

doi: 10.13241/j.cnki.pmb.2021.05.034

瞬时弹性成像技术对非酒精性单纯性脂肪肝的诊断价值 及受控衰减系数与糖脂代谢的相关性分析*

王 雨¹ 王 楠^{2Δ} 韩 璐³ 曲长君⁴ 刘媛媛² 付建军²

(1 西安市中心医院消化科 陕西 西安 710004; 2 西安市中心医院感染科 陕西 西安 710004;

3 西安市中心医院超声诊断科 陕西 西安 710004; 4 西安市中心医院影像科 陕西 西安 710004)

摘要 目的:探讨瞬时弹性成像技术(FibroTouch)对非酒精性单纯性脂肪肝(NAFLD)的诊断价值及受控衰减系数(CAP[™])与糖脂代谢的相关性分析。**方法:**选取 2017 年 8 月~2019 年 8 月期间本院收治的 NAFLD 患者 117 例为研究对象,纳入实验组,另选同期在我院进行健康体检的健康受试者 80 例为对照组。对实验组患者和对照组受试者进行 FibroTouch 检查、腹部彩色多普勒超声检查、糖脂代谢指标生化检查。对比两组受试者的糖脂代谢指标水平、CAP[™]水平、FibroTouch 检查与彩色多普勒超声检查诊断 NAFLD 的准确率,分析 CAP[™]水平与糖脂代谢指标水平的相关性。**结果:**实验组空腹血糖(FPG)、糖化血红蛋白(HbA1C)、空腹胰岛素(FINS)水平均高于对照组($P<0.05$)。实验组甘油三酯(TG)、总胆固醇(TC)、低密度脂蛋白(LDL-C)、载脂蛋白 A(apoA)、CAP[™]水平均高于对照组($P<0.05$)。FibroTouch 检查 NAFLD 的准确率高于彩色多普勒超声检查($P<0.05$)。经 Pearson 相关性分析显示,CAP[™]与各项糖脂代谢指标均呈正相关性($P<0.05$)。**结论:**相比于彩色多普勒超声检查,FibroTouch 用于 NAFLD 的诊断准确率更高,FibroTouch 检查参数 CAP[™]与糖脂代谢指标存在明显的相关性,可辅助用于 NAFLD 的诊断和病情评估。

关键词:非酒精性单纯性脂肪肝;瞬时弹性成像技术;彩色多普勒超声;受控衰减系数;糖脂代谢

中图分类号:R575.5;R445.1 **文献标识码:**A **文章编号:**1673-6273(2021)05-958-04

The Diagnostic Value of Transient Elastography in Nonalcoholic Simple Fatty Liver and the Correlation between Controlled Attenuation Coefficient and Glycolipid Metabolism*

WANG Yu¹, WANG Nan^{2Δ}, HAN Lu³, QU Chang-jun⁴, LIU Yuan-yuan², FU Jian-jun²

(1 Department of Gastroenterology, Xi'an Central Hospital, Xi'an, Shaanxi, 710004, China; 2 Department of Infectious Disease, Xi'an Central Hospital, Xi'an, Shaanxi, 710004, China; 3 Department of Ultrasound Diagnosis, Xi'an Central Hospital, Xi'an, Shaanxi, 710004, China; 4 Department of Imaging, Xi'an Central Hospital, Xi'an, Shaanxi, 710004, China)

