

## · 综 述 ·

## 急性肺栓塞合并右心功能不全的诊断及预后评估

蒋 娅 综述, 李 波 审校

〔摘要〕 急性肺栓塞(acute pulmonary embolism, APE)是常见的心血管急症,肺动脉栓子堵塞后引起右心室负荷的增加,导致右心功能不全(right ventricular dysfunction, RVD),继而发展为右心衰竭。合并 RVD 的患者死亡率高。超声心动图(TTE)、心电图、心肌损伤标志物、N 端-前脑钠肽(NT-proBNP)、CT 肺动脉造影等对评价 RVD 有一定价值。本文综述各种检查手段评估 RVD 的特点以及与预后的关系。

〔关键词〕 肺栓塞,右心功能不全,预后

〔中图分类号〕 R541;R563.5 〔文献标志码〕 A doi:10.3969/j.issn.1672-271X.2015.05.023

急性肺栓塞(acute pulmonary embolism, APE)是一种潜在的致命性疾病,右心功能不全(right ventricular dysfunction, RVD)是 APE 患者危险分层的重要指标,也是住院期间临床死亡的预测因素<sup>[1]</sup>。RVD 是 APE 常见的严重并发症,栓子阻塞肺动脉引起血管机械因素、神经反射及体液调节等因素发生变化,轻者不会引起显著改变,重者可出现肺循环阻力增加,右心负荷增大,室壁张力增高,引起右心衰竭。研究显示 RVD 与 APE 患者的预后密切相关<sup>[2]</sup>。早期识别这类患者有助于临床决策的快速实施,合并 RVD 的患者可从溶栓疗法、外科取栓术中获益<sup>[1]</sup>。近年来,心肌损伤标志物、超声心动图、CT 肺血管成像等作为评估心室大小及心脏功能的重要检查手段已广泛开展<sup>[3,4]</sup>。本文主要探讨 APE 患者右心功能相关指标的临床变化及临界诊断值。

## 1 超声心动图评价右心功能不全

超声心动图对评价心功能有独特的优势,可测量心房及心室的形态、运动幅度、大小,室间隔的厚度以及测定肺动脉内径和肺动脉压,同时能测定三尖瓣返流情况、右心室射血分数等心功能指数,可在检出肺栓塞的同时观察到患者右心功能异常<sup>[5]</sup>。是目前评估急性肺栓塞患者合并 RVD 的主要诊断手段,Beccattini 等<sup>[6]</sup>认为符合以下标准至少一项以上可诊断为 RVD:①右心室运动功能减退(右心室的收缩不对称或延迟);②室间隔反常运动或右心室扩大(四腔心切面右室舒张末期内径  $>30$  mm 或右室/左室舒张末期内径  $>1$ );③肺动脉高压:肺动

脉收缩压  $>40$  mmHg。Jaff 等<sup>[7]</sup>认为超声心动图评价 RVD 的指南不够准确。目前 RVD 的各种诊断标准如下。定性评估:①右心室游离壁运动减弱<sup>[6,8]</sup>;②室间隔反常运动<sup>[6]</sup>;③McConnell 征<sup>[6,8]</sup>。定量评估:①右心室扩大<sup>[6,9]</sup>;舒张末期右室/左室横向间隔直径  $>0.9$ <sup>[7]</sup>;胸骨旁观右室舒张末期直径  $>30$  mm<sup>[6,9]</sup>;②肺动脉高压<sup>[6,9]</sup>:三尖瓣返流<sup>[6,9]</sup>、肺动脉收缩压  $>30$  mmHg<sup>[6,9]</sup>。Cho 等<sup>[10]</sup>以超声诊断标准将 3283 名血流动力学稳定的 APE 患者分为 RVD 和非 RVD 组, RVD 组患者短期死亡率增加 2.29 倍,其中住院期间死亡率增加 2.60 倍,30 d 死亡率增加 1.98 倍。研究表明通过超声心动图评价的 RVD 的患者属于临床高危人群,其住院期间并发症和远期死亡率增加。

