临床经验 CLINICAL PRACTICE

血清谷丙转氨酶在正常范围内对非酒精性脂肪性肝病的预测

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Predictive significance of normal serum alanine aminotransferase in patients with nonalcoholic fatty liver disease

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Abstract

AIM: To investigate the predictive significance of normal serum alanine aminotransferase (ALT) in patients with nonalcoholic fatty liver disease (NAFLD).

METHODS: Ultrasonography was used to diagnose cholecystolithiasis in 4 076 subjects who underwent routine health examination in the People's Hospital of Hunan Province from April 2006 to January 2010. A total of 2 830 subjects were enrolled, of them 1 367 were followed up for 1-3 years. Body height, body weight, blood pressure, lipid profile, ALT, white blood cell (WBC) count, and fasting blood glucose were tested. Individuals with normal serum ALT were divided into four groups according to the quartile of ALT from the lowest to the highest: A, B, C and D. Those with normal serum ALT were also divided into four groups according to the quartile of ALT from the lowest to the highest: E, F, G and H.

RESULTS: Compared with subjects without NAFLD, the mean level of ALT in patients with NAFLD was higher (36.57 ± 26.17 vs 25.29 ± 24.27, $P < 0.05$). Compared with group A, the prevalence of NAFLD was higher in group D (44.26% vs 19.38%, $P < 0.05$). Compared with group A, the levels of diastolic blood pressure (125.93 ± 18.43 vs 123.00 ± 19.81, $P < 0.05$), systolic blood pressure (80.77 ± 11.61 vs 76.65 ± 11.36, $P < 0.05$), body mass index (24.94 ± 2.80 vs 22.67 ± 3.01, $P < 0.05$), triglyceride (2.00 ± 1.47 vs 1.41 ± 0.89, $P < 0.05$), fasting blood glucose (5.38 ± 1.53 vs 5.16 ± 1.26, $P < 0.05$), WBC count (6.43 ± 151 vs 5.99 ± 1.50, $P < 0.05$) were much higher in group D, while the level of high density lipoprotein was significantly lower (1.36 ± 0.36 vs 1.50 ± 0.39, $P < 0.05$). During 1 to 3 years of follow-up, the incidence of NAFLD was significantly higher in group H than in group E (28.67% vs 13.04%, OR = 2.679; 95% CI: 1.610-4.457; $P < 0.05$), in group G than in group E (26.67% vs 13.04%, OR = 2.424; 95% CI: 1.494-3.935; $P < 0.05$), and in group F than in group E (20.09% vs 13.04%, OR = 1.676; 95% CI: 1.024-2.745; $P < 0.05$).

CONCLUSION: The levels of serum ALT in patients with NAFLD are higher than those without NAFLD. Even within normal range, elevated ALT can be used as a predictive parameter for NAFLD.

Key Words: Nonalcoholic fatty liver disease; Alanine aminotransferase; Insulin resistance

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摘要

目的: 分析血清谷丙转氨酶(ALT)与非酒精性脂肪性肝病(NAFLD)之间的关系, 探讨正常范围ALT对NAFLD发生的预测价值.

方法: 选择2006-04-07/2010-01-09湖南省人民医院体检个体共4 076例, 排除过量饮酒、乙肝标志物阳性、严重感染及MS资料不全者, 共2 830例纳入研究, 其中1 367例在1-3年后再次体检. B超诊断NAFLD, 记录身高、体质量、血压、血脂、外周血白细胞计数、尿酸、空腹血糖及ALT. 将ALT正常个体(n = 2 445)四分位为A、B、C、D 4组, 上四分位组为D组, 下四分位组为A组, 比较4组代谢特征. 将随访个体(n = 1 367)中ALT正常个体(n = 1 183)四分位为E、F、G、H 4组, 上四分位组为H组, 下四分位组为E组, 比较随访后4组NAFLD发病情况.

结果: 与非NAFLD组相比, NAFLD组患者ALT升高(36.57±26.17 vs 25.29±24.27, $P<0.05$); 与A组比较, D组NAFLD患病率增高(44.26% vs 19.38%, $P<0.05$); 与A组比较, D组收缩压(125.93±18.43 vs 123.00±19.81, $P<0.05$)、舒张压(80.77±11.61 vs 76.65±11.36, $P<0.05$)、体质量指数(24.94±2.80 vs 22.67±3.01, $P<0.05$)、三酰甘油(2.00±1.47 vs 1.41±0.89, $P<0.05$)、空腹血糖(5.38±1.53 vs 5.16±1.26, $P<0.05$)及外周血白细胞计数增高(6.43±151 vs 5.99±1.50, $P<0.05$), 高密度脂蛋白降低(1.36±0.36 vs 1.50±0.39, $P<0.05$). 随访1-3年后(n = 1 367), H组NAFLD发病率高于E组(28.67% vs 13.04%, OR = 2.679, 95%CI: 1.610-4.457, $P<0.05$). G组NAFLD发病率高于E组(26.67% vs 13.04%, OR = 2.424, 95%CI: 1.494-3.935, $P<0.05$). F组NAFLD发病率高于E组(20.09% vs 13.04%, OR = 1.676, 95%CI: 1.024-2.745, $P<0.05$).

