

# 老年非瓣膜性心房颤动患者血清 Periostin, UAR 水平表达与射频消融术后复发的相关性研究

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**摘要:** **目的** 探究老年非瓣膜性心房颤动 (NVA) 患者血清骨膜蛋白 (Periostin)、尿酸/清蛋白比率 (UAR) 水平与射频消融术 (RFCA) 后复发的相关性。**方法** 选取 2019 年 1 月 ~ 2022 年 10 月在首都医科大学附属北京同仁医院心血管中心接受 RFCA 治疗的 108 例老年 NAVF 患者为观察组, 选取同期在首都医科大学附属北京同仁医院体检的 108 例健康者作为对照组, 对患者进行为期一年的随访, 根据随访情况将其分为复发组 ( $n=42$ ) 和未复发组 ( $n=66$ )。收集患者性别、年龄、体质指数 (BMI)、高血压史、糖尿病史、高脂血症、吸烟史、饮酒史、左心室射血分数 (LVEF)、左心室舒张末期直径 (LVEDD) 和白细胞计数 (WBC); 采用酶联免疫吸附测定法 (ELISA) 检测血清 Periostin 含量; 采用全自动生化分析仪测定血清清蛋白 (ALB) 和尿酸 (UA) 含量, 其比值即为 UAR 水平。采用 Logistic 回归分析 NAVF 患者 RFCA 后复发的影响因素; 受试者工作特征 (ROC) 曲线分析血清 Periostin, UAR 水平对老年 NAVF 患者 RFCA 后复发的预测价值。**结果** 观察组术前 Periostin ( $53.53 \pm 6.27$  ng/L), UAR ( $4.09 \pm 0.78$ ) 水平显著高于术后 ( $50.53 \pm 7.23$  ng/L,  $3.41 \pm 0.91$ ) 和对照组 ( $31.29 \pm 4.21$  ng/L,  $1.24 \pm 0.27$ ), 差异具有统计学意义 ( $t=3.258$ ,  $30.603$ ;  $5.896$ ,  $35.883$ , 均  $P<0.05$ )。复发组 LVEF ( $51.16\% \pm 6.49\%$ ) 低于未复发组 ( $55.39\% \pm 6.71\%$ ), UAR ( $4.01 \pm 0.92$ )、Periostin ( $55.77 \pm 6.56$  ng/L) 和高血脂史占比 ( $66.67\%$ ) 水平高于未复发组 ( $3.02 \pm 0.63$ ,  $47.19 \pm 5.44$  ng/L,  $34.85\%$ ), 差异具有统计学意义 ( $\chi^2/t=3.234$ ,  $6.458$ ,  $7.180$ ,  $10.426$ , 均  $P<0.05$ )。血清 Periostin[OR(95% CI):  $1.856(1.148 \sim 3.000)$ ], UAR[OR(95% CI):  $2.127(1.145 \sim 3.951)$ ] 为患者 RFCA 后复发的独立危险因素 (均  $P<0.05$ ); 血清 Periostin, UAR 水平预测老年 NAVF 患者 RFCA 后复发的曲线下面积 (95% 置信区间) [AUC(95%CI)] 分别为  $0.856(0.776 \sim 0.916)$ ,  $0.817(0.731 \sim 0.884)$ , 截断值分别为  $53.00$  ng/L,  $3.99$ , 约登指数分别为  $0.569$ ,  $0.509$ , 敏感度分别为  $88.10\%$ ,  $85.71\%$ , 特异度分别为  $71.21\%$ ,  $65.15\%$ ; 二者联合预测的 AUC(95%CI), 约登指数、敏感度、特异度分别为  $0.924(0.857 \sim 0.966)$ ,  $0.736$ ,  $85.71\%$  和  $87.88\%$ , 二者联合预测高于各指标单独预测 ( $Z=2.296$ ,  $2.880$ ;  $P=0.022$ ,  $0.004$ )。**结论** 老年 NAVF 患者血清 Periostin, UAR 水平上调, 与 RFCA 后复发存在一定的关联, 二者联合预测老年 NAVF 患者 RFCA 后复发具有较高效能。

**关键词:** 非瓣膜性心房颤动; 骨膜蛋白; 尿酸/清蛋白比率; 射频消融术

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## Correlation between Expression of Serum Periostin and UAR Levels in Elderly Patients with Nonvalvular Atrial Fibrillation and Recurrence after Radiofrequency Ablation