ABSTRACT Objective: To study the diagnostic value of FibroTouch(FibroTouch) in nonalcoholic simple fatty liver (NAFLD) and the correlation between controlled attenuation coefficient (cap[™]) and glycolipid metabolism. **Methods:** 117 patients with NAFLD who were admitted to our hospital from August 2017 to August 2019 were selected as the study subjects and 80 healthy subjects who had physical examination in our hospital at the same time were selected as the control group. The patients in the experimental group and the control group were examined by FibroTouch, abdominal color Doppler ultrasound and biochemical examination of glycolipid metabolism. The level of glycolipid metabolism index, cap[™], the accuracy rate of fibroscan and color Doppler ultrasound in diagnosing NAFLD, and the correlation between cap[™] and glycolipid metabolism index were analyzed. **Results:** The levels of Fasting blood glucose (FPG), Glycosylated hemoglobin (HbA1c), and Fasting insulin (fins) in the experimental group were higher than those in the control group ($P<0.05$). Triglyceride (TG), total cholesterol (TC), low density lipoprotein (LDL-C), apolipoprotein A (ApoA) and cap[™] in the experimental group were higher than those in the control group ($P<0.05$). The accuracy of NAFLD in fibrotouch was higher than that in CDUS ($P<0.05$). By Pearson correlation analysis, cap[™] was positively correlated with each index of glycolipid metabolism ($P<0.05$). **Conclusion:** Transient elastography can be used in the diagnosis of nonalcoholic simple fatty liver with higher accuracy than ultrasound. There is a significant correlation between cap[™] and glycolipid metabolism index, it can be used for diagnosis and evaluation of NAFLD.

Key words: Nonalcoholic simple fatty liver; Transient elastography; Color Doppler ultrasound diagnosis; Controlled attenuation coefficient; Glycolipid metabolism

Chinese Library Classification(CLC): R575.5; R445.1 **Document code:** A

Article ID: 1673-6273(2021)05-958-04

* 基金项目:陕西省社会发展科技攻关项目(2016SF-624);西安市科技计划项目[2019115413YX009SF042(4)]

作者简介:王雨(1988-),男,硕士研究生,主治医师,研究方向:肝病及胃肠疾病诊治,E-mail:wangyu19880628@sina.com

Δ 通讯作者:王楠(1988-),女,博士研究生,主治医师,研究方向:脂肪肝临床及基础,E-mail:pumpkingua@126.com

(收稿日期:2020-06-27 接受日期:2020-07-21)

前言

非酒精性单纯性脂肪肝 (Nonalcoholic simple fatty liver, NAFLD) 是临床常见的一类肝脏性疾病, 是指患者排除酒精和其他明确的损肝因素所致的肝细胞内脂肪过度沉积为主要特征的临床病理综合征^[1,2]。根据流行病学调查显示, 随着物质生活水平的提高, 不良生活习惯的增加及饮食结果的改变, NAFLD 的发病率逐年升高, 已成为威胁人类生命健康的重要肝脏性疾病。NAFLD 早期并无明显症状, 而随着疾病的发展后期可并发肝硬化及多种代谢性疾病。因此, 如何进行早期的诊断和治疗, 对于 NAFLD 的防治有重要作用^[3,4]。目前对于 NAFLD 的诊断以组织病理学检查为金标准, 但为有创性检查, 限制了其临床应用。瞬时弹性成像技术 (FibroTouch) 是一种新型的影像学检查方法, 在肝纤维化及慢性肝病诊断上具有临床意义, 并具有无创、无痛、快捷、准确等优点^[5,6]。受控衰减系数 (Controlled attenuation parameter, CAPTM) 是基于 FibroTouch 检测技术的一种无创性的方法, 是一种定量检测指标, 通过 CAPTM 量化指标的判断对于 NAFLD 疾病的诊断发挥重要作用, 目前关于此类方面的研究在临床上的报道较少^[7,8]。为此, 在本研究中以近期收治的 NAFLD 患者为研究对象, 对其实施 FibroTouch 检查, 并与腹部超声检查的准确率进行统计对比。同时对各组受试者的糖脂代谢指标进行检测对比, 分析探讨 FibroTouch 检测的量化指标 CAPTM 与糖脂代谢间的相关性。

