心外膜脂肪组织的无创影像学在心房颤动中的研究进展

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【摘要】心外膜脂肪组织是位于心包与心肌之间的特殊内脏脂肪库，可能通过脂肪细胞直接浸润心肌、炎性介导和自主神经作用等机制诱导心房颤动的发生。研究显示心外膜脂肪与心房颤动的发生、进展程度及术后复发密切相关。用无创影像学方法，如计算机断层扫描、磁共振成像及超声定量检测心外膜脂肪的体积、厚度和密度等相关指标对评价心房颤动的发生、进展及预后有重要意义。现主要就心外膜脂肪组织影像学指标与心房颤动的发生、预后及并发症关系的研究进展进行综述。

【关键词】心外膜脂肪组织；心房颤动；心外膜脂肪体积；心外膜脂肪厚度；心外膜脂肪密度
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Non-invasive Imaging of Epicardial Adipose Tissue in Atrial Fibrillation

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【**Abstract**】Epicardial adipose tissue is a special visceral fat bank located between the pericardium and the myocardium. Atrial fibrillation may be induced by adipocytes directly infiltrating the myocardium, inflammatory mediation and autonomic nerve action. Studies have shown that epicardial fat is closely related to the occurrence, progression and postoperative recurrence of atrial fibrillation. Non-invasive imaging methods such as computed tomography, magnetic resonance imaging and ultrasound quantitative detection of epicardial fat volume, thickness, density and other related indicators are of great significance in evaluating the occurrence, progress and prognosis of atrial fibrillation. This article reviews the research progress of the relationship between epicardial adipose tissue imaging indicators and the occurrence, prognosis and complications of atrial fibrillation.

【**Key words**】Epicardial adipose tissue; Atrial fibrillation; Epicardial adipose tissue volume; Epicardial adipose tissue thickness; Epicardial adipose tissue density

心房颤动（房颤）是临床常见的室上性心律失常，发病率和死亡率日趋升高[1]。既往研究已证实房颤的发生与全身性肥胖有关[2]，而随着对房颤机制的不断深入研究，发现心外膜脂肪组织（epicardial adipose tissue, EAT）与房颤的关系似乎更为密切[3-4]，用EAT评价房颤可能更有意义。现就EAT影像学指标与房颤发生、预后及并发症关系的研究进展进行综述。

1　EAT的解剖结构及生理功能

EAT是贮存于脏层心包与心肌之间的特殊内脏脂肪库，几乎覆盖了心脏表面的80%，占整个心脏质量的20%，主要位于右心室表面和左心室前壁，围绕房室沟和冠状动脉主要分支，具有储存能量的作用及内分泌功能[5]。EAT直接包绕在心肌及冠状动脉表面，无筋膜分隔，可通过自分泌或旁分泌促炎因子，直接影响心肌与冠状动脉的微环境[3]。生理情况下，EAT对心肌和冠状动脉起保护作用，而在病理条件下（如肥胖、高脂血症和心力衰竭等），EAT分泌的脂肪因子和炎性介质等会促进心房结构和功能的重构，促进房颤的发生和发展[3,5]。

2　EAT影响房颤的可能机制

EAT影响房颤的机制尚未完全明确。目前研究表明EAT可能通过直接机制和间接机制影响心脏结构和功能，从而导致房颤的发生和进展。

2.1　EAT增加房颤风险的直接机制

EAT通过脂肪细胞的直接浸润，渗透到心房心肌细

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胞，使得心肌细胞的同一性消失，导致电生理传导减慢或各向异性，从而使除极波异常传播，增加折返波的形成和电冲动的异常，促进房颤的发生[3]。

