

doi: 10.13241/j.cnki.pmb.2019.09.016

冠心病患者心率变异性与冠状动脉病变狭窄范围及严重程度的关系研究*

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摘要 目的:探讨冠心病患者心率变异性(HRV)与冠状动脉病变狭窄范围及严重程度的关系。**方法:**选取上海市第十人民医院2015年1月至2018年7月期间收治的冠心病患者220例,所有患者均行冠脉造影及24h动态心电图检查。按狭窄范围分为单支狭窄组(n=68)、双支狭窄组(n=82)、三支狭窄组(n=70),按狭窄严重程度分为轻度组(狭窄 \leq 50%,n=62),中度组(50% $<$ 狭窄 $<$ 70%,n=66),重度组(狭窄 \geq 70%,n=92),另选取51例同期于我院体检的健康志愿者作为对照组。记录冠心病患者与对照组HRV各项指标,比较不同冠脉病变狭窄范围患者、不同狭窄严重程度患者正常平均N-N间期(SDNN)、正常相邻每5minR-R间期均数标准差(SDANN)、正常相邻正常N-N间期的均方根(RMSSD)、正常相邻间期差值高于50ms心搏数占总心搏数的百分比(pNN50)、低频(LF)、高频(HF)及低频/高频比值(LF/HF)。**结果:**冠心病患者与对照组RMSSD、pNN50、LF、HF比较差异无统计学意义($P>0.05$),冠心病患者SDNN、SDANN低于对照组,LF/HF值高于对照组($P<0.05$)。不同冠脉狭窄范围、不同冠脉病变狭窄严重程度患者pNN50、LF、HF整体比较无统计学差异($P>0.05$),随着冠脉狭窄范围的增加或狭窄病变严重程度的加重SDNN、SDANN、RMSSD逐渐降低,LF/HF值逐渐升高($P<0.05$)。**结论:**HRV是评估心脏自主功能的良好指标,该指标中SDNN、SDANN、RMSSD、LF/HF值可作为评估冠心病患者冠状动脉的狭窄程度和狭窄范围的良好指标,具有重要的临床指导意义。

关键词:心率变异性;冠状动脉狭窄;冠心病;狭窄程度;狭窄范围

中图分类号:R541.4 文献标识码:A 文章编号:1673-6273(2019)09-1679-04

Relationship between Heart Rate Variability and Range of Stenosis and Severity of Coronary Artery Stenosis in Patients with Coronary Heart Disease*

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ABSTRACT Objective: To investigate the relationship between heart rate variability (HRV) and the range of stenosis and severity of coronary artery stenosis in patients with coronary heart disease. **Methods:** 220 patients with coronary heart disease who were admitted to Shanghai Tenth People's Hospital from January 2015 to July 2018 were selected, all patients underwent coronary angiography and 24-hour dynamic electrocardiogram examination. They were divided into single-vessel stenosis group (68 cases), double-vessel stenosis group (82 cases) and three-vessel stenosis group (70 cases) according to the range of stenosis. They were divided into mild group (stenosis \leq 50%, n=62), moderate group (50% $<$ stenosis $<$ 70%, n=66) and severe group (stenosis \geq 70%, n=92) according to the severity of stenosis. Another 51 healthy volunteers who received physical examination in our hospital during the same period were selected as control group. The indexes of HRV in patients with coronary heart disease and control group were recorded. The different coronary artery disease patients with range of stenosis, and severity of stenosis in patients with normal average N-N interphase (SDNN), the normal period between adjacent every 5 min R-R mean standard deviation (SDANN), the normal period between adjacent normal N-N RMS (RMSSD), the phase difference between adjacent normal number above 50 ms cardiac accounted for the percentage of the total number of cardiac (pNN50), low frequency (LF), high frequency (HF) and low frequency/high frequency ratio (LF/HF) were compared. **Results:** There were no significant differences in RMSSD, pNN50, LF and HF between the patients with coronary heart disease and the control group ($P>0.05$). The SDNN and SDANN of patients with coronary heart disease were lower than those of the control group, and the LF/HF value was higher than that of the control group ($P<0.05$). There were no significant differences in pNN50, LF and HF among patients with different coronary stenosis range and severity ($P>0.05$). With the increase of coronary stenosis or the severity of the severity of coronary stenosis, the SDNN, SDANN and RMSSD decreased gradually, the LF/HF value gradually increased ($P<0.05$). **Conclusion:** HRV is a good indicator for assessing cardiac autonomic function, the values of SDNN, SDANN, RMSSD and LF/HF can be used as a good index to evaluate the degree and range of coronary artery stenosis in patients with coronary heart disease, which have important clinical guiding significance.

