·临床研究·

血清胃泌素与老年冠心病患者冠状动脉病变程度的相关分析

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【摘 要】 **目的** 探讨血清胃泌素水平与老年冠心病(CHD)患者冠状动脉病变程度的相关性。**方法** 入选2015年10月至2016年12月东南大学医学院附属盐城医院住院并行冠状动脉造影(CAG)的老年CHD患者104例,根据冠状动脉狭窄程度分为CHD组($n=82$)和对照组($n=22$)。CHD组患者根据病变血管数又分为单支病变组($n=42$)、双支病变($n=27$)和三支病变组($n=13$),按照Gensini评分计算冠状动脉病变狭窄程度的总评分,酶联免疫吸附法测定空腹血清胃泌素(FG)及餐后1 h血清胃泌素(PG1h)水平。计量资料用均数±标准差($\bar{x}\pm s$)表示,两组比较采用t检验。计数资料用百分率表示,组间比较用χ^2检验。**结果** 两组患者年龄、性别、吸烟、CHD家族史、消化道疾病、血肌酐(SCr)水平、质子泵抑制剂(PPIs)使用方面差异无统计学意义($P>0.05$)。CHD组患者体质量指数(BMI)、甘油三酯(TG)、低密度脂蛋白胆固醇(LDL-C)、FG、FG1h、及高血压和糖尿病患者例数高于对照组,差异有统计学意义($P<0.05$)。三支病变组患者PG1h、PG1h/FG和Gensini评分显著高于单支和双支病变组患者,差异具有统计学意义($P<0.05$)。Spearman相关分析结果表明,血清胃泌素与性别、BMI、吸烟、CHD家族史、TG、LDL-C无关,与年龄、消化道疾病、使用PPIs、高血压史、SCr、病变血管数和Gensini评分有关($P<0.05$)。偏相关分析校正混杂因素后,血清胃泌素水平与病变血管数($r=0.58$)和Gensini评分($r=0.63$)呈正相关。**结论** 血清胃泌素水平与老年CHD患者冠状动脉病变程度呈正相关,提示血清胃泌素水平越高,越可能对老年冠状动脉粥样硬化的发生和发展存在潜在不利影响。

【关键词】 冠心病;血清胃泌素;Gensini评分
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Correlation between serum gastrin level and severity of coronary lesions in elderly patients with coronary artery disease

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【**Abstract**】 **Objective** To investigate the relationship of serum gastrin level with severity of coronary lesions in the elderly patients with coronary heart disease (CHD). **Methods** A total of 104 elderly CHD patients who received coronary artery angiography (CAG) in our hospital from October 2015 to December 2016 were recruited in this study. According to their coronary artery stenosis, they were divided into CHD group ($n=82$) and control group ($n=22$). By the number of involved branches, the former group were further assigned into 3 subgroups: single vessel subgroup ($n=42$), double vessel subgroup ($n=27$) and triple vessel subgroup ($n=13$). The severity of coronary arterial stenosis was evaluated by Gensini scoring system. Enzyme-linked immunosorbent assay was used to measure the levels of fasting serum gastrin (FG) and postprandial 1 hour serum gastrin (PG1h). The measurement data were expressed as mean ± standard deviation ($\bar{x}\pm s$), and Student's t test was employed for the comparison between groups. Enumeration data were expressed as percentage, and inter-group comparison was carried out with Chi-square test. **Results** There were no significant differences in age, sex, smoking, family history of CHD, gastrointestinal disease, serum level of creatinine (SCr), and usage of proton pump inhibitors (PPIs) between the CHD group and control group ($P>0.05$). The CHD group had significantly higher body mass index (BMI), triglycerides (TG), low density lipoprotein-cholesterol (LDL-C), FG, and FG1h, and notably larger proportions of hypertension and diabetes when compared with the control group ($P<0.05$). The patients with triple vessel disease had remarkably higher PG1h, ratio of PG1h/FG and Gensini score than those with single and double vessel disease ($P<0.05$). Spearman correlation analysis showed that serum gastrin level had no correlation with sex, BMI, smoking, family history of CHD, TG and LDL-C, but was correlated with age, gastrointestinal disease, usage of PPIs, hypertension, SCr, number of lesioned branches and Gensini score ($P<0.05$). After partial correlation analysis and correction of confounding factors, serum gastrin level was positively correlated with the number of lesioned branches ($r=0.58$) and Gensini score ($r=0.63$). **Conclusion** Serum gastrin is positively correlated with the lesion severity

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of coronary artery disease in elderly CHD patients. It suggests that higher serum gastrin might negatively contribute to the occurrence and development of coronary atherosclerosis in the elderly.

