

心律失常

超声心动图结合生物标记物在非瓣膜性心房颤动患者左心房血栓诊断中的意义*

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[摘要] **目的:**通过联合检测左心耳流速、左房前后径及血清生物学标记物,探讨其对非瓣膜性房颤(NVAF)患者左心房血栓的诊断意义。**方法:**入选2017年12月—2019年12月内蒙古医科大学附属医院收治的NVAF患者,通过食管超声心动图结果将患者分为无血栓组和血栓组,并测量左心耳流速,经胸超声心动图测量患者的左房前后径及左室射血分数。计算CHA2DS2-VASc评分,检测D-二聚体、同型半胱氨酸及脑钠肽前体。**结果:**①两组患者一般情况(年龄、性别、高血压、糖尿病)及CHA2DS2-VASc评分无统计学差异($P>0.05$)。②血栓组患者左心耳流速减慢、左房前后径增大、LVEF减低($P<0.05$)。单因素Logistic回归分析显示,左心耳流速、左房前后径、左室射血分数在左心房血栓诊断中具有重要意义。③血栓组患者血清D-二聚体、脑钠肽前体、同型半胱氨酸高于无血栓组。④多因素logistic回归分析显示,左心耳流速($OR=0.83,95\%CI:0.78\sim 10.87,P<0.001$)、左房前后径($OR=1.09,95\%CI:1.00\sim 1.18,P=0.044$)是左心房血栓诊断的重要指标。当左心耳流速截点值为25.5 cm/s时,诊断左心房血栓形成的灵敏度和特异度分别为98%、45%,ROC曲线下面积为0.939。左心耳流速联合左房前后径诊断左心房血栓形成ROC曲线下面积为0.945。在二者基础上联合D-二聚体及脑钠肽前体诊断左心房血栓形成ROC曲线下面积为0.948。**结论:**左心耳流速减慢在NVAF患者左心房血栓诊断中具有重要作用。左心耳流速联合左房前后径及血清D-二聚体、脑钠肽前体,提高了对NVAF患者左心房血栓的诊断能力,其敏感性及其有效性增加。

[关键词] 心房颤动;左心耳流速;左心房血栓;左心结构及功能;生物学标记物

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Echocardiography combined with biomarkers in the diagnosis of left atrial thrombosis in patients with nonvalvular atrial fibrillation

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Abstract Objective: To explore the diagnostic significance of left atrial appendage velocity (LAAV), Left atrial diameter (LAD) and serum biomarkers in patients with non-valvular atrial fibrillation (NVAF). **Method:** Patients with NVAF admitted to the Affiliated Hospital of Inner Mongolia Medical University from December 2017 to December 2019 were divided into non-thrombotic group and thrombotic group by transesophageal echocardiography (TEE). The LAAV was measured, and the LAD and LVEF were measured by transthoracic echocardiography (TTE). We calculated CHA2DS2-VASc score, and measured D-dimer and pro-brain natriuretic peptide. **Result:** ① There was no significant difference in general condition (age, sex, hypertension, diabetes) and CHA2DS2-VASc score between the two groups ($P>0.05$). ② LAAV decreased, LAD increased and LVEF decreased in

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thrombus group ($P < 0.05$). Univariate logistic regression analysis showed that LAAV, LAD and LVEF had played the important roles in the diagnosis of LAT. ③ Serum D-dimer, pro-brain natriuretic peptide and homocysteine in patients with thrombosis were higher than those in patients without thrombosis. ④ Multivariate logistic regression analysis showed that LAAV ($OR = 0.83, 95\%CI: 0.78 - 1.07, P < 0.001$) and LAD ($OR = 1.09, 95\%CI: 1.00 - 1.18, P = 0.044$) were important indicators in the diagnosis of LAT. When LAAV was 25.5 cm/s, the sensitivity and specificity of diagnosing LAT were 98% and 45%, and the area under ROC curve was 0.939. The area under ROC curve of LAAV combined LAD diagnosis LAT was 0.945. On the basis of both, combined with D-dimer and pro-brain natriuretic peptide, the area under ROC curve for diagnosing LAT was 0.948. **Conclusion:** The slow velocity of left atrial appendage plays an important role in the diagnosis of left atrial thrombus in patients with NVAF. The LAAV combined with LAD, serum D-dimer and pro-brain natriuretic peptide precursor, can improve the diagnostic ability, sensitivity and effectiveness of LAT in NVAF patients.