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**Abstract: Objective** To exploring the correlation between serum periostin, uric acid/albumen ratio(UAR) levels and recurrence after radiofrequency ablation (RFCA) in elderly patients with nonvalvular atrial fibrillation (NVA). **Methods** The 108 elderly NAVF patients who received RFCA treatment at the Cardiovascular Center of Peking Tongren Hospital Affiliated to Capital Medical University from January 2019 to October 2022 were selected as the observation group, selected 108 healthy individuals who had medical checkups at Beijing Tongren Hospital Affiliated to Capital Medical University during the same period as the control group, and the patients were followed up for a period of 1 year. And according to the follow-up, they were divided into the recurrence group ( $n=42$ ) and the non-recurrence group ( $n=66$ ). Sex, age, body mass index (BMI), history of hypertension, diabetes mellitus, hyperlipidemia, smoking, alcohol consumption, left ventricular ejection fraction (LVEF), left ventricular end-diastolic diameter (LVEDD), white blood cell counts were collected. Enzyme linked immunosorbent assay (ELISA) was applied to detect serum Periostin level. Fully automated biochemical analyzer was applied to measure the levels of serum albumin (ALB) and uric acid (UA), whose ratio was the level of UAR. Logistic regression was applied to analyze the influencing factors of

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recurrence in NAVF patients after RFCA. Receiver Operating Characteristic (ROC) curve was applied to analyze the predictive value of serum Periostin and UAR levels for recurrence after RFCA in elderly NAVF patients. **Results** Preoperative Periostin, UAR levels in the observation group were significantly higher than serum Periostin ( $53.53 \pm 6.27 \text{ ng/L}$ ), UAR ( $4.09 \pm 0.78$ ) in the postoperative ( $50.53 \pm 7.23 \text{ ng/L}$ ,  $3.41 \pm 0.91$ ) and control groups ( $31.29 \pm 4.21 \text{ ng/L}$ ,  $1.24 \pm 0.27$ ), and the differences were statistically significant ( $t=3.258, 30.603; 5.896, 35.883$ , all  $P<0.05$ ). The LVEF was lower in the recurrent group ( $51.16\% \pm 6.49\%$ ) than in the non-recurrent group ( $55.39\% \pm 6.71\%$ ), the levels of UAR ( $4.01 \pm 0.92$ ), Periostin ( $55.77 \pm 6.56 \text{ ng/L}$ ) and percentage of history of hyperlipidemia ( $66.67\%$ ) were higher in the relapse group than those in the non-relapse group ( $3.02 \pm 0.63$ ,  $47.19 \pm 5.44 \text{ ng/L}$ ,  $34.85\%$ ), and the differences were statistically significant ( $\chi^2/t=3.234, 6.458, 7.180, 10.426$ , all  $P<0.05$ ). Serum Periostin[OR(95% CI):  $1.856(1.148 \sim 3.000)$ ] and UAR[OR(95% CI):  $2.127(1.145 \sim 3.951)$ ] were independent risk factors for recurrence after RFCA in patients ( $P<0.05$ ). The area under the curve (95% confidence interval) [AUC(95%CI)] of serum Periostin and UAR levels to predict relapse after RFCA in elderly NAVF patients were  $0.856(0.776 \sim 0.916)$ ,  $0.817(0.731 \sim 0.884)$ , respectively, the cutoff values were  $53.00 \text{ ng/L}$ ,  $3.99$ , the Youden index was  $0.569$ ,  $0.509$ , the sensitivity was  $88.10\%$ ,  $85.71\%$  and the specificity was  $71.21\%$ ,  $65.15\%$ , respectively. The combined predicted of the AUC(95%CI), Youdon index, sensitivity and specificity by the two method were as flows  $0.924(0.857 \sim 0.966)$ ,  $0.736$ ,  $85.71\%$  and  $87.88\%$ , respectively. The combined prediction was significantly higher than that of each index alone ( $Z=2.296, 2.880$ ,  $P=0.022, 0.004$ ). **Conclusion** Serum Periostin and UAR levels are upregulated in elderly patients with NAVF, there is a certain correlation with recurrence after RFCA, the combination of the two has a high efficacy in predicting recurrence in elderly NAVF patients after RFCA.

