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男性内源性性激素水平与冠心病范围及左心室射血分数的相关性*

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摘要 目的:探究男性内源性性激素水平与冠心病范围及左心室射血分数(LVEF)的相关性。**方法:**将 2018 年 6 月至 2020 年 6 月于我院接受治疗的 96 例经冠状动脉造影术(CAG)确诊为冠心病的 96 例患者纳入研究,按照临床分型将其区分为稳定型心绞痛(SAP,30 例)、不稳定型心绞痛(UAP,30 例)、急性心肌梗死(AMI,36 例),另选同期 CAG 检测结果提示冠状动脉管腔直径狭窄率<50%的 50 例个体为对照组,检测入组对象的睾酮(Ts)、雌二醇(E₂)水平,评估计算入组对象的 Gensini 积分以及 LVEF,对比不同组别之间 Ts、E₂、Gensini 积分以及 LVEF 差异,Spearman 相关分析探究 Ts、E₂与 Gensini 积分、LVEF 的相关性,最后将患者按照 Gensini 评分区分为狭窄轻型组与严重组,Logistic 回归分析影响冠脉狭窄的危险因素。**结果:**(1)比较显示,冠心病各组间 Ts、E₂、Gensini 积分以及 LVEF 差异明显,以 AMI 组患者 Ts、E₂和 LVEF 水平最低,Gensini 积分最高($P<0.05$);(2)Spearman 相关性分析显示,Ts、E₂均与 Gensini 积分呈负相关,与 LVEF 呈正相关($P<0.05$);(3)多因素 Logistic 回归分析显示 Ts、E₂水平是影响冠脉狭窄程度的独立危险因素($P<0.05$)。**结论:**男性内源性性激素水平同其冠心病范围和 LVEF 呈现密切相关性,是影响冠脉狭窄程度的独立危险因素,可以考虑将其应用于临床冠脉狭窄的诊断与鉴别中。

关键词:内源性性激素;冠心病范围;LVEF;相关性

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The Correlation of Endogenous Sex Hormone Levels with Coronary Heart Disease and Left Ventricular Ejection Fraction in Men*

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ABSTRACT Objective: To explore the correlation between endogenous sex hormone levels and the range of coronary heart disease and left ventricular ejection fraction (LVEF) in men. **Methods:** 96 patients with coronary heart disease diagnosed by coronary angiography (CAG) in our hospital from June 2018 to June 2020 were included in the study. According to the clinical classification, they were divided into stable angina pectoris (SAP, 30 cases) and unstable angina pectoris UAP (30 cases), acute myocardial infarction (AMI), Another 50 individuals whose CAG results showed that the stenosis rate of coronary artery lumen diameter was less than 50% were selected as the control group. The levels of testosterone (Ts) and estradiol (E₂) were detected, the Gensini score and LVEF were evaluated and calculated, and the differences of Ts, E₂, Gensini score and LVEF between different groups were compared. Spearman correlation analysis was used to explore the relationship between Ts, E₂ and Gensini score and LVEF. **Results:** (1) There were significant differences in Ts, E₂, Gensini score and LVEF among the groups, with the lowest level of Ts, E₂ and LVEF in AMI group and the highest Gensini score ($P<0.05$). (2) Spearman correlation score Analysis showed that Ts and E₂ levels were negatively correlated with Gensini score, and positively correlated with LVEF ($P<0.05$). (3) multivariate logistic regression analysis showed that Ts and E₂ levels were independent risk factors for the degree of coronary artery stenosis ($P<0.05$). **Conclusion:** The level of endogenous sex hormone in men is closely correlated with the range of coronary heart disease and LVEF, and is an independent risk factor for the degree of coronary artery stenosis. It can be used in the diagnosis and differential diagnosis of coronary artery stenosis.

Key words: Endogenous sex hormone; Coronary heart disease range; LVEF; Correlation