## 2 心电图评价右心功能不全

APE 的严重程度与心电图改变呈正相关,急性肺栓塞的患者常常合并胸前导联 T 波倒置。研究表明,前壁导联 T 波倒置(NTW)是 APE 患者合并 RVD 的最常见的心电图表现<sup>[11]</sup>。NTW 出现可能与急性肺源性心脏病的进展有关,肺动脉主干或分支阻塞,肺血管床容量减少,肺内血液循环阻力增加,进而引起肺动脉高压,急性右室负荷增加,右心室急剧扩张,导致右室功能不全,右室排血量减少,此外右室扩张会引起室间隔左移,左心室舒张期充盈不足,左室心搏量下降,主动脉与右心室之间压力差变小,冠状动脉灌注不足,而且肺栓塞发生时,各种化学介质、如儿茶酚胺、组胺的释放引起冠状动脉收缩,共同引起心肌缺血,心肌复极顺序发生改变,出现 ST-T 改变<sup>[11-12]</sup>。Choi 等<sup>[13]</sup>通过多因素回归分析证实 NTW 与 RVD 相关( $OR = 22.8, P = 0.007$ ),相

作者单位: 650101 云南昆明,昆明医科大学第二附属医院  
心功能科

通讯作者: 李 波, E-mail: xgnlibo@sina.com

比其他心电图特征和实验室指标,胸前导联 T 波倒置大于 3 个以上是 RVD 的重要预测因素,NTW 的动态变化伴随右心功能的变化,前壁导联倒置 T 波的消失可以预测右心功能的恢复。Punukollu 等<sup>[14]</sup>发现 V1 ~ V3 导联 T 波倒置诊断 RVD 的特异性高,敏感性中等。Kukla 等<sup>[15]</sup>发现 T 波倒置个数是评估 APE 患者住院期间相关并发症和死亡率的独立预测因子。S1Q3T3 可反映 QRS 初始向量向右上偏移,提示急性右心扩张,是 APE 患者的典型心电图表现,新发的右束支阻滞(RBBB)提示肺动脉主干栓塞,RBBB 及 S1Q3T3 诊断 RVD 特异性高,敏感性低,其出现强烈提示 APE 患者合并右心功能不全,但排除诊断价值不高<sup>[16]</sup>。RBBB、S1Q3T3、V1 ~ V4 导联 T 波倒置与右心室负荷增加有关,这些心电图表现增加了对 RVD 患者预后的评估价值<sup>[11]</sup>。

### 3 生物标志物评价右心功能不全

N 端-前脑钠肽(NT-proBNP)是由 76 个氨基酸残基组成的 N 端肽片段。心室壁负荷增加是导致 NT-proBNP 血中含量升高的最强刺激因素,对于预测心力衰竭具有较高的灵敏度和特异度<sup>[17]</sup>。临床上已广泛应用于左心功能不全的评估以及慢性心衰患者预后的分析。近年来国外学者研究应用生物标志物对 APE 患者进行风险评估,在无其他导致 BNP 释放的因素(左心衰竭、肾脏疾病等)影响下,NT-proBNP 是右心功能不全的有效标志物。肌钙蛋白 T(cTnT)是心肌损伤标志物,具有高度特异性、敏感性,国内外学者发现肺栓塞并发 RVD 的患者 cTnT 显著升高,可能与肺栓塞所致右室急剧扩张,心肌缺血坏死以及继发冠状动脉痉挛有关,近来研究发现 cTnT 升高与 APE 疾病严重程度及预后明显相关<sup>[18]</sup>。Choi 等<sup>[19]</sup>通过受试者工作特征曲线(ROC)分析相关生物标志物在 RVD 中的诊断作用,其最佳临界值标准如下,NT-proBNP 620 pg/mL, cTnT 0.016 ng/mL,肌钙蛋白 I(cTnI) 0.055 ng/mL,这些重要血清学指标诊断 RVD 敏感性高,特异性中等,多因素回归分析提示 NT-proBNP > 620 pg/mL, cTnT > 0.016 ng/mL 是预测 RVD 的独立生化因子,也是住院期间 APE 患者死亡率的有效预测因素。研究发现 cTnT、cTnI 的水平能反应 RVD 的严重程度及 APE 疾病的严重性<sup>[2]</sup>。cTnT 和 NT-proBNP 升高提示心肌损害、右心功能不全严重,临床中可伴随血流动力学不稳定,意识障碍等严重表现,NT-proBNP 预测 APE 患者 30 d 全因死亡率的最佳临界值为 4740 pg/mL,此标志物的检测对于短期预后的评估尤其

