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风湿性心脏病瓣膜置换术患者围术期血浆脑钠肽水平的表达及临床意义

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摘要 目的:探讨风湿性心脏病瓣膜置换术患者围手术期血浆脑钠肽(BNP)水平及其临床意义。**方法:**选取 2015 年 1 月至 2016 年 12 月在我院接受心脏瓣膜置换术的风湿性心脏病患者 98 例为研究对象,分别于术前、术后 12 h、24 h、48 h、术后 1 周进行血浆 BNP、磷酸肌酸同工酶(CK-MB)、高敏 C 反应蛋白(hs-CRP)水平检测,观察纽约心脏病协会(NYHA)不同心功能分级、不同时间点患者血浆 BNP、CK-MB、hs-CRP 水平变化,同时观察并比较术后发生严重心律失常与否的患者在不同时间点血浆 BNP、CK-MB、hs-CRP 水平变化。**结果:**随 NYHA 心功能分级升高,患者血浆 BNP、CK-MB、hs-CRP 水平升高,不同 NYHA 心功能分级患者血浆 BNP、hs-CRP 水平比较差异有统计学意义($P<0.05$),CK-MB 水平比较差异无统计学意义($P>0.05$);不同 NYHA 心功能分级患者血浆 BNP、hs-CRP 两两比较差异有统计学意义($P<0.05$),CK-MB 两两比较差异无统计学意义($P>0.05$)。患者术后 12 h、24 h、48 h 血浆 BNP、hs-CRP 水平均显著高于术前,术后 24 h、48 h 血浆 CK-MB 水平均显著高于术前,而术后 1 周血浆 BNP、CK-MB、hs-CRP 显著低于术前($P<0.05$)。术后发生严重心律失常(严重心律失常组)患者 16 例,未发生严重心律失常(无严重心律失常组)患者 82 例,两组患者术后 12 h、24 h、48 h 血浆 BNP、CK-MB、hs-CRP 水平均显著高于术前($P<0.05$);两组患者术后 1 周 BNP 与术前比较差异无统计学意义($P>0.05$),而 CK-MB、hs-CRP 水平均显著低于术前($P<0.05$),但严重心律失常组术后 12 h、24 h、48 h、1 周血浆 BNP、CK-MB、hs-CRP 水平均显著高于无严重心律失常组($P<0.05$)。**结论:**风湿性心脏病瓣膜置换术患者术前血浆 BNP 可以反映患者心功能情况,术后患者血浆 BNP、CK-MB、hs-CRP 异常升高,发生严重心律失常患者升高更为明显。

关键词:风湿性心脏病;脑钠肽;磷酸肌酸同工酶;高敏 C 反应蛋白

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Expression of Plasma Brain Natriuretic Peptide in Patients with Rheumatic Heart Disease Undergoing Valve Replacement and its Clinical Significance