1 资料与方法

1.1 临床资料

选取 2017 年 8 月~2019 年 8 月期间本院收治的 NAFLD 患者 117 例为研究对象, 纳入实验组, 纳入标准: ① 患者经定期超声检查及相关血液生化检查确诊为 NAFLD, 符合中华医学会肝病学会脂肪肝和酒精性肝病学会制定的《非酒精性脂肪性肝病诊疗指南》中的相关诊断标准^[9]; ② 患者均可耐受本研究的检查方式; ③ 患者精神状态、认知功能良好, 能够配合调查研究过程的进行; ④ 患者均自愿参与本研究。排除标准: ① 患者并发其他肝脏功能疾病; ② 患者检查前已服用相应治疗药物影响检查结果的判断。另选同期在我院进行健康体检的健康受试者 80 例为对照组, 患者各项生命体征指标检查正常, 无肝脏疾病史。实验组: 男性 63 例、女性 54 例, 年龄 43~78 岁, 平均年龄 (57.34±12.39) 岁, 体质指数 (Body mass index, BMI) 21~28 kg/m², 平均 BMI 为 (25.48±1.98) kg/m²。对照组: 男性 45 例、女性 35 例, 年龄 41~76 岁, 平均年龄 (56.10±12.37) 岁, BMI 为 20~27 kg/m², 平均 BMI 为 (24.91±1.56) kg/m²。两组性别、年龄、BMI 等一般资料无明显差异 ($P>0.05$), 均衡可比。研究方案经医院伦理学委员会审查通过。

1.2 研究方法

1.2.1 糖脂代谢生化指标检查 实验组患者入院后、对照组受试者体检当日采集晨起空腹静脉血约 5 mL, 经 Pic17 型高速离心机 (美国赛默飞世尔公司) 离心分离, 转速 5000 rpm、离心 5 min, 半径 10 cm, 分离得到血清样本, 置于冰箱中保存备用, 采用 AU5800 型全自动生化分析仪 (美国贝克曼公司) 检测患者的血脂指标包括甘油三酯 (triglyceride, TG)、总胆固醇 (total

cholesterol, TC)、低密度脂蛋白 (Low density lipoprotein, LDL-C)、载脂蛋白 A (Apolipoprotein A, apoA) 水平, 采用 HGM-114 型多功能血糖仪检测患者的血糖指标包括空腹血糖 (Fasting blood glucose, FPG)、糖化血红蛋白 (glycosylated hemoglobin, HbA1C)、空腹胰岛素 (Fasting insulin, FINS) 水平, 检测试剂盒均购置于美国西格玛-阿尔德里奇公司, 操作步骤严格按仪器、试剂盒说明书要求进行。

1.2.2 FibroTouch 检查 两组均采用 FibroTouch FT7000 型瞬时弹性成像诊断仪 (海斯凯尔医学技术有限公司) 进行 FibroTouch 检查, 患者取仰卧位, 探查区域包括右腋中线与腋前线间的第 7~9 肋间隙、距离右腋中线下 5 cm 处, 在探头上涂抹耦合剂, 与探查区域皮肤垂直, 并在显示器成像技术的辅助下, 确定最合适的检测部位进行测量。测量深度设置为 2~5 cm, 对患者测量所得到的图像进行分析, 其中直线为 A 波, TM 波显示层状均匀, 表明患者的受检者弹性图显示波形正常, 将测量得到的有效值去平均数得到 CAPTM 值。根据测量的结果, 当 CAPTM 值 > 238 db/m 时确诊为脂肪肝, 当患者的 CAPTM 值 ≤ 238 db/m 时为正常^[10]。

1.2.3 腹部超声检查 采用 HD7 型彩色多普勒超声诊断仪 (飞利浦公司) 对两组受试者进行腹部超声检查, 设置超声探头频率 5.0 MHz, 患者取仰卧位进行探查, 探查部位为患者的整个肝脏区域, 探查时从左至右、从上到下依次探查, 在显示器上密切观察患者的肝脏大小、包膜形态、边界轮廓清晰度以及肝区回声情况, 超声信号的衰减情况。根据超声情况对患者的结果进行判断, NAFLD 超声诊断标准为^[11]: ① 患者肝脏的近场回声呈弥漫型增强, 且强于肾区超声信号; ② 患者的肝内管道结构不清晰; ③ 肝脏的远场信号逐步衰减。