重要<sup>[20]</sup>。多因素回归分析提示 NT-proBNP > 300 pg/mL, cTnT > 0.027 ng/mL 是预测患者全因死亡率的最佳指标组合。Logeart 等<sup>[21]</sup>认为 cTnI 升高与重度 RVD 相关, cTnI > 0.1  $\mu$ g/L 可预测严重右心功能不全,阳性预测值为 85%。心肌特异性标记物是心肌损伤的可靠证据, cTnI 升高会增加血流动力学恶化的风险, APE 合并 cTnI 显著升高的患者住院期间死亡率增加,临床严重并发症较多,更加需要溶栓治疗<sup>[22-23]</sup>。D-二聚体是可疑性 APE 的诊断指标, Rydman 等<sup>[24]</sup>发现 D-二聚体 > 3 mg/L 可识别次大面积肺栓塞合并 RVD 的患者,有助于风险评估。Jeebun 等<sup>[25]</sup>发现升高的 D-二聚体水平与血栓负荷过重、血栓位置靠近中心动脉密切相关。

### 4 CT 诊断右心功能不全

CT 肺动脉造影(CTPA)扫描时间分辨力和空间分辨力的提高,使得通过 CT 评价肺栓塞合并右心功能不全成为可能,近年来有大量 CT 诊断 RVD 相关征象的报道,He 等<sup>[26]</sup>发现 CT 提示的右心室增大和室间隔左移可作为区分 RVD 的主要征象,当采用 CT 血栓负担评分系统对肺血管阻塞程度进行分级时, RVD 组的平均血栓负担分值更高。CT 肺动脉栓塞指数(PAOI)评分可以定量分析肺动脉树的阻塞程度,并对右心功能进行评价,结合心血管结构的测量,可预测致命事件,有助于风险评估,帮助临床医生选择最佳治疗手段<sup>[27]</sup>。CT 肺动脉阻塞指数率(PACTOIR)不仅提供了血栓存在的客观证据,还可以估测血栓的重量,诊断 RVD 的临界值为 PACTOIR > 37.5%<sup>[28]</sup>。目前较为普遍采用的评分为 Mastora 和 Qanadli 评分方法, Apfaltrer 等<sup>[29]</sup>发现合并 RVD 组的肺动脉栓塞评分,双侧心室直径比和容积比明显高于无 RVD 组, Qanadli 评分和 Mastora 评分还可以筛选出重度 RVD 患者,研究人员通过受试者工作特征曲线诊断合并 RVD 的患者,其中当轴向切面右室与左室内径比值(RV/LVaxial) > 1.18,重建四腔心切面右室与左室内径比值(RV/LV4ch) > 1.29,三维右室容积与左室容积(RVV/LVV) > 1.39, Qanadli 评分 > 20, Mastora 评分 > 46 可以认为 APE 患者合并有右心功能不全。Aribas 等<sup>[30]</sup>发现轴向切面心室内径比值诊断 RVD 的价值优于肺动脉阻塞评分,多因素回归分析示 RV/LVaxial 比值和肺动脉内径是 RVD 的独立预测因子<sup>[31-33]</sup>。Kang 等<sup>[34]</sup>用 CT 相关的右心功能参数评价 APE 患者的预后。室间隔位置异常,下腔静脉对比返流, RVD/LVD4-CH > 1.0,以及 RVV/LVV > 1.2 是患者临床

预后不佳的独立预测因子,其中重建四腔心切面心室直径比和三维心室容积比是 30 d 死亡的预测因素<sup>[32]</sup>。Trujillo-Santos 等<sup>[35]</sup>对来自 10 个研究机构的 1188 例患者进行系统评价与荟萃分析,CT 相关右心功能参数与 APE 患者死亡率、住院期间并发症密切相关。CT 对右心功能不全的评价尚无统一标准,其诊断价值需要进行大量病例的分析。