Key words atrial fibrillation; left atrial appendage velocity; left atrial thrombus; left ventricular structure and function; biological markers

心房颤动(房颤)是临床常见的心律失常。据统计,30~85岁发病率为0.77%,40~50岁发病率为0.5%;80岁以上发病率为7.5%,随年龄增长而增加,到2060年在原有基础上将增长2.3倍^[1-2]。研究表明^[3-4],90%以上的房颤患者存在左心房血栓,血栓脱落增加了缺血性卒中和动脉栓塞的风险,其病死率、致残率分别约为20%、60%。研究者提出,抗凝治疗是房颤管理的基石,然而目前中国房颤有效抗凝率仍然较低^[5]。因而如何高效准确诊断非瓣膜性房颤(NVAF)患者左心房血栓是我们临床工作的重点。

CHA₂DS₂-VASc评分 ≥ 2 分时,认为发生栓塞危险性较高,应予以抗凝治疗。研究表明,评分为0分的NVAF患者卒中发生率约为1.9%,评分为1分的NVAF患者卒中发生率为2.8%,其可能忽视了一部分实际需要抗凝的房颤患者^[6-7]。目前,临床主要依据经食管超声诊断左心耳有无血栓。2010年欧洲房颤指南提出,如果经食管超声心动图检查未发现血栓,可进行房颤复律^[8],在实际工作中却存在复律后血栓栓塞情况^[9]。其原因为,机械转复与电转复不同步,以及左心耳流速减慢促进复律后左心房血栓的形成^[10-11]。

研究表明多种血清生物学标志物可预测血栓形成的不良事件^[12-13]。李雪博等^[14]研究提出,房颤组患者血清炎症生物学标志物较高,且在房颤患者的心房肌细胞活检中,炎症浸润和纤维化的发生率很高。本实验研究左心耳流速、左心结构功能改变及血清生物学标记物,探讨其对NVAF患者左心房血栓诊断的意义。

1 对象与方法

1.1 对象

2017年12月—2019年12月就诊于我院的NVAF患者170例,其中男98例,女72例,平均年龄(64.21 \pm 10.12)岁。完善食管超声心动图及经胸超声心动图检查。签署知情同意书。

纳入标准:①所有患者均严格按照2014年

AHA/ACC/HRS房颤管理诊断标准纳入。②能配合完成食管超声心动图及经胸超声心动图检查。

排除标准:①先天性心脏病、风湿性心脏病、甲亢性心脏病、心脏瓣膜病换瓣史、既往房颤射频消融史;②中度至重度二尖瓣反流或狭窄;③长期口服抗凝剂者;④新发急性冠脉综合征及严重心血管疾病;⑤存在严重感染或合并严重肝肾功能不全者。

1.2 方法

超声心动图检查:采用Philips公司iE33彩色多普勒超声诊断仪,在左心耳最大舒张状态下经食管超声心动图测量左心耳的血流频谱。经胸多普勒超声测量左房前后径、左室射血分数(LVEF)。

生物学指标:所有研究对象禁食水8h,空腹采集肘静脉血,采用酶联免疫法测定D-二聚体值、脑钠肽数值,采用ELISA法测定患者的同型半胱氨酸值。

1.3 统计学处理

采用SPSS 20.0统计学软件进行处理,计量资料以 $\bar{x} \pm s$ 表示,两组均数比较采用 t 检验。不服从正态分布的采用秩和检验。采用多因素两分类非条件Logistic逐步回归分析筛选影响血栓形成的因素。绘制ROC曲线并计算曲线下面积。