1.3 统计学处理

采用 SPSS 21.0 进行数据处理与分析, 计量资料以 ($\bar{x} \pm s$) 表示, 两组间比较采用 t 检验, 计数资料采用 [n(%)]。组间对比实施 χ^2 检验, 相关性分析采用 Pearson 法, 检验水准 $\alpha=0.05$ 。

2 结果

2.1 两组患者糖代谢指标、CAPTM 水平对比

实验组 FPG、HbA1C、FINS、CAPTM 水平均高于对照组 ($P<0.05$), 见表 1。

2.2 两组患者脂代谢指标水平对比

实验组 TG、TC、LDL-C、apoA 水平均高于对照组 ($P<0.05$), 见表 2。

2.3 FibroTouch 与超声检查准确率对比

FibroTouch 检查 NAFLD 准确率高于彩色多普勒超声检查 ($P<0.05$), 见表 3。

2.4 CAPTM 与糖脂代谢指标相关性分析

经 Pearson 相关性分析, CAPTM 与各项糖脂代谢指标均呈正相关性 ($P<0.05$), 见表 4。

3 讨论

NAFLD 是脂肪肝类疾病中的一种, 是由机体的各种代谢异常引起的肝实质细胞脂肪变性和脂肪贮积为特征的肝脏病变^[12,13]。目前, 随着研究的深入, 人们对于 NAFLD 发病机制有

表 1 两组患者糖代谢指标、CAPTM 水平对比($\bar{x} \pm s$)Table 1 Comparison of glucose metabolism indexes and captm levels between the two groups($\bar{x} \pm s$)

Groups	n	FPG (mmol/L)	HbA1C (mmol/L)	FINS (mU/L)	CAP TM (db/m)
Experience group	117	7.51±0.79	10.98±2.98	17.11±3.34	251.23±17.92
Control group	80	5.11±0.75	6.23±1.78	12.02±2.87	213.56±18.12
t		16.967	6.205	11.190	14.424
P		0.000	0.000	0.000	0.000

表 2 两组患者脂代谢指标对比($\bar{x} \pm s$)Table 2 Comparison of lipid metabolism indexes between the two groups($\bar{x} \pm s$)

Groups	n	TG (mmol/L)	TC (mmol/L)	LDL-C (mmol/L)	apoA (g/L)
Experience group	117	3.98±0.97	7.01±2.34	4.80±1.23	1.59±0.62
Control group	80	2.63±0.72	5.17±1.34	3.32±0.93	0.97±0.45
t		10.606	6.354	9.123	7.667
P		0.000	0.000	0.000	0.000

表 3 FibroTouch 与超声检查准确率对比[n(%)]

Table 3 Comparison of accuracy between fibrotouch and ultrasonic examination[n(%)]

Test method	n	Diagnosis	Undiagnosed
FibroTouch test	117	103 (88.03)	14 (11.97)
Ultrasonography	117	91 (77.78)	26 (22.22)
χ^2	-		4.342
P	-		0.037

表 4 CAPTM 与糖脂代谢指标相关性分析Table 4 Correlation Analysis of captm and glycolipid metabolism index

Index	CAP TM	
	r	P
FPG	0.471	0.011
HbA1C	0.502	0.004
FINS	0.512	0.001
TG	0.487	0.009
TC	0.508	0.003
LDL-C	0.493	0.006
apoA	0.517	0.000