临床上将右心功能不全列为急性肺栓塞风险分层的主要指标<sup>[36]</sup>,及时识别这类高危患者对于制订合理的治疗方案、改善近远期预后尤为重要。评估右心功能不全的任何一种检查手段都不是独立的,对各项指标进行综合分析,有利于提高对 RVD 的诊断准确率。

## 【参考文献】

- [1] Kreit JW. The impact of right ventricular dysfunction on the prognosis and therapy of normotensive patients with pulmonary embolism[J]. Chest, 2004, 125(4):1539-1545.
- [2] McKie PM, Cataliotti A, Lahr BD, et al. The prognostic value of N-terminal pro-B-type natriuretic peptide for death and cardiovascular events in healthy normal and stage A/B heart failure subjects[J]. J Am Coll Cardiol, 2010, 55(19):2140-2147.
- [3] Lankeit M, Friesen D, Aschoff J, et al. Highly sensitive troponin T assay in normotensive patients with acute pulmonary embolism[J]. Eur Heart J, 2010, 31(15):1836-1844.
- [4] Becattini C, Vedovati MC, Agnelli G. Prognostic value of troponins in acute pulmonary embolism: a meta-analysis[J]. Circulation, 2007, 116(4):427-433.
- [5] Bernhardt P, Stiller S, Kottmair E, et al. Myocardial scar extent evaluated by cardiac magnetic resonance imaging in ICD patients: relationship to spontaneous VT during long-term follow-up[J]. Int J Cardiovasc Imaging, 2011, 27(6):893-900.
- [6] Becattini C, Vedovati MC, Agnelli G. Right ventricle dysfunction in patients with pulmonary embolism[J]. Int Emergency Med, 2010, 5(5):453-455.
- [7] Jaff MR, McMurtry MS, Archer SL, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association[J]. Circulation, 2011, 123(16):1788-1830.
- [8] Torbicki A, Perrier A, Konstantinides S, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the task force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC)[J]. Eur Heart J, 2008, 29(18):2276-2315.
- [9] Lankeit M, Gomez V, Wagner C, et al. A strategy combining imaging and laboratory biomarkers in comparison with a simplified clinical score for risk stratification of patients with acute pulmonary embolism[J]. Chest, 2012, 141(4):916-922.
- [10] Cho JH, Kutti Sridharan G, Kim SH, et al. Right ventricular dysfunction as an echocardiographic prognostic factor in hemodynamically stable patients with acute pulmonary embolism: a meta-analysis[J]. BMC Cardiovasc Disord, 2014, 14:64.
- [11] Vanni S, Polidori G, Vergara R, et al. Prognostic value of ECG among patients with acute pulmonary embolism and normal blood pressure[J]. Am J Med, 2009, 122(3):257-264.
- [12] Kosuge M, Kimura K, Ishikawa T, et al. Prognostic significance of inverted T waves in patients with acute pulmonary embolism[J]. Circul J, 2006, 70(6):750-755.
- [13] Choi BY, Park DG. Normalization of negative T-wave on electrocardiography and right ventricular dysfunction in patients with an acute pulmonary embolism[J]. Korean J Intern Med, 2012, 27(1):53-59.
- [14] Punukollu G, Gowda RM, Vasavada BC, et al. Role of electrocardiography in identifying right ventricular dysfunction in acute pulmonary embolism[J]. Am J Cardiology, 2005, 96(3):450-452.
- [15] Kukla P, Dlugopolski R, Krupa E, et al. Electrocardiography and prognosis of patients with acute pulmonary embolism[J]. Cardiol J, 2011, 18(6):648-653.
- [16] Kim SE, Park DG, Choi HH, et al. The best predictor for right ventricular dysfunction in acute pulmonary embolism: comparison between electrocardiography and biomarkers[J]. Korean Circulation J, 2009, 39(9):378-381.
- [17] Coutance G, Le Page O, Lo T, et al. prognostic value of brain natriuretic peptide in acute pulmonary embolism[J]. Critical Care, 2008, 12(4):R109.
- [18] Musani MH. Asymptomatic saddle pulmonary embolism: case report and literature review[J]. Clin Appl Thromb Hemost, 2011, 17(4):337-339.
- [19] Choi HS, Kim KH, Yoon HJ, et al. usefulness of cardiac biomarkers in the prediction of right ventricular dysfunction before echocardiography in acute pulmonary embolism[J]. J Cardiol, 2012, 60(6):508-513.
- [20] Dores H, Fonseca C, Leal S, et al. NT-proBNP for risk stratification of pulmonary embolism[J]. Rev Port Cardiol, 2011, 30(12):881-886.
- [21] Logeart D, Lecuyer L, Thabut G, et al. biomarker-based strategy for screening right ventricular dysfunction in patients with non-massive pulmonary embolism[J]. Intensive Care Med, 2007, 33(2):286-292.
- [22] Amorim S, Dias P, Rodrigues RA, et al. Troponin I as a marker of right ventricular dysfunction and severity of pulmonary embolism[J]. Rev Port Cardiol, 2006, 25(2):181-186.
- [23] Margato R, Carvalho S, Ribeiro H, et al. cardiac troponin levels in acute pulmonary embolism[J]. Rev Port Cardiol, 2009, 28(11):1213-1222.
- [24] Rydman R, Soderberg M, Larsen F, et al. d-Dimer and simplified pulmonary embolism severity index in relation to right ventricular function[J]. Am J Emergency Medicine, 2013, 31(3):482-486.
- [25] Jeebun V, Doe SJ, Singh L, et al. Are clinical parameters and biomarkers predictive of severity of acute pulmonary emboli on CTPA? [J] QJM, 2010, 103(2):91-97.
- [26] He H, Stein MW, Zalta B, et al. Computed tomography evaluation of right heart dysfunction in patients with acute pulmonary embolism.