【Key words】 coronary artery disease; serum gastrin; Gensini score

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冠心病(coronary heart disease,CHD)是指由于冠状动脉粥样硬化致管腔狭窄或阻塞而引起心肌缺血和缺氧,是动脉粥样硬化导致器官病变的最常见类型[1]。据世界卫生组织(world health organization,WHO)报道,2020年CHD将成为全球重要的医疗负担,其中急性心肌梗死是发病和死亡的主要原因[2]。我国CHD的发病率和死亡率总体也呈上升趋势,尤其是老年人群。研究表明老年人患CHD的风险明显高于青年人[3]。胃泌素(gastrin)是一种主要由胃肠道G细胞合成和分泌的肽类激素,存在于全身多个器官,主要通过其受体发挥生物活性,研究表明其受体也存在于血管[4]。研究结果表明,胃泌素与高血压、心肌梗死等疾病也存在相关性[5,6],但关于老年CHD患者的冠状动脉病变严重程度和血清胃泌素水平关系的研究甚少。本研究探讨了血清胃泌素与老年CHD患者冠状动脉病变程度的相关性。

1 对象与方法

1.1 研究对象

入选2015年10月至2016年12月在东南大学医学院附属盐城医院住院并行冠状动脉造影(coronary angiography, CAG)的老年CHD患者104例,根据冠状动脉狭窄程度分为CHD组82例(至少有1支冠状动脉狭窄≥50%)和对照组22例(冠状动脉正常)。CHD组患者根据病变血管数又分为单支病变组42例(前降支、回旋支或右冠状动脉任一支病变,血管狭窄≥50%)、双支病变组27例(前述3支冠状动脉中任意2支病变,且至少有1处血管狭窄≥70%,左主干病变为2支病变)和三支病变组13例(冠状动脉3大分支均有病变,至少有1处血管狭窄≥90%)[7]。纳入标准:(1)年龄≥65岁;(2)拟诊为CHD并行CAG检查的患者[8]。排除标准:(1)遭受严重创伤以及1个月内进行了外科手术;(2)6个月内发生过急性心肌梗死;(3)确诊或怀疑恶性肿瘤;(4)心脏瓣膜中度疾病、非缺血性心肌病;(5)自身免疫性疾病或重度感染;(6)无肝肾等重要器官疾病。

1.2 方法

1.2.1 CAG 采用单盲法由两位临床医师对造影结果进行评估,不一致时由两位医师协商解决。

1.2.2 Gensini评分 按照美国心脏协会规定的冠状动脉血管图像分段评价,应用Gensini评分系统对每支血管狭窄程度进行定量分析[8]。首先用直径法评定狭窄程度,以最严重处直径狭窄的比例表示冠状动脉狭窄程度,即狭窄直径1%~25%计为1分,26%~50%计为2分,51%~75%计为4分,76%~90%计为8分,91%~99%计为16分,100%计为32分。然后根据不同冠状动脉分支确定相应系数:左主干病变×5.0;右冠状动脉病变×1.0;左前降支病变:近段×2.5,中段×1.5,远段×1.0;左回旋支病变:近段×2.5,中远段×1.0,后降支、钝缘支×1.0,其余×0.5。以每一条动脉的狭窄程度基本评分乘以病变部位的系数,即为该病变血管的评分,各病变血管得分总和即为该患者冠状动脉病变狭窄程度的总评分。