**Keywords:** non valvular atrial fibrillation; periostin; uric acid/albumen; radiofrequency catheter ablation

心房颤动是一种在临床上常表现为心悸、胸闷、心慌等症状的快速心律失常疾病<sup>[1]</sup>, 60岁以上的群体年龄越大出现心房颤动的可能性越高<sup>[2]</sup>。非瓣膜性心房颤动(non-valvular atrial fibrillation, NAVF)主要表现为与心室无关的心律不齐, 主要包括阵发性房颤、持续性房颤、永久性房颤三种类型<sup>[3]</sup>。射频消融术(radiofrequency ablation, RFCA)是目前治疗心房颤动最有效的方式, 通过动/静脉血管将电极导管放入心脏特定部位, 通过释放电流引发心内膜及心内膜下的心肌凝固性坏死, 进而阻止心律失常的传导和起源点的技术, 但该方法仍存在较大的复发概率, 影响患者的恢复<sup>[4]</sup>。血清骨膜蛋白(Periostin)是一种可以作为细胞外基质中构建复杂结构支架的细胞外基质蛋白, 具有改善分子间相互作用并增强结缔组织力学性能的作用, 导管消融后 Periostin 表达水平较高的患者房颤复发率也较高, 是导管消融后房颤早期复发的预测因子<sup>[5]</sup>。尿酸/清蛋白比率(uric acid/albumin ratio, UAR)是尿酸(uric acid, UA)与血清清蛋白(albumen, ALB)的比值, 在预测 ST 段抬高型心肌梗死患者新发房颤具有较高价值<sup>[6]</sup>。UA 是嘌呤代谢的最终产物, 有研究指出, 尿酸升高与心脏疾病之间的联系密切<sup>[7]</sup>。ALB 是血液中脂肪酸的携带者, 可为细胞及细胞内所有的生物膜提供能量, ALB 水平降低与阵发性房颤显著相关<sup>[8]</sup>。但是, 目前临床上鲜有关于 Periostin, UAR 对老年 NAVF 患者 RFCA 后复发的预测研究。因此本研究通过探究 Periostin, UAR 与老年 NAVF 患者 RFCA 后复发的

相关性, 为改善预后提供一定的参考依据。

## 1 材料与方法

1.1 研究对象 选取 2019 年 1 月 ~ 2022 年 10 月在首都医科大学附属北京同仁医院心血管中心接受 RFCA 治疗的 108 例老年 NAVF 患者作为观察组, 其中男性 55 例, 女性 53 例; 年龄  $60 \sim 75(67.50 \pm 7.14)$  岁, 体质指数(BMI)为  $23.21 \pm 4.89 \text{ kg/m}^2$ 。选择同期在我院进行体检的健康者 108 例作为对照组, 其中男性 49 例, 女性 59 例; 年龄  $60 \sim 77(67.79 \pm 7.11)$  岁, BMI 为  $23.57 \pm 4.35 \text{ kg/m}^2$ 。观察组纳入标准: ①符合 NAVF 的诊断标准<sup>[9]</sup>; ②均在我院进行 RFCA 治疗; ③未接受过其他心脏类手术; ④临床资料完整; ⑤年龄  $\geq 60$  岁; ⑥患者及家属同意参与此研究, 并签署知情书。排除标准: ①患有精神疾病且无法正常交流者; ②瓣膜性心脏病、先天性心脏病、限制性心肌病者; ③并发其他肿瘤或免疫系统疾病者; ④肝肾损伤者; ⑤不配合随访者。本研究已获得本院伦理委员会批准(批号: 2018-KY-0037)。

1.2 仪器与试剂 血清 Periostin 检测试剂盒[生工生物工程(上海)股份有限公司, 货号: D711384-0048], 全自动生化分析仪及配套试剂(日立高新技术国际贸易有限公司, 型号: 日立 008AS)。

## 1.3 方法

1.3.1 血清 Periostin, UAR 水平检测: 采集观察组患者术前、术后第 1 天和对照组健康者体检时的空腹静脉血 10ml,  $3\ 500 \text{ r/min}$  离心 10min 得到血清,  $-80^\circ\text{C}$  保存。采用酶联免疫吸附测定法(ELISA)

检测血清 Periostin 含量，实验步骤严格按照试剂盒说明书进行操作。

采用全自动生化分析仪检测患者血清 ALB 和 UA 含量，计算 UAR 比值。

1.3.2 随访：术后对患者进行为期一年的随访，随访方式可以为微信、电话或门诊，患者出现复发症状并在医院确诊，即随访结束，根据随访结果将患者分为复发组（ $n=42$ ）和未复发组（ $n=66$ ）。

1.4 统计学分析 使用 SPSS25.0 软件对数据进行统计学分析，计数资料以  $n(\%)$  表示，进行  $\chi^2$  检验；计量数据均符合正态分布，以均数  $\pm$  标准差