了深刻的认识,肥胖、糖尿病、高脂血症等代谢综合征均是诱发 NAFLD 发生的重要影响因素,相关的临床报道显示肥胖、糖脂代谢功能紊乱与 NAFLD 间有紧密的关联。患者发病后可进一步进展为脂肪肝炎,进一步发展至肝硬化、肝癌等终末期肝病,严重威胁患者的生命健康和生活质量^[14-16]。而 NAFLD 在发病早期无明显症状,极不利于患者病情的诊断和评估。目前对于 NAFLD 的检查主要依赖于病理组织活检和超声检查,其中病理组织活检作为金标准方法,虽有较高的诊断正确率,但作为有创性检查一定程度上限制了其临床广泛应用,影响了患者检查的顺应性^[17-19]。另外,肝脏超声检查也是 NAFLD 等肝脏疾病常用的影像学检查手段,但检查结果受到观察者的主管判断因

素的影响,且对于轻度 NAFLD 患者的诊断灵敏度欠佳。因此,如何提高 NAFLD 患者的早期诊断正确率,寻找一种新的有效的诊断方法对于 NAFLD 患者的早期诊断和病情防治有着重要作用^[20]。

随着研究的不断深入,更多新的检测技术应用于临床,其中 FibroTouch 则是近几年逐步发展成熟的一种新型检测手段,其检测原理是利用弹性波和超声波进行检测,通过仪器探头发射出低频率、低振幅的弹性波,探头上的超声换能器进行连续的超声采集以跟踪弹性波的传播并测量其速度,而弹性波的传播速度与组织的硬度及脂肪度密切相关^[21-23]。因此,可通过对患者的弹性波的传播速率的测量,并将其转化为量化指标 CAPTM,

由此评估患者的肝纤维化和肝脏脂肪病变程度, 从而实现对NAFLD的病情检测与诊断^[24,25]。在本研究中, 对实验组患者分别进行了FibroTouch检查和腹部超声检查, 结果显示经FibroTouch检查的准确率要高于彩色多普勒超声检查, 表明了FibroTouch检查对于NAFLD患者的诊断价值更高。这是因为当患者的脂肪肝病灶大小为不足20%的轻度病变时, 超声的检出NAFLD的能力将大大降低, 并且超声检查只是定性检测的方法, 难以实现对患者脂肪变的定量评估。FibroTouch检查则是形成了CAPTM这一量化指标, 进而更为灵敏的判断患者的脂肪肝程度, 特别是对于轻度脂肪肝患者也有较好的诊断正确率^[26,27]。在实验组与对照组糖脂代谢指标、CAPTM对比中, 实验组患者的FPG、HbA1C、FINS、TG、TC、LDL-C、apoA及CAPTM水平均高于对照组, 表明与正常者对比, NAFLD患者存在明显的糖脂代谢异常, 这是因为NAFLD的发病与肥胖、糖尿病、胰岛素抵抗、高脂血症等代谢综合征有紧密关联, 在多数情况下糖尿病、高脂血症等疾病可诱发加重NAFLD的病情, 因此在NAFLD患者体内表现为糖脂代谢指标异常^[28,29]。进一步经相关性分析显示, FibroTouch检查得到的量化指标CAPTM与患者的糖脂代谢各项指标存在正相关性, 因此经过本项研究调查, 初步表明FibroTouch检查可以在NAFLD疾病的辅助诊疗中发挥重要作用^[30]。

综上所述, 与彩色多普勒超声检查相比, 对于NAFLD患者实施FibroTouch检查有更高的准确率, 且CAPTM与NAFLD患者的糖脂代谢指标呈明显的正相关性。因此, 对于NAFLD患者实施FibroTouch检测, 观察患者的CAPTM水平可辅助NAFLD的疾病诊断, 病情评估和预后效果判断。

参考文献(References)

