

· 临床研究 ·

维、汉民族冠心病住院患者胰岛素敏感性与多种危险因素分析

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【摘要】目的 探讨维、汉民族冠心病患者胰岛素敏感性的异质性和多种危险因素的分布特点。**方法** 选取2001年至2002年新疆维吾尔自治区人民医院住院的冠心病患者164例(维吾尔族50例, 汉族114例)和对照组71例(维族35例, 汉族36例), 进行葡萄糖耐量试验和胰岛素释放试验, 运用稳态模式法评价胰岛素敏感性(HOMA IS)。**结果** (1)维、汉民族冠心病患者胰岛素敏感性较对照组明显减低[维族(204.02 ± 180.43) vs (409.14 ± 181.06), 汉族(258.09 ± 105.66) vs (479.09 ± 200.97), $P < 0.05$]; 冠心病组代谢综合征患病率明显增多[维族(54.0% vs 25.7%), 汉族(66.7% vs 22.7%), $P < 0.05$]。糖尿病患病率明显高于对照组[维族(52.0% vs 0.0%), 汉族(64.0% vs 0.0%), $P < 0.01$]。冠心病组1h胰岛素水平下降和2h血糖水平升高($P < 0.05$)。其余各项虽有变化, 但差异无统计学意义。代谢综合征患病率和胰岛素敏感性变化无论在对照组或冠心病组内维、汉民族间差异均无统计学意义。(2)维、汉民族冠心病患者存在体质量[(78.06 ± 12.69) vs (72.32 ± 12.03) kg]和体质量指数[BMI(27.29 ± 3.53) vs (25.61 ± 3.42) kg/m²]的显著差异($P < 0.01$)。对照组中维、汉两个民族各种危险因素差异无统计学意义($P > 0.05$)。(3)多个危险因素对冠心病危险性比较(logistic回归分析)看出, 饮酒、糖尿病、高血压与冠心病正相关($P < 0.05$)。高密度脂蛋白胆固醇与冠心病呈负相关($P < 0.05$)。**结论** 住院患者中维、汉民族冠心病存在较低的胰岛素敏感性和较高的代谢综合征、糖尿病患病率; 维族冠心病患者肥胖显著。该地区饮酒、糖尿病、高血压是维、汉民族冠心病的危险因素。

【关键词】 维吾尔族; 汉族; 冠状动脉疾病; 胰岛素敏感性; 代谢疾病; 糖尿病; 体质量指数

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Insulin sensitivity and cardiovascular risk factors in Uygur and Han inpatients with coronary heart diseases

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【Abstract】 Objective To explore the heterogeneity of insulin sensitivity (IS) and the distribution of cardiovascular risk factors in the races of the Uygur and Han patients with coronary heart diseases (CHD) in Urumqi. **Methods** A total of 164 CHD patients (50 Uygurs and 114 Hans) hospitalized in the Autonomous Regional Hospital from 2001 to 2002 were recruited in this study. Another 71 healthy individuals (35 Uygurs and 36 Hans) served as normal controls. Oral glucose tolerance test (OGTT) and insulin release test were used to measure the concentrations of blood glucose and insulin before and after oral 75 g glucose in 0, 0.5, 1, 2 and 3h. The Homeostasis Model Assessment of Insulin Sensitivity (HOMA IS) was calculated by the HOMA model. **Results** The IS was significantly lower in the CHD patients than in the normal controls [the Uygurs: (204.02 ± 180.43) vs (409.14 ± 181.06); the Hans: (258.09 ± 105.66) vs (479.09 ± 200.97); $P < 0.05$]. The CHD patients also had higher morbidities of metabolic syndrome (the Uygurs: 54% vs 25.7%; the Hans: 66.7% vs 22.7%; $P < 0.05$) and of diabetes mellitus (the Uygurs: 52.0% vs 0.0%; the Hans: 64.0% vs 0.0%, $P < 0.01$) when compared with the normal controls. The CHD patients had significantly decreased 1h insulin and increased 2h glucose than the normal controls ($P < 0.05$). No significant difference was found in other indices between the CHD patients and normal controls. There was no difference in the morbidity of metabolic syndrome and IS between the 2 ethnics no matter for CHD patients or the normal controls. Significant differences were seen in the body mass [(78.06 ± 12.69) vs (72.32 ± 12.03)kg, $P < 0.01$] and body mass index [BMI(27.29 ± 3.53) vs (25.61 ± 3.42)kg/m², $P < 0.01$] in the two ethnic patients with CHD. But no such difference was

