先天性心脏病患儿介入封堵术治疗前后 CRP、NT-proBNP、心率变异性的变化及与术后心功能的关系研究 *

郭　军　赵　胜　黄晓碧　杨贵明　祁晓慧

（安徽省儿童医院心内科 安徽 合肥 230000）

摘要 目的：探讨先天性心脏病(CHD)患儿介入封堵术治疗前后 C-反应蛋白(CRP)、N 末端 B 型利钠肽原(NT-proBNP)、心率变异性(HRV)的变化及与术后心功能的关系。方法：选择 2020 年 10 月至 2021 年 6 月在本院行介入封堵术治疗的 95 例 CHD 患儿为研究对象，采用化学发光法检测血清 CRP 水平，采用电化学发光免疫技术检测血清 NT-proBNP 水平，采用 24 h 动态心电图及 12 导联同步心电图分析 HRV 指标，观察手术前后患儿的血清 CRP、NT-proBNP 水平及 HRV 指标变化，比较术后不同 NYHA 心功能分级患儿的血清 CRP、NT-proBNP 水平和 HRV 指标，分析患儿术前血清 CRP 水平、血清 NT-proBNP 水平、HRV 指标与术后 NYHA 心功能分级的相关性。结果：介入封堵术后患儿血清 CRP、NT-proBNP、LF/HF 水平逐渐降低，术后 3 d、术后 1 个月时均低于术前，术后 1 个月时均低于术后 3 d 时($P<0.025$)；而 TP、HF、LF、R-R、PNN50%、ASDNN、SDANN、SDNN、rMSSD 水平逐渐升高，术后 3 d、术后 1 个月时均高于术前，术后 1 个月时均高于术后 3 d 时($P<0.025$)。患儿术后 3 d 的血清 CRP、NT-proBNP 水平及 LF/HF 水平随着 NYHA 心功能分级的升高而升高，TP、HF、LF、R-R、PNN50%、ASDNN、SDANN、SDNN、rMSSD 水平随着 NYHA 心功能分级的升高而降低(多有 $P<0.05$)。患儿术后 3 d 的 NYHA 心功能分级与治疗前血清 CRP、NT-proBNP 及 LF/HF 水平呈负相关，与 TP、HF、LF、R-R、PNN50%、ASDNN、SDANN、SDNN、rMSSD 水平呈正相关($P<0.05$)。结论：CHD 患儿经介入封堵术治疗后，血清 CRP、NT-proBNP 及 HRV 指标变化明显，与术后 NYHA 心功能分级显著相关，血清 CRP、NT-proBNP 及 HRV 指标有望成为评估 CHD 患儿介入封堵术后预后的较敏感性指标。

关键词：先天性心脏病；介入封堵术；C-反应蛋白；N 末端 B 型利钠肽原；心率变异性；心功能

中图分类号：R541.1　文献标识码：A　文章编号：1673-6273(2022)09-1760-06

Changes of CRP, NT-proBNP, Heart Rate Variability and their Relationship Research with Postoperative Cardiac Function in Children with Congenital Heart Disease before and after Interventional Closure*

GUO Jun, ZHAO Sheng, HUANG Xiao-bi, YANG Gui-ming, QI Xiao-hui

(Department of Internal Medicine-Cardiovascular, Anhui Children's Hospital, Hefei, Anhui, 230000, China)

ABSTRACT Objective: To investigate the changes of C-reactive protein (CRP), N-terminal pro-B-type natriuretic peptide (NT-proBNP), heart rate variability (HRV) and their relationship with postoperative cardiac function in children with congenital heart disease (CHD) before and after interventional closure. Methods: From October 2020 to June 2021, 95 children with CHD who received interventional occlusion in our hospital were selected as the research subjects. The serum CRP level was detected by chemiluminescence method, the serum NT-proBNP level was detected by electrochemiluminescence immunoassay, the HRV indexes were analyzed by 24 h ambulatory electrocardiogram and 12 lead synchronous electrocardiogram, and the changes of serum CRP, NT proBNP levels and HRV indexes before and after operation were observed. The serum CRP, NT-probNP levels and HRV indexes were compared before and after operation, and the serum CRP, NT-probNP levels and HRV indexes of children with different NYHA cardiac function grades after operation were compared. The correlation between preoperative serum CRP level, serum NT-probNP level, HRV index and postoperative NYHA cardiac function grading were analyzed. Results: The serum CRP, NT-proBNP and LF/HF levels in children with CHD after interventional occlusion decreased gradually, which at 3 days and 1 month after operation were lower than those before operation, and 1 month after operation were lower than those 3 days after operation($P<0.025$). The TP, HF, LF, R-R, PNN50%, ASDNN, SDANN, SDNN and rMSSD levels increased gradually, which at 3 days and 1 month after operation were higher than those before operation, and 1 month after operation were higher than those 3 days after operation ($P<0.025$). The serum CRP, NT-probNP and LF/HF levels in children with CHD at 3 d after operation increased with the increase of NYHA cardiac function grading. The TP, HF, LF, R-R, PNN50%, ASDNN, SDANN, SDNN and rMSSD levels decreased with the increase of NYHA cardiac function grading (most have $P<0.05$). The NYHA car-