- [1] Yvelise Ferro, Ilaria Carè, Elisa Mazza, et al. Protein and vitamin B6 intake are associated with liver steatosis assessed by transient elastography, especially in obese individuals [J]. Clin Mol Hepatol, 2017, 23(3): 249-259
- [2] Friedrichrust M, Schoelzel F, Maier S, et al. Severity of coronary artery disease is associated with non-alcoholic fatty liver disease: A single-blinded prospective mono-center study[J]. Plos One, 2017, 12(10): 6720-6727
- [3] Guo Y, Dong C, Lin H, et al. Evaluation of Non-alcoholic Fatty Liver Disease Using Acoustic Radiation Force Impulse Imaging Elastography in Rat Models [J]. Ultrasound in Medicine & Biology, 2017, 43(11): 2619
- [4] 卢莎莎, 郭晓林. 受控衰减参数对非酒精性脂肪性肝病患者肝脂肪变性无创诊断准确性的系统性回顾和Meta分析[J]. 临床肝胆病杂志, 2019, 31(6): 1230-1230
- [5] Jacob Søholm, Maja Sofie Thiele, Peer Brehm Christensen. Controlled attenuation parameter is a novel technique in screening for non-alcoholic fatty liver disease [J]. Ugeskrift for Laeger, 2018, 180(5): 281-286
- [6] Zeng J, Cai S, Liu J, et al. Dynamic Changes in Liver Stiffness Measured by Transient Elastography Predict Clinical Outcomes Among Patients With Chronic Hepatitis B [J]. J Ultrasound Med, 2017, 36(2): 261-268
- [7] 杨光, 窦琳, 唐蔚青, 等. 高脂饮食和西方饮食诱导的非酒精性脂肪肝小鼠模型的特征比较 [J]. 医学分子生物学杂志, 2018, 15(1): 281-284
- [8] Sporea I. Ultrasound and liver elastography - tools for detection and quantification of severity in Nonalcoholic Fatty Liver Disease (NAFLD) in general population [J]. Medical Ultrasonography, 2017, 19(3): 247-255
- [9] 中华医学会肝病学分会脂肪肝和酒精性肝病学组. 非酒精性脂肪性肝病诊疗指南(2010年修订版)[J]. 中华肝脏病杂志, 2010, 18(3): 163-166
- [10] 陈虹燕, 邓婉萍, 吴嘉嘉, 等. 瞬时弹性成像指标受控衰减参数与代谢综合征组分的相关分析[J]. 中华内分泌代谢杂志, 2019, 35(6): 468-474
- [11] Ignatius Bima Prasetya, Irsan Hasan, Wismandari Wisnu, et al. Prevalence and Profile of Fibrosis in Diabetic Patients with Non-alcoholic Fatty Liver Disease and the Associated Factors[J]. Acta Medica Indonesiana, 2017, 49(2): 91-98
- [12] 鲍轶. 免疫细胞在非酒精性脂肪性肝病中的作用机制及研究进展 [J]. 中华肝脏病杂志, 2017, 25(7): 553-556
- [13] Sugihara T, Koda M, Matono T, et al. Risk Assessment of Hepatocellular Carcinoma in General Population by Liver Stiffness in Combination with Controlled Attenuation Parameter using Transient Elastography: A Cross Sectional Study [J]. Yonago Acta Medica, 2017, 60(2): 106-112
- [14] 杨秀珍, 肖丽, 咸建春, 等. 瞬时弹性成像技术对非酒精性脂肪性肝病的诊断及相关因素分析 [J]. 中华全科医师杂志, 2018, 17(7): 548-550
- [15] 庞鹏宇, 任小宁, 王沁易, 等. 2型糖尿病伴脂肪肝患者血浆FGF21水平与肥胖、脂代谢及胰岛素抵抗的相关性[J]. 现代生物医学进展, 2016, 16(27): 5340-5342, 5308
- [16] Bril F, Millán L, Kalavalapalli S, et al. Use of a metabolomic approach to non-invasively diagnose non-alcoholic fatty liver disease in patients with type 2 diabetes mellitus [J]. Diabetes Obes Metab, 2018, 20(7): 1702-1709
- [17] 陈容容, 林志辉. 瞬时弹性成像技术和超声诊断非酒精性脂肪性肝病的一致性分析[J]. 海峡预防医学杂志, 2019, 29(1): 105-107
- [18] Guo L, Zheng L, Hu L, et al. Transient Elastography (FibroTouch) Performs Better Than Non-Invasive Markers in Assessing Liver Fibrosis and Cirrhosis in Autoimmune Hepatitis Patients [J]. Med Sci Monit, 2017, 23(12): 5106-5112
- [19] Mahady SE, Macaskill P, Craig JC, et al. Diagnostic Accuracy of Noninvasive Fibrosis Scores in a Population of Individuals With a Low Prevalence of Fibrosis [J]. Clin Gastroenterol Hepatol, 2017, 15(9): 1453-1460.e1
- [20] Khaled K Aldossari, Dhalia Ghoraba, Sara Mahmoud Abdelhakam, et al. Clinicopathological and immunological characteristics and outcome of concomitant coeliac disease and non-alcoholic fatty liver disease in adults: a large prospective longitudinal study[J]. Bmj Open Gastroenterology, 2018, 5(1): 123-129
- [21] Zobair M. Younossi, Rohit Loomba, Quentin M. Anstee, et al. Diagnostic Modalities for Non-alcoholic Fatty Liver Disease (NAFLD), Non-alcoholic Steatohepatitis (NASH) and Associated Fibrosis[J]. Hepatology, 2017, 68(1): 182-189