1.2.3 血液检测 抽取清晨空腹和餐后1 h外周静脉血5 ml,检测甘油三酯(triglycerides,TG)、低密度脂蛋白胆固醇(low-density lipoprotein cholesterol,LDL-C)、血肌酐(serum creatinine,SCr)等生化指标。采血前一周,患者没有接受质子泵抑制剂(proton pump inhibitors,PPIs)和H2受体拮抗剂以及制酸剂(铝碳酸镁等)治疗。空腹血清胃泌素(fasting serum gastrin,FG)和餐后1 h胃泌素(postprandial 1 h serum gastrin,PG1h)水平检测采用必欧瀚生物技术有限公司生产的人类血浆和血清胃泌素17检测试剂盒检测。

1.3 统计学处理

应用SPSS 17.0统计软件对数据进行统计学分析。计量资料用均数±标准差($\bar{x} \pm s$)表示,两组比较采用t检验,多组比较采用单因素方差分析。计数资料用百分率表示,两组比较采用χ^2检验或Fisher确切概率法。Spearman相关分析血清胃泌素与老年人冠状动脉病变程度的相关性,并用偏相关分析进行混杂因素的校正。$P<0.05$为差异有统计学意义。

2 结 果

2.1 两组患者一般资料比较

两组患者年龄、性别、吸烟、CHD家族史、消化道疾病、SCr水平、PPIs使用方面差异无统计学意义($P>0.05$)。CHD组患者体质量指数(body mass index,BMI)、TG、LDL-C、FG、FG1h、及高血压和糖尿病患者例数均高于对照组,差异有统计学意义($P<0.05$;表1)。

表 1 两组患者基线资料比较

Table 1 Comparison of baseline data between two groups

Item	CHD group (n = 82)	Control group (n = 22)	t/χ^2	P value
Age (years, $\bar{x} \pm s$)	68.21 ± 9.47	67.94 ± 8.25	0.12	0.452
Gender (male/female, n/n)	59/23	12/10	2.43	0.119
BMI (kg/m^2, $\bar{x} \pm s$)	24.62 ± 2.96	22.93 ± 3.05	2.36	0.012
Smoking [n (%)]	25 (30.49)	6 (27.27)	0.09	0.769
Digestive tract disease [n (%)]	21 (25.61)	5 (22.73)	0.07	0.782
Usage of PPIs [n (%)]	12 (14.63)	4 (18.18)	0.01	0.938
Hypertension [n (%)]	48 (58.54)	7 (31.82)	4.97	0.026
Diabetes mellitus [n (%)]	32 (39.02)	3 (13.64)	5.01	0.025
CHD family history [n (%)]	16 (19.51)	4 (18.18)	0.03	0.870
Abnormal SCr level [n (%)]	7 (8.54)	1 (4.55)	0.03	0.862
TG (mmol/L, $\bar{x} \pm s$)	1.94 ± 0.58	1.54 ± 0.62	2.83	0.004
LDL-C (mmol/L, $\bar{x} \pm s$)	2.68 ± 0.07	2.20 ± 0.64	3.51	0.001
FG (ng/L, $\bar{x} \pm s$)	94.52 ± 15.21	74.68 ± 12.35	5.63	< 0.001
PG1h (ng/L, $\bar{x} \pm s$)	243.09 ± 30.57	163.88 ± 25.16	11.17	< 0.001

CHD: coronary heart disease; BMI: body mass index; PPIs: proton pump inhibitors; SCr: serum creatinine; TG: triglycerides; LDL-C: low-density lipoprotein cholesterol; FG: fasting serum gastrin; PG1h: postprandial 1 h serum gastrin

2.2 不同病变血管组 FG 和 PG1h 水平以及 Gensini 评分比较

不同病变血管组患者 FG 水平差异无统计学意义(P > 0.05);三支病变血管组患者 PG1h、PG1h/FG 和 Gensini 评分显著高于单支和双支病变组患者,差异具有统计学意义(P < 0.05;表 2)。

2.3 血清胃泌素的相关性分析

Spearman 相关分析结果表明,血清胃泌素与性别、BMI、吸烟、CHD 家族史、TG、LDL-C 无关(P > 0.05),与年龄、消化道疾病、使用 PPIs、高血压史、SCr、病变血管数和 Gensini 评分有关(P < 0.05)。偏相关分析校正混杂因素后,血清胃泌素水平与病变血管数(r = 0.58)和 Gensini 评分(r = 0.63)呈正相关(表 3)。

