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血清 Hcy 和 BNP 水平对心房颤动患者射频消融术后复发的预测价值

谢丽¹, 度伟¹, 付华²

(1. 成都市龙泉驿区第一人民医院心内科, 成都 610100; 2. 四川大学华西医院心内科, 成都 610041)

[摘要] 目的: 探究血清同型半胱氨酸(homocysteine, Hcy)、脑钠肽(brain natriuretic peptide, BNP)水平对心房颤动(atrial fibrillation, AF)患者射频消融术后复发的预测价值。方法: 选择2016年1月至2018年10月成都市龙泉驿区第一人民医院心内科收治的95例AF患者为AF组, 选择同期体格检查健康的成年人为对照组。两组受试者均于入院后测定血清Hcy和BNP水平, AF组接受射频消融术后进行为期12个月的随访, 统计复发情况, 分析AF患者复发的危险因素及血清Hcy和BNP的预测价值。结果: AF组患者血清Hcy和BNP水平显著高于对照组受试者($P<0.05$)。AF患者术后随访复发32例, 复发率为33.68%; 经比较, 复发组患者高血压、糖尿病比例显著高于未复发组($P<0.05$); 左心房直径、血清Hcy和BNP水平显著高于未复发组, 差异具统计学意义($P<0.05$)。Logistic多因素分析示: 在矫正其他影响因素后, 高血清Hcy和BNP水平是AF患者射频消融术后复发的独立危险因素($P<0.05$)。血清Hcy和BNP预测复发的曲线下面积(area under the area, AUC)分别为0.774, 0.828, 预测最佳截点值分别为25.7 $\mu\text{mol/L}$, 78.4 pg/mL ; 两者联合预测复发的曲线下面积为0.865。结论: 血清Hcy和BNP水平与AF患者射频消融术后复发相关, 临床可根据截点值筛选复发高风险人群, 进行病情检测及早期干预。

[关键词] 同型半胱氨酸; 脑钠肽; 心房颤动; 射频消融术; 复发

Predictive value of serum homocysteine and brain natriuretic peptide levels for recurrence of patients with atrial fibrillation after radiofrequency ablation

XIE Li¹, TUO Wei¹, FU Hua²

(1. Department of Cardiology, First People's Hospital, Longquanyi District, Chengdu 610100;
2. Department of Cardiology, West China Hospital, Sichuan University, Chengdu 610041, China)

Abstract **Objective:** To explore predictive value of serum homocysteine (Hcy) and brain natriuretic peptide (BNP) levels for recurrence of patients with atrial fibrillation (AF) after radiofrequency ablation (RFA). **Methods:** During the period from January 2016 to October 2018, 95 AF patients who were admitted to cardiology department of the

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通信作者 (Corresponding author): 付华, Email: ye63857@163.com

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hospital and healthy adults who underwent physical examination during the same period were enrolled as study objects. They were included into AF group and control group, respectively. After admission, all in both groups were tested for serum Hcy and BNP levels. After RFA, AF group underwent 12-month follow-up. The recurrence situation was statistically analyzed. The risk factors of recurrence in AF patients and predictive value of serum Hcy and BNP were analyzed. **Results:** The levels of serum Hcy and BNP in AF group were significantly higher than those in control group ($P<0.05$). The postoperative follow-up for AF patients showed that there were 32 cases with recurrence, with recurrence rate of 33.68%. After comparison, proportion of patients with hypertension and diabetes mellitus in recurrence group was significantly higher than that in non-recurrence group ($P<0.05$), left atrial diameter, levels of serum Hcy and BNP were significantly higher than those in non-recurrence group ($P<0.05$). Logistic multivariate analysis showed that after correcting other influencing factors, high serum Hcy and BNP levels were independent risk factors of recurrence in AF patients after RFA ($P<0.05$). The areas under the curve (AUC) of serum Hcy and BNP for predicting recurrence were 0.774 and 0.828, respectively. Their best cut-off values were 25.7 $\mu\text{mol/L}$ and 78.4 pg/mL , respectively. The area under the curve of the two for predicting recurrence was 0.865. **Conclusion:** Serum Hcy and BNP levels are related to recurrence in AF patients after RFA. Clinically, high-risk recurrence populations can be screened out based on cut-off values for disease detection and early intervention.

