·现场调查·

北京市1680名社区居民血清同型半胱氨酸与代谢综合征关系的横断面研究

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【摘要】 **目的**　分析血清同型半胱氨酸(Hcy)与代谢综合征(MS)间的关系。**方法**　1680名北京市社区居民纳入调查。MS依据NCEP-ATPⅢ标准定义。以多因素logistic回归分析计算MS发病危险比值比(*OR*),多元线性回归分析Hcy与各指标间的相关关系。**结果**　校正性别、年龄后MS组Hcy水平高于非MS组(17.99 μmol/L *vs.* 17.18 μmol/L, $P=0.007$),随着MS组分由0个增加至4或5个,Hcy水平逐渐升高为16.71、16.94、17.62、18.20和17.82 μmol/L(线性趋势$P=0.044$)。MS的5个组分中,表现为腹型肥胖、高血压和高甘油三酯血症者,其Hcy水平相应较高。多元logistic回归分析显示,Hcy最高四分位水平(Hcy Ⅳ)与MS发生相关。校正年龄、性别、肌酐、肾小球滤过率(eGFR)、低密度脂蛋白胆固醇(LDL-C)、尿酸、吸烟、饮酒、运动等因素后,与Hcy最低四分位水平(Hcy Ⅰ)相比,Hcy Ⅳ的MS发生风险$OR=1.379$(1.005～1.892)。排除性别及年龄因素,偏相关分析显示Hcy与体重指数(BMI)、腰围、血压、LDL-C、甘油三酯、尿酸、肌酐、eGFR呈正相关,与高密度脂蛋白胆固醇呈负相关。多元线性回归分析显示,年龄、男性、BMI、LDL-C、肌酐、尿酸与Hcy水平呈独立正相关。**结论**　高Hcy水平是MS发生的相关因素,Hcy与年龄、男性、BMI、LDL-C、肌酐、尿酸独立相关。

【关键词】 代谢综合征; 同型半胱氨酸; 横断面研究

Relationship between serum homocysteine and metabolic syndrome: a cross-sectional study

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【**Abstract**】 **Objective**　To explore the relationship between serum homocysteine and metabolic syndrome (MS). **Methods**　A cohort with 1680 people involved in a community-based population in Beijing was investigated. Metabolic syndrome was defined by NCEP-ATPⅢ criteria. Multivariate logistic regression analysis was used to estimate the odds ratios (*OR*) of MS. Multiple linear regression analysis was performed to analyze the association between Hcy and characteristic variables. **Results**　Homocysteine was higher in MS population compared to those without MS (17.99 μmol/L *vs.* 17.18 μmol/L, $P=0.007$) after adjusted for age and sex. Levels of homocysteine increased with the presence of MS components (from 0 to 4 or 5) (16.71, 16.94, 17.62, 18.20, 17.82 μmol/L respectively, $P=0.044$ for linear trend). Among the components, groups with larger waist circumference, higher blood pressure and triglycerides showed significantly higher Hcy level than their counterparts. Results from multiple logistic regression analysis revealed that the highest Hcy quartile (Hcy Ⅳ) was significantly associated with MS. Compared with the lowest Hcy quartile (Hcy Ⅰ), the adjusted odds ratio of having MS in Hcy Ⅳ was 1.379 (1.005-1.892) after adjusting for age, sex, levels on creatinine/estimated glomerular filtration rate (eGFR)/low-density lipoprotein cholesterol (LDL-C) and uric acid, smoking, alcohol intake and exercise. In the partial correlation analyses, Hcy was positively associated with body mass index (BMI), waist circumsternece, blood pressure, LDL-C, triglycerides (TG), uric acid, serum creatinine, eGFR, but inversely associated

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with high-density lipoprotein cholesterol (HDL-C) and independently with age and sex. In multiple linear regression analysis, age, male sex, BMI, LDL-C, creatinine and uric acid were found to be independently associated with Hcy level. **Conclusion** There was an association noticed between the MS using NCEP-ATPⅢcriteria and the highest quartile level of Hcy in this study. Factors as age and being male, the levels of BMI, LDL-C, creatinine and uric acid were independently associated with the Hcy level.