diac function grading of children with CHD at 3 d after operation was negatively correlated with the CRP, NT-proBNP and LF/HF levels in serum before treatment($P<0.05$), and positively correlated with the TP, HF, LF, R-R, PNN50%, ASDNN, SDANN, SDNN and rMSSD levels ($P<0.05$). **Conclusion:** After interventional closure, the indexes of serum CRP, NT-proBNP and HRV in children with CHD changed significantly, which are significantly correlated with the postoperative NYHA cardiac function grade. The indexes of serum CRP, NT-proBNP and HRV are expected to be sensitive indexes to evaluate the prognosis of children with CHD after interventional occlusion.

Key words: Congenital heart disease; Interventional closure; C-reactive protein; N-terminal pro-B-type natriuretic peptide; Heart rate variability; Cardiac function

前言

先天性心脏病(Congenital heart disease,CHD)是由心脏或大血管结构异常所引起的一类心脏病，我国是世界上 CHD 发病率较高的国家，儿童 CHD 的发病率约为 0.7%~0.8%，CHD 是我国及世界各发达国家婴儿死亡的主要原因之一，严重危害了患儿的健康和生命安全[1,2]。介入封堵术是治疗 CHD 患儿的主要方式[3]，具有操作方法简单、术后恢复快、疗效好等优点，得到广大医患人员的青睐。然而，手术过程中导管导丝的牵拉及封堵材料的挤压和磨损等，均不可避免地会对心肌造成一定的损伤，且对术后心功能的恢复造成一定的影响。心率变异性(Heart rate variability,HRV)是目前临床上 CHD 是否进行介入治疗的依据，同时也是预测患者术后心功能的重要指标[4]。C-反应蛋白(C-reactive protein,CRP)是一种由肝脏合成的急性时相蛋白，以微量形式存在于人体血清中，当机体发生创伤或有急性炎症时，CRP 水平升高，是急性炎症反应的一个敏感可靠的指标，可以有效预测术后心血管事件发生情况及监测术后恢复情况[5,6]。N 末端 B 型利钠肽原(N-terminal pro-B-type natriuretic peptide,NT-proBNP)是 B 型利尿钠肽（Brain natriuretic peptide,BNP）降解的产物，通过检测血清 NT-proBNP 可以反映 BNP 浓度[7]。BNP 主要由心室分泌，左室收缩功能降低和心室壁张力增加可促进 BNP 分泌,BNP 浓度水平与心功能有关[8]。本文拟探明 CHD 患儿经介入封堵术治疗前后 CRP、NT-proBNP、HRV 的变化及与术后心功能的关系，以期为 CHD 的治疗及预后评估提供参考。

1 对象与方法

1.1 一般资料

选择 2020 年 10 月至 2021 年 6 月在本院行介入封堵术治疗的 95 例 CHD 患儿为研究对象。其中，男 37 例，女 58 例；年龄 8 月 ~16 岁，平均年龄（10.37± 4.53）岁；疾病类型：房间隔缺损 47 例，动脉导管未闭 24 例，室间隔缺损 24 例。本研究方案经本院伦理委员会审核通过。纳入标准：① 经心脏超声心动图或心血管造影确诊为 CHD[9]；② 符合介入封堵术治疗指征；③ 患儿家属签署知情同意书；④ 年龄 8 月 ~16 岁。排除标准：① 合并风湿性心脏病、肺源性心脏病等其它器质性心脏病者；② 无法配合完成本研究中所有检查项目者；③ 有心脏外科手术史、其他心脏介入手术史者；④ 手术过程中有发生心跳骤停或呼吸骤停等严重并发症者。

1.2 检查指标及方法

1.2.1 血清 CRP、NT-proBNP 水平检测　所有 CHD 患儿均于术前 1 d、术后 3 d、术后 1 个月采集清晨空腹静脉血 3 mL，置于无抗凝的空心试管中，采血后 2 h 内在 3000 r/min 下离心 10 min,有效离心半径 8 cm,常规分离血清保存于 -80℃低温冰箱,2 个月内平衡至室温。运用日立 7060C 型全自动生化分析仪及配套试剂盒，采用化学发光法检测 CRP 水平;采用电化学发光免疫技术检测血清 NT-proBNP 水平，试剂盒为美国 Roche proBNP 试剂盒,仪器为罗氏 Elecsys 2010 型电化学分析仪。检测过程中严格按照试剂盒说明进行操作。