结论: NAFLD患者血清谷丙转氨酶升高. 在正常范围内, ALT的升高可预测NAFLD的发生.

关键词: 非酒精性脂肪性肝病; 血清谷丙转氨酶; 胰岛素抵抗

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0 引言

非酒精性脂肪性肝病(nonalcoholic fatty liver disease, NAFLD)是指除外酒精和其他明确的损肝因素所致的, 以弥漫性肝细胞大泡性脂肪变为主要特征的临床病理综合征. 有研究认为, NAFLD的发生与肝脏胰岛素抵抗密切相关[1,2], 而血清谷丙转氨酶(alanine aminotransferase, ALT)的升高是反映肝脏损伤的标志之一. ALT是否可作为对NAFLD发生的预测指标? 目前仍不清楚. 本研究通过分析2 830例湖南省人民医院体检人群临床及生化资料, 阐明NAFLD患者血清ALT变化; 对1 367例患者随访1-3年, 探讨ALT对NAFLD发病的预测价值.

1 材料和方法

1.1 材料 2006-04-07/2010-01-09湖南省人民医院体检个体4 067例, 排除377例乙肝标志物阳性、860例代谢综合征代谢组分资料缺失及过量饮酒者, 共2 830例纳入研究. NAFLD诊断采用南京会议定义[3], B超进行诊断. 排除标准包括: (1)过量饮酒(每日折含乙醇量>50 g或每周乙醇摄入量>350 g); (2)乙型肝炎标志物阳性: HbsAg、HbeAg、HbeAb、HbcAb及HbcAb-IgM中任意一项阳性; (3)代谢综合征代谢组分资料缺失者: 体质量指数(body mass index, BMI)、血压、血糖及血脂任一资料缺失; (4)严重感染或处于应激状态患者.

1.2 方法

1.2.1 分组: 将2 445例血清ALT正常个体, 根据血清ALT水平进行四分位数分组, A组(n = 614): 血清ALT水平≤15.7 U/L; B组(n = 621): 15.7 U/L<血清ALT水平≤21.0 U/L; C组(n = 600): 21.0 U/L<血清ALT水平≤28.5 U/L; D组(n = 610): 血清ALT水平>28.5 U/L. 将1 183例随访的ALT正常个体, 根据血清ALT水平进行四分位数分组, E组(n = 301): 血清ALT水平≤16.1 U/L; F组(n = 293): 16.1 U/L<血清ALT水平≤21.6 U/L; G组(n = 303): 21.6 U/L<血清ALT水平≤29.0 U/L; H组(n = 286): 29.0 U/L<血清ALT水平≤45.0 U/L.

1.2.2 检测: 研究对象于清晨空腹状态行肝脏B超检查, 测量身高、体质量、血压. 计算体质量指数, BMI = 体质量(kg)/身高^2(m^2). 采空腹静脉血用于检测空腹血糖、血脂、ALT、尿酸、外周血白细胞计数及乙肝三对. 空腹血糖、血

表 1　正常范围内不同血清ALT水平组代谢特征 (mean ± SD)

代谢特征	A组(n = 614)	B组(n = 621)	C组(n = 600)	D组(n = 610)
BMI(kg/m^2)	22.67 ± 3.01	23.63 ± 2.90[a]	24.28 ± 2.82[ac]	24.94 ± 2.80[ace]
收缩压(mmHg)	123.00 ± 19.81	124.89 ± 18.30	125.81 ± 18.05	125.93 ± 18.43[a]
舒缩压(mmHg)	76.65 ± 11.36	78.46 ± 10.88[a]	79.37 ± 11.46[a]	80.77 ± 11.61[ace]
三酰甘油(mmol/L)	1.41 ± 0.89	1.52 ± 0.78	1.93 ± 1.52[ac]	2.00 ± 1.47[ac]
高密度脂蛋白(mmol/L)	1.50 ± 0.39	1.47 ± 0.37	1.42 ± 0.40[ac]	1.36 ± 0.36[ace]
空腹血糖(mmol/L)	5.16 ± 1.26	5.18 ± 1.16	5.44 ± 1.48[ac]	5.38 ± 1.53[a]
外周血白细胞计数(10^9/L)	5.99 ± 1.50	6.10 ± 1.46	6.28 ± 1.68[ac]	6.43 ± 151[ac]

[a]$P<0.05$ vs A组; [c]$P<0.05$ vs B组; [E]$P<0.05$ vs C组.

表 2　随访1-3年后, 正常范围ALT水平四分位分组NAFLD发病率

分组	随访后发生NAFLD n = 172(%)	随访后未发生NAFLD n = 645(%)	OR值	95%CI	P值
E	33(13.04)	220(86.96)	–	–	–
F	44(20.09)	175(79.91)	1.676	1.024-2.745	0.039
G	52(26.67)	143(73.33)	2.424	1.494-3.935	0.000
H	43(28.67)	107(71.33)	2.679	1.610-4.457	0.000

脂、谷丙转氨酶、尿酸检测采用日立7600全自动生化分析仪; 外周血白细胞计数检测采用Byer 2120全自动血细胞分析仪; 乙肝三对检测采用Micro Labfame全自动酶免分析仪. 肝脏B超检测采用东芝TOSHIBA彩超, 探头频率3.5 MHZ.