- [20] Khasawneh MA, Ugarte ML, Srivastian B, et al. Role of gastrografin challenge in early postoperative small bowel obstruction [J]. *J Gastrointest Surg*, 2014, 18(2): 363-8
- [21] Burneikis D, Stocchi L, Steiger E, et al. Parenteral Nutrition Instead of Early Reoperation in the Management of Early Postoperative Small Bowel Obstruction[J]. *J Gastrointest Surg*, 2020, 24(1): 109-114
- [22] Lee SY, Park KJ, Ryou SB, et al. Early postoperative small bowel obstruction is an independent risk factor for subsequent adhesive small bowel obstruction in patients undergoing open colectomy [J]. *World J Surg*, 2014, 38(11): 3007-3014
- [23] Tan YQ, Chen HW, Li J, et al. Efficacy, Chemical Constituents, and Pharmacological Actions of Radix Paeoniae Rubra and Radix Paeoniae Alba[J]. *Front Pharmacol*, 2020, 11(2): 1054
- [24] Fu Y, Yan M, Zeng X, et al. Meta-analysis of the efficacy of Xuebijing combined with hemoperfusion in treating paraquat poisoning[J]. *Ann Palliat Med*, 2020, 9(4): 2152-2162
- [25] Li C, Wang P, Zhang L, et al. Efficacy and safety of Xuebijing injection (a Chinese patent) for sepsis: A meta-analysis of randomized controlled trials[J]. *J Ethnopharmacol*, 2018, 224(1): 512-521
- [26] Qian L, Huang J, Qin H. Probiotics and dietary intervention modulate the colonic mucosa-associated microbiota in high-fat diet populations [J]. *Turk J Gastroenterol*, 2020, 31(4): 295-304
- [27] Hibberd AA, Lyra A, Ouwehand AC, et al. Intestinal microbiota is altered in patients with colon cancer and modified by probiotic intervention[J]. *BMJ Open Gastroenterol*, 2017, 4(1): e000145
- [28] Musa AE, Shabeeb D, Alhilfi HSQ. Protective Effect of Melatonin Against Radiotherapy-Induced Small Intestinal Oxidative Stress: Biochemical Evaluation[J]. *Medicina (Kaunas)*, 2019, 55(6): 308
- [29] Poprac P, Jomova K, Simunkova M, et al. Targeting Free Radicals in Oxidative Stress-Related Human Diseases [J]. *Trends Pharmacol Sci*, 2017, 38(7): 592-607
- [30] Guo Y, Li H, Liu Z, et al. Impaired intestinal barrier function in a mouse model of hyperuricemia[J]. *Mol Med Rep*, 2019, 20(4): 3292-3300
- [31] Xu Q, Liu J, Wang Z, et al. Heat stress-induced disruption of endothelial barrier function is via PAR1 signaling and suppressed by Xuebijing injection[J]. *PLoS One*, 2015, 10(2): e0118057
- [32] Jakubczyk D, Leszczyńska K, Górka S. The Effectiveness of Probiotics in the Treatment of Inflammatory Bowel Disease (IBD)-A Critical Review[J]. *Nutrients*, 2020, 12(7): 1973
- [33] Shieh A, Epeldegui M, Karlamangla AS, et al. Gut permeability, inflammation, and bone density across the menopause transition [J]. *JCI Insight*, 2020, 5(2): e134092
- [34] Zhang Q, Li J, Liang X, et al. The preventive effect of Chinese herbal preparation Xuebijing against hyperactive inflammation after hepatopancreato-biliary surgery[J]. *Ann Transl Med*, 2019, 7(18): 481
- [35] Chen X, Feng Y, Shen X, et al. Anti-sepsis protection of Xuebijing injection is mediated by differential regulation of pro- and anti-inflammatory Th17 and T regulatory cells in a murine model of polymicrobial sepsis[J]. *J Ethnopharmacol*, 2018, 211(1): 358-365

