

· 临床研究 ·

经食道超声心动图结合声学造影对卵圆孔未闭的评估价值

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[摘要] 目的: 对比研究经胸超声心动图(transsthoracic echocardiography, TTE)及经食道超声心动图(transesophageal echocardiography, TEE)结合声学造影对卵圆孔未闭(patent foramen ovale, PFO)右向左分流(right-to-left shunt, RLS)的评估价值, 提出最佳诊断策略。方法: 回顾性纳入2020年2月—2022年2月南京医科大学第一附属医院心血管内科收治的186例隐源性卒中(cryptogenic stroke, CS)、短暂性脑缺血发作(transient ischemic attack, TIA)、偏头痛的患者, 并经TEE或心导管检查证实为PFO的患者, 分别进行经胸超声心动图下声学造影(contrast transthoracic echocardiography, cTTE)及经食道超声心动图下声学造影(contrast transesophageal echocardiography, cTEE)。另外在cTEE下配合患者自主Valsalva动作增加1次检查者握拳放置患者腹部按压放松的操作, 分别观察3个心动周期内左房左室内微气泡出现的数量, 评估房间隔水平的RLS分流程度。结果: 静息时cTTE检测到RLS 136例, cTEE检测到RLS 140例。Valsalva动作下, cTTE检测到RLS 186例, cTEE检测到RLS 186例, 提示Valsalva动作时无论cTTE还是cTEE, PFO-RLS检出率均有显著提升。检出RLS的PFO患者, cTTE检测到I级27例, II级31例, III级128例; cTEE检测到I级80例, II级56例, III级50例。110例患者cTTE检出的RLS分流程度高于cTEE, 其中46例cTTE时III级, cTEE时II级; 43例cTTE时III级, cTEE时I级; 21例cTTE时II级, cTEE时I级。cTEE下进行Valsalva动作时, 同时配合检查者握拳放置腹部按压放松时, 检测到RLS I级35例, II级46例, III级105例, 76例患者RLS分流程度提升, 其中21例患者从I级提升到II级, 24例患者从I级提升到III级, 31例患者从II级提升到III级, 中-大量分流的比例显著增加。结论: cTTE检出的RLS分流程度高于cTEE。cTEE检查时, 患者配合检查者按压, Valsalva动作下检出的RLS分流程度增加。cTTE结合TEE对PFO解剖结构的判断、对PFO治疗及封堵术前评估有较大价值。

[关键词] 经胸超声心动图声学造影; 经食道超声心动图声学造影; 卵圆孔未闭; 右向左分流; 评估价值

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The value of transesophageal echocardiography combined with contrast echocardiography in the evaluation of patent foramen ovale

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[Abstract] **Objective:** This study aims to compare transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) combined with contrast echocardiography in the evaluation of right-to-left shunt (RLS) of patent foramen ovale (PFO), and propose the optimal diagnostic strategy. **Methods:** A retrospective study was conducted on 186 patients admitted the cardiovascular department of the First Affiliated Hospital of Nanjing Medical University from February 2020 to February 2022 with cryptogenic stroke (CS), transient ischemic attack (TIA) and migraine who were confirmed to have a patent foramen ovale (PFO) through TEE or cardiac catheterization. Both contrast transthoracic echocardiography (cTTE) and contrast transesophageal echocardiography (cTEE) were performed. In addition, during cTEE, the operator clenched their fist and placed it on the patient's abdomen, applying pressure and then releasing it, while the patient performed a Valsalva maneuver. The number of microbubbles appearing in the left atrium and left ventricle within three cardiac cycles was observed to assess the degree of RLS at the level of the interatrial septum. **Results:** During rest, cTTE detected 136 cases of RLS, while cTEE detected 140 cases of RLS. During the Valsalva maneuver, cTTE detected 186