统计学处理　采用SPSS13.0统计软件. 计量资料以mean±SD表示, 两样本均数的比较采用t检验, 多样本均数的比较采用单因素方差分析, 组间两两比较采用LSD检验; 计数资料以百分率(%)表示, 各组之间的比较采用χ^2检验; $P<0.05$认为差异具有统计学意义.

2 结果

2.1 NAFLD患者血清ALT变化　NAFLD组(n = 979)血清ALT水平为36.57 U/L±26.17 U/L, 非NAFLD组(n = 1 851)血清ALT水平为25.29 U/L±24.27 U/L, NAFLD组与非NAFLD组比较, 差异有统计学意义($P<0.05$).

2.2 正常范围内, 不同血清ALT水平个体发生NAFLD情况　A组NAFLD患病率为19.38%(n = 119), B组NAFLD患病率为24.96%(n = 155), C组NAFLD患病率为33.67%(n = 202), D组NAFLD患病率为44.26%(n = 270), D组较A组NAFLD患病率增高, 差异有统计学意义($P<0.05$). D组BMI、收缩压、舒张压、三酰甘油、外周血白细胞计数及空腹血糖较A组明显升高, 高密度脂

蛋白降低, 差异有统计学意义($P<0.05$, 表1).

2.3 血清ALT水平预测NAFLD的发生　1 367例个体在1-3年内随访, 其中第1次检查时184例血清ALT水平高于正常, 占13.46%. 随访14.81 mo±6.05 mo后, H组150例体检个体中, 43例新发NAFLD, 发病率为28.67%; 随访14.77 mo±7.32 mo后, G组195例体检个体中, 52例新发NAFLD, 发病率为26.67%; 随访15.11 mo±7.21 mo后, F组219例体检个体中, 44例新发NAFLD, 发病率为20.09%; 随访14.97 mo±6.99 mo后, E组253例体检个体中, 33例新发NAFLD, 发病率为13.04%. 各组间随访时间差异无统计学意义($P>0.05$). H组NAFLD发病率高于E组, 差异有统计学意义($P<0.05$), H组个体中28.67%发生NAFLD(OR = 2.679, 95%CI: 1.610-4.457, $P<0.05$); G组NAFLD发病率高于E组, 差异有统计学意义($P<0.05$), G组个体中26.67%发生NAFLD(OR = 2.424, 95%CI: 1.494-3.935, $P<0.05$); F组NAFLD发病率高于E组, 差异有统计学意义($P<0.05$), F组个体中20.09%发生NAFLD(OR = 1.676, 95%CI: 1.024-2.745, $P<0.05$, 表2).

3 讨论

近年来随着人们生活水平的提高, NAFLD的发病率显著增高[4-6], NAFLD的不仅可危害肝脏, 还

可促进心脑血管疾病的发生. 血清ALT升高是反映肝脏损伤的标志之一, 在临床上较常见. 探讨正常范围内血清ALT升高对NAFLD发生的预测作用具有重要临床价值.

ALT正常主要分布于肝细胞质, 谷草转氨酶主要分布于肝细胞线粒体, 不同的转氨酶升高反映肝脏受损的程度亦有不同. 肝脏的轻度损伤, 以肝细胞膜通透性增强为主, 此时血清ALT增高. 如伴有肝线粒体的破坏, 即可出现谷草转氨酶也明显升高. 随着世界范围肥胖患病率的增加, NAFLD被认为是无明显诱因肝酶异常的最常见原因之一[7]. 而在ALT、谷草转氨酶及谷酰转肽酶等肝酶中, ALT与肝脏脂肪聚集关系最为密切[8]. 本研究结果显示, NAFLD患者血清ALT水平升高明显, 即使处于正常范围内, 随着血清ALT水平的升高, BMI、收缩压、舒张压、三酰甘油、外周血白细胞计数及空腹血糖升高, 高密度脂蛋白降低, 且NAFLD患病率亦升高明显. 正常范围内上四分位血清ALT可预测NAFLD的发生(OR = 2.679). NAFLD患者血清ALT升高[9,10], 具体机制尚不清楚. 而正常参考范围内血清ALT的升高与NAFLD密切相关[11]. 而韩国一项对健康体检人群的研究同样发现, 正常参考范围内血清ALT的升高可预测NAFLD的发生[12]. 提示血清ALT的升高并非仅仅为NAFLD作用肝脏的结果, 其发生可能早于NAFLD, 是肝细胞早期损伤的指标, 可预测NAFLD的发生, 是NAFLD的早期表现之一.

血清ALT的升高可能早于NAFLD的发生, 正常范围内血清ALT的升高对NAFLD具有预测意义, 需进行早期干预.

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