Key words: Heart rate variability; Coronary artery stenosis; Coronary heart disease; Severity of stenosis; Range of stenosis

Chinese Library Classification(CLC): R541.4 **Document code:** A

Article ID: 1673-6273(2019)09-1679-04

* 基金项目:上海市卫计委基金项目(2015SY384)

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(收稿日期:2018-09-27 接受日期:2018-10-21)

前言

冠心病是一种常见的心血管系统疾病,其发病率较高,严重危及患者的生活质量及生命安全^[1-3]。冠心病的主要诱因包括高脂饮食、吸烟、高血压等,上述病因均可引起血管内膜损伤,脂质代谢紊乱,粥样斑块形成,最终导致冠脉狭窄,引发冠心病^[4-6]。目前,多项研究表明,冠脉狭窄可引起心脏自主神经功能失调,心率变异性(Heart rate variability, HRV)是反映心脏自主功能神经活性的无创指标,其本质是分析窦性心律在一定时间内的每次心动周期内的时间与频率变化,反映心率快慢变化的规律性^[7-9]。有研究表明,HRV降低可引起心律失常或心源性猝死,与冠心病预后存在密切关系,可作为评估冠脉狭窄的良好指标^[10-12]。本研究主要探究冠心病患者心率变异性与冠状动脉病变狭窄范围及严重程度之间的关系,旨在为临床冠心病防治提供参考,现报道如下。

1 资料与方法

1.1 一般资料

选取上海市第十人民医院 2015 年 1 月至 2018 年 7 月期间收治的冠心病患者 220 例,纳入标准:(1)符合世界卫生组织关于冠心病的有关诊断标准^[13];(2)患者均接受冠脉造影及 24h 动态心电图确诊为冠心病患者,临床症状表现为胸痛、胸闷;(3)入院前未接受相关治疗者;(4)患者及其家属均签署知情同意书。排除标准:(1)合并自主神经系统类疾病,如帕金森病,糖尿病;(2)失代偿性心力衰竭者;(3)各种原因引起的心律失常,如房颤,预激综合征;(4)起搏器植入者;(5)肝肾功能不全者;(6)急性心梗、心肌梗患者。另选取 51 例同期于我院体检的健康志愿者作为对照组,冠心病患者与对照组一般资料比较差异无统计学意义($P>0.05$),具有可比性,见表 1。上海市第十人民医院伦理委员会已批准本研究。

表 1 两组患者一般资料比较

Table 1 Comparison of general information between two groups of patients

Groups	n	Age (year)	Sex (male / female)	Body mass index (kg/m ²)	Combined hypertension (n)	Diabetes mellitus (n)
Patients with coronary heart disease	220	61.35± 5.24	121/99	24.15± 3.16	135	74
Control group	51	60.52± 6.42	30/21	23.25± 4.12	35	14
χ^2/t	-	0.687	0.245	0.152	0.934	0.722
P	-	0.494	0.620	0.563	0.334	0.395

1.2 检测方法

所有患者均由 2 名经验丰富的介入医师行冠脉造影,共同评估右冠状动脉、左回旋支、左前降支及左主干狭窄程度,按狭窄范围分为单支狭窄组(n=68)、双支狭窄组(n=82)、三支狭窄组(n=70),按狭窄严重程度分为轻度组(狭窄 \leq 50%,n=62),中度组(50% $<$ 狭窄 $<$ 70%,n=66),重度组(狭窄 \geq 70%,n=92)。由同一医师行 24 h 动态心电图检查,检查仪器为美国 GE 公司 Seer Light 24 h 心电图仪及自带分析软件,检查前告知受试者 12 h 内避免烟酒、咖啡、浓茶及剧烈运动。24h 动态心电图记录 HRV 指标,包括时阈参数:正常平均 N-N 间期(SDNN)、正常相邻每 5minR-R 间期均数标准差(SDANN)、正常相邻正常 N-N 间期的均方根(RMSSD)、正常相邻间期差值高于 50 ms 心搏数占总心搏数的百分比(pNN50),频域参数:0.14~0.30HZ

低频(LF)、0.15~0.40HZ 高频(HF)及低频 / 高频比值(LF/HF)。

1.3 统计学方法

本研究数据均采用 SPSS20.0 软件进行检测分析,计数资料用率(%)表示,采用 χ^2 检验,计量资料用均数 \pm 标准差($\bar{x}\pm s$)表示,组间两两比较采用 t 检验,多组间对比采用单因素方差分析。检验水准 $\alpha=0.05$ 。