- ism[J]. J Comput Assist Tomogr, 2006, 30(2):262-266.
- [27] Attina D, Valentino M, Galie N, et al. Application of a new pulmonary artery obstruction score in the prognostic evaluation of acute pulmonary embolism: comparison with clinical and haemodynamic parameters[J]. Radiol Med, 2011, 116(2):230-245.
- [28] Rodrigues AC, Guimaraes L, Guimaraes JF, et al. Relationship of clot burden and echocardiographic severity of right ventricular dysfunction after acute pulmonary embolism[J]. Int J Cardiovasc Imaging, 2015, 31(3):509-515.
- [29] Apfaltrer P, Henzler T, Meyer M, et al. Correlation of CT angiographic pulmonary artery obstruction scores with right ventricular dysfunction and clinical outcome in patients with acute pulmonary embolism[J]. Eur J Radiol, 2012, 81(10):2867-2871.
- [30] Aribas A, Keskin S, Akilli H, et al. The use of axial diameters and CT obstruction scores for determining echocardiographic right ventricular dysfunction in patients with acute pulmonary embolism[J]. Jpn J Radiol, 2014, 32(8):451-460.
- [31] Kumamaru KK, Hunsaker AR, Wake N, et al. The variability in prognostic values of right ventricular-to-left ventricular diameter ratios derived from different measurement methods on computed tomography pulmonary angiography: a patient outcome study[J]. J Thorac Imaging, 2012, 27(5):331-336.
- [32] Lu MT, Demehri S, Cai T, et al. Axial and reformatting four-chamber right ventricle-to-left ventricle diameter ratios on pulmonary ct angiography as predictors of death after acute pulmonary embolism[J]. AJR Am J Roentgenol, 2012, 198(6):1353-1360.
- [33] Lu MT, Cai T, Ersoy H, et al. Interval increase in right-left ventricular diameter ratios at ct as a predictor of 30-day mortality after acute pulmonary embolism: initial experience[J]. Radiology, 2008, 246(1):281-287.
- [34] Kang DK, Thilo C, Schoepf UJ, et al. CT signs of right ventricular dysfunction: prognostic role in acute pulmonary embolism[J]. JACC Cardiovasc Imaging, 2011, 4(8):841-849.
- [35] Trujillo-Santos J, den Exter PL, Gomez V, et al. Computed tomography-assessed right ventricular dysfunction and risk stratification of patients with acute non-massive pulmonary embolism: systematic review and meta-analysis[J]. J Thromb Haemost, 2013, 11(10):1823-1832.
- [36] 刘畅, 曹小织. 自发性肺血栓栓塞症的早期诊断及分析[J]. 东南国防医药, 2014, 16(6):605-607.  
(收稿日期:2015-06-03; 修回日期:2015-08-01)  
(本文编辑:齐 名; 英文编辑:王建东)