2.2 EAT增加房颤风险的间接机制

（1）EAT分泌脂肪因子：EAT可能充当代谢活性组织，分泌脂肪因子（如激活素A、基质金属蛋白酶-2和基质金属蛋白酶-7）[6-8]，这些脂肪因子通过促进心肌纤维化，导致心房结构重构，诱导房颤发生。（2）EAT释放炎症介质：多项研究已表明房颤的发生与局部炎症的过程相关[9]，EAT分泌的炎症介质，如C反应蛋白、白介素-6、白介素-8和肿瘤坏死因子-α等炎症介质[10-12]，产生局部促炎作用，促进心律失常，尤其是在缺血性心肌病、肥胖症或糖尿病患者中。（3）EAT激活自主神经：EAT通过激活位于EAT内的神经节神经丛，刺激交感神经，增加Ca^{2+}内流，刺激副交感神经，缩短动作电位持续时间[13-14]，从而诱发房颤。

3 EAT的影像学测量方法

目前常用检测EAT的无创影像学方法主要有磁共振成像、超声及计算机断层扫描（computed tomography，CT）。

磁共振成像一直以来被认为是测量心外膜脂肪体积（epicardial adipose tissue volume, EATV）的金标准[3]，但其费时费力，且价格偏高，易产生伪影，不宜广泛应用于临床。

超声通常在胸骨旁的左心室长轴和短轴切面上测量收缩末期右心室游离壁处EAT的厚度。超声具有廉价、简单和易于重复操作等优势，适合大样本研究，但由于超声声窗的限制，区分EAT与其他心脏脂肪尚有难度，且无法直接测量EATV，限制了其在临床方面的应用。

目前大多数研究更倾向使用CT进行EATV和EAT密度的测量，因为其分辨率和重复性高。CT测量EAT的方法一般多为手动或半自动勾画EAT范围，设置CT值为–190～–30 HU，通过半自动后处理软件，识别出此CT值范围内的EAT，再由容积或密度测量工具计算出相关指标[15]。

4 EAT的影像学指标与房颤的关系

目前多数研究已证实EAT与房颤的发生、发展、预后及并发症的发生密切相关，可用EAT的相关影像学指标预测房颤的发生，识别高危个体，从而积极干预治疗，提高患者预后及生活质量，也可用EAT进行预后评估，评价患者术后房颤复发及出现卒中并发症的风险。

4.1 EATV与房颤的关系

4.1.1 EATV与房颤发生和进展的关系

相关研究表明EATV与房颤的发生和进展有关，EATV增大是房颤发生的独立危险因素，持续性房颤患者的EATV高于阵发性房颤患者[3,15-16]，EATV随着房颤的存在和严重程度的增加而逐步增加，即EATV及EATV指数（EATVI）（EATVI=EATV/体表面积）与房颤的程度成正比[15]。此外，EATV也与心脏手术后房颤的发生相关，Kogo等[17]发现左心房EATV/总EATV的比值越高，术后房颤发生的可能性越大。

4.1.2 EATV与房颤预后的关系

大多数研究认为EATV增大与房颤术后的复发有关。Maeda等[18]发现CT测定的EATVI是导管消融后房颤复发的独立危险因素，高EATVI界值（阵发性房颤：EATVI≥85 mL/m²或持续性房颤：EATVI≥116 mL/m²）可预测导管消融后的房颤复发。Sepehri Shamloo等[19]的荟萃分析纳入了10篇文章共计1 208例房颤消融患者，统计分析结果提示复发房颤患者中的左心房周围EATV和总EATV高于未复发房颤患者（左心房周围EATV：界值为0.862 mL，95% *CI* 0.567～1.156; 总EATV：界值为1.017 mL, 95% *CI* 0.748～1.286），左心房周围EATV和总EATV的增加与房颤消融后复发相关。

然而，也有研究表明EATV与房颤术后复发无关，Vroomen等[20]回顾性研究了EATV与房颤患者混合性房颤消融术（心外膜外科手术和心内膜导管消融）预后之间的关系，发现阵发性房颤与持续性房颤和长期持续性房颤患者之间EATV无差异，EATV既不会影响手术消融的结果，也不会影响术前或术中的决策。上述研究结果存在差异的原因可能是与样本的选择及样本数量有关，这也表明EATV与房颤术后复发之间的关系仍需进一步探究。