2 结果

2.1 NVAF患者的一般情况

NVAF患者的一般情况见表1。

2.2 NVAF血栓组与无血栓组患者超声心动图参数比较

血栓组左心耳流速减慢、左心房直径增大、左心室射血分数减低($P < 0.05$),见表2。

2.3 NVAF血栓组与无血栓组患者血清生物学标记物比较

房颤血栓组血清D-二聚体及脑钠肽前体升高($P < 0.05$)。两组患者同型半胱氨酸差异无统计学意义($P > 0.05$),见表3。

表 1 NVAF 患者的一般情况

Table 1 General data		$\bar{x} \pm s$		
项目	血栓组(65 例)	无血栓组(105 例)	χ^2/t 值	P 值
年龄/岁	65.05±10.5	63.69±9.9	0.851	0.396
女/例(%)	25(38.5)	46(43.8)	0.472	0.492
高血压/例(%)	43(66.2)	61(58.1)	1.098	0.295
糖尿病/例(%)	6(9.2)	18(17.1)	2.073	0.150
CHA ₂ DS ₂ -VASc 评分	3.0(2.0,4.0)	3.0(2.0,4.0)	1.958	0.051

表 2 NVAF 患者心脏结构及功能

Table 2 Heart structure and function in NVAF patients		$\bar{x} \pm s$		
项目	血栓组(65 例)	无血栓组(105 例)	t 值	P 值
左心耳流速/(cm·s ⁻¹)	26.5±9.1	51.7±14.5	13.904	<0.001
左心房前后径/mm	47.5±6.5	41.8±7.9	4.822	<0.001
左心室射血分数/%	56.9±9.5	61.6±10.1	3.020	0.003

表 3 NVAF 患者血清生物学标记物

Table 3 Serum biomarkers in NVAF patients		$\bar{x} \pm s$		
项目	血栓组(65 例)	无血栓组(105 例)	t 值	P 值
脑钠肽前体/(pg·ml ⁻¹)	1196.0(463.3,2211.0)	502.0(244.8,1107.9)	3.393	<0.001
同型半胱氨酸/(μmol·L ⁻¹)	17.2(15.0,20.0)	15.6(11.7,20.0)	2.322	0.562
D-二聚体/(μg·L ⁻¹)	1.2(0.3,1.7)	0.34(0.2,0.8)	4.591	<0.001

2.4 单因素 Logistic 回归分析

经 Logistic 回归分析,左心耳流速减慢、左心房直径增大、左心室射血分数减低及 D-二聚体、脑钠肽前体增高在 NVAF 患者左心房血栓诊断中具有重要作用($P < 0.05$),见表 4。

2.5 多因素 Logistic 回归分析

以 NVAF 左心房血栓形成为因变量(赋值:否=0,是=1),表 4 中有统计学意义的因素为自变量,进行多因素 Logistic 回归分析,结果显示,NVAF 患者左心耳流速($OR = 0.83, 95\%CI: 0.78 \sim 10.87, P < 0.001$)、左心房前后径($OR = 1.09,$

$95\%CI: 1.00 \sim 1.18, P = 0.044$)是左心房血栓诊断的重要指标,见表 5。

2.6 ROC 曲线

绘制 ROC 曲线,左心耳流速诊断左心房血栓的曲线下面积为 0.939($95\%CI: 0.899 \sim 0.978$),左心耳流速联合左房前后径诊断左心房血栓的曲线下面积为 0.945($95\%CI: 0.907 \sim 0.982$)。二者基础上联合血清脑钠肽前体、D-二聚体诊断左心房血栓的曲线下面积为 0.948($95\%CI: 0.914 \sim 0.983$)。多因素联合后对 NVAF 患者左心房血栓诊断敏感性及其有效性均增加,见图 1。

表 4 单因素 Logistic 回归分析

Table 4 Logistic regression analysis		$\bar{x} \pm s$				
项目	B	S.E	Wald	OR	95%CI	P 值
年龄	0.01	0.02	0.73	1.01	0.98~1.05	0.394
性别	-0.22	0.32	0.47	0.80	0.43~1.50	0.492
高血压	0.34	0.33	1.09	1.41	0.74~2.68	0.296
糖尿病	-0.71	0.50	2.01	0.49	0.18~1.31	0.156
左心耳流速	-0.20	0.03	47.14	0.82	0.78~0.87	<0.001
左心房前后径	0.11	0.03	17.69	1.11	1.06~1.17	<0.001
LVEF	-0.06	0.02	8.38	0.95	0.91~0.98	0.004
脑钠肽前体	0.01	0.01	6.12	1.00	1.00~1.00	0.013
同型半胱氨酸	0.01	0.16	0.34	1.00	0.98~1.00	0.562
D-二聚体	0.55	0.17	10.70	1.74	1.25~2.42	0.001
CHA ₂ DS ₂ -VAS 评分	0.22	0.10	4.12	1.24	1.00~1.54	0.052