【Key words】 Metabolic syndrome; Homocysteine; Cross-section study

代谢综合征(MS)是多种心血管危险因素聚集于个体的病理状态,其组分包括腹型肥胖、高血压、高甘油三酯、低高密度脂蛋白胆固醇和高血糖等[1,2]。已有研究证实MS是心血管病的独立危险因子[3]。同型半胱氨酸(Hcy)被认为是动脉硬化的危险因子,通过损伤血管内皮,促进血管平滑肌细胞增殖,同时激活凝血因子,引起血栓发生[4]。目前少有Hcy与MS关系的大样本研究,且结果并不一致[5-8]。本研究利用较大样本探讨Hcy与MS间的关系。

对象与方法

1. 研究对象和指标测定:研究对象来自2007—2009年解放军总医院在北京市石景山区苹果园地区2个社区进行的横断面研究。共随机抽取社区居民1859人,排除严重系统性疾病如胶原性疾病、内分泌代谢性疾病(糖尿病除外)、炎症、严重肝肾疾病等。共收集资料完整调查对象1680名。所有参加人员以问卷调查方式填写病史、家族史、用药史、生活方式如吸烟、饮酒、运动等。所有参加人员签署知情同意书,由受专门培训的医生和护士做体格检查。血压测量以安静环境下休息5 min,坐位测量右上臂血压,连续测量3次,间隔5 min,取其平均值记录为受试者血压。所有受试者均经全套实验室检测,包括血脂、肝肾功能、血糖、血尿酸(UA)、Hcy。Hcy使用Roche酶法试剂盒,批间变异为4.1%。

2. 相关定义:①高血压定义为既往有高血压病史或体检发现SBP≥140 mm Hg(1 mm Hg=0.133 kPa)和(或)DBP≥90 mm Hg或服用抗高血压药物。②体重指数(BMI)以体重(kg)除以身高(m)的平方计算[9]。③腰围以受试者站立位时肋骨最低点和髂嵴之间中点为基点测定。④吸烟和饮酒定义为每天至少1支,连续1年以上;平均每周饮用1次白酒、啤酒或其他酒类即视为饮酒。⑤不论采用何种锻炼方式,平均每日运动量不少于30 min即视为运动[10]。⑥依据NCEP-ATPⅢ定义[11],凡以下5项中有≥3项者定义为MS:腰围男性≥90 cm或女性≥80 cm,甘油三酯(TG)≥1.7 mmol/L,高密度脂蛋白胆固醇(HDL-C)男性<1.03 mmol/L或女性<1.3 mmol/L,SBP≥130 mm Hg或DBP≥85 mm Hg,空腹血糖(FBG)≥5.6 mmol/L。⑦肾小球滤过率(eGFR)根据四变量MDRD(midification of diet in renal disease)公式基础上修正的中国人计算公式:eGFR=175×标准化血清肌酐(Cr,mg/dl)$^{-1.234}$×年龄(岁)$^{-0.179}$×0.79(女性)[12,13]。

3. 统计学分析:计量资料以均数($\bar{x}$)±标准差(s)或中位数(四分位数)表示;不符合正态分布变量(Hcy、UA、Cr、eGFR、TG)以对数转换后进入Pearson相关分析及多元线性回归分析。组间比较计数资料用χ^2检验,计量资料用t检验或非参检验。组间校正年龄、性别因素比较用一般线性模型(GLM)。以多因素logistic回归分析计算不同模型下MS发病危险比值比(OR)。logistic回归分析时变量赋值:①性别赋值:男性=1,女性=2;②Hcy以相对应的四分位(HcyⅠ~Ⅳ)分别赋值1~4。P值取双侧,P<0.05表示差异有统计学意义。用SPSS 13.0软件完成统计学分析。