2 结果

2.1 冠心病患者与对照组 HRV 指标比较

冠心病患者与对照组 RMSSD、pNN50、LF、HF 比较差异无统计学意义 ($P>0.05$),冠心病患者 SDNN、SDANN 低于对照组,LF/HF 值高于对照组($P<0.05$)。见表 2。

表 2 冠心病患者与对照组 HRV 指标比较($\bar{x}\pm s$)

Table 2 Comparison of HRV indexes between patients with coronary heart disease and control group($\bar{x}\pm s$)

Groups	n	SDNN(ms)	SDANN(ms)	RMSSD(ms)	pNN50(%)	LF(HZ/ms)	HF(HZ/ms)	LF/HF
Patients with coronary heart disease	220	126.63± 21.42	123.24± 31.45	35.25± 11.53	13.16± 13.14	15.14± 7.24	9.43± 6.36	1.74± 0.45
Control group	51	147.14± 20.41	144.13± 32.13	38.45± 10.25	13.84± 10.42	16.97± 8.42	10.28± 6.42	1.56± 0.25
t	-	3.241	2.513	1.822	1.425	0.649	0.536	2.536
P	-	0.000	0.000	0.070	0.063	0.241	0.231	0.000

2.2 不同冠脉病变狭窄范围患者 HRV 指标比较

不同冠脉狭窄范围患者 pNN50、LF、HF 整体比较无统计

学差异 ($P>0.05$),随着冠脉狭窄范围的增加 SDNN、SDANN、RMSSD 逐渐降低,LF/HF 值逐渐升高($P<0.05$)。见表 3。

表 3 不同冠脉病变狭窄范围患者 HRV 指标比较($\bar{x} \pm s$)

Table 3 Comparison of HRV indexes in patients with different range of coronary artery stenosis($\bar{x} \pm s$)

Groups	n	SDNN(ms)	SDANN(ms)	RMSSD(ms)	pNN50(%)	LF(HZ/ms)	HF(HZ/ms)	LF/HF
Single-vessel stenosis group	68	138.24± 34.42	136.58± 31.14	42.15± 13.13	13.36± 4.24	15.87± 6.42	9.49± 4.14	1.69± 0.23
Double-vessel stenosis group	82	124.25± 33.24 ^a	125.83± 25.24 ^a	35.06± 15.24 ^a	13.29± 3.34	15.03± 5.42	9.48± 2.53	1.73± 0.35 ^a
Three-vessel stenosis group	70	118.14± 24.25 ^{ab}	107.25± 36.53 ^{ab}	28.76± 13.52 ^{ab}	12.80± 3.24	14.57± 5.14	9.32± 3.24	1.81± 0.41 ^{ab}
F	-	31.465	47.441	6.253	4.425	1.535	0.524	24.255
P	-	0.000	0.000	0.032	0.072	0.341	0.645	0.000

Note: compared with single-vessel stenosis group, ^aP<0.05; compared with double-vessel stenosis group, ^bP<0.05.

2.3 不同冠脉病变狭窄严重程度患者的 HRV 指标比较

不同冠脉病变狭窄严重程度患者 pNN50、LF、HF 整体比较无统计学差异 (P>0.05), 随着冠脉病变狭窄严重程度的加

重, SDDN、SDANN、RMSSD 逐渐降低, LF/HF 值逐渐升高 (P<0.05)。见表 4。

表 4 不同冠脉病变狭窄严重程度患者的 HRV 指标比较($\bar{x} \pm s$)

Table 4 Comparison of HRV indexes in patients with different severity of coronary artery stenosis($\bar{x} \pm s$)

Groups	n	SDNN(ms)	SDANN(ms)	RMSSD(ms)	pNN50(%)	LF(HZ/ms)	HF(HZ/ms)	LF/HF
Mild group	62	143.56± 29.64	140.27± 37.16	39.98± 7.81	13.68± 7.75	16.32± 5.62	10.19± 6.75	1.51± 1.21
Moderate group	66	126.36± 35.25 ^a	125.17± 41.16 ^a	35.63± 7.24 ^a	13.24± 6.53	15.31± 4.42	9.44± 6.23	1.77± 1.35 ^a
Severe group	92	115.41± 27.25 ^{ab}	110.37± 35.63 ^{ab}	31.79± 6.42 ^{ab}	12.75± 6.24	14.22± 4.14	8.91± 4.24	1.87± 1.42 ^{ab}
F	-	43.146	35.145	5.134	4.387	4.914	0.921	28.942
P	-	0.000	0.000	0.046	0.069	0.172	0.367	0.000

Note: compared with mild group, ^aP<0.05; compared with moderate group, ^bP<0.05.