seen in the normal controls. Logistic regression analysis showed that alcohol drinking ($OR=2.532$), diabetes mellitus ($OR=2.466$), and hypertension ($OR=2.355$) had positive correlation with CHD ($P < 0.05$), and high-density lipoprotein cholesterol had negative correlation with CHD ($P < 0.05$). **Conclusion** Both Uygur and Han CHD patients in Urumqi have lower IS and higher morbidity of metabolic syndrome and diabetes mellitus. The Uygur CHD patients have higher prevalence of obesity. Alcohol drinking, diabetes mellitus, and hypertension are risk factors of CHD in the two ethnics in the Xinjiang Uygur Autonomous Region.

【Key words】 Uygur nationality; Han nationality; coronary disease; insulin sensitivity; metabolic diseases; diabetes mellitus; body mass index

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美国国家胆固醇教育计划成人治疗组第三次指南 (National Cholesterol Education Program Adult Treatment Panel III, NCEP ATP-III) 确定糖尿病为冠心病的等危症。大量研究证明糖尿病是冠心病的独立危险因素, 胰岛素抵抗 (insulin resistance, IR) 与心血管疾病密切相关。胰岛素敏感性 (insulin sensitivity, IS) 的降低, 即IR是超重伴发高脂血症、糖尿病和高血压的主要影响因素, 对心血管病危险因素的影响存在种族、性别、年龄差异, 并受超重程度的影响^[1-3]。关于新疆维吾尔和汉民族IR的研究甚少, 为此我们对该地区冠心病患者进行研究, 以了解维、汉民族间IR的异质性和多种危险因素的分布特点。

1 对象与方法

1.1 研究对象

随机选取2001年至2002年新疆维吾尔自治区人民医院内科(心脏、内分泌和干保科)住院患者。研究对象235例(维吾尔族85例, 汉族150例), 其中男性159例, 女性76例。其中正常对照组71例(维吾尔族35例, 汉族36例), 冠心病组164例(维吾尔族50例, 汉族114例), 心绞痛者64例, 心肌梗死者52例, 合并高血压者81例, 合并2型糖尿病者99例(非胰岛素治疗)。冠心病的诊断根据1979年世界卫生组织颁布的缺血性心脏病定义。研究对象在收住院后, 经病史、体检、心电图、心脏超声以及冠状动脉造影或心脏放射性核素检查如发射型计算机断层摄像(emission computed tomography, ECT), 证实为冠心病或非冠心病。

1.2 方法

1.2.1 口服葡萄糖糖耐量(oral glucose tolerance test, OGTT)试验和胰岛素释放试验 入院1周内, 研究对象禁食12h后, 清晨口服75g葡萄糖, 采集空腹和糖负荷后30, 60, 120, 180min静脉血, 测定血糖和胰岛素浓度。同时测定空腹总胆固醇(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)、甘油三酯(triglycerides, TG)及脂蛋白(a)[lipoprotein(a), Lp(a)]、血尿酸(blood uric acid, BUA)、谷氨酰氨转肽酶(gamma glutamyl transpeptidase, GGT)等。使用美国Beckman公司全自动生化仪, 采用酶法完成TC, HDL-C, TG和血糖等检测。根据Friedewald公式: $LDL-C = TC - HDL-C - TG / 2.2$ 计算LDL-C值(mmol/L)。胰岛素测定使用放射免疫法。

1.2.2 OGTT试验检测方法 (1) 在OGTT检查前3d内保证碳水化合物摄入 $\geq 150\text{g/d}$; (2) 试验当天空腹时间至少12h, 没有过强负荷的运动; (3) 要求受试者口服溶于300ml水内的75g葡萄糖粉, 3~5min内喝完糖水; (4) 两次采血期间应安静休息, 禁止剧烈活动、饮食、喝水、喝茶、吸烟以及饮酒。(5) 试验前3~7d, 停用可能影响血糖的药物, 如避孕药、利尿药、苯妥英钠等。

1.2.3 代谢综合征的临床判断(1998年世界卫生组织工作定义) 糖耐量减低或糖尿病, 和(或)IR(由高胰岛素葡萄糖钳夹技术测定的葡萄糖利用率低于下位1/4位点), 并且同时存在下列 ≥ 2 种的其他情况: (1) 高血压 $\geq 140/90\text{mmHg}$ (1mmHg=0.133kPa); (2) 高TG $\geq 1.7\text{mmol/L}$, 和(或)低HDL-C男性 $< 0.9\text{mmol/L}$, 女性 $< 1.0\text{mmol/L}$; (3) 中心性肥胖腰/臀围比(waist-hipratio, WHR)男性 > 0.9 , 女性 > 0.85 和(或)体质指数(body mass index, BMI) > 30 ; (4) 微量白蛋白尿 尿白蛋白排泄率 $\geq 20\mu\text{g/min}$ 或白蛋白/肌酐比值 $\geq 30\text{mg/h}$ 。