结　果

1. 研究人群基本特征:男女两组间除年龄、BMI、TG、FBG差异无统计学意义(P>0.05)外,其余差异均有统计学意义。其中男性Hcy水平显著高于女性(19.50 μmmol/L *vs.* 15.80 μmmol/L),男性MS患病率显著低于女性(34.56% *vs.* 42.22%,P<0.01)。见表1。

2. 不同MS组分间Hcy水平比较:由表2可见,校正年龄、性别因素后,腰围、血压、TG较高者Hcy水平亦高(P<0.05)。MS组Hcy水平高于非MS组(17.99 μmmol/L *vs.* 17.18 μmmol/L,P=0.007)。

3. MS不同组分个数间与Hcy水平比较:由表3可见,校正年龄、性别因素,当MS组分个数由0、1、2、3、4或5递增时,Hcy水平差异有统计学意义(P=0.015),并呈线性升高趋势(P=0.044)。

4. MS相关因素的多因素logistic回归分析:本研究以3种模型进行logistic回归分析。模型1校正因素包括年龄、性别、Cr水平、eGFR、吸烟、饮酒、运动;模型2在模型1基础上增加UA水平作为校正因

表 1　研究人群基本情况

项　目	男性(n=709)	女性(n=971)	P值
年龄(岁)[a]	62.29±11.46	61.34±10.58	>0.05
BMI(kg/m^2)[a]	25.48±3.19	25.56±3.78	>0.05
腰围(cm)[a]	89.79±9.22	84.95±10.05	<0.001
SBP(mm Hg)[a]	133.34±18.00	128.24±18.26	<0.001
DBP(mm Hg)[a]	78.73±10.76	75.00±10.30	<0.001
TC(mmol/L)[a]	4.90±0.87	5.18±0.94	<0.001
HDL-C(mmol/L)[a]	1.30±0.34	1.46±0.38	<0.001
LDL-C(mmol/L)[a]	2.85±0.70	3.09±0.73	<0.001
TG(mmol/L)[b]	1.45(1.06 ~ 2.13)	1.51(1.12 ~ 2.12)	>0.05
FBG(mmol/L)[a]	5.34±1.36	5.40±1.80	>0.05
Hcy(μmol/L)[b]	19.50(15.90 ~ 24.75)	15.80(13.00 ~ 19.20)	<0.001
UA(mmol/L)[b]	320.60(274.65 ~ 369.35)	263.00(222.40 ~ 306.50)	<0.001
Cr(mmol/L)[b]	76.30(68.20 ~ 85.80)	56.70(50.20 ~ 63.80)	<0.001
eGFR[ml·(min·1.73 m^2)$^{-1}$][b]	85.90(76.58 ~ 95.26)	87.48(79.00 ~ 97.13)	<0.05
体力活动[c]	533(75.18)	745(76.73)	>0.05
吸烟[c]	337(47.54)	81(8.34)	<0.001
饮酒[c]	273(38.50)	37(3.81)	<0.001
冠心病[c]	132(18.62)	108(11.12)	<0.001
脑卒中[c]	44(6.21)	37(3.81)	<0.05
糖尿病[c]	144(20.31)	196(20.19)	>0.05
高血压[c]	396(55.85)	490(50.46)	<0.05
MS[c]	245(34.56)	410(42.22)	<0.01

注：[a] $\bar{x}\pm s$；[b]括号外数据为中位数，括号内数据为四分位数；[c]括号外数据为人数，括号内数据为百分比(%)

表 2　不同MS组分年龄、性别校正后Hcy水平比较

指　标		人数	Hcy水平(μmol/L)	P值
MS	是	655	17.99(17.54 ~ 18.49)	
	否	1025	17.18(16.83 ~ 17.54)	0.007
腰围(cm)	是	1042	17.95(17.58 ~ 18.32)	
≥90(男)或≥80(女)	否	638	16.79(16.33 ~ 17.22)	<0.001
血压(mm Hg)	是	912	17.86(17.46 ~ 18.24)	
SBP≥130或DBP≥85	否	768	17.10(16.67 ~ 17.54)	0.013
HDL-C≤1.03 mmol/L	是	515	17.70(17.18 ~ 18.24)	
	否	1165	17.42(17.06 ~ 17.74)	0.358
TG≥1.7 mmol/L	是	663	17.95(17.50 ~ 18.45)	
	否	1017	17.22(16.83 ~ 17.58)	0.011
FBG≥5.6 mmol/L	是	446	17.10(16.56 ~ 17.66)	
	否	1234	17.66(17.30 ~ 17.99)	0.101

