

心率变异性在心血管疾病中的应用进展

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摘要

心率变异性(heart rate variability, HRV)是临床常用于评价心脏自主神经活性的无创性检测指标之一, 在多种心血管疾病的筛查、危险分层、治疗调整及预后判断等均有重要价值。本文着重于HRV的研究背景、分析方法、临床应用等进行综述。

关键词

心率变异性, 心力衰竭, 心律失常, 心源性猝死, 冠心病, 高血压

Application Progress of Heart Rate Variability in Cardiovascular Diseases

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Abstract

Heart rate variability (HRV) is one of the non-invasive detection indicators commonly used in the clinical evaluation of cardiac autonomic nerve activity. It plays an important role in screening, risk stratification, treatment adjustment and prognosis judgment of various cardiovascular diseases. This article focuses on the research background, analysis methods and clinical application of HRV.

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Keywords

Heart Rate Variability, Heart Failure, Arrhythmia, Sudden Cardiac Death, Coronary Heart Disease, Hypertension

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1. 引言

心率变异性(heart rate variability, HRV)是指每搏心动周期之间差异的变化情况, 由机器对动态心电图的计算分析得出, 临床上多用于反映自主神经张力的变化趋势, 具有无创性、简便性及良好的应用潜力等诸多优点。目前, HRV 已成为评价自主神经功能的最常用检测方法之一, 在涉及自主神经功能的多种疾病中均有较广泛的应用, 尤其在心血管等疾病的疾病诊断、预后评估、危险分层等多方面均有重要价值。

2. 心率变异性的分析方法及常用指标

2.1. 时域分析

时域分析为利用统计学上的离散趋势法, 对心率或 RR 间期的变化进行分析。临床上常用的 24 小时长时程分析指标有: (1) SDNN: 全部正常窦性心搏间期的标准差, 成人正常参考值为 141 ± 39 ms, 儿童正常参考值为 145 ± 35 ms, 适用于 HRV 的总体分析, 是反映心脏自主神经系统平衡的重要指标, 其降低反映交感神经活性的增强; (2) SDANN: 每 5 min 正常窦性心搏间期平均值的标准差, 成人正常参考值为 127 ± 35 ms, 儿童正常参考值为 132 ± 48 ms, 用于交感神经系统的评价, 数值降低反映交感神经的活性增强; (3) rMSSD: 全程相邻正常窦性心搏间期之差的均方根, 成人正常参考值为 27 ± 12 ms, 儿童正常参考值为 49 ± 20 ms, 其数值与迷走神经活性成正相关; (4) pNN50: 相邻 RR 间期差值超过 50 ms 的个数占总窦性心搏个数的百分比, 与 rMSSD 均反映迷走神经的活跃程度, 数值降低均反映迷走神经活性减弱。

2.2. 频域分析

频域分析常用快速傅里叶变换和自动回归参数模型法等计算方法, 将心率信号转换为频域上的频谱图以得到各频率的功率密度分布及变化情况。根据所用时程分短时程分析(<5 min)和长时程分析(24 h), 短时程分析因能通过避免生理因素、病理状态及外界环境等因素对自主神经活动的干扰, 使结果相对于长时程分析更能反映出被检者自身的自主神经活动情况[1]。常用的频域分析指标有总功率(TP)、超低频功率(ULF)、极低频功率(VLF)、低频功率(LF)和高频功率(HF)。TP (0~0.4 Hz)反映整体的自主神经调节能力; HF (0.15~0.4 Hz)反映迷走神经的调节作用, 且受呼吸深度的调控; LF (0.04~0.15 Hz)通常认为受到迷走神经和交感神经的共同调节影响, 但也有学者认为其主要受到交感神经的调控[1]; LF/HF 比值在临床上可用于定量反映心脏自主神经活性中迷走神经和交感神经的平衡变化[2]; ULF (0~0.003 Hz)和 VLF (0.003~0.04 Hz)两指标占总功率的极小部分, 应用相对较少。