1.2.4 运用数学模型[稳态模式评估法(HOMA)^[4]]计算IR指数(Homeostasis Model Assessment of Insulin Resistance, HOMA IR)和IS指数(HOMA of insulin Sensitivity, HOMA IS)及李光伟^[5]胰岛素敏感指数 (1) HOMA IR=(空腹胰岛素mU/L×空腹血糖mmol/L) $\div 22.5$; (2) HOMA IS=20×空腹胰岛素mU/L \div (空腹血糖mmol/L-3.5); (3) 李光伟胰岛素敏感指数CNL IS=1 \div (空腹胰岛素mU/L

×空腹血糖mmol/L)。

1.2.5 体脂含量及分布 总体脂含量以BMI表示, $BMI = \text{体质量 (kg)} / \text{身高 (m}^2\text{)}$; 局部体脂含量以腰围(即腰部骨性胸廓最下缘与髂嵴最上缘之中点周径)和臀围(即臀部最大周径)表示, $WHR = \text{腰围 (cm)} / \text{臀围 (cm)}$ 。

1.3 统计学处理

资料分析应用SPSS 10.0 (Statistics Package for Social Science 10.0 for Windows) 软件完成。测定数据以均值±标准差($\bar{x} \pm s$)表示。计量资料用t检验和方差分析, 率的比较用 χ^2 检验。危险因素用logistic回归分析。 $P < 0.05$ 为差异有统计学意义。

2 结 果

2.1 维吾尔族和汉族冠心病与正常对照组多个常见危险因素比较

从表1中看出, 维、汉民族冠心病组患者HOMA IS较对照组明显减低[维族(204.02 ± 180.43) vs (409.14 ± 181.06), 汉族(258.09 ± 105.66) vs (479.09 ± 200.97), $P < 0.05$]; 维、汉民族冠心病组患者较对照组代谢综合征患病率明显增多[维族($54.0\% vs 25.7\%$), 汉族($66.7\% vs 22.7\%$), $P < 0.05$]; 维、汉民族冠心病组患者较对照组糖尿病患病率明显增多[维族($52.0\% vs 0.0\%$), 汉族($64.0\% vs 0.0\%$), $P < 0.01$]; 1h胰岛素水平下降和2h血糖水平升高($P < 0.05$)。其余各项虽有变化, 但差异无统计学意义(表1)。

维、汉民族冠心病组患者体质量[(78.06 ± 12.69) vs (72.32 ± 12.03) kg]和BMI[(27.29 ± 3.53) vs (25.61 ± 3.42) kg/m²]差异有统计学意义($P < 0.01$)。对照组中维、汉两个民族各种危险因素差异无统计学意义($P > 0.05$; 表1)。

2.2 多个危险因素对冠心病危险性比较(logistic回归分析)

从表2看出, 饮酒、糖尿病、高血压与冠心病呈正相关($P < 0.05$)。HDL-C与冠心病呈负相关($P < 0.05$)。对冠心病影响的危险因素大小依次为饮酒[相对危险性比值比(odds ratio, OR)=2.532]、糖尿病(OR=2.466)、高血压(OR=2.355)。说明有糖尿病、高血压者患冠心病是无糖尿病、高血压者的近2.5倍。

3 讨 论

IR是指机体对正常胰岛素的反应减弱, 即组

织对IS下降。IR时, 血浆葡萄糖不能有效地从循环中移除, 而进一步刺激β细胞释放胰岛素, 导致高胰岛素血症。因此高胰岛素血症只是IR的一种代偿机制。当β细胞功能无力维持高胰岛素状态时即发生明显高血糖。长期高血糖可使血管内皮细胞功能障碍, 引起胰岛素受体分布和功能变化而产生IR。IR和代偿性高胰岛素血症常伴有脂代谢紊乱。

胰岛素反映性降低与心血管病危险因素聚集有关。本文研究显示新疆地区维、汉民族冠心病患者IS显著减低, 空腹和餐后血糖显著高于对照组。说明该地区冠心病患者存在IR。IR的存在预示着冠心病多种危险因素并存^[6]。