表 3　MS组分个数在年龄、性别校正后与Hcy水平的比较

MS组分个数	人数	Hcy水平(μmol/L)
0	227	16.71(15.96 ~ 17.46)
1	348	16.94(16.33 ~ 17.54)
2	450	17.62(17.06 ~ 18.20)
3	355	18.20(17.54 ~ 18.84)
4或5	300	17.82(17.14 ~ 18.49)
P值		0.015(0.044[a])

注：[a]线性趋势P值

素；模型3在模型2基础上增加LDL-C水平作为校正因素。由模型1可见，以HcyⅠ为基准比较，HcyⅣ水平 OR=1.538(95%CI：1.130 ~ 2.095，P<0.01)；模型2的HcyⅣ水平 OR=1.378(95% CI：1.006 ~ 1.888，P<0.05)；模型3的HcyⅣ水平 OR=1.379(95%CI：1.005 ~ 1.892，P<0.05)。见表4。

5. Hcy水平与各项指标的相关性及多元线性回归分析：由表5可见，Hcy与男性、年龄、BMI、腰围、血压、TG、UA、Cr呈显著正相关，与HDL-C、血糖、eGFR呈显著负相关；校正性别、年龄后，Hcy与BMI、腰围、血压、LDL-C、TG、UA、Cr呈显著正相关，与HDL-C、eGFR呈显著负相关。纳入多元线性回归分析的因素经多因素分析，Hcy与年龄、男性、BMI、LDL-C、UA、Cr呈正相关。

讨　论

本研究采用多因素logistic分析表明，调整年龄、性别、Cr、eGFR、UA、LDL-C等因素后，HcyⅣ较HcyⅠ的MS发生风险增加，说明血清Hcy水平升高是MS发病相关因素。

瑞典一项研究(纳入1108例40岁以上人群)校正年龄、性别因素后，发现Hcy与血清胰岛素呈现正相关(P=0.004)，在排除

表 4　MS相关因素的多因素logistic回归分析[OR值(95%CI)]

因素	模型1	模型2	模型3
性别	2.037(1.37 ~ 3.028)[a]	2.465(1.692 ~ 3.590)[a]	2.308(1.564 ~ 3.407)[a]
年龄	1.019(1.008 ~ 1.031)[a]	1.017(1.006 ~ 1.029)[a]	1.016(1.004 ~ 1.027)[a]
HcyⅠ	1.000	1.000	1.000
HcyⅡ	1.231(0.916 ~ 1.654)	1.111(0.822 ~ 1.500)	1.092(0.807 ~ 1.477)
HcyⅢ	1.242(0.917 ~ 1.681)	1.125(0.827 ~ 1.532)	1.134(0.832 ~ 1.546)
HcyⅣ	1.538(1.130 ~ 2.095)[a]	1.378(1.006 ~ 1.888)[b]	1.379(1.005 ~ 1.892)[b]
UA		1.006(1.004 ~ 1.007)[a]	1.006(1.004 ~ 1.007)[a]
LDL-C			1.305(1.129 ~ 1.507)[a]