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cases of RLS, and cTEE also detected 186 cases of RLS, indicating a significant increase in the detection rate of PFO-RLS during the Valsalva maneuver compared to the rest state, regardless of the cTTE or cTEE method. Among the PFO patients with RLS detected, cTTE classified 27 cases as grade I, 31 cases as grade II, and 128 cases as grade III. On the other hand, cTEE classified 80 cases as grade I, 56 cases as grade II, and 50 cases as grade III. Among these cases, 110 patients had a higher RLS degree in cTTE compared to cTEE, with 46 cases being grade III in cTTE and grade II in cTEE, 43 cases being grade III in cTTE and grade I in cTEE, and 21 cases being grade II in cTTE and grade I in cTEE. During the Valsalva maneuver with cTEE, while the operator clenched their fist and applied pressure on the patient's abdomen and then released it, 35 cases were classified as grade I, 46 cases as grade II, and 105 cases as grade III. There were 76 patients with an increase in RLS degree, including 21 patients who upgraded from grade I to grade II, 24 patients who upgraded from grade I to grade III, and 31 patients who upgraded from grade II to grade III. The proportion of patients with moderate to large shunting significantly increased. **Conclusion:** The RLS level detected by cTTE is higher than that of cTEE. During the cTEE examination, when the patient cooperates with the examiner to press, the degree of RLS detected under Valsalva's action increases. The combination of cTTE and TEE in diagnosing the anatomical structure and morphology of PFO is of great value for the treatment and preoperative evaluation of PFO occlusion.

[Key words] contrast transthoracic echocardiography; contrast transesophageal echocardiography; patent foramen ovale; right-left shunt; evaluation value

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卵圆孔未闭(patent foramen ovale, PFO)是胎儿循环系统的残余, PFO的患病率随着年龄的增长而下降, 0~30岁组为34.3%, 80~99岁组为20.2%^[1-2]。PFO与许多疾病的发生相关, 例如隐源性卒中(cryptogenic stroke, CS)、短暂性脑缺血发作(transient ischemic attack, TIA)、偏头痛等^[3]。PFO患者中, 随着右向左分流(right-to-left shunt, RLS)分级程度的增加, 脑卒中发生风险随之上升, 因为RLS较大时血栓通过隔膜的可能性增大, 因此中-大量的RLS是增加CS等发生的一个重要危险因素^[4], 因此准确及时诊断PFO尤为重要。目前诊断PFO的方法有经颅多普勒声学造影(contrast transcranial doppler, cTCD)、经胸超声心动图声学造影(contrast transthoracic echocardiography, cTTE)及经食道超声心动图声学造影(contrast transesophageal echocardiography, cTEE)。虽然cTEE是目前诊断PFO-RLS的参考标准^[5-6], 但在食管探头的干扰下, 进行Valsalva动作常常不充分, 且经食道超声心动图(transesophageal echocardiography, TEE)一般在空腹状态下进行, 此时右房压降低, 导致左右房压梯度降低, 因此cTEE往往难以准确评估大的RLS^[7]。而由于部分患者透声条件差等, cTTE也常常无法准确诊断评估PFO患者RLS的量和类型。有研究表明PFO封堵后的闭合率更依赖于PFO的解剖结构而非器械类型^[8], 因此在封堵前综合评估PFO形态和RLS程度具有重要临床意义。本研究旨在了解cTTE和cTEE在诊断PFO引起的RLS中的不同价值, 并寻求确定最佳的

综合性诊断策略。

1 对象和方法

1.1 对象

回顾性纳入2020年2月—2022年2月南京医科大学第一附属医院心血管内科收治的186例PFO患者。纳入标准:①TEE或心导管检查证实为PFO;②同时具有神经系统症状包括头痛、偏侧无力、视物模糊、口角歪斜等且被神经内科医生明确诊断为偏头痛或CS/TIA;③具有不明原因脑梗死症状。排除标准:①年龄<16岁或>70岁;②经查已明确病因的脑卒中(根据TOAST分型排除动脉粥样硬化、血管炎、心源性等原因引发的脑卒中^[9]);③明确原因的继发性头痛, 如感染、外伤等引起的头痛等;④既往有CT或磁共振成像诊断为肺动静脉瘘或无法进行Valsalva动作的患者。本课题已由南京医科大学第一附属医院医学伦理委员会审议通过(伦理审查号2021-NT-17), 研究对象及家属均签署知情同意书。