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前言

心血管疾病是当前世界上发病率最高、患病人数最多、死

亡率最高的疾患,研究显示目前冠心病是发展中国家和发达国家第一大死因。冠心病是一种因冠状动脉发生粥样病变而引起血管腔狭窄或阻塞,进而使个体出现心肌缺血、缺氧或坏死

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而导致的心脏病。冠心病易导致心肌缺血、缺氧或坏死,使患者出现胸痛、恶心、呕吐等^[1-3]。该病发病机理较为复杂,现阶段临床研究认为高血压、高血脂、高血糖、易怒、过饱等都是诱发其发作的危险因素,该病初次发作时,约有 1/3 的患者会出现猝死^[4,5]。数据显示,全球每年因冠心病死亡人数高达 700 万,位于单病种死因首位。文献报道,我国冠心病患病率呈逐年增长趋势,如不加控制,到 2030 年,冠心病发病率将是 2000 年的 3.7 倍^[6,7]。早期诊断的治疗是改善冠心病患者预后的重要途径,CAG 是目前冠心病诊断的金标准,但该检测方式属于有创操作,临床推广性较差^[8]。近些年针对冠心病的流调学发现,男性群体心血管发病率要较女性明显升高,经分析发现男性性别是心血管疾病发病的独立危险因素,提示性激素可能与心血管疾病之间存在一定的关联^[9]。学者 Tung^[10]等的研究就发现,雌激素能够通过调节机体的凝血功能进而对心血管发挥保护作用,绝经后女性发生冠心病的几率要高于未绝经女性。本研究拟通过设立对照研究的方式,探究男性内源性性激素水平与冠心病范围及 LVEF 的相关性,以期为冠心病患者的临床诊疗提供新思路。

1 资料与方法

1.1 一般资料

将 2018 年 6 月至 2020 年 6 月于我院接受治疗的 96 例经冠状动脉造影术(CAG)确诊为冠心病的 96 例患者纳入研究,按照临床分型将其区分为稳定型心绞痛(SAP,30 例)、不稳定型心绞痛(UAP,30 例)、急性心肌梗死(AMI,36 例),另选同期 CAG 检测结果提示冠状动脉管腔直径狭窄率 <50% 的 50 例个体为对照组。

纳入标准:(1) 入组对象均出现类似冠心病临床症状;(2) 意识清晰能够配合开展调研;(3) 调研对象临床资料齐全;(4) 调研相关资料提报医院伦理学会批准实施;(5) 患者或其家属签署知情同意书;(6) 均为男性。

排除标准:(1) 伴发精神疾患者;(2) 伴发主动脉瘤患者;(3) 既往 PCI 术史者;(4) 伴发房颤患者;(5) 既往冠脉旁路移植术者;(6) 伴发严重肝肾功能障碍者;(7) 伴发严重心律失常者;(8) 恶性肿瘤者。

1.2 干预方法

采集入组对象空腹 12 h 以上外周静脉血,分离血清后分装,置于 -20℃ 冰箱中保存,使用放射免疫法对入组对象的血清 Ts 及 E₂ 水平进行检测。入组对象均实施冠状动脉造影及冠状动脉狭窄程度评估,一般选择经桡动脉途径实施检测,采取 Judkin's 法对患者实施多体位投照,冠脉造影结果由两名经验丰富的医师进行双盲判读,如出现分歧则请第三位医师分析,冠脉狭窄程度评估采取改良 Gensini 评分法^[11];在冠脉 8 个主要节段中,将每个节段最重的狭窄病变计入评分系统并进行定量评分,无异常记为 0 分,狭窄程度 1%~49% 记为 1 分,狭窄程度 50%~74% 记为 2 分,狭窄程度 75%~99% 记为 3 分,完全闭塞记为 4 分,各段评分之和为患者总积分。LVEF 的检测采用飞利浦 iE33 彩色多普勒超声诊断仪开展,每名对象连续检测 3 次取平均值作为最终结果。

1.3 观察指标及评测标准

入组对象的分组标准参照美国心脏病学会基金会 / 美国心脏病协会标准^[12]进行区分,冠脉狭窄程度的分组参考 Gensini 积分进行,将 Gensini 积分 ≤ 25 分者记为冠脉狭窄轻型组 (n=40 例),将 Gensini 积分 >25 分者记为冠脉狭窄严重组 (n=56 例),Logistic 回归分析 Ts 和 E₂ 是否会对冠脉狭窄产生影响。

1.4 统计学方法

将采集的数据录入到 EXCEL 表格中,使用 SPSS 22.0,计数资料以 [n(%)] 表示,选择卡方检验,计量资料以 ($\bar{x} \pm s$) 表示,选择 t 检验,相关性分析使用 Spearman 进行, $P < 0.05$ 有统计学意义^[13]。

2 结果

2.1 冠心病各组一般临床资料差异性比较

将 SAP、UAP、AMI 以及对照组 4 组个体的一般临床资料诸如年龄、体重、受教育程度、婚姻状态、吸烟 (≥ 1 根 / 日,持续 1 年以上)、饮酒 (≥ 2 次 / 日,持续 5 年以上)、疾病史等,并开展组间比较,结果显示,在一般临床资料方面,几组患者差异并不明显 ($P > 0.05$),具有可比性,具体数据如表 1 所示。

2.2 冠心病各组 Ts、E₂、Gensini 积分以及 LVEF 差异

将 4 组冠心病组患者的 Ts、E₂、Gensini 积分以及 LVEF 实施组间差异性比较,结果显示,4 组患者的上述资料组间差异较为明显 ($P < 0.05$),其中 AMI 组患者的 Ts、E₂ 以及 LVEF 水平最低,Gensini 积分最高 ($P < 0.05$),对照组个体的 Ts、E₂ 以及 LVEF 水平最高,Gensini 积分最低 ($P < 0.05$),具体数据如表 2 所示。