(上接第 516 页)

- [16] Planes R, BenMohamed L, Leghmari K, et al. HIV-1 Tat protein induces PD-L1 (B7-H1) expression on dendritic cells through tumor necrosis factor alpha- and toll-like receptor 4-mediated mechanisms[J]. J Virol, 2014, 88(12):6672-6689.
- [17] Penalzoa-MacMaster P, Kamphorst AO, Wieland A, et al. Interplay between regulatory T cells and PD-1 in modulating T cell exhaustion and viral control during chronic LCMV infection[J]. J Exp Med, 2014, 211(9):1905-1918.
- [18] Su SS, He H, Kong LB, et al. Regulatory phenotype, PD-1 and TLR3 expression in T cells and monocytes from HCV patients undergoing antiviral therapy: a randomized clinical trial[J]. PLoS One, 2014, 9(4):e93620.
- [19] Shi F, Shi M, Zeng Z, et al. PD-1 and PD-L1 upregulation promotes CD8(+) T-cell apoptosis and postoperative recurrence in hepatocellular carcinoma patients[J]. Int J Cancer, 2011, 128(4):887-896.
- [20] Palmer BE, Neff CP, Lecureux J, et al. In vivo blockade of the PD-1 receptor suppresses HIV-1 viral loads and improves CD4<sup>+</sup> T cell levels in humanized mice[J]. J Immunol, 2013, 190(1):211-219.
- [21] Dai B, Xiao L, Bryson PD, et al. PD-1/PD-L1 blockade can enhance HIV-1 Gag-specific T cell immunity elicited by dendritic cell-directed lentiviral vaccines[J]. Mol Ther, 2012, 20(9):1800-1809.
- [22] Iwai Y, Terawaki S, Ikegawa M, et al. PD-1 inhibits antiviral immunity at the effector phase in the liver[J]. J Exp Med, 2003, 198(1):39-50.
- [23] Dong H, Zhu G, Tamada K, et al. B7-H1 determines accumulation and deletion of intrahepatic CD8(+) T lymphocytes[J]. Immunity, 2004, 20(3):327-336.
- [24] Cai G, Nie X, Li L, et al. B and T lymphocyte attenuator is highly expressed on intrahepatic T cells during chronic HBV infection and regulates their function[J]. J Gastroenterol, 2013, 48(12):1362-1372.
- [25] Xu P, Chen YJ, Chen H, et al. The expression of programmed death-1 in circulating CD4<sup>+</sup> and CD8<sup>+</sup> T cells during hepatitis B virus infection progression and its correlation with clinical baseline characteristics[J]. Gut Liver, 2014, 8(2):186-195.
- [26] Boni C, Fiscaro P, Valdatta C, et al. Characterization of hepatitis B virus (HBV)-specific T-cell dysfunction in chronic HBV infection[J]. J Virol, 2007, 81(8):4215-4225.
- [27] Hou FQ, Wu XJ, Wang Y, et al. Rapid downregulation of programmed death-1 and interferon-gamma-inducible protein-10 expression is associated with favourable outcome during antiviral treatment of chronic hepatitis B[J]. J Viral Hepat, 2013, 20(Suppl 1):18-26.  
(收稿日期:2015-04-14; 修回日期:2015-06-22)  
(本文编辑:齐 名; 英文编辑:王建东)