1.2 方法

所有PFO患者均于同一天在经胸超声心动图(transthoracic echocardiography, TTE)和TEE下进行声学造影检查(生理盐水血液混悬液:将9 mL生理盐水+1 mL空气+1滴回抽静脉血在2个10 mL注射器中搅拌至少10次, 注射器由3通旋塞连接)。

cTTE检查时, 患者采取平卧或左侧卧体位, 选取心尖四腔切面进行观察, 分别在静息状态下和Valsalva动作时经左肘静脉注入生理盐水血液混悬

液,观察3个心动周期内左房左室内微气泡出现的数量,用以评估房间隔水平RLS的量。

cTEE时患者采取右侧卧位,选取两房心切面进行观察,首先观察房间隔向左突出的程度以及第一隔与第二隔裂隙的大小及形态,并评估Valsalva动作的有效性,之后分别在静息状态下和Valsalva动作时经左肘静脉注入生理盐水血液混悬液,观察3个心动周期内左房左室内微气泡出现的数量,评估房间隔水平RLS的量。最后增加1次患者在Valsalva动作下,操作者握拳放置患者腹部按压后放松,观察3个心动周期内左房左室内微气泡出现的数量,并评估房间隔水平RLS的量。

当右房右室混浊后3个心动周期内左房左室出现微气泡时,可诊断为PFO-RLS。采用RLS分级来量化分流程度:0级(阴性);I级(轻度,1~10个微气泡);II级(中等,11~20个微气泡);III级(≥ 21 个微气泡或左房左室内几乎充满,呈雪花样)^[10]。

1.3 统计学方法

使用SPSS 24.0进行统计学分析。正态分布的连续变量以均值±标准差($\bar{x} \pm s$)表示,非正态分布的变

量以中位数(四分位数) $[M(P_{25}, P_{75})]$ 表示,分类变量按频数和百分比 $[n(\%)]$ 表示。连续变量组间比较采用*t*检验,分类变量采用 χ^2 检验,采用McNemar卡方检验比较配对两组间比率的差异,采用Cochran's *Q*检验进行多组间率的比较,采用Dunn's检验进行事后两两比较。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 基线临床资料

选取2020年2月—2022年2月南京医科大学第一附属医院心血管内科收治的186例高度疑似PFO患者,其中偏头痛99例,CS/TIA 87例。基线临床资料方面(表1),患者年龄为(41.0±14.3)岁,男性占33.9%,在年龄、性别上差异有统计学意义($P < 0.05$):偏头痛组患者更年轻、女性更多,而CS/TIA组年龄更大、男性占比更多。两组患者收缩压、舒张压、心率差异无统计学意义($P > 0.05$)。

2.2 PFO-RLS的检出率

静息时cTTE检测到RLS 136例(73.11%),cTEE检测到RLS 140例(75.27%)。Valsalva动作下,

表1 基线水平的指标比较

Table 1 Comparison of indicators at baseline level

指标	全部(n=186)	CS/TIA组(n=87)	偏头痛组(n=99)	P值
年龄(岁, $\bar{x} \pm s$)	41.0 ± 14.3	45.3 ± 14.2	37.2 ± 13.3	<0.001
男性[n(%)]	63(33.9)	45(51.7)	18(18.2)	<0.001
收缩压(mmHg, $\bar{x} \pm s$)	122.0 ± 14.5	123.3 ± 13.6	120.7 ± 15.2	0.211
舒张压(mmHg, $\bar{x} \pm s$)	78.2 ± 10.4	78.8 ± 9.9	77.7 ± 10.9	0.455
心率[次/min, $M(P_{25}, P_{75})$]	76(70, 84)	74(69, 85)	71(68, 81)	0.501