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ABSTRACT Objective: To investigate the level of plasma brain natriuretic peptide (BNP) in patients with rheumatic heart disease undergoing valve replacement and its clinical significance. **Methods:** 98 patients with rheumatic heart disease who were underwent valve replacement in our hospital from January 2015 to December 2016 were selected as the subjects, the levels of plasma BNP, creatine phosphate isoenzyme (CK-MB) and high sensitive C reactive protein (hs-CRP) were detected before operation and 12 h, 24 h, 48 h and 1 weeks after operation respectively, the changes of plasma BNP, CK-MB and hs-CRP levels in patients with different cardiac function classification of New York Heart Association (NYHA) and different time points, at the same time, the changes of plasma BNP, CK-MB and hs-CRP levels were observed and compared at different time points in patients with Severe arrhythmia or not. **Results:** With the increase of NYHA cardiac function classification, the plasma BNP, CK-MB and hs-CRP levels increased, and there were significant differences in the plasma BNP and hs-CRP levels between different NYHA cardiac function classification ($P<0.05$), there was no significant difference in CK-MB level between different NYHA cardiac function classification ($P>0.05$). There were significant differences in plasma BNP and hs-CRP between patients with different NYHA cardiac function classification ($P<0.05$), there was no significant difference in CK-MB ($P>0.05$). The plasma BNP and hs-CRP levels in patients with 12 h, 24 h and 48 h after operation were significantly higher than those before operation, the CK-MB levels in 24 h and 48 h after operation were significantly higher than those before operation, the plasma BNP, CK-MB and hs-CRP at 1 weeks after operation were significantly lower than those before operation ($P<0.05$). There were 16 patients with severe arrhythmia (severe arrhythmia group) after operation, there were 82 patients without severe arrhythmia (no severe arrhythmia group), the plasma BNP, CK-MB and hs-CRP levels in the two groups at 12 h, 24 h and 48 h after operation were significantly higher than those before operation ($P<0.05$). There was no significant difference in BNP of the two groups between 1 weeks after operation and before operation ($P>0.05$), the CK-MB and hs-CRP levels were significantly lower than those before operation ($P<0.05$), however, the plasma BNP, CK-MB and hs-CRP levels in the severe arrhythmia group 12 h, 24 h, 48 h and 1 weeks after operation were significantly higher than those no severe arrhythmia ($P<0.05$). **Conclusion:** Preoperative plasma BNP can reflect the cardiac function in patients with

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rheumatic heart disease undergoing valve replacement, the plasma BNP, CK-MB and hs-CRP levels were abnormally elevated after operation, the increase of the patients with severe arrhythmia is more obvious.

Key words: Rheumatic heart disease; Brain natriuretic peptide; Creatine phosphate isoenzyme; High sensitivity C reactive protein

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前言

风湿性心脏病是一种由 A 组乙型溶血性链球菌感染引起的变态反应性疾病,心脏瓣膜是其主要的病变部位,其将引起心脏血流动力学改变^[1-3]。随着疾病的发展,大多数风湿性心脏病患者需要进行瓣膜置换术治疗,通过瓣膜置换术可以改善患者生活质量^[4-6]。然而由于大多数接受瓣膜置换术的患者病史较长,部分患者术前心功能较差,从而影响了治疗效果^[7-9]。因此,选择合理的手术时机已成为提高患者生存率的重要问题。脑钠肽(Brain natriuretic peptide, BNP)是利钠肽家族的重要成员,主要由心室肌细胞合成,具有利尿、排钠和降低血容量等生理作用^[10-12]。同时近年来有研究发现,心力衰竭患者通常存在血浆 BNP 水平异常升高现象,其水平可以反映心功能情况^[13-15]。但对于血浆 BNP 水平在风湿性心脏病瓣膜置换术患者围手术期的临床意义报道较少。本研究对我院收治的 98 例患者进行研究,旨在为风湿性心脏病患者瓣膜置换术手术时机选择提供依据,现报道如下。

1 资料与方法

1.1 一般资料

选取 2015 年 1 月至 2016 年 12 月在我院接受心脏瓣膜置换术的风湿性心脏病患者 98 例为研究对象。纳入标准:① 所有患者均参照第 8 版《内科学》中的诊断标准确诊为风湿性心脏病;② 患者均首次接受心脏瓣膜置换手术治疗;③ 患者及其家属对本研究知情并签署知情同意书。排除标准:① 合并急性心肌梗死者;② 近两个月内有严重感染病史者;③ 严重心律失常者;④ 1 年内有手术、创伤史者;⑤ 高血压、慢性阻塞性肺疾病及肺心病者;⑥ 严重肝肾功能不全者。其中男性 46 例,女性 52 例,年龄 28~75 岁,平均年龄(48.54±8.39)岁,病程 3~12 年,平均病程(7.94±2.73)年;患者术前纽约心脏病协会(New York Heart Association, NYHA)心功能分级 I 级 15 例、II 级 29 例、III 级 36 例、IV 级 18 例。本研究经医院伦理委员会批准同意。