2.3. 非线性分析

心率的调控中存在非线性现象, 对于使用时域分析及频域分析均难以描述的心率变异情况, 临床上

常用散点图的形态进行定性分析, 并通过散点图的分布图像进行判断, 正常图像多呈彗星状, 而 HRV 异常时, 可表现为鱼雷形、短棒形及其他复杂图像。此外还存在参数估算法、非线性预测、改良散点图等分析方法, 但目前其他方法临床应用较少, 且多局限于理论水平, 仍需要进一步研究。

3. 心率变异性在心血管疾病中的临床应用

3.1. HRV 与心力衰竭

心力衰竭是多种病因导致的心脏收缩或舒张功能障碍的临床综合征, 是心脏疾病发展的终末阶段, 其病理生理学特征是严重的血流动力学异常, 同时伴有心脏自主神经系统功能的失衡, 表现为交感神经活性增加和迷走神经活性减弱[3], 而自主神经功能的紊乱, 在疾病的发展和进展中有着重要作用。Ksela 等[4]通过对射血分数保留型心力衰竭(heart failure with preserved ejection fraction, HFpEF)患者进行预后的随访及动态心电图的持续监测后发现, 相较于存活者, 死亡患者的 SDNN 显著降低, 并提出 HRV 参数能帮助区分 HFpEF 患者中潜在不良结局风险较大者, 有助于评估 HFpEF 患者的预后及危险分层。Patel 等[5]对 1401 例无症状老年人群随访发生心力衰竭的相关性研究表明, 平均心率校正后 24 小时内 5 分钟节段 N-N 间期的平均方差(the average variance of N-N intervals in 5-min segments over 24 h when corrected for the average heart rate, CV%)与心力衰竭的发生显著独立相关[(95%CI (0.90~0.99), $P < 0.05$), 提示识别 HRV 异常的无症状老年人, 可能有助于指导心力衰竭的预防策略。Ostrowska 等[6]的一项老年群体队列研究表明, 较低的 LF/HF 比值是发生心力衰竭的强预测因子, 尤其是当 LF/HF 比值 <30 时, 与新发心衰相关, 且在加入传统心血管疾病的危险因素后, 可进一步提高心衰的预测准确性, 较以往的预测模型准确性提高 3.3% ($P < 0.03$), 此外, 研究还显示 HF 功率较高的个体, 其心力衰竭的发生风险有所增加, 这可能与以往迷走神经活性减少是心衰发生前自主神经功能失衡的主要原因有冲突。呼吸性窦性心律不齐(respiratory sinus arrhythmia, RSA), 即正常呼吸运动所引起的心率变异, 在心血管疾病患者中可以观察到 RSA 的降低, 在心力衰竭群体这一现象则消失[7]。Shanks 等[8]通过构建慢性心力衰竭动物模型, 并对起搏器编程以重新恢复 RSA, 可显著改善心衰患者的心输出量并重塑心肌细胞的形态。因此, HRV 检测对心力衰竭患者的预测、危险分层、预防等具有重要价值。