1.2.2 HRV 指标检测　分别于术前 1 d、术后 3 d、术后 1 个月采用动态心电图(纳龙公司生产的 AECG-12C 型动态心电图分析仪）及纳龙 12 导联同步心电图记录仪对所有患儿进行 24 h 动态心电图监测和同步心电图记录，心律失常分型、检出率统计以及 HRV 时域和频域指标计算均由同一组专业医师完成。时域指标包括：正常 R-R 间期平均值(R-R)、相邻正常心动周期≥ 50 ms 的 R-R 间期差值构成比(PNN50%)、24 h 内 R-R 间期标准差(SDNN)、相邻正常 R-R 间期标准差(rMSSD)、1 d 内每 5 min 节段 R-R 间期均值标准差（ASDNN)、1 d 内每 5 min 节段 R-R 间期平均标准差(SDANN)。频域指标包括：总功率(TP)、高频功率(HF)、低频功率(LF)、低频功率 / 高频功率比值(LF/HF)。

1.2.3 术后心功能分级　于术后 3 d 对患儿进行 NYHA 心功能分级，分级标准[10]：Ⅰ级：有心脏病但日常活动量不受限制，一般体力活动不会引起过度疲劳、心悸、气喘或心绞痛等症状；Ⅱ级：心脏病患者的体力活动受到轻度的限制，休息时无自觉症状，但平时一般活动下可出现疲劳、心悸、气喘或心绞痛；Ⅲ级：心脏病患者体力活动明显受限制。小于平时一般体力活动即可引起过度疲劳、心悸、气喘或心绞痛；Ⅳ级：心脏病患者不能从事任何体力活动，休息状态下也出现心衰症状，体力活动后加重。

1.3 统计学方法

研究数据采用 SPSS25.0 进行统计学分析。血清 CRP、NT-proBNP 及 HRV 指标等计量资料经正态性检验符合正态分布，采用均数± 标准差($\bar{x}\pm s$)描述，同组不同时间数据比较采用重复测量方差分析，多组比较采用方差分析，两两组间比较采用独立样本 t 检验，两两时间比较采用差值 t 检验。运用 Spearman 法分析血清 CRP、NT-proBNP 及 HRV 指标与 NYHA 心功能分级的相关性;检验水准以 $P<0.05$ 为差异有统计学

意义。多次比较时按 Bonferroni 校正法进行检验水准调整。

2 结果

2.1 治疗前后 CRP、NT-proBNP 水平及 HRV 频域指标比较

CHD 患儿经介入封堵术后血清 CRP、NT-proBNP、LF/HF

水平逐渐降低，术后 3 d、术后 1 个月时均低于术前，术后 1 个月时均低于术后 3 d 时（$P < 0.025$）；而 TP、HF、LF 水平逐渐升高，术后 3 d、术后 1 个月时均高于术前，术后 1 个月时均高于术后 3 d 时（$P < 0.025$）。详见表 1。

表 1 治疗前后 CRP、NT-proBNP 及 HRV 频域指标比较（$\bar{x} \pm s$）

Table 1 Comparison of CRP, NT-proBNP and HRV frequency domain indexes before and after treatment（$\bar{x} \pm s$）

Time	n	CRP(mg/L)	NT-proBNP (pg/mL)	TP(mW)	HF(mW)	LF(mW)	LF/HF
Before operation	95	5.67± 1.24	148.74± 16.03	872.67± 84.36	63.23± 14.35	275.35± 26.53	4.34± 1.90
3d after operation	95	4.28± 1.15[t]	106.73± 14.20[t]	1,372.15± 92.51[t]	116.92± 21.94[t]	356.04± 33.20[t]	3.09± 1.56[t]
1 month after operation	95	3.05± 1.04[t]	72.62± 11.09[t]	1,516.17± 101.09[t]	172.91± 38.18[t]	429.09± 44.73[t]	2.52± 1.20[t]
Sphericity test	HF coefficient	1.0077	0.9785	1.0184	0.7510	0.8943	0.8901
Overall analysis	F, P	126.966, 0.000	729.808, 0.000	1,151.597, 0.000	384.069, 0.000	442.700, 0.000	33.049, 0.000
T1 vs T0	t, P	8.851, 0.000	19.559, 0.000	35.286, 0.000	20.749, 0.000	19.638, 0.000	4.670, 0.000
T2 vs T0	t, P	16.066, 0.000	37.465, 0.000	44.789, 0.000	25.695, 0.000	27.834, 0.000	8.326, 0.000

Note: The overall analysis was one-way repeated measurement analysis of variance, and the correction of sphericity test was HF coefficient method. The time pairwise comparison was the difference t-test, and the significance marker t was compared with the first time point in the group $P < \alpha'$. $\alpha' = 0.05 / 2 = 0.025$, 2 was the number of multiple comparisons (Bonferroni correction method).