1.2 方法

1.2.1 手术方法 所有患者均在中度低温和中度血液稀释条

件下进行体外循环,将冷血心肌保护剂通过体外循环间断的灌注到患者体内。观察患者生命体征,进行二尖瓣置换术 51 例、三尖瓣置换术 5 例、主动脉瓣置换术 22 例、主动脉瓣置换术+二尖瓣置换术 20 例。术中常规应用血管活性药物,并监测患者电解质情况,维持酸碱平衡和电解质含量。

1.2.2 血清学指标检测 分别于术前、术后 12 h、24 h、48 h、术后 1 周抽取患者清晨空腹静脉血 5 mL,置于 EDTA 试管中,静置 5 min 后 3500 r/min 离心 10 min,离心半径 12 cm,分离血浆,应用免疫荧光分析法测定血浆 BNP 水平,应用免疫比浊法检测血浆磷酸肌酸同工酶(Creatine kinase isozyme, CK-MB)、高敏 C 反应蛋白(High sensitive C reactive protein, hs-CRP)水平,试剂盒购自雅培有限公司,严格按照试剂盒操作进行。

1.2.3 严重心律失常的判定标准 以患者术后频发室性早搏、室性心动过速、多形室性期前收缩、心室颤动判定为严重心律失常。

1.3 观察指标

对比不同 NYHA 心功能分级、不同时间点患者血浆 BNP、CK-MB、hs-CRP 水平,同时观察并对比术后发生严重心律失常与否患者不同时间点血浆 BNP、CK-MB、hs-CRP 水平。

1.4 统计学分析

采用 SPSS23.0 软件进行相关统计学分析,计量资料以($\bar{x} \pm s$)表示,多组数据比较应用单因素方差分析,两组数据比较应用 t 检验;计数资料以百分率表示,应用 χ^2 检验, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 不同 NYHA 心功能分级患者血浆 BNP、CK-MB、hs-CRP 水平比较

随 NYHA 心功能分级升高,患者血浆 BNP、CK-MB、hs-CRP 水平升高,不同 NYHA 心功能分级患者血浆 BNP、hs-CRP 水平整体比较差异有统计学意义($P < 0.05$),CK-MB 比较差异无统计学意义($P > 0.05$);不同 NYHA 心功能分级患者血浆 BNP、hs-CRP 两两比较差异有统计学意义($P < 0.05$),CK-MB 两两比较差异无统计学意义($P > 0.05$)。见表 1。

表 1 不同 NYHA 心功能分级患者血浆 BNP、CK-MB、hs-CRP 水平比较($\bar{x} \pm s$)

Table 1 Comparison of plasma BNP, CK-MB and hs-CRP levels in patients with different grades of cardiac function

NYHA grade	n	BNP(pg/mL)	CK-MB(U/L)	hs-CRP(mg/L)
Class I group	15	164.31±57.64	16.45±4.58	8.22±2.51
Class II group	29	238.75±64.21 ^a	20.12±5.12	12.18±2.58 ^a
Class III group	36	542.42±88.73 ^{ab}	22.78±5.28	15.18±2.11 ^{ab}
Class IV group	18	942.41±107.81 ^{abc}	24.78±5.21	17.29±2.68 ^{abc}
F	-	104.037	2.756	10.822
P	-	0.000	0.165	0.000

Note: compared with the class I group, ^a $P < 0.05$; compared with the class II group, ^b $P < 0.05$; compared with the class III, ^c $P < 0.05$.

2.2 不同时间点患者血浆 BNP、CK-MB、hs-CRP 水平比较 术后 1 周血浆 BNP、CK-MB、hs-CRP 水平显著低于术前($P<0.05$),见表 2。
患者术后 12 h、24 h、48 h 血浆 BNP、hs-CRP 水平均显著高于术前,术后 24 h、48 h 血浆 CK-MB 水平均显著高于术前,

表 2 不同时间点患者血浆 BNP、CK-MB、hs-CRP 水平比较($\bar{x} \pm s$)
Table 2 Comparison of plasma BNP, CK-MB and hs-CRP levels in patients with different observation time