Keywords homocysteine; brain natriuretic peptide; atrial fibrillation; radiofrequency ablation; recurrence

心房颤动(atrial fibrillation, AF)是一种常见的心律失常疾病,好发于老年人群。流行病学调查^[1]显示:75~84岁老年人AF患病率可达12%,而超过84岁的高龄人群患病率高达33.3%。AF的发生可造成心房收缩丧失,心搏量减少,极易引发血流动力学损害及血栓栓塞等情况的发生,具有较高的致残率及病死率。研究^[2]表明:合并AF的患者全因性病死率是非AF人群的1.4~1.9倍。射频消融术是治疗AF的有效术式,被广泛应用于临床治疗中,但其高复发率也是困扰医学界及患者的重大难题,早期预测AF的复发对于早期干预措施的采取具有一定临床意义^[3-4]。同型半胱氨酸(homocysteine, Hcy)是机体含硫氨基酸的重要代谢产物,现有研究^[5]表明高水平Hcy可导致心肌肥大及心肌组织损伤,可作为心血管事件的风险预测因子。脑钠肽(brain natriuretic peptide, BNP)是心脏分泌的肽类物质,可反映心肌缺血、损伤及心室壁压力等状态,有研究^[6]表明其在AF发生时高表达。已有研究^[7-8]报道Hcy和BNP与AF发生及病情的关系,但其与AF术后复发之间的关系及其预测价值仍有待研究验证。本研究以成都市龙泉驿区第一人民医院(以下简称我院)行射频消融术的AF患者作为研究对象,分析术前血清Hcy和BNP水平对患者术后复发的预测价值及预测截点值,为高风险复发患者术后的干预治疗

提供一定指导。

1 对象与方法

1.1 对象

选择2016年1月至2018年10月我院心内科收治的95例AF患者作为研究对象,纳入AF组。纳入标准:患者完善心电监护及心电图检查,提示有AF发作,心电图表现为正常P波被大小、时限不等的快速振荡波或纤维颤动替代(图1);AF发作持续时间超过7 d,阵发性AF窦性心律恢复时间为24 h内;心功能 \geq II级;有射频消融术适应证,拟行手术治疗者;对本研究知情并签署知情同意书。排除标准:存在缩窄性心脏病者;存在肺炎、肺气肿、肺栓塞等肺病者;肾功能不全者;未能接受术后随访者。另择同期于我院体格检查的50例健康成年人纳入对照组,对照组受试者经全面的体格检查及生化检查排除器质性病变。本研究获得我院医学伦理委员会批准,受试者对本研究知情并签署同意书。

AF组男42例,女53例,年龄(60.67 ± 9.56)岁;病程(6.01 ± 1.52)年;合并高血压者45例,合并糖尿病者23例;对照组男25例,女25例,年龄(59.86 ± 10.27)岁。两组受试者性别组成及年龄比较差异无统计学意义($P>0.05$,表1)。