2.2 治疗前后 HRV 时域指标比较

CHD 患儿经介入封堵术后 R-R、PNN50% 、ASDNN、

SDANN、SDNN、rMSSD 水平逐渐升高,术后 3 d 和术后 1 月均高于术前,术后 1 月时均高于术后 3 d 时（$P < 0.025$）。详见表 2。

表 2 治疗前后 HRV 时域指标比较（$\bar{x} \pm s$）

Table 2 Comparison of HRV time domain indexes before and after treatment（$\bar{x} \pm s$）

Time	n	R-R(ms)	PNN50%(%)	ASDNN(ms)	SDANN(ms)	SDNN(ms)	rMSSD(ms)
Before operation	95	657.01± 52.78	12.26± 4.74	51.27± 8.17	77.64± 14.40	84.87± 22.40	31.50± 5.91
3 d after operation	95	709.52± 62.40[t]	14.64± 4.97[t]	56.57± 8.22[t]	98.19± 19.62[t]	108.98± 34.09[t]	37.87± 6.01[t]
1 month after operation	95	773.19± 73.82[t]	17.90± 5.34[t]	59.89± 9.89[t]	114.96± 21.08[t]	132.78± 49.70[t]	45.45± 7.26[t]
Sphericity test	HF coefficient	0.9140	0.9933	0.9850	1.0018	0.9346	0.9875
Overall analysis	F, P	81.108, 0.000	31.111, 0.000	25.530, 0.000	93.386, 0.000	39.917, 0.000	107.437, 0.000
T1 vs T0	t, P	6.251, 0.000	3.080, 0.003	4.727, 0.000	7.961, 0.000	5.284, 0.000	7.391, 0.000
T2 vs T0	t, P	14.066, 0.000	8.394, 0.000	6.537, 0.000	13.777, 0.000	8.018, 0.000	13.909, 0.000
T2 vs T1	t, P	6.027, 0.000	4.622, 0.000	2.763, 0.007	5.770, 0.000	4.364, 0.000	7.676, 0.000

Note: The overall analysis was one-way repeated measurement analysis of variance, and the correction of sphericity test was HF coefficient method. The time pairwise comparison was the difference t-test, and the significance marker t was compared with the first time point in the group $P < \alpha'$. $\alpha' = 0.05 / 2 = 0.025$, 2 was the number of multiple comparisons (Bonferroni correction method).

2.3 术后 3 d 不同 NYHA 心功能分级患儿血清 CRP、NT-proB-NP 水平及 HRV 频域指标比较

术后 3 d 时，CHD 患儿的血清 CRP、NT-proBNP、LF/HF 水平随着 NYHA 心功能分级的升高而升高，而 TP、HF、LF 水平随着 NYHA 心功能分级的升高而降低，三组间比较差异多有统计学意义（$P < 0.05$），仅Ⅱ级组与Ⅰ级组 LF/HF 水平两两比较无统计学意义（$P > 0.05$），Ⅲ级与Ⅱ级组 LF/HF 水平两两比较无统计学意义（$P > 0.05$）。详见表 3。

2.4 术后 3 d 不同 NYHA 心功能分级患儿 HRV 时域指标比较

术后 3 d 时，CHD 患儿的 HRV 时域指标 R-R、PNN50%、ASDNN、SDANN、SDNN、rMSSD 水平随着 NYHA 心功能分级的升高而降低，但三组间比较差异仅部分有统计学意义（$P < 0.05$）。详见表 4。

表 3　术后 3 d 不同 NYHA 心功能分级患儿血清 CRP、NT-proBNP 水平及 HRV 频域指标比较($\bar{x}\pm s$)

Table 3　Comparison of serum CRP, NT-proBNP levels and HRV frequency domain indexes in children with different NYHA cardiac function grades 3 days after operation($\bar{x}\pm s$)

NYHA grades	n	CRP(mg/L)	NT-proBNP (pg/mL)	TP(mW)	HF(mW)	LF(mW)	LF/HF
Grade Ⅰ	58	3.82± 0.81	103.02± 12.46	1,415.01± 81.35	129.37± 21.96	367.16± 38.46	2.86± 1.81
Grade Ⅱ	33	4.94± 0.86[a]	112.39± 14.77[a]	1,334.50± 72.27[a]	98.80± 19.07[a]	342.98± 33.69[a]	3.43± 1.76
Grade Ⅲ	4	5.92± 1.25[ab]	130.87± 21.15[ab]	1,129.86± 60.20[ab]	72.49± 15.32[ab]	293.66± 22.98[ab]	4.03± 1.50[a]
Sphericity test	F, P	26.044, 0.000	11.086, 0.000	32.093, 0.000	31.977, 0.000	10.675, 0.000	1.665, 0.195
Ⅱ vs Ⅰ	LSD-t, P	4.573, 0.000	2.375, 0.020	3.589, 0.001	5.087, 0.000	2.298, 0.024	1.121, 0.265
Ⅲ vs Ⅰ	LSD-t, P	8.599, 0.000	7.060, 0.000	12.710, 0.000	9.465, 0.000	6.983, 0.000	2.283, 0.025
Ⅲ vs Ⅱ	LSD-t, P	4.026, 0.000	4.685, 0.000	9.121, 0.000	4.378, 0.000	4.685, 0.000	1.162, 0.248

Note: The overall analysis was one-way ANOVA. LSD-t test or hsd-q test was used to compare the two groups. The significant markers a and b were compared with grad Ⅰ and grade Ⅱ, respectively ($P<0.05$).