Times	n	BNP(pg/ml)	CK-MB(U/L)	hs-CRP(mg/L)
Before operative	98	524.72± 96.72	21.05± 6.11	14.12± 3.01
12 h after operative	98	1072.28± 105.28 ^a	22.78± 7.12	18.32± 3.18 ^a
24 h after operative	98	1642.42± 145.72 ^a	23.72± 6.23 ^a	21.44± 4.15 ^a
48 h after operative	98	1124.72± 138.54 ^a	26.22± 7.11 ^a	23.11± 2.51 ^a
1 week after operative	98	418.27± 81.28 ^a	17.73± 5.28 ^a	10.25± 3.15 ^a
F	-	612.851	10.185	14.282
P	-	0.000	0.017	0.000

Note: compared with before operation, ^a $P<0.05$.

2.3 术后发生严重心律失常与否患者血浆 BNP、CK-MB、hs-CRP 水平比较 于术前($P<0.05$),两组患者术后 1 周 BNP 与术前比较差异无统计学意义($P>0.05$),两组术后 1 周 CK-MB、hs-CRP 水平均低于术前($P<0.05$),但严重心律失常组术后 12 h、24 h、48 h、1 周血浆 BNP、CK-MB、hs-CRP 水平均显著高于无严重心律失常组($P<0.05$),见表 3。
术后发生严重心律失常患者(严重心律失常组)16 例,未发生严重心律失常患者(无严重心律失常组)82 例,两组患者术后 12 h、24 h、48 h 血浆 BNP、CK-MB、hs-CRP 水平均显著高

表 3 术后发生严重心律失常与否患者血浆 BNP、CK-MB、hs-CRP 水平比较($\bar{x} \pm s$)
Table 3 Comparison of plasma BNP,CK-MB and hs-CRP levels in patients with severe arrhythmia or not after operation

Groups	Times	BNP(pg/ml)	CK-MB(U/L)	hs-CRP(mg/L)
Severe arrhythmia (n=16)	Before operative	682.22± 81.24	22.14± 5.13	16.42± 3.23
	12 h after operative	1228.12± 125.84 ^{ab}	24.78± 7.12 ^{ab}	20.22± 3.12 ^{ab}
	24 h after operative	1840.8± 121.08 ^{ab}	25.72± 6.23 ^{ab}	23.51± 3.53 ^{ab}
	48 h after operative	1428.84± 128.76 ^{ab}	27.22± 7.11 ^{ab}	25.23± 2.12 ^{ab}
	1 week after operative	688.84± 71.85 ^b	20.73± 5.28 ^{ab}	12.31± 2.13 ^{ab}
No severe arrhythmia (n=82)	Before operative	284.12± 78.25	17.22± 5.01	10.56± 2.12
	12 h after operative	824.11± 95.24 ^a	21.12± 5.12 ^a	15.12± 3.34 ^a
	24 h after operative	958.83± 112.53 ^a	23.72± 6.23 ^a	18.06± 2.14 ^a
	48 h after operative	614.75± 98.84 ^a	24.11± 5.13 ^a	20.25± 2.14 ^a
	1 week after operative	282.44± 68.73	15.71± 5.28 ^a	8.11± 3.16 ^a

Note: compared with before operative, ^a $P<0.05$; compared with no severe arrhythmia, ^b $P<0.05$.

3 讨论

心脏瓣膜是风湿性心脏病最重要的病变部位,当患者发生心脏瓣膜病变时,可引起心脏血流动力学改变。由于心脏代偿能力较强,风湿性心脏病患者早期往往并无明显的临床表现,随着时间的推移,大多数患者存在心功能降低,从而影响了瓣膜置换术效果^[16]。选择合适的手术时机对于瓣膜置换术成功与否有着重要的意义。有研究表明^[17,18],随着心功能分级升高,风湿性心脏病患者瓣膜置换术并发症风险将降低 23.4~38.3%。目前临床上对于心功能分级主要包括 NYHA 分级和超声心动图心功能分级^[19]。前者主要依据患者临床症状分级,主观性较强,但对于卧床患者无法进行分级。而后者虽然客观性较强,但受检测者和设备限制,同时仅能反映患者心脏的功能,分级标准