3 讨论

冠心病是由于冠状动脉粥样硬化后管腔狭窄或完全闭塞, 致使心肌缺血缺氧引起的一类常见的心血管系统疾病, 其主要病理特征是动脉粥样硬化^[14-16]。目前, 有研究表明动脉粥样硬化可能是由于心脏自主神经功能受损, 失去正常调节功能所致^[17-19]。动脉粥样硬化形成的机制复杂, 一般认为存在以下过程: 内皮功能受损, 血管平滑肌增殖, 泡沫细胞生成引起炎症反应而形成粥样物质, 而自主神经均参与上述病理过程^[20-22]。心脏自主神经由交感神经及迷走神经组成, 迷走神经兴奋时, 通过扩张冠脉增加冠脉血流, 增加心肌供血供氧, 从而保护心肌细胞, 避免心肌细胞负荷。其次, 迷走神经兴奋时还可阻断肿瘤坏死因子- α 表达, 减轻炎症反应, 预防粥样斑块形成^[23,24]。交感神经兴奋时, 可使心率增快, 增加心脏负荷, 导致血流动力学紊乱和心脏内皮细胞受损, 从而启动炎症损伤机制, 逐步形成粥样斑块。其次, 交感神经还可分泌去甲肾上腺素作为神经递质, 促使前脂肪细胞 P56 蛋白转位, 加速炎症因子及粘附因子表达, 加重炎症反应^[25,26]。两者功能相互拮抗, 促使自主神经功能稳定。因此, 迷走神经与交感神经调节功能的改变均能影响粥样斑块的形成, 其功能紊乱与冠心病的形成存在密切关联。冠脉造影是诊断冠脉狭窄的“金标准”, 但其具有创伤性且价格昂贵, 制约了其在临床的应用。冠脉狭窄时, 相较常规的冠脉造影, HRV 更具无创性、经济性, 可替代冠脉造影行冠脉狭窄早期的筛查。

本研究结果显示, 冠心病患者 SDNN、SDANN 低于对照

组, LF/HF 值高于对照组 (P<0.05), 冠心病患者发生冠脉病变时, 心肌缺血, 心肌或内膜下自主神经功能末梢坏死, 自主神经功能受损, 常表现为交感神经张力增加, SDNN、SDANN 等对应反映其张力的指标出现明显下降, 且张力越大, 下降幅度越明显, 而 LF/HF 作为反映其张力平衡的指标, 则出现上升的情况。冠脉病变狭窄范围主要反映心肌缺血范围, 而冠脉病变狭窄严重程度主要反映心肌的缺血程度。本研究结果显示, 随着冠脉病变支数的增加或病变狭窄严重程度的加重, SDDN、SDANN、RMSSD 逐渐降低, LF/HF 值逐渐升高 (P<0.05), 但不同冠脉狭窄范围、不同冠脉病变狭窄严重程度患者 pNN50、LF、HF 整体比较无统计学差异 (P>0.05)。HRV 是窦性心律 R-R 间期随时间所发生的数值变化, 是检测心脏自主功能的无创性指标。HRV 作为自主神经对环境刺激的一种自我应答, 其本质是分析窦性心律在一定时间内的每次心动周期内的时间与频率变化, 反映心率快慢变化的规律性, 是评判心脏自主功能的敏感指标。HRV 指标中 SDNN、LF/HF 值等被认为是反映心脏自主神经张力的良好指标, RMSSD 可反映迷走神经兴奋性, SDANN 可反映交感神经兴奋性。罗春苗等^[27]发现冠心病患者心率变异性与冠脉病变程度存在相关性, Maestri 等^[28]研究发现, HRV 可作为疑似冠心病患者心肌缺血的检测指标。李昭蓉等^[29]研究发现 HRV 还与心率失常存在密切关系。HRV 部分指标无差异可能是由于单支或双支冠脉狭窄是虽有心肌缺血改变, 但相应神经末梢尚未受损, 自主神经功能尚未受明显影响, 对应 pNN50、LF、HF 指标未见明显异常。陆艳等^[30]认为可能是

当冠脉狭窄时心肌缺血时,主要是交感神经张力发生改变,对应SDNN、SDANN、LF/HF值等反映交感神经兴奋性的指标明显改变,而迷走神经张力无明显变化,对应pNN50、HF等指标等也无明显变化,提示冠脉狭窄的程度可能主要与交感神经兴奋性改变有关,与本研究结果相同。

综上所述,HRV指标中SDDN、SDANN、RMSSD随冠脉狭窄范围或狭窄严重程度的增加而下降,LF/HF值则相反,其可作为评估冠心病患者冠状动脉的狭窄程度和狭窄范围的指标。

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