表 4　术后 3 d 不同 NYHA 心功能分级患儿 HRV 时域指标比较($\bar{x}\pm s$)

Table 4　Comparison of HRV time domain indexes in children with different NYHA cardiac function grades 3 days after operation($\bar{x}\pm s$)

NYHA grades	n	R-R(ms)	PNN50%(%)	ASDNN(ms)	SDANN(ms)	SDNN(ms)	rMSSD(ms)
Grade Ⅰ	58	718.82± 57.46	15.70± 2.79	57.07± 7.95	106.87± 17.38	116.24± 35.09	39.31± 5.27
Grade Ⅱ	33	703.88± 57.87	14.73± 2.50	56.19± 7.94	94.91± 14.72[a]	96.86± 30.68[a]	34.98± 4.78[a]
Grade Ⅲ	4	681.78± 52.99[a]	13.54± 1.64[a]	54.97± 7.70	87.47± 13.80[a]	83.19± 27.72[a]	31.97± 4.01[ab]
Sphericity test	F, P	1.291, 0.280	2.283, 0.108	0.227, 0.797	7.215, 0.001	4.703, 0.011	10.170, 0.000
B vs A	LSD-t, P	0.900, 0.370	1.263, 0.210	0.386, 0.701	2.527, 0.013	2.009, 0.047	2.960, 0.004
C vs A	LSD-t, P	2.232, 0.028	2.810, 0.006	0.918, 0.361	4.096, 0.000	3.426, 0.001	5.018, 0.000
C vs B	LSD-t, P	1.331, 0.186	1.548, 0.125	0.533, 0.595	1.570, 0.120	1.417, 0.160	2.058, 0.042

Note: The overall analysis was one-way ANOVA. LSD-t test or hsd-q test was used to compare the two groups. The significant markers a and b were compared with grad Ⅰ and grade Ⅱ, respectively ($P<0.05$).

2.5 治疗前血清 CRP、NT-proBNP 水平及 HRV 指标与术后 NYHA 心功能分级的相关性分析

Spearman 相关性分析显示, CHD 患儿经介入封堵术后 3 d 的 NYHA 心功能分级与治疗前血清 CRP、NT-proBNP 及 LF/HF 水平呈负相关关系（$P<0.05$）, 与 TP、HF、LF、R-R、PNN50%、ASDNN、SDANN、SDNN、rMSSD 水平呈正相关关系（$P<0.05$）。详见表 5。

3 讨论

CHD 是指胎儿出生即携带的心脏病, 其病理类型主要有房间隔缺损、动脉导管未闭和室间隔缺损等, 由于其病因不同, 其临床症状差异也较大, 其临床症状主要取决于畸形大小和复杂程度, 以心悸、发绀、反复呼吸道感染、气喘等为主要临床表现, 不仅会影响患儿循环系统功能, 还影响患儿的生长发育, 严重者可危及生命安全[11,12]。由于 CHD 患儿心脏结构存在解剖畸形, 导致左右分流引起心室高容量负荷, 使其心室经常处于高动力循环状态, 进而对心功能造成不利影响[13,14]。介入封堵术可有效矫正心脏结构的解剖畸形及阻断异常分流问题, 有效减轻心室负荷, 改善心功能, 加上介入封堵术本身具有微创、操作简单等优点, 是目前临床上治疗 CHD 患儿的首选术式[15,16]。然而, 凡是手术均会造成一定的创伤, CHD 患儿介入手术过程中导管导丝的牵拉及封堵材料的挤压和磨损等, 均会对心肌造成一定的损伤, 影响患儿的术后恢复。因此, 术前精准评估术后心功

能恢复情况在 CHD 患儿介入封堵术中具有重要意义。

CRP 作为一种急性时相蛋白, 参与组织损伤、炎症反应的病理生理过程, 可反映机体炎症状态, 临床上常用于术后患者机体恢复情况检测和心血管事件的预测[17,18]。BNP 是一种在心室中合成的多肽类心脏神经激素, 由 32 个氨基酸残基组成, 是利尿钠肽家族成员, 主要存在于心室肌内, 多由心肌细胞合成和分泌, 具有扩张血管、利尿(促进尿钠排泄)的作用, 可作为评估心力衰竭预后及急性冠脉综合征患者的危险分层和预后判断的有效指标[19,20]。而 NT-proBNP 是 BNP 降解的产物, 通过检测血清 NT-proBNP 水平可反映血清 BNP 水平[21,22]。心脏节律能够随着昼夜变化和机体状况变化而发生改变的规律被称之为 HRV, HRV 的异常改变与患者病死率和严重心律失常的发生率有密切的关联[23,24]。临床上对于 HRV 的评估, 目前主要分为时域指标和频域指标两种, 其中频域指标(包括 TP、HF、LF、HF\LF)临床上用的较少, 主要应用以 R-R 间期变异为基础的时域指标, 常见的时域指标包括 R-R、PNN50%、ASDNN、SDANN、SDNN、rMSSD[25,26], 本研究结合时域指标和频域指标进行分析。