较为局限。近年来,随着血清学指标的不断发现,大量血清学标志物被用于临床诊断,并取得了显著成效。BNP 是由 32 个氨基酸残基组成的多肽,主要由心室肌细胞合成并分泌。生理情况下 BNP 主要发挥利尿、排钠的功能,当心脏容量负荷增加时,可以导致心室壁张力增加,心室肌细胞合成 BNP 增加,并分泌到血液中,起到扩张血管、阻断肾素-血管紧张素-醛固酮系统功能的作用^[20-22]。

本研究通过对我院 98 例接受心脏瓣膜置换术的风湿性心脏病患者观察发现,术前随 N 者血浆 BNP、hs-CRP 两两比较差异有统计学意义($P<0.05$),CK-MB 两两比较差异无统计学意义($P>0.05$)。表明术前不同心功能分级的风湿性心脏病患者血浆 BNP、hs-CRP 存在差异。其中 BNP 可以反映患者心功能情况,对于接受心脏瓣膜置换术的风湿性心脏病患者术前心功

能分级有一定价值^[23]。而 hs-CRP 是一种非特异性炎症标志物,其水平可以反映机体炎症反应情况^[24]。YHA 心功能分级升高,患者血浆 BNP、CK-MB、hs-CRP 升高,不同 NYHA 心功能分级患而风湿性心脏病是一种由 A 组乙型溶血性链球菌感染引起的变态反应性疾病,患者心功能降低往往由于体内炎症反应较强引起,因此术前随 NYHA 分级升高,患者血浆 hs-CRP 水平升高。而 CK-MB 是反映心肌损伤情况的标志物,由于风湿性心脏病主要病变部位在心脏瓣膜,因此术前血清 CK-MB 并无显著差异。从不同时间点患者血清学指标比较来看,患者术后 12 h、24 h、48 h 血浆 BNP、hs-CRP 水平均显著高于术前,术后 24 h、48 h 血浆 CK-MB 水平均显著高于术前。表明术后患者血浆 BNP 水平可以反映心功能变化,同时也提示瓣膜置换术患者心肌损伤、患者体外循环、病情长短及炎症反应程度均是术后 BNP 水平的影响因素^[25,26]。另外值得注意的是接受心脏瓣膜置换术患者术后 12 h 血浆 BNP、hs-CRP 即出现显著升高,而血浆 CK-MB 则在术后 24 h 显著升高,表明血浆 BNP 变化较 CK-MB 更为敏感,这可能与接受心脏瓣膜置换术造成的心肌损伤,释放 CK-MB 更为缓慢有关。

另外,本组术后发生严重心律失常患者 16 例,未发生严重心律失常患者 82 例,两组患者术后 12 h、24 h、48 h 血浆 BNP、CK-MB、hs-CRP 均显著高于术前水平,两组术后 1 周 CK-MB、hs-CRP 水平均显著低于术前,但严重心律失常组术后 12h、24h、48h、1 周血浆 BNP、CK-MB、hs-CRP 均显著高于无严重心律失常组($P<0.05$)。表明瓣膜置换术患者术后常见并发症后发生心律失常患者 BNP、CK-MB、hs-CRP 均存在不同程度的异常。心律失常是瓣膜置换术患者术后常见并发症,也是影响患者预后的重要指标^[27],本研究提示血浆 BNP、CK-MB、hs-CRP 水平升高可能是瓣膜置换术后发生严重心律失常的预测指标。因此临床上可以对接受心脏瓣膜置换术患者血浆 BNP、CK-MB、hs-CRP 进行检测,对存在严重心律失常风险的患者进行干预,降低患者死亡率。

综上所述,风湿性心脏病瓣膜置换术患者术前血浆 BNP 可以反映患者心功能情况,术后患者血浆 BNP、CK-MB、hs-CRP 异常升高,发生严重心律失常患者升高更为明显,临床上可以对患者血浆 BNP、CK-MB、hs-CRP 进行检测,改善患者预后。

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