3.2. 心率变异性与心律失常和心源性猝死

随着人类预期寿命的增长, 心律失常的患病率也不断增加[9]。预测潜在心律失常的发生对于心律失常早期干预和管理的重要性不言而喻。现有研究认为, 心律失常的发生及过程的维持与自主神经功能失调密切相关, 心率变异性可能有助于早期预测心律失常的发生。一项针对于阵发性心房颤动的动态心电图研究[10]表明, 与正常对照组相比, 房性早搏(PACs)、房性心动过速以及 rMSSD 是阵发性心房颤动患者的独立危险因素, 且列线图表明, rMSSD 每增加一个单位, 发生心房颤动的几率可增加约 1.0357 倍。一项孟德尔随机化研究[11]显示, SDNN 是房颤[OR: 0.515; 95%CI: 0.278~0.954; $P = 0.03$]和心动过缓[OR: 0.988; 95%CI: 0.976~1.000; $P = 0.0045$]发生的独立预后危险因素。Geurts 等[12]对一般人群的纵向和孟德尔随机化研究也显示较高的 SDNN (HR: 1.24; 95%CI: 1.04~1.47; $P = 0.0213$)和较高的 rMSSD [HR: 1.33; 95%CI: 1.13~1.54; $P = 0.001$]与新发房颤显著相关, 尤其在女性群体中更为突出。快速性室性心律失常(ventricular tachyarrhythmias, VTAs)包括心室颤动(ventricular fibrillation, VF)和室性心动过速(ventricular tachycardia, VT), VTAs 是未能及时就医的情况下导致心源性猝死(Sudden cardiac death, SCD)的主要原因之一, 约占心源性猝死的 80% [13], 因此早期预测快速型心律失常的发生可能有助于降低心源性猝死的死亡率。以往的基于 HRV 分析预测 VTAs 的多项研究表明 HRV 在预测 VT 的发生具有潜在应用潜力[14]-[16]。Zhang 等[17]发现 HRV 在老年心梗患者的 VF 具有一定预测价值, 有望成为 VF 的辅助诊断方法。Thong

等[16]通过对 HRV 分析建立基于神经网络的 VTAs 预测模型, 该模型通过短程(5 min)的 HRV 分析在 VT 事件发生前 10 秒预测可能出现的 VT 事件, 并表现出 73.3%的敏感性, 73.8%的特异性和 75.6%的准确性, 但 10 秒的预测长度在临床上缺乏实际价值, 在后续研究[18]中对 HRV 参数进一步调整后, 引入 11 个 HRV 参数的预测模型在预测 1 小时后可能出现的 VT 事件上表现出 73.5%的准确性、70.6%的敏感性、76.5%的特异性、75.0%的阳性预测值和 72.2%的阴性预测值, AUC 为 0.75。这一模型的预测性在加入呼吸频率变异性(respiratory rate variability, RRV)分析后其准确率(85.3%)、敏感性(88.2%)及特异性(82.4%)得到进一步提升。Panjaitan 等[19]也基于 HRV 的时域分析构建 SCD 的卷积神经网络模型对 SCD 进行风险预测, 模型表现出较高的预测水准, 平均准确率为 99.30%、敏感性为 97.00%、特异性为 99.60%、精准度为 97.87%, 表明 HRV 在预测 SCD 事件上的潜在价值, 但研究只涉及到 HRV 的时域分析方法, 且样本量较小, 未来仍需要多中心大样本研究及更多分析方法的验证。Yan 等[20]通过个体化的心率对 HRV 进行调整, 调整后得到的 HRV₁ 在 SCD 的危险分层上展现出更高的可靠性, 其曲线下面积中位数为 0.72, 高于长程 HRV 分析(0.63)及短程 HRV 分析(0.58)。Martinez-Alanis 等[21]基于 135 名受试者其短期心电图记录(长度为 1000 次心搏周期)所得到的 HRV, 通过支持向量机法检测其对 SCD 事件的预测价值, 向量机性能测试显示其 AUC 为 0.68, 准确性为 67%, 表明以此开发的支持向量机可能有助于 SCD 的早期预警。这些研究均表明 HRV 异常与心律失常(尤其恶性心律失常)和心源性猝死密切相关。