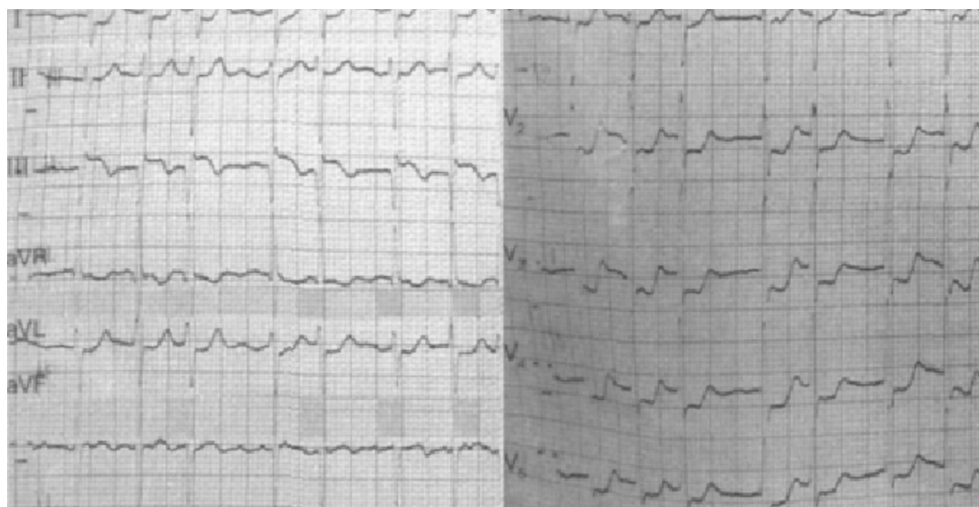


图1 心房颤动典型心电图

Figure 1 Typical ECG picture of atrial fibrillation

表1 两组受试者一般资料比较

Table 1 Comparison of general information between the two groups

组别	n	男/[例(%)]	年龄/岁
AF组	95	42(44.21)	60.67 ± 9.56
对照组	50	24(48.00)	59.86 ± 10.27
χ^2/t		0.190	0.473
P		0.663	0.637

1.2 方法

AF患者入院后常规行射频消融术治疗, 选择左、右股静脉作为穿刺点, 左侧股静脉放置冠状静脉窦导管, 右侧进行房间隔穿刺并放置长鞘管, 经长鞘管放置消融导管后行心房模型重建及静脉消融术, 以肺静脉完全电隔状态作为消融终点, 所有AF患者射频消融术由同一组手术医师完成。

血清学指标检测: 入院后, 采集晨起空腹静脉血, 离心分离血清, Hcy采用荧光免疫分析法, BNP采用双抗体夹心法, 检测仪器及试剂为美国雅培公司I-2000全自动发光分析仪及其配套试剂。

随访: 患者术后1, 3, 6, 12个月时进行门诊随访, 统计患者复发情况, 随访以心电图检查为复查手段。

1.3 统计学处理

采用SPSS 19.0统计软件进行数据分析, 符合正态分布的资料以均数±标准差($\bar{x} \pm s$)表示, 两组间比较行独立样本t检验, 采用logistic单因素及多

因素分析AF患者术后复发的影响因素, 绘制ROC曲线评价各血清学指标预测患者复发的价值, 以 $P < 0.05$ 表示差异具统计学意义。

2 结果

2.1 AF组及对照组血清学指标比较

AF组患者血清Hcy和BNP水平显著高于对照组受试者, 差异具统计学意义($P < 0.05$, 表2)。

2.2 AF组复发及未复发患者临床指标比较

AF患者术后随访复发32例, 复发率为33.68%; 经比较, 复发患者高血压、糖尿病比例显著高于未复发患者($P < 0.05$); 左心房直径、血清Hcy和BNP水平显著高于未复发患者, 差异具统计学意义($P < 0.05$, 表3)。

2.3 AF组复发的logistic多因素分析

Logistic多因素分析示: 在矫正其他影响因素

后, 高血清Hcy和BNP水平是AF患者射频消融术后复发的独立危险因素($P < 0.05$)。AF患者术后复发的logistic单因素及多因素分析结果详见表4。

2.4 血清 Hcy 和 BNP 水平对 AF 患者术后复发的预测价值分析

绘制血清Hcy和BNP预测AF患者术后复发的

受试者特征工作(receiver operating characteristic, ROC)曲线, 血清Hcy和BNP预测复发的曲线下面积(area under the curve, AUC)分别为0.774和0.828, 预测最佳截点值分别为25.7 $\mu\text{mol/L}$, 78.4 pg/mL ; 两者联合预测复发的曲线下面积为0.865(表5, 图2)。