(上接第 961 页)

- [22] Wai Ling Leong, Lee Lai Lai, Nik Raihan Nik Mustapha, et al. Comparing point shear wave elastography (ElastPQ) and transient elastography for diagnosis of fibrosis stage in nonalcoholic fatty liver disease [J]. *Journal of Gastroenterology and Hepatology*, 2019, 29(11): 281-284
- [23] 马丽雪, 张宇虹, 苏本利, 等. 应用 FibroTouch 技术评价 2 型糖尿病患者肝脏脂肪变和纤维化程度及二者相关性[J]. *中国临床医学影像杂志*, 2018, 29(9): 636-639
- [24] 丁智勇, 卜乐, 鲁鸿燕, 等. 非酒精性脂肪性肝病者血清维生素 A 水平、肝脏脂肪含量与胰岛素抵抗的相关性分析[J]. *临床肝胆病杂志*, 2017, 33(12): 290-293
- [25] Christian A. Hudert, Heiko Tzschätzsch, Jing Guo, et al. US Time-Harmonic Elastography: Detection of Liver Fibrosis in Adolescents with Extreme Obesity with Nonalcoholic Fatty Liver Disease [J]. *Radiology*, 2018, 288(1): 928-935
- [26] Harshit Garg, Sandeep Aggarwal, Shalimar, et al. Utility of Transient Elastography (FibroTouch) and Impact of Bariatric Surgery on Non-Alcoholic Fatty Liver Disease (NAFLD) in Morbidly Obese Patients [J]. *Surgery for Obesity & Related Diseases*, 2017, 14(1): 280-286
- [27] 陈默, 王满才, 倪睿, 等. 益生菌在非酒精性脂肪肝病治疗中的作用 [J]. *中华肝脏病杂志*, 2017, 25(1): 77-80
- [28] Toshihide Shima, Kyoko Sakai, Hirohisa Oya, et al. Diagnostic accuracy of combined biomarker measurements and vibration-controlled transient elastography (VCTE) for predicting fibrosis stage of non-alcoholic fatty liver disease [J]. *Journal of Gastroenterology*, 2019, 29(12): 389-397
- [29] SeyedSaeed Seyedian, Eskandar Hajiani, SeyedJalal Hashemi, et al. Relationship between serum ferritin level and transient elastography findings among patients with nonalcoholic fatty liver disease [J]. *Journal of Family Medicine & Primary Care*, 2017, 6(4): 750-757
- [30] Thomson Chi Wang Loong, Jeremy Lok Wei, Jonathan Chung Fai Leung, et al. Application of the combined FibroMeter vibration controlled transient elastography algorithm in Chinese patients with non alcoholic fatty liver disease [J]. *Journal of Gastroenterology & Hepatology*, 2017, 32(7): 281-287