表 2 不同病变血管组 FG 和 PG1h 水平以及 Gensini 评分比较

Table 2 Comparison of FG, PG1h and Gensini score among different involved vessel subgroups ($\bar{x} \pm s$)

Item	Single vessel subgroup (n = 42)	Double vessel subgroup (n = 27)	Triple vessel subgroup (n = 13)
FG (ng/L)	91.14 ± 14.82	93.45 ± 16.09	95.18 ± 15.99
PG1h (ng/L)	169.18 ± 20.45 *	220.71 ± 29.00 *	264.06 ± 32.11
PG1h/FG	1.94 ± 0.75 *	2.52 ± 0.71 *	2.93 ± 0.57
Gensini score	10.44 ± 4.00 *	28.62 ± 6.48 *	70.59 ± 17.33

FG: fasting serum gastrin; PG1h: postprandial 1 h serum gastrin. Compared with triple vessel subgroup, * P < 0.05

表 3 血清胃泌素影响因素的相关性分析

Table 3 Correlation analysis of influencing factors of serum gastrin level

Factor	Spearman analysis		Partial analysis	
	r	P value	r	P value
Age	0.25	0.02	0.16	0.18
Gender	−0.18	0.34	–	–
BMI	0.26	0.11	–	–
Smoking	0.21	0.07	–	–
Digestive tract disease	0.35	0.01	0.10	0.24
PPIs	0.19	0.03	0.07	0.31
Hypertension	0.22	< 0.01	0.16	< 0.01
Diabetes mellitus	0.34	0.01	0.10	0.09
CHD family history	0.10	0.24	–	–
SCr	0.31	0.01	0.17	0.15
TG	0.06	0.68	–	–
LDL-C	−0.09	0.13	–	–
Involved vessel	0.73	< 0.01	0.58	< 0.01
Gensini score	0.81	< 0.01	0.63	< 0.01

BMI: body mass index; PPIs: proton pump inhibitors; CHD: coronary heart disease; SCr: serum creatinine; TG: triglycerides; LDL-C: low-density lipoprotein cholesterol

3 讨 论

胃泌素主要由胃肠道 G 细胞分泌,是主要的胃肠道激素,在血液循环中是其他肠道激素的 10 ~ 20 倍。胃泌素有两类代表性受体,即 CCK1 和 CCK2 受体,均属于 G 蛋白偶联受体[9]。有研究表明胃泌素与心血管系统间存在密切联系,其受体在心肌及冠状动脉中均有表达,胃泌素可通过冠状动脉内皮细胞上的 CCK2 受体扩张冠状动脉,增加冠状动脉血流

量[4,10]。也有研究证实胃泌素及其受体通过与多巴胺受体的相互作用,促进大鼠肾脏排钠,从而影响大鼠血压,而在高血压大鼠中,这种作用则明显减弱[11]。在脑组织中,也有其他学者发现胃泌素水平能反映脑梗死病变的严重程度[12-14]。

研究表明,饱食后受影响最大的是胃肠道激素,其中胃泌素在循环中的浓度比其他胃肠道激素显著升高。本研究结果显示CHD组与对照组FG水平差异无统计学意义,而CHD组患者PG1h水平显著高于对照组,这与其他学者的研究结果[15]相似,可能是由于CHD患者进食后需要分泌更多的胃泌素来扩张冠状动脉,从而保证心脏供血。同时研究表明,三支病变血管组CHD患者PG1h水平较单支和双支病变组患者高,提示餐后胃泌素水平反映冠状动脉的病变程度。

Gensini评分综合考虑了冠状动脉病变的范围和程度,能更精确地判断冠状动脉病变的情况,Gensini评分越高,提示冠状动脉病变越严重[16]。本研究采用Gensini评分系统对CHD患者冠状动脉病变程度进行定量分析,结果显示CHD患者随着病变血管严重程度的增加,Gensini评分增高,PG1h与FG的比值也随着升高,并且,CHD患者血清胃泌素水平与病变血管数和Gensini评分呈正相关,提示血清胃泌素越高,越可能对冠状动脉粥样硬化的发生、发展存在潜在的不利影响,而能否作为老年冠心病危险因素,则尚需长期大样本临床研究进一步证实。

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