表2 AF组及对照组血清学指标比较

Table 2 Comparison of serological indicators between the two groups

组别	<i>n</i>	Hcy/ $(\mu\text{mol}\cdot\text{L}^{-1})$	BNP/ $(\text{pg}\cdot\text{mL}^{-1})$
AF组	95	25.09 \pm 6.85	77.9 \pm 20.41
对照组	50	12.45 \pm 4.63	38.56 \pm 12.45
χ^2/t		11.707	12.453
<i>P</i>		<0.001	<0.001

表3 复发组及未复发组患者临床参数比较

Table 3 Comparison of clinical parameters between relapsed and non-relapsed patients

组别	<i>n</i>	男/ [例(%)]	年龄/岁	病程/年	高血压/ [例(%)]	糖尿病/ [例(%)]	左心房 直径/mm	Hcy/ $(\mu\text{mol}\cdot\text{L}^{-1})$	BNP/ $(\text{pg}\cdot\text{mL}^{-1})$
复发	32	17 (53.12)	62.15 \pm 8.59	6.25 \pm 1.52	20 (62.50)	12 (37.50)	50.41 \pm 10.27	29.60 \pm 5.46	92.04 \pm 20.45
未复发	63	25 (39.68)	60.11 \pm 10.27	5.88 \pm 1.74	25 (39.68)	11 (17.46)	43.12 \pm 8.59	22.78 \pm 4.12	70.52 \pm 15.63
χ^2/t		1.400	0.965	1.021	4.432	4.644	3.657	6.815	5.702
<i>P</i>		0.237	0.337	0.310	0.035	0.031	0.001	<0.001	<0.001

表4 AF患者术后复发的logistic多因素分析

Table 4 Logistic multivariate analysis of postoperative recurrence in AF patients

因素	单因素分析			多因素分析		
	β	OR(95%CI)	<i>P</i>	β	OR(95%CI)	<i>P</i>
性别组成	0.201	1.223 (0.139~10.789)	0.856			
年龄	0.526	1.692 (0.736~3.893)	0.217			
病程	0.174	1.190 (0.974~1.453)	0.089			
高血压	0.748	2.113 (1.330~3.355)	0.002	0.386	1.471 (1.151~1.879)	0.002
2型糖尿病	0.613	1.846 (1.181~2.886)	0.007	0.412	1.510 (1.018~2.239)	0.041
左心房直径	0.926	2.524 (1.119~5.694)	0.026	0.526	1.692 (1.112~2.574)	0.014
Hcy	0.415	1.514 (1.021~2.246)	0.039	0.271	1.311 (1.076~1.598)	0.008
BNP	0.333	1.395 (1.142~1.704)	0.001	0.286	1.331 (1.098~1.613)	0.004

表5 血清Hcy和BNP预测AF患者术后复发的价值

Table 5 Value of serum Hcy and BNP in predicting recurrence of AF patients

指标	曲线下面积	截点值	灵敏度/%	特异度/%	95%CI	P
Hcy	0.774	25.7 $\mu\text{mol/L}$	71.9	71.4	0.671~0.876	<0.001
BNP	0.828	78.4 pg/mL	75.0	68.9	0.744~0.912	<0.001
联合	0.865	—	87.5	73.0	0.789~0.941	<0.001