表 5 多因素 Logistic 回归分析
 Table 5 Multivariate logistic regression analysis

项目	B	S. E	Wald	OR	95%CI	P 值
左心耳流速	-0.19	0.29	42.64	0.83	0.78~10.87	<0.001
左心房前后径	0.08	0.41	4.04	1.09	1.00~1.18	0.044

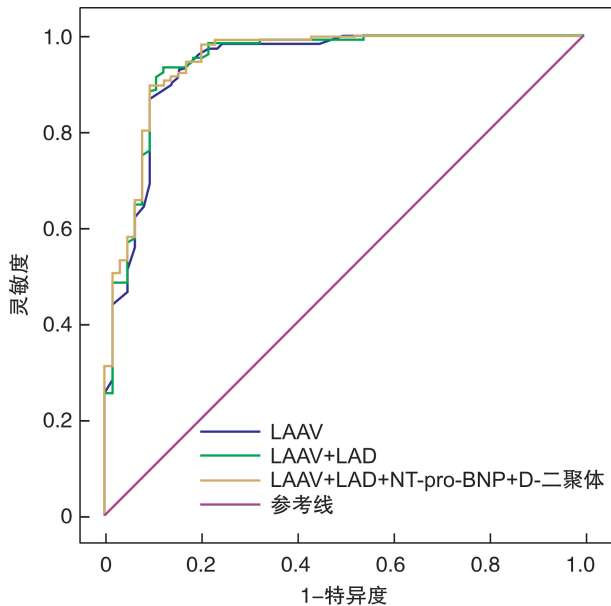


图 1 ROC 曲线分析
 Figure 1 ROC curve

3 讨论

目前,房颤的发病机制尚未明确,较为肯定的是房颤的发生需要触发因素和维持机制,其中电重构及结构重构较为重要。研究认为,不可调控因素如性别、年龄及可调控因素高血压、糖尿病等均可致心房重构,进而促进房颤的发生^[15]。

年龄被认为是房颤的危险因素,研究结果显示,年龄<75岁房颤发病率男性多于女性,年龄≥75岁发病率则男性少于女性^[16]。认为房颤与患者年龄及性别有关。此外,研究提出,NVAF患者高血压患病率为49%~90%^[17]。田刚等^[18]认为,高血压患者房颤发病率增加,长期高血压可致心房重构及心肌纤维化。一项Meta结果显示,糖尿病患者房颤发病风险较非糖尿病患者增加39%^[19]。CHA2DS2-VASc评分提出女性、高龄、高血压、糖尿病均会增加血栓栓塞风险。在本研究中,两组患者性别、年龄与血栓形无明显相关性,可能与实验样本量少有关,需扩大样本量进一步研究。

Xing等^[20]和Michael等^[21]研究认为,左心耳流速减慢及左房前后径增大促进左房血栓的形成。Costa等^[22]研究发现,当左心耳流速<25 cm/s时自发显影率显著增加,当左心耳流速<20 cm/s时,脑栓塞发病率升高2.5倍。本研究与既往研究

结果一致。

研究认为D-D试验阳性与卒中及栓塞风险相关^[23]。在心肌细胞受到拉伸时,BNP前体在蛋白酶作用下裂解为NT-pro-BNP。同型半胱氨酸可能参与NVAF的发生与维持^[24]。本实验研究认为血清生物学标记物升高有利于评估患者整体情况,尚不能作为左心房血栓形成的独立诊断指标。

综上,经食管超声测左心耳流速减慢,在NVAF患者左心房血栓诊断过程中具有重要作用。左心耳流速减慢联合增大的左心房直径及血清脑钠肽前体、D-二聚体对NVAF左心房血栓的诊断更意义。

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