3.3. HRV 与冠心病

冠心病在成年人群中是最常见的心脏病, 且患病率逐年增长, 发生心梗死后的心肌组织因缺血缺氧而导致心脏自主神经功能失衡, 冠心病患者后期往往更易发生 VT、VF 等不良心血管事件。多项研究均显示心梗后较低的 HRV 与全因死亡[22]和心源性死亡[23][24]的风险增加有关, 以往的研究证明 24 小时动态心电图 SDNN < 70 ms 是急性心梗后死亡的有利预测指标和独立危险因素, 且 HRV 能够预测心梗后患者的心室颤动和症状性持续性室性心动过速[25]。一项研究测试了基于 10 秒心电图所获取的超短期心率变异性(ultra-short heart rate variability, usHRV)的有效性, 发现单个 10 秒心电图也能产生有效的 rMSSD 和 SDNN 测量值, 且与较长时间记录有中等到强的相关性[26], 这意味着 10 秒心电图能提供更多有价值的预后信息, 尤其是在门诊、重症监护室等环境下能更早期识别高危患者。一项研究表明, 在 ST 段抬高型心肌梗死(ST-elevation Myocardial infarction, STEMI)后 1 个月和 6 个月以及 1 年和 2 年, 入院心电图的 usHRV 减少与死亡率增加有关[27]。另一项有关非 ST 段抬高型心肌梗死(non-ST-elevation Myocardial infarction, USTEMI)预后的研究也表明, 较低的 usHRV 与 USTEMI 患者 2 年后较高的全因死亡率有显著相关性, SDNN 每增加 1 ms, USTEMI 患者 2 年死亡风险降低约 4.4% [28]。运动心脏康复能恢复 STEMI 患者的 HRV 值, 改善自主神经功能, 减少心血管不良事件的发生[29], 且中等强度连续运动的远期收益要优于高强度间歇运动[30]。一项单中心前瞻性队列研究[31]显示经皮冠状动脉介入(percutaneous coronary intervention, PCI)术后 24 小时和 6 个月后的 HRV 值较术前有明显增加, 且 HRV 分析显示完全血运重建患者的恢复程度优于不完全血运重建, 提示 PCI 可以改善冠心病患者的自主神经调节功能。

3.4. HRV 与原发性高血压

高血压患者在临床上常常能够观察到存在交感神经的活性增强与副交感神经的活性降低, 后续对高血压患者自主神经功能的研究表明, 自主神经功能的障碍在高血压发病之前就已经出现[32][33], 且非杓型高血压患者的交感神经较杓型高血压患者更加活跃[34]。Alp 等[35]研究发现非杓型高血压患者的 LF/HF 比值较杓型高血压患者更高, 而 HF 及 rMSSD 则低于杓型高血压患者, 提示自主神经昼夜节律和

自主神经功能恶化可能是导致这一现象出现的原因。有效的降压治疗对高血压患者的自主神经功能的平衡和血流动力学的改善有一定帮助[36],但也有观点认为即便通过药物控制血压,与正常血压人群相比,高血压患者的 HRV 仍可能持续降低[37]。HRV 在高血压发病预测上也具有一定参考价值, Kang 等[38]通过一项对未罹患高血压人群的长期随访研究发现,HRV 的降低与未来发生高血压的风险增加成反比关系,提示 HRV 可以在预测未来高血压的发病方面发挥作用,尤其在青中年人群中影响更大。现有观点认为心室重构与心脏自主神经功能独立相关[39][40],提示在防止心室重构的高血压治疗方案中,具有调节自主神经功能的药物有着重要地位,对高血压患者 HRV 的监测,也有助于了解其自主神经功能变化,帮助早期预测及减少高血压患者的靶器官损害的发生。

4. 小结

综上所述,作为临床上常用且容易获得的心电图指标,心率变异性可以反映心脏自主神经的活性及调节功能,在心血管疾病的疾病进展、疗效评估、预后判断及并发症风险评估等多个方面均有重要作用,但由于 HRV 受年龄、药物、生活习惯、昼夜节律等多种因素影响,且随自主神经活性的平衡变化而变化,现有研究尚不能确定某一个具体的标准用于疾病的诊断、危险分层及预后判断,usHRV、非线性心率变异性分析以及神经网络或机器学习的 HRV 分析方法展现出的潜力可能有助于帮助我们寻找某个或综合疾病评估标准。

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