$(\bar{x} \pm s)$  描述，两组间比较采用  $t$  检验；Logistic 回归分析老年 NAVF 患者 RFCA 后复发的影响因素；受试者工作特征（ROC）曲线分析血清 Periostin，UAR 水平对老年 NAVF 患者 RFCA 后复发的预测价值。 $P<0.05$  为差异具有统计学意义。

2 结果

2.1 观察组与对照组血清 Periostin，UAR 水平比较 见表 1。观察组术前 Periostin，UAR 水平显著高于术后和对照组（ $t=3.258, 30.603; 5.896, 35.883$ ），术后高于对照组（ $t=23.899, 23.758$ ），差异具有统计学意义（均  $P<0.05$ ）。

表 1 观察组与对照组血清 Periostin，UAR 水平比较（ $n=108, \bar{x} \pm s$ ）

项 目	观察组		对照组	<i>F</i>	<i>P</i>
	术前	术后			
Periostin (ng/L)	53.53 $\pm$ 6.27	50.53 $\pm$ 7.23	31.29 $\pm$ 4.21	431.662	<0.001
UAR	4.09 $\pm$ 0.78	3.41 $\pm$ 0.91	1.24 $\pm$ 0.27	475.596	<0.001

2.2 复发组与未复发组血清 Periostin，UAR 水平及临床资料比较 见表 2。复发组患者的性别、年龄、BMI，吸烟史、饮酒史、糖尿病史、高血压史、左心室舒张末期直径（left ventricular end-diastolic diameter，LVEDD）、白细胞计数与未复发组相比，

差异均无统计学意义（均  $P>0.05$ ）；复发组左室射血分数（left ventricular ejection fraction，LVEF）显著低于未复发组，高血脂史占比、血清 Periostin，UAR 水平显著高于未复发组，差异具有统计学意义（均  $P<0.05$ ）。

表 2 复发组与未复发组血清 Periostin，UAR 水平及临床资料比较 [ $n(\%)$ ， $\bar{x} \pm s$ ]

类 别		复发组（ $n=42$ ）	未复发组（ $n=66$ ）	$t/\chi^2$	<i>P</i>
性别	男	23 (54.76)	32 (48.48)	0.405	0.525
	女	19 (45.24)	34 (51.52)		
年龄（岁）		67.15 $\pm$ 7.08	67.73 $\pm$ 6.91	0.421	0.674
BMI（kg/m <sup>2</sup> ）		23.14 $\pm$ 4.26	23.26 $\pm$ 5.29	0.124	0.902
高血压史	是	24 (57.14)	30 (45.45)	1.403	0.236
	否	18 (42.86)	36 (54.55)		
糖尿病史	是	20 (47.62)	32 (48.48)	0.008	0.930
	否	22 (52.38)	34 (51.52)		
高血脂史	是	28 (66.67)	23 (34.85)	10.426	0.001
	否	14 (33.33)	43 (65.15)		
吸烟史	是	19 (45.24)	33 (50.00)	0.233	0.639
	否	23 (54.76)	33 (50.00)		
饮酒史	是	16 (38.10)	35 (53.03)	2.297	0.230
	否	26 (61.90)	31 (46.97)		
LVEF（%）		51.16 $\pm$ 6.49	55.39 $\pm$ 6.71	3.234	0.001
LVEDD（mm）		47.31 $\pm$ 5.15	49.36 $\pm$ 6.34	1.758	0.082
白细胞计数（ $\times 10^9/L$ ）		6.93 $\pm$ 0.74	7.16 $\pm$ 0.83	1.462	0.146
Periostin（ng/L）		57.97 $\pm$ 6.83	50.70 $\pm$ 5.50	7.180	0.001
UAR		4.60 $\pm$ 0.73	3.76 $\pm$ 0.61	6.458	0.001

2.3 Logistic 回归分析影响老年 NAVF 患者 RFCA 后复发的影响因素 见表 3。以老年 NAVF 患者 RFCA 后复发情况（复发=1，未复发=0）为因变量，

以高血脂史（是=1，否=0）、LVEF（实测值）、Periostin（实测值）、UAR（实测值）为自变量，进行 Logistic 回归分析。结果显示，Periostin，





重要的应用价值。

综上所述,老年NAVF患者血清Periostin, UAR水平上调与RFCA后复发联系密切,是老年NAVF患者RFCA后复发的危险因素,二者联合预测老年NAVF患者RFCA后复发具有较高效能,可作为临床预测老年NAVF患者RFCA后复发的生物标志物。但是本研究缺乏血清Periostin, UAR水平在老年NAVF患者RFCA后复发机制中的研究,因此,后续还应设计更合理的方案进一步深入研究。

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