本研究显示, CHD 患儿经介入封堵治疗后 3 d、术后 1 个月, 血清 CRP、NT-proBNP、LF/HF 水平较治疗前明显降低, TP、HF、LF、R-R、PNN50%、ASDNN、SDANN、SDNN、rMSSD 水平较治疗前明显升高, 表明 CHD 患儿经介入封堵后炎症状态明显改善, 心功能明显好转。其原因可能是介入治疗纠正了血

表 5 治疗前血清 CRP、NT-proBNP 水平及 HRV 指标与术后 NYHA 心功能分级的相关性分析

Table 5 Correlation analysis between serum CRP, NT-proBNP levels and HRV indexes before treatment and postoperative NYHA cardiac function grade

Indexes	NYHA cardiac function grade	
	r_s	P
CRP	-0.652	0.000
NT-proBNP	-0.675	0.000
TP	0.532	0.007
HF	0.483	0.022
LF	0.476	0.024
LF/HF	-0.635	0.000
R-R	0.446	0.016
PNN50%	0.373	0.025
ASDNN	0.388	0.021
SDANN	0.347	0.031
SDNN	0.395	0.018
rMSSD	0.304	0.035

Note: rs was Spearman correlation coefficient.

流动力学异常情况,阻断了左向右分流,缓解了右心室循环状态[27,28]。另外,介入封堵术纠正了患儿心脏解剖畸形,使心室容量负荷降低、室壁张力下降、心室结构得以逆转,从而消除炎症反应,降低心室细胞分泌 BNP。这一结论在前人的研究[29,30]中也得到佐证。本研究显示,术后 3 d 时,CHD 患儿的血清 CRP、NT-proBNP 水平及 LF/HF 水平随着 NYHA 心功能分级的升高而升高,TP、HF、LF、R-R、PNN50% 、ASDNN、SDANN、SDNN、rMSSD 水平随着 NYHA 心功能分级的升高而降低,提示血清 CRP、NT-proBNP 水平及 HRV 指标与 CHD 患儿术后心功能有密切的关系,术后不同 NYHA 心功能分级的 CHD 患儿,其血清 CRP、NT-proBNP 水平及 HRV 指标呈现出差异性,通过检测血清 CRP、NT-proBNP 水平及 HRV 指标可对 CHD 患儿术后心功能恢复评估提供非常有价值的信息。然而,本研究中,在对术后不同 NYHA 心功能分级患儿 HRV 指标进行组间两两配对比较时,发现 HRV 的部分时域和频域指标比较无统计学差异的情况,如 LF/HF、PNN50%水平 Ⅱ级组与 Ⅰ级组比较差异不明显,PNN50%、ASDNN 水平Ⅲ级与Ⅱ级比较差异不明显。其原因可能是:其一,NYHA 心功能 Ⅰ级和Ⅱ级患儿其疗效接近,NYHA 心功能Ⅲ级与Ⅱ级级疗效接近,导致 HRV 部分指标比较无统计学意义;其二,本研究中介入封堵术治疗后 NYHA 心功能Ⅲ的病例资料较少,导致数据的代表性不强。本研究相关分析显示,CHD 患儿术后 3 d 的 NYHA 心功能分级与治疗前血清 CRP、NT-proBNP 及 LF/HF 水平呈负相关,与 TP、HF、LF、R-R、PNN50%、ASDNN、SDANN、SDNN、rMSSD水平呈正相关,进一步证实血清 CRP、NT-proBNP 水平及 HRV 指标可预判术后 CHD 患儿心功能情况。

综上所述,CHD 患儿血清 CRP、NT-proBNP 水平及 HRV 指标水平治疗前后变化明显,术后不同 NYHA 心功能分级的患儿血清 CRP、NT-proBNP 水平及 HRV 指标水平不同,术前血清 CRP、NT-proBNP 水平及 HRV 指标水平与术后 NYHA 心功能分级呈现出明显的相关性,CRP、NT-proBNP、HRV 有望成为评估 CHD 患儿预后的敏感性指标。

参 考 文 献 (References)

[1] 陈瑜, 陈梅. 南京地区学龄前儿童先天性心脏病的患病情况调查与发病因素分析[J]. 实用预防医学, 2020, 27(11): 1384-1387

[2] 赵晓蕾, 王理, 张辉. 先天性心脏病的表观遗传学研究进展[J]. 心肺血管病杂志, 2018, 37(11): 1033-1037

[3] Santens B, Van De Bruaene A, De Meester P, et al. Diagnosis and treatment of right ventricular dysfunction in congenital heart disease [J]. Cardiovasc Diagn Ther, 2020, 10(5): 1625-1645