不同年龄、种族和地区人群中均普遍存在IR, 但有差异性。这些种族间的异质性, 引起试验结果之间的差异性。在南亚地区(新加坡), 对印度、马来和华人3个不同民族的研究^[6]显示, 马来人有较高的BMI, 印度人有较高的WHR、空腹血糖和较多的异常糖耐量。本研究显示维、汉族冠心病患者存在体质 (78.06 ± 12.69) vs (72.32 ± 12.03) kg]和BMI[(27.29 ± 3.53) vs (25.61 ± 3.42) kg/m²]的显著差异。中国北部地区人群平均BMI为(25.5 ± 3.68) kg/m²^[7]。美国黑人男性BMI均值为 $25.6\text{kg}/\text{m}^2$, 女性为 $27.4\text{kg}/\text{m}^2$, 爱斯基摩人为 $26.9\text{kg}/\text{m}^2$, 皮马(Pima)印第安人为 $35.8\text{kg}/\text{m}^2$ 。所有这些可增加动脉硬化和血栓的危险性, 至少可部分解释他们较高的冠心病发病率^[8]。

Ford等^[9]对>20岁美国人进行了代谢综合征患病率的流行病学调查, 结果发现患病率为23.7%, 在60~70岁的老年人中达43.5%。中国11省市队列人群代谢综合征的流行病学研究^[10], 代谢综合征患病率平均为13.3%, >55岁者高达20%。本研究发现在正常对照组代谢综合征患病率为23.9%(年龄45~65岁), 与国内外报道接近。代谢综合征的存在将增加心血管意外事件的发生^[11,12]。

经logistic逐步回归分析后, 年龄、饮酒、高血压、糖尿病、和2h葡萄糖(G 2h)与冠心病呈正相关; 男性、糖尿病、代谢综合征与心肌梗死高度相关。与国外学者^[13]研究一致。

乌鲁木齐地区维、汉民族冠心病住院患者存在较低的IS和较高的糖尿病、代谢综合征患病率; 维吾尔族冠心病患者肥胖显著。以代谢综合征为基础的多个危险因素并存是该地区冠心病患者的重要特征。提示我们应进行多重危险因素干预以防治冠心病。

表1 维、汉民族冠心病患者多个危险因素比较
Table 1 Comparison of risk factors between the Uygurs and the Hans with or without CHD