cTTE检测到RLS 186例(100.00%),cTEE检测到RLS 186例(100.00%,表2),结果提示Valsalva动作时,无论cTTE还是cTEE,PFO-RLS检出率均有显著提升($P < 0.05$)。图1为典型PFO患者cTTE及cTEE的检查结果。

cTTE检出PFO-RLS患者中I级27例,II级31例,

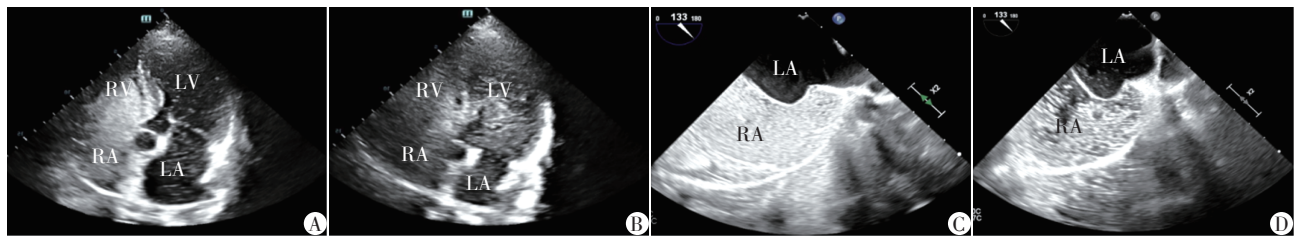
表2 静息状态及Valsalva动作下cTTE和cTEE的PFO-RLS检出率

Table 2 Detection rates of PFO-RLS under resting state and Valsalva action by cTTE and cTEE [n(%)]

类别	cTTE	cTEE
静息状态RLS(n=186)	136(73.11)	140(75.27)
Valsalva动作下RLS(n=186)	186(100.00)	186(100.00)
χ^2 值	54.558	40.758
P值	<0.001	<0.001

III级128例;cTEE中检出PFO-RLS患者I级80例,II级56例,III级50例;其中110例(59.1%)患者RLS分流程度cTTE高于cTEE,其中46例(24.7%)cTTE时III级,cTEE时II级,43例(23.1%)cTTE时III级,cTEE时I级,21例(11.3%)cTTE时II级,cTEE时I级。59例(31.7%)患者在cTTE和cTEE检出的RLS分流程度相同。仅17例(9.14%)患者cTTE检出的RLS分流程度低于cTEE(表3)。

cTEE下进行Valsalva动作时,同时配合操作者握拳放置患者腹部按压放松时,检测到RLS 186例(100%),其中RLS I级35例,II级46例,III级105例,76例患者RLS分流程度提升,其中有21例患者从I级提升到II级,24例患者从I级提升到III级,31例患者从II级提升到III级(表4);图2为cTEE下典型患者在配合操作者加压后PFO-RLS的分流程度提升。



同一患者静息状态下 cTTE RLS II 级(A), Valsalva 动作下 RLS III 级(B); 同一患者静息状态下 cTEE RLS 0 级(C), Valsalva 动作下 RLS II 级(D)。LA: 左心房; LV: 左心室; RA: 右心房; RV: 右心室。

图1 典型PFO患者cTTE及cTEE的检查结果

Figure 1 The examination results of cTTE and cTEE in typical PFO patients

表3 cTTE与cTEE检出PFO-RLS分流程度比较

Table 3 Comparison of PFO-RLS detection degree between cTTE and cTEE (n)

cTTE	cTEE			总计
	I 级	II 级	III 级	
RLS I 级	16	6	5	27
RLS II 级	21	4	6	31
RSL III 级	43	46	39	128
总计	80	56	50	186