[4] Sarah BM, Rathinaswamy G, Marina M, et al. Heart rate variability is depressed in the early transitional period for newborns with complex congenital heart disease[J]. Clin Auton Res, 2020, 30(2): 165-172

[5] Qian Z, Chong S, Yanchun C, et al. Association of high sensitive C-reactive protein with coronary heart disease: a Mendelian randomization study[J]. BMC Med Genet, 2019, 20(1): 170

[6] Yuelin S, Tianxin Z, Dong L, et al. Predictive value of C-reactive protein and the Pediatric Risk of Mortality III Score for occurrence of postoperative ventilator-associated pneumonia in pediatric patients with congenital heart disease[J]. Pediatr Investig, 2019, 3(2): 91-95

[7] Nicole M, Stefanie TR, Nicolas B, et al. Perioperative urinary NT-ProBNP values and their usefulness as diagnostic and prognostic markers in children with congenital heart disease[J]. Clin Chim Acta, 2021, 5(18): 28-32

[8] Lamia AA, Giovanni DA, Giuseppe P, et al. Cardiac Magnetic Resonance Evaluation of Pulmonary Transit Time and Blood Volume in Adult Congenital Heart disease [J]. J Magn Reson Imaging, 2019, 50(3): 779-786

[9] 梁峰, 沈珠军, 方全, 等. 2015 年欧洲心脏病学会关于心肌病、遗传性心律失常、小儿和先天性心脏病患者室性心律失常治疗和心脏性猝死预防指南解读[J]. 中国心血管杂志, 2016, 21(5): 413-418

[10] Bennett JA, Riegel B, Bittner V, et al. Validity and reliability of the NYHA classes for measuring research outcomes in patients with cardiac disease[J]. Heart Lung, 2002, 31(4): 262-270

[11] 贾兵, 李守军. 先天性心脏病外科治疗中国专家共识(二):小儿先天性主动脉瓣狭窄 [J]. 中国胸心血管外科临床杂志, 2020, 27(3): 246-250

[12] 韩月英, 王厚照, 张雪梅, 等. 先天性心脏病患儿术后并发医院感染的危险因素及其病原菌分布和药敏实验分析[J]. 现代生物医学进展, 2021, 21(4): 683-687, 682

[13] 莫绪明, 李守军. 先天性心脏病外科治疗中国专家共识 (十三):先天性二尖瓣畸形 [J]. 中国胸心血管外科临床杂志, 2020, 27(12): 1382-1388

[14] 龙向淑, 杨太, 张长海, 等. 先天性心脏病复合畸形患者行同期介入治疗的长期疗效及安全性观察[J]. 临床心血管病杂志, 2019, 35 (12): 1141-1144

[15] Bergmann M, Germann CP, Nordmeyer J, et al. Short- and Long-term Outcome After Interventional VSD Closure: A Single-Center Experience in Pediatric and Adult Patients [J]. Pediatr Cardiol, 2021, 42(1): 78-88

[16] 王宁, 王瑜, 林晓丹, 等. 超声诊断及心血管造影在先天性心脏病介入封堵术中的联合应用研究[J]. 解放军预防医学杂志, 2019, 37 (7): 71-72, 75

[17] Stephen MC, Ahmet F, Nick S, et al. Diagnostic triage and the role of natriuretic peptide testing and echocardiography for suspected heart failure: an appropriateness ratings evaluation by UK GPs[J]. Br J Gen Pract, 2011, 61(588): e427-e435

[18] McClelland S, Zhou S, O'Connell E, et al. New-onset heart failure in the STOP-HF programme. Natriuretic peptide defines and tracks risk and enables earlier diagnosis of heart failure [J]. Eur J Heart Fail, 2020, 22(2): 378-380

[19] Liu Y, Guo D, Wang A, et al. Combined effect of serum N-terminal pro-brain natriuretic peptide and galectin-3 on prognosis 1 year after ischemic stroke[J]. Clin Chim Acta, 2020, 5(11): 33-39

[20] Zheng X, Zhang Y, Liu L, et al. N-terminal pro-brain natriuretic peptide as a biomarker for predicting coronary artery lesion of Kawasaki disease[J]. Sci Rep, 2020, 10(1): 5130

[21] Siegmund AS, Pieper PG, Bouma BJ, et al, van Veldhuisen DJ, Dickinson MG. Early N-terminal pro-B-type natriuretic peptide is associated with cardiac complications and function during pregnancy in congenital heart disease[J]. Neth Heart J, 2021, 29(5): 262-272

[22] Zheng H, Cui Y, Li K, et al. The association between the pattern of change in N-terminal pro-B-type natriuretic peptide and short-term outcomes in children undergoing surgery for congenital heart disease [J]. Interact Cardiovasc Thorac Surg, 2021, 32(4): 601-606

[23] Elena SB, Kathleen MH, Cristopher AA, et al. Psychological Traits, Heart Rate Variability, and Risk of Coronary Heart Disease in Healthy Aging Women-The Women's Health Initiative [J]. Psychosom Med, 2019, 81(3): 256-264