Item	Control group(n = 71)		CHD group(n = 164)	
	Hans(n = 36)	Uygur(n = 35)	Hans(n = 114)	Uygur(n = 50)
Male[n(%)]	21/36 (58.3)	20/35 (57.1)	81/114 (71.1)	37/50 (74.0)
Age(years, $\bar{x} \pm s$)	54.78 ± 11.36	53.37 ± 9.44	57.35 ± 9.52	55.26 ± 8.72
Drinking[n(%)]	19/36 (52.8)	10/35 (28.6)	50/114 (43.9)	29/50 (58.0) [#]
MS[n(%)]	8/36 (22.7)	9/35 (25.7)	76/114 (66.7) ^{**}	27/50 (54.0) [#]
DM[n(%)]	0/36 (0.0)	0/35 (0.0)	73/114 (64.0) ^{**}	26/50 (52.0) [#]
CNL IS($\bar{x} \pm s$)	0.0147 ± 0.0110	0.0130 ± 0.0110	0.0152 ± 0.0129	0.0149 ± 0.0124
HOMA IR($\bar{x} \pm s$)	4.64 ± 2.70	5.69 ± 3.42	5.13 ± 3.87	5.25 ± 3.69
HOMA IS($\bar{x} \pm s$)	479.09 ± 200.97	409.14 ± 181.06	258.09 ± 105.66 [*]	204.02 ± 180.43 [#]
BMI(kg/m ² , $\bar{x} \pm s$)	25.81 ± 2.87	25.78 ± 3.83	25.61 ± 3.42	27.29 ± 3.53 ^{△△}
Body mass(kg, $\bar{x} \pm s$)	72.20 ± 11.33	76.14 ± 12.47	72.32 ± 12.03	78.06 ± 12.69 ^{△△}
WHR($\bar{x} \pm s$)	0.94 ± 0.06	0.95 ± 0.05	0.94 ± 0.06	1.12 ± 0.13
Waist(cm, $\bar{x} \pm s$)	93.24 ± 8.04	96.48 ± 10.00	94.37 ± 8.86	96.53 ± 11.27
TC(mmol/L, $\bar{x} \pm s$)	4.46 ± 1.05	4.32 ± 0.87	4.52 ± 1.07	4.25 ± 1.04
HDL-C(mmol/L, $\bar{x} \pm s$)	1.31 ± 0.45	1.29 ± 0.58	1.18 ± 0.29	1.20 ± 0.35
LDL-C(mmol/L, $\bar{x} \pm s$)	2.76 ± 0.96	2.44 ± 0.73	2.72 ± 0.91	2.56 ± 0.95
TG(mmol/L, $\bar{x} \pm s$)	2.19 ± 1.41	2.03 ± 1.09	2.40 ± 1.47	2.23 ± 1.65
Lp(a)(mg/L, $\bar{x} \pm s$)	184.77 ± 113.00	163.17 ± 76.51	172.28 ± 125.10	175.43 ± 92.24
UA(μmol/L, $\bar{x} \pm s$)	289.86 ± 73.87	265.35 ± 96.15	295.09 ± 89.15	274.37 ± 94.95
GGT(IU/L, $\bar{x} \pm s$)	26.31 ± 17.56	24.10 ± 13.00	29.33 ± 20.43	30.29 ± 18.56
G 0h(mmol/L, $\bar{x} \pm s$)	5.20 ± 1.73	5.59 ± 2.53	6.89 ± 3.13 ^{**}	6.81 ± 3.41 ^{**}
G 1h(mmol/L, $\bar{x} \pm s$)	9.42 ± 3.80	10.41 ± 4.46	16.04 ± 5.02	13.51 ± 4.90
G 2h(mmol/L, $\bar{x} \pm s$)	8.08 ± 4.11	9.01 ± 4.75	14.58 ± 6.68 ^{**}	12.91 ± 6.88 [#]
In 0h(mU/L, $\bar{x} \pm s$)	19.87 ± 10.53	22.73 ± 12.94	16.87 ± 10.43	17.07 ± 10.17 [#]
In 1h(mU/L, $\bar{x} \pm s$)	102.91 ± 42.33	97.02 ± 45.18	72.07 ± 46.72 ^{**}	67.77 ± 46.94 [#]
In 2h(mU/L, $\bar{x} \pm s$)	89.86 ± 47.76	91.38 ± 47.48	76.22 ± 51.04	71.59 ± 50.56

CHD: coronary heart disease; MS: metabolic syndrome; DM: diabetes mellitus; CNL IS: Guangwei Li's insulin sensitivity index; HOMA IR: Homeostasis Model Assessment of Insulin Resistance; HOMA IS: Homeostasis Model Assessment of Insulin Sensitivity; BMI: body mass index; WHR: waist hip ratio; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TG: triglycerides; Lp(a): lipoprotein (a); UA: uric acid; GGT: gamma-glutamyl transpeptidase; G 0h: fasting glucose; G 1h: 1-hour glucose; G 2h: 2-hour glucose; In 0h: fasting insulin; In 1h: 1-hour insulin; In 2h: 2-hour insulin. Compared with Hans in control group, ^{*}P < 0.05, ^{**}P < 0.01; compared with Uygur in control group, [#]P < 0.05, ^{##}P < 0.01; compared with Hans in CHD group, ^{△△}P < 0.01

表2 冠心病危险因素logistic回归分析(最大似然估计法)
Table 2 Logistic regression analysis in risk factors of coronary heart disease (maximum likelihood estimation)

Factor	Regression coefficient (B)	Standard error(SE)	Wald χ^2	P	Exp(B)OR
Drinking	0.929	0.368	6.380	0.012	2.532
EH	0.848	0.366	5.361	0.021	2.355
DM	0.902	0.429	4.433	0.035	2.466
HDL-C	-1.190	0.494	5.795	0.016	0.304
GGT	0.018	0.010	3.269	0.071	1.019
G 2h	0.080	0.036	4.998	0.025	1.083
Constant	-5.841	1.447	16.290	0.000	0.003

OR: odds ratio; EH: essential hypertension; DM: diabetes mellitus; HDL-C: high-density lipoprotein cholesterol; GGT: gamma-glutamyl transpeptidase; G 2h: 2-hour glucose

总之，提倡改变不良生活方式，增加运动量。

每日30min的中等强度的户外体力活动。因为适量运动和合理膳食可以升高HDL-C、提高IS和降低血压^[14,15]。同时，降压降糖、调脂抗凝、戒烟限酒、保持平稳心态等这些减少危险因素的措施，也是预防冠心病致死和致残的首要临床处理方案。

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