2.3 冠心病各组 Ts、E₂ 与 Gensini 积分、LVEF 相关性分析

将纳入对象的 Ts、E₂ 与 Gensini 积分、LVEF 开展 Spearman 相关性分析,结果显示 Ts、E₂ 与 Gensini 积分均呈现负相关联系 ($r = -0.9437, r = -0.9858, P < 0.05$),Ts、E₂ 与 LVEF 均呈现正相关联系 ($r = 0.9851, r = 0.9230, P < 0.05$),具体数据如表 3 和图 1 所示。

2.4 冠脉狭窄轻型组与冠脉狭窄严重组影响因素二元 Logistic 回归分析

经分析显示冠心病患者 Ts、E₂ 水平同其 Gensini 积分、LVEF 均具有密切的关联性,为进一步分析 Ts、E₂ 是否为影响冠脉狭窄的危险因素,将纳入的 96 例冠心病患者按照 Gensini 积分区分为冠脉狭窄轻型组 (40 例) 和冠脉狭窄严重组 (56 例),就两组患者的年龄、BMI、高血压、糖尿病、Ts、E₂ 因素纳入研究并开展二元 Logistic 回归分析,结果显示 Ts 和 E₂ 均为冠脉狭窄的独立危险因素 ($P < 0.05$),具体数据如表 4 所示。

3 讨论

近些年随着我国居民生活水平的提升以及饮食结构的改变,冠心病的发病率有逐年递增趋势^[14-16],数据显示,全球前五位死亡病因中,冠心病是 60 岁以下患者死亡的第二大原因,仅次于艾滋病,60 岁以上人群死亡病因中冠心病位列第一^[17-19]。我国一项针对上海浦东新区 11230 例合格人群的抽查发现,居民冠心病粗患病率为 6.53%,标准患病率为 1.94%,其中男性粗患病率 5.88%,女性粗患病率 6.93%^[20,21],上述数据均显示,

表 1 两组患者一般临床指标比较

Table 1 Comparison of general clinical indexes between the two groups

General clinical data		Control group(n=50)	SAP group(n=30)	UAP group(n=30)	AMI group(n=36)
Age (years)		40.33±4.33	39.98±4.51	40.19±3.98	40.43±3.29
Body weight (kg)		71.29±3.22	71.11±3.44	70.28±4.00	71.28±3.98
Educational level	University or above	5	5	6	7
	high school	15	14	15	16
	Junior high school and below	30	31	29	27
Junior high school and below	Yes	15	10	9	8
	No	35	20	21	28
Diabetes	Yes	14	9	8	10
	No	36	21	22	26
Smoke	Yes	15	8	8	7
	No	35	22	22	29
Drink wine	Yes	18	7	8	7
	No	32	23	22	29

表 2 冠心病各组 Ts、E₂、Gensini 积分以及 LVEF 差异($\bar{x} \pm s$)Table 2 The difference of TS, E₂, Gensini score and LVEF in CHD groups($\bar{x} \pm s$)

Groups	n	Ts(ng/mL)	E ₂ (pg/mL)	Gensini integral	LVEF(%)
Control group	50	4.39±1.34	13.21±3.22	0	62.39±5.54
SAP	30	3.78±1.11*	6.59±1.21*	54.19±5.55*	60.18±3.29*
UAP	30	2.87±0.32*#	4.21±1.32*#	63.29±4.30*#	51.29±8.19*#
AMI	36	2.11±0.32*#&	3.29±1.11*#&	89.18±5.40*#&	41.98±5.69*#&

Note: compared with the control group, * $P < 0.05$, compared with SAP group, # $P < 0.05$, compared with UAP group, & $P < 0.05$.

表 3 冠心病各组 Ts、E₂ 与 Gensini 积分、LVEF 相关性分析Table 3 Correlation Analysis of T_s, E₂, Gensini score and LVEF in coronary heart disease groups

Groups	Ts	E ₂	Gensini integral	LVEF
Ts	-	-	-0.9437	0.9851
E ₂	-	-	-0.9858	0.9230
Gensini integral	-0.9437	-0.9858	-	-
LVEF	0.9851	0.9230	-	-

冠心病已对我国居民正常生活造成严重影响。

本研究通过设立不同分组的方式,就男性内源性性激素水平同冠心病范围及 LVEF 的相关性进行了探究,结果显示,将纳入的 96 例冠心病患者按照疾病类型实施分组后,与对照组相比较,冠心病各组患者的 Ts、E₂、LVEF 水平均明显更低, Gensini 积分明显更高,这提示冠心病确实会对个体的内源性性激素水平产生一定的影响。文中按照该思路就不同疾病类型冠心病患者的上述指标差异开展了进一步分析,结果显示 AMI 组患者的 Ts、E₂、LVEF 水平在冠心病各组中处于最低水平, Gensini 积分处于最高水平,其次为 UAP 组, SAP 组患者的 Ts、E₂、LVEF 水平在冠心病各组中最高, Gensini 积分最低,各组间