[24] 魏传菊, 任长明, 庄海峰, 等. 先天性心脏病介入治疗前后心律失常及心率变异性变化与术后心功能的相关性分析 [J]. 中国医刊, 2020, 55(2): 159-162

[25] 董宁, 崔海玲. 心率变异性对急性心肌梗死患者心脏自主功能的评价作用[J]. 广西医科大学学报, 2020, 37(3): 474-478

[26] 迟晔虹, 张明玥, 梁娟, 等. 心率变异性在散点图指标和时域指标中的对比分析[J]. 临床心血管病杂志, 2019, 35(7): 628-630

[27] 李芬, 全勇, 宋青青, 等. 儿童先天性心脏病封堵术后发生心血管事件的影响因素分析[J]. 临床药物治疗杂志, 2019, 17(12): 44-48

[28] 博宁, 刘琮, 张智伟. 小儿先天性心脏病介入治疗进展 [J]. 中华实用儿科临床杂志, 2020, 35(1): 19-23

[29] 蒋海清, 黄霞, 夏俊. 小儿先天性心脏病合并心力衰竭外周血NT-proBNP、cTnI 和 CRP 水平变化及其临床意义 [J]. 华南国防医学杂志, 2019, 33(11): 748-750, 763

[30] 张小龙. NT-ProBNP 及 BNP 在儿童先天性心脏病中的应用价值 [J]. 国际儿科学杂志, 2019, 46(10): 713-717

---

[19] Crozeta BM, Chaves de Souza L, Correa Silva-Sousa YT, et al. Evaluation of Passive Ultrasonic Irrigation and GentleWave System as Adjuvants in Endodontic Retreatment [J]. J Endod, 2020, 46(9): 1279-1285

[20] Ghoniem N, Vaidyanathan V, Zealand C M, et al. Mineral Trioxide Aggregate and Diluted Formocresol Pulpotomy: Prospective and Retrospective Study Outcomes [J]. J Mich Dent Assoc, 2018, 100(4): 40-65

[21] Junqueira M A, Cunha N N O, Caixeta F F, et al. Clinical, Radiographic and Histological Evaluation of Primary Teeth Pulpotomy Using MTA And Ferric Sulfate [J]. Braz Dent J, 2018, 29 (2): 159-165

[22] Kahvand M, Mehran M, Haghgoo R, et al. Clinical and Radiographic Evaluation of Allium sativum Oil （Garlic Oil) in Comparison with Formocresol in Primary Molar Pulpotomy [J]. J Int Soc Prev Community Dent, 2019, 9(4): 390-395

[23] Konyala H R, Mareddy A R, Puppala N, et al. Clinical, Radiological, and Histological Assessment of Magnetic Nanoparticles as Pulpotomy Medicament in Primary Molars [J]. Int J Clin Pediatr Dent, 2018, 11 (4): 283-287

[24] Kuo H Y, Lin J R, Huang W H, et al. Clinical outcomes for primary molars treated by different types of pulpotomy: Aretrospective cohort study[J]. J Formos Med Assoc, 2018, 117(1): 24-33

[25] Maroto M, Barreiro S, Barberí a E. Portland cement as pulp dressing agent in pulpotomy treatment of primary molars: a 12-month clinical study[J]. Eur J Paediatr Dent, 2019, 20(1): 23-26

[26] Căpută PE, Retsas A, Kuijk L, et al. Ultrasonic Irrigant Activation during Root Canal Treatment: A Systematic Review [J]. J Endod. 2019, 45(1): 31-44.e13

[27] Musale P K, Kothare S S, Soni A S. Mineral trioxide aggregate pulpotomy: patient selection and perspectives [J]. Clin Cosmet Investig Dent, 2018, 10(12): 37-43

[28] Pei S L, Shih W Y, Liu J F. Outcome comparison between diode laser pulpotomy and formocresol pulpotomy on human primary molars[J]. J Dent Sci, 2020, 15(2): 163-167

[29] Prabhakar A R, Mandroli P S, Bhat K. Pulpotomy with curcumin: Histological comparison with mineral trioxide aggregate in rats [J]. Indian J Dent Res, 2019, 30(1): 31-36

[30] vi Praja V, Muttath A L, Duraisamy V, et al. A Clinical and Radiographic Comparison of Platelet-rich Fibrin and Lyophilized Platelet-derived Preparation as Pulpotomy Agent in Primary Molars [J]. J Pharm Bioallied Sci, 2020, 12(Suppl 1): 155-160

[31] Orozco EIF, Toia CC, Cavalli D, et al. Effect of passive ultrasonic activation on microorganisms in primary root canal infection: a randomized clinical trial[J]. J Appl Oral Sci, 2019, 28(1): e20190100

[32] Shafie L, Esmaili S, Parirokh M, et al. Efficacy of Pre-Medication with Ibuprofen on Post-Operative Pain after Pulpotomy in Primary Molars[J]. Iran Endod J, 2018, 13(2): 216-220