表4 常规cTEE与配合操作者握拳加压患者腹部检测的PFO-RLS程度

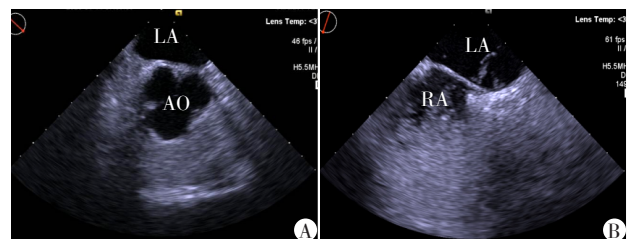
Table 4 PFO-RLS degree between routine cTEE and cTEE with the operator to press the patient's abdomen (n)

常规cTEE	cTEE(配合操作者握拳加压)			总计
	I 级	II 级	III 级	
RLS I 级	35	21	24	80
RLS II 级	0	25	31	56
RSL III 级	0	0	50	50
总计	35	46	105	186

以 RLS II 级+ III 级为中-大量分流标准, 3 种方式中, cTTE 对中-大量分流的检出率为 159 例(85.48%), cTEE 的检出率为 106 例(56.99%), cTEE+配合操作者加压的检出率为 151 例(81.18%), 其中 cTTE 对中-大量 RLS 检出率较高, 常规 cTEE 对中-大量分流的检出率比 cTTE 低, 但配合操作者加压后的 cTEE 对中-大量分流的检出率与 cTTE 相比, 差异无统计学意义(表 5)。

3 讨论

PFO 的人群患病率为 20%~25%^[11-12]。研究表明, 通过未闭卵圆孔的 RLS 与包括 CS、TIA、偏头痛等在内的临床病症密切相关^[13]。PFO 的解剖结构复杂多样, 本研究发现 PFO 的常见解剖结构有 3 种类



同一患者在静息状态下 RLS I 级(A), 配合操作者握拳放置患者腹部按压放松时继发隔向左房面膨出, 左心房见团块状微气泡, RLS 达到 III 级(B)。AO: 主动脉; LA: 左心房; RA: 右心房。

图2 典型患者在静息状态及配合操作者加压情况下的cTEE检查结果

Figure 2 cTEE examination results of a typical patient in a resting state and under pressure with the operator

表5 3种方式对PFO-RLS中-大量分流(II+III级)的检出率
Table 5 Detection rates of medium-large shunt (II+III) in PFO-RLS by three methods [n(%)]

方式	RLS I 级	RLS II 级+ III 级
cTTE(n=186)	27(14.52)	159(85.48)
cTEE(n=186)	80(43.01)*#	106(56.99)*#
cTEE+配合操作者加压(n=186)	35(18.82)	151(81.18)

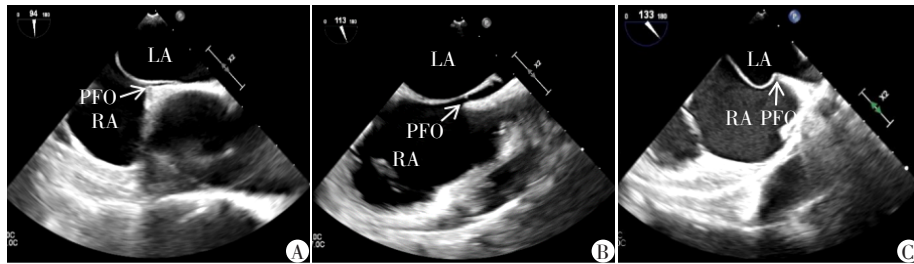
与 cTTE 比较, * $P < 0.05$; 与 cTEE+配合操作者加压比较, # $P < 0.05$ 。