差异明显。学者 Lindholm^[22]等通过将 164 例冠心病患者于 52 例非冠心病患者进行对比发现,冠心病组患者的 E₂ 和 TSH 水平与非冠心病存在显著差异,我们进一步将 164 例冠心病患者按照 Gensini 积分为 A 组(≤ 50 分)和 B 组(>50 分),对比发现, A 组和 B 组间的性激素水平同样存在明显差异,这与本文结果类似。我们分析认为,性激素水平往往与机体的代谢能力密切相关,以往有的研究指出,性激素水平的变化会对个体 TC、TG 等脂质代谢指标产生影响^[23-25],这可能也是影响冠心病发生的重要机制。

文中进一步通过 Spearman 相关性分析以及 Logistic 回归分析印证了上文的观点,我们分析认为,男性内源性性激素水

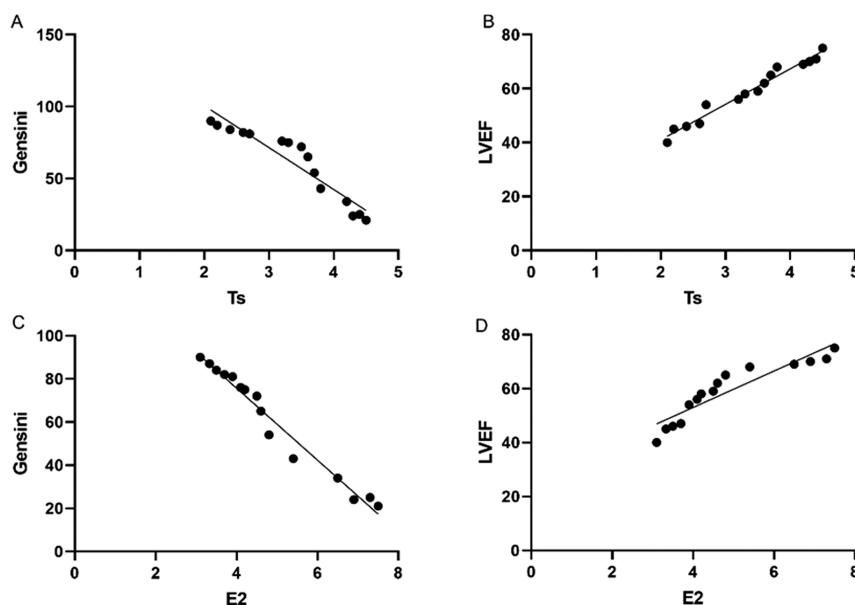
图1 冠心病各组 Ts、E₂ 与 Gensini 积分、LVEF 相关性分析Fig.1 Correlation Analysis of TS, E₂, Gensini score and LVEF in coronary heart disease groups

表4 冠脉狭窄轻型组与冠脉狭窄严重组影响因素二元 Logistic 回归分析

Table 4 Binary logistic regression analysis of influencing factors between mild coronary stenosis group and severe coronary stenosis group

Factor	B	Wald	P	OR	OR95%CI
Age	0.028	0.677	0.414	1.023	0.981-1.101
BMI	-0.155	1.822	0.172	0.849	0.682-1.087
Hypertension	0.663	1.212	0.271	1.921	0.593-5.489
Diabetes	0.781	1.211	0.293	2.091	0.555-7.192
Ts	0.013	5.481	0.012	1.023	1.003-1.023
E ₂	0.021	4.980	0.015	1.028	1.031-1.041

平会对冠心病患者产生影响的机制可能有如下几点:(1) 冠心病患者机体处于严重持续应激状态,而内源性性激素对应激状态较为敏感,持续的应激状态会导致性激素水平的迅速下降^[27,28];(2)冠心病患者相对心输出量会出现降低,这可能会影响机体的周围循环,从而导致睾丸缺血缺氧,使其合成分泌性激素能力降低;(3)冠心病状态的,机体性激素合成的降低也是一种代偿性反应,通过减少性激素的合成来减少对性活动的驱动,从而降低心脏负担;(4)冠心病状态下,肾素-血管紧张素-醛固酮系统被激活,这会阻断睾酮的合成^[29,30]。

综上所述,男性内源性性激素水平同其冠心病范围和LVEF 呈现密切相关性,是影响冠脉狭窄程度的独立危险因素,可以考虑将其应用于临床冠脉狭窄的诊断与鉴别中。

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