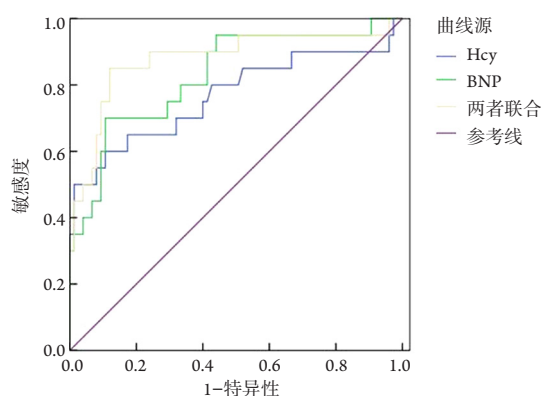


图2 血清Hcy和BNP预测AF患者术后复发的ROC曲线

Figure 2 ROC curve of serum Hcy and BNP to predict recurrence of AF patients

3 讨论

Hcy作为一种血管损伤因子被逐渐关注,其被证实与高血压、糖尿病、冠心病等多种代谢性疾病的发生及发展相关^[9-10]。研究^[11]表明:长期高水平的Hcy可导致内皮损伤,刺激血管的炎症反应及氧化应激,影响纤溶系统,导致血液黏稠度改变,另外其也可通过调控脂质过氧化物导致间质胶原的沉积及脂质代谢紊乱,促进胆固醇在血管壁的沉积,引起动脉粥样硬化等心脑血管疾病的发生。BNP是一种心肌标志物,目前认为AF发生与血浆BNP水平密切相关,其机制可能为AF的发生可引起机体血液动力学的改变,心房收缩下降,心输出量减少,另外AF时循环周期不规则可导致心输出量减少,加大肺动脉及心房压力,刺激心房肌细胞合成BNP,导致血浆中BNP水平升高^[12]。在本研究中,与健康成年人比较,AF患者出现血清Hcy和BNP水平的升高,这一结果与既往多数研究^[13-14]结果类似。

目前有关AF患者射频消融术后复发率及复发的影响因素已有部分研究报道,但不同研究的结果存在一定差异:早期国内一项研究^[15]调查显

示AF患者射频消融术中晚期复发率约为26.5%;Ito等^[16]研究证实中长期持续性AF患者术后复发率可高达53%~60%;本研究患者术后复发率为33.68%,与前人研究结果均存在一定差异,分析其原因可能与患者病情程度及术后随访时间差异所致。本研究结果显示:在矫正患者合并症、左心房直径等因素后,血清Hcy和BNP水平仍是患者术后复发的独立影响因素,证实这两个指标可独立预测AF患者预后。江华等^[17]研究证实:AF患者复发情况与血清Hcy水平呈正相关,多因素分析显示其风险值为1.17(95%CI: 1.01~1.36);国外一项研究^[18]证实:血清BNP水平是AF患者预后的独立影响因素;郭丽珠等^[19]开展的一项研究证实:BNP水平在复发组及未复发组患者中存在显著差异,但进行多因素分析后未被纳入方程;本研究与前人研究存在一定异同。

血清Hcy和BNP水平是影响患者预后的影响因素,若能找到预测复发的截点值可能为筛选复发高危人群并进行早期干预提供一定基础。本研究采用ROC曲线分析两者预测复发的效能,结果显示:血清Hcy和BNP预测复发的AUC分别为0.774, 0.828,两者联合预测的AUC为0.865,提示两种指标对AF术后复发有较高的诊断效能,而两者联合诊断价值更高。汤泽生等^[20]开展的一项研究显示:血清BNP水平预测AF患者复发的AUC为0.690,预测截点值为90.10 pg/mL ,本研究与其报道的AUC及最佳预测截点值均有一定差异,可能与样本量差异及检测方式的差异所致。目前有关血清Hcy及Hcy和BNP两者联合预测术后复发效能的研究不多,本研究结果可能为该指标的应用及AF患者术后复发的早期预测提供一定参考,有一定临床应用价值。

综上,血清Hcy和BNP水平与AF患者射频消融术后复发相关,临床可根据截点值筛选复发高风险人群,术后密切关注病情变化并采取一定干预措施延缓、降低患者术后复发。本研究存在的局限性在于术后随访有一部分为电话随访,这就导

致部分患者可能难以明确是否复发, 导致术后复发的比例偏低; 另外本研究样本量不大, 存在一定计算误差, 未来仍有待完善患者的心电图检查明确复发时间, 提高样本量进行验证。

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