型, 分别为长隧道型(图 3A)、开口型(图 3B)、房间隔膨出瘤型(图 3C)。其中长隧道型卵圆孔是一个长且间隔紧密粘连的通道; 开口型原发隔与继发隔间距很大, 这可能是由于左心房侧的组织褶皱将原发隔与继发隔隔开, 形成保持开放的开口, 这可能会影响封堵装置的固定及密封性; 而房间隔膨出瘤的可活动性可导致原发隔回缩, 从而引发大的 RLS^[14-15]。临床上针对不同类型的 PFO 使用不同尺寸的封堵器, 伴有房间隔膨出瘤的 PFO 甚至使用房间隔缺损的封堵器。TEE 对于确定卵圆孔的解剖结构及其与周围结构的关系非常关键, 因此为了提高封堵成功率, TEE 及在 TEE 下进行的声学造影可能对 PFO 经皮介入手术封堵器的选择极为重要。

目前已有多项研究报道了 cTCD、cTTE 和 cTEE

在诊断PFO方面的有效性,但对于最适合PFO的诊断策略,仍存在很多争议。周芳等^[16]研究表明cTCD可用于CS/TIA或偏头痛患者是否合并PFO的病因筛查,是经导管介入封堵治疗PFO患者较好的术后疗效评价手段。Clarke等^[17]研究得出cTTE和cTEE对PFO检测的结果相似,而Mojadidi等^[18]研究报道,相比cTEE,cTTE的灵敏度较低(46%),马杰等^[19]研究表明cTTE、cTEE分别联合cTCD均可诊断PFO,

但cTEE联合cTCD的诊断效能更高。本研究结果显示,Valsalva动作下,cTTE及cTEE检测到RLS均为100.00%。因为在正常呼吸下,由于右房压低于左房压,左房左室内只能检测到少量微气泡,当进行Valsalva动作时,足够的胸腔内压力导致下肢和上肢静脉回流减少和前负荷降低,瞬时右房压高于左房压^[20],微气泡可从右房通过未闭的卵圆孔进入左房内。而日常生活中,咳嗽、负重、排便等活动都可



A:长隧道型;B:开口型;C:房间隔膨出瘤型。

图3 TEE视角下PFO常见3种类型

Figure 3 Three common types of PFO under the TEE perspective

导致瞬时右房压大于左房压,因此无论cTTE还是cTEE,足够充分的Valsalva动作都是准确检出RLS及其程度的关键。在本研究检出RLS的PFO患者中,110例(59.1%)患者cTTE检测的RLS分流程度高于cTEE。这可能与患者在空腹状态下伴随紧张、经食道超声探头的干扰下无法进行充分的Valsalva动作密切相关,由于胸腔内压力不足,未能降低前负荷,无法在释放期实现左、右心房压力倒置。因此在本研究中,cTEE时增加了1次检测,患者在Valsalva动作下,操作者握拳放置患者腹部按压,观察房间隔水平RLS的量,目的是为了通过腹部压迫增强Valsalva动作的有效性,结果显示有76例患者RLS分流程度提升。

由于可以进行充分的Valsalva动作,相比cTEE,cTTE观察房间隔水平RLS的量及分流程度更为有效^[21],但是临床上需要TEE来评估PFO的形态学特征,区分PFO的形态和类型,以及辨别是否伴有房间隔缺损,进而选择封堵器类型及大小。研究表明虽然PFO的长度与分流程度并无密切关联,但PFO的孔径确是经皮介入封堵闭合术后24个月残留心房间分流的最具预测力的独立因素^[22]。同时TEE对排除肺动静脉畸形、评估左心耳血栓形成和寻找其他合并症同样重要。

综上所述,TEE及经过改善操作的cTTE可以对PFO患者的RLS及分流程度进行准确评估判断。

cTTE简单、操作便捷,建议应作为筛查PFO-RLS的首选,但在决定进行PFO封堵术前,必须进行TEE观察卵圆孔形态及孔径大小,而为了克服cTEE检查时Valsalva动作的不充分,操作者握拳放置患者腹部按压后放松以观察房间隔水平RLS的步骤极为重要,这一综合性的诊断策略可能有助于临床医生对PFO患者的评估和治疗。

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