(metabolic syndrome, MetS)的主要特征。而 NAFLD 与 MetS 常平行出现,互为危险因素。有研究表明,NAFLD 是 MetS 在肝脏的表现[1,3]。MetS、肥胖症和糖尿病同时合并 NAFLD 比例高达 70%~90%。高甘油三酯血症会导致血中游离脂肪酸升高,而血中游离脂肪酸及血糖的升高均可促使胰岛素抵抗,使游离脂肪酸不受抑制地输送至肝脏,从而超出肝脏脂质代谢能力,导致 NAFLD[15]。

最后,本研究 ROC 曲线分析显示,年龄、女性、BMI、FBG 及 TG 多指标联合预测老年人群 NAFLD 的曲线下面积为 0.782(95% CI 0.751~0.811),对疾病有良好的预测价值。

综上所述,本研究分析了老年人群 NAFLD 的临床特点,提示女性、肥胖、糖尿病、血脂异常尤其是 TG 升高是老年人 NAFLD 的危险因素,且老年人群随着年龄的增长,NAFLD 呈自然下降趋势。科学管理 NAFLD 的影响因素对预防疾病的发生、发展具有重大意义。本研究不足之处:(1)纳入对象年龄较大,吸烟、饮酒、运动史、用药史及既往病史等均为患者的自我报告,存在回忆偏倚。(2)腹部超声对轻度脂肪肝敏感性较低,结果可能存在偏倚。

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