注：[a] P<0.01，[b]P<0.05

表 5　研究人群Hcy与其他指标Pearson相关、校正年龄、性别后偏相关系数及多元线性回归系数

因素	Pearson相关		偏相关		多元线性回归	
	Hcy[a]	P值	Hcy[a]	P值	Hcy[a]	P值
性别	−0.317	<0.001	−	−	−0.199	<0.001
年龄	0.309	<0.001	−	−	0.267	<0.001
BMI	0.119	<0.001	0.130	<0.001	0.085	<0.001
腰围	0.217	<0.001	0.097	<0.001	−0.033	0.360
SBP	0.169	<0.001	0.064	0.009	0.013	0.662
DBP	0.079	0.001	0.076	0.002	0.043	0.063
HDL-C	−0.165	<0.001	−0.099	<0.001	−0.031	0.332
LDL-C	0.031	0.20	0.052	0.034	0.102	0.023
TC	−0.012	0.622	0.025	0.308	−0.085	0.063
TG[a]	0.074	0.002	0.078	0.001	0.046	0.059
FBG	−0.069	0.05	−0.064	0.07	−0.073	0.545
UA[a]	0.253	<0.001	0.115	<0.001	0.051	0.046
Cr[a]	0.278	<0.001	0.109	<0.001	0.093	<0.001
eGFR[a]	−0.186	<0.001	−0.111	<0.001	−0.031	0.471

注：[a]经log转换数据

了糖尿病和Cr水平升高者后，其余999例这种正相关仍然显著（$P=0.003$），同时还发现Hcy与胰岛素抵抗也有类似相关性。由此认为MS与Hcy具有相关性[6]。Cankurtaran等[7]在一项纳入1255例65岁以上老年人的研究中发现，经多元logistic分析显示高Hcy水平是MS独立相关因素。Gideon等[14]研究显示MS者Hcy水平高于非MS者[（14.9±0.2 *vs.* 14.1±0.2）μmol/L，$P=0.002$]，且MS伴Hcy水平较高者，心血管事件发病风险增高，$HR=2.5$，95%*CI*：1.4～4.6。本研究中，校正性别、年龄因素，MS者Hcy水平显著高于非MS者（$P=0.007$），且随MS组分个数增加，Hcy水平呈线性升高趋势（$P=0.044$），与文献报道相似[14]。多因素logistic回归分析显示，在校正年龄、性别、Cr、eGFR、UA、LDL-C等因素后，高Hcy水平（HcyⅣ）仍是MS发病相关因素，$OR=1.379$（95%*CI*：1.005～1.892）。

本研究校正性别及年龄因素后，偏相关分析显示Hcy与BMI、腰围、血压、TG呈正相关。在MS组分中，表现为腹型肥胖、高血压和高甘油三酯血症者，其Hcy水平也相应较高。MS的核心机制是胰岛素抵抗，腰围和BMI已被认为是胰岛素抵抗的临床替代指标[11]。腹型肥胖可以诱导$CD8^+$T细胞、巨噬细胞等炎症细胞的浸润、分化，形成局部炎症[15]，而慢性炎症进一步加重了胰岛素抵抗[16]。已有多项研究证实Hcy水平与胰岛素抵抗呈正相关[6,17,18]。Hcy水平升高的原因可能系机体胰岛素抵抗时，Hcy代谢中的限速酶——胱硫醚β合酶活性下调所致[19]。

本研究多元线性回归分析显示，Hcy与年龄、男性、BMI、LDL-C、Cr、UA呈显著正相关。Hcy水平与年龄、男性、Cr呈正相关，这与以往的研究一致[5,6,8,20]，与UA呈正相关，与Rhee等[8]研究一致。业已证实，年龄、性别、LDL-C和UA是心血管病独立危险因素。Hcy也是动脉硬化的危险因素，可引起血管内膜弹力层断裂，血管平滑肌细胞增殖，动、静脉血栓，增加LDL-C氧化并在动脉壁沉积[21]。但Hcy、LDL-C和UA三者在心血管病发病中是否有相互协同作用，尚需进一步研究。

本研究存在不足之处：首先Hcy水平的影响因素很多，如基因、饮食、药物干扰[8,22]，但在研究中控制这些因素比较困难；其次本研究是横断面研究，并不能提供Hcy与MS关系直接的证据，因此两者关系还需进一步探索。

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