4.1.3 EATV与房颤相关卒中的关系

EATV可用来预测房颤相关卒中的发生。Ahn等[21]纳入3 464例房颤消融术后的患者，通过（47.2±36.4）个月的随访，发现左心房周围EATV的增加与房颤消融术后栓塞性卒中的发生有关（界值为20.15 mL，*OR* 1.065，95% *CI* 1.005～1.128，$P<0.05$）。也有相关报道称在阵发性和持续性房颤患者中，左心房周围EATV与心脏栓塞性卒中的发生有关[22]。在此研究基础上，或许可用EATV评估房颤相关卒中及其他并发症发生的风险，进行风险分级，采取预防措施并指导相关治疗。

4.2 EAT厚度与房颤的关系

4.2.1 EAT厚度与房颤发生和进展的关系

不仅EATV与房颤发生和进展有关，也有研究认为EAT厚度同样与房颤发生和进展密切相关。Yorgun等[23]研究发现与窦性心律组相比，永久性、持续性和阵发性房颤组EAT厚度明显更高（$P<0.001$），且阵发性房颤、持续性房颤和永久性房颤的EAT厚度呈增加的趋势，这可能与心房结构性重构和炎性浸润有关。

4.2.2 EAT厚度与房颤预后的关系

EAT厚度的增加可能是术后房颤复发的独立危险

因素[24-25]。Mirolo等[25]对使用第二代冷冻球囊行首次肺静脉隔离术的房颤患者进行随访，用磁共振成像测定EAT厚度，发现复发患者EAT厚度高于未复发患者[（4.9±0.9）mm vs（4.3±0.9）mm，*P*=0.001]，EAT厚度增加与房颤复发有关（*OR* 1.96，95% *CI* 1.20～3.18，*P*=0.007，EAT厚度界值为4.35 mm）。Dereli等[26]也证实这一结论，通过研究发现房颤复发组患者的平均EAT厚度为（8.7±1.2）mm，而房颤未复发组患者的平均EAT厚度为（6.8±0.8） mm，房颤复发组的EAT明显较厚（*P*=0.001），EAT厚度的增加（*OR* 3.029，95% *CI* 1.013～9.055，*P*=0.047）是房颤复发的独立危险因素。

4.2.3　EAT厚度与房颤相关卒中的关系

EAT厚度同EATV一样，也可为临床评估房颤相关并发症的发生提供依据。Cho等[27]通过研究发现EAT厚度也与房颤的相关卒中密切相关。房颤组缺血性卒中患者的EAT厚度较大[（6.5±1.2） mm vs（5.3±1.2）mm，*P* < 0.001]，logistic多元回归分析也表明，EAT的厚度（*OR* 1.740）与房颤缺血性卒中独立相关。

4.3　EAT密度与房颤的关系

密度能反映组织特征的变化，提供潜在的生物学信息。目前EAT密度这一指标多应用于冠状动脉相关疾病的研究中，而EAT密度与房颤之间关系的研究尚少[28-29]。Kusayama等[30]纳入32例射频消融前阵发性房颤患者及临床资料与其匹配的32例窦性心律患者，通过对左心房周围EAT密度的测量，发现左心房周围EAT密度的增高与阵发性房颤的发生相关，而皮下脂肪密度与房颤的发生无关，左心房周围EAT密度可能是阵发性房颤发生的独立危险因素之一，这可能与炎症浸润左心房有关，支持了炎症假说这一观点。Klein等[1]则发现有房颤病史患者的左心房周围EAT低密度与低电压区的存在有关（心房纤维化表现为低电压区），而EAT厚度、EATV及总EAT密度与低电压区的存在无关。

5　问题及展望

尽管已有很多研究证实EAT与房颤之间存在相关性，但在二者关系的机制研究和临床应用上仍存在一些问题：（1）目前研究多集中于EAT与房颤之间关系的临床研究，缺少相关动物模型的研究。（2）EAT与房颤发生和发展之间是因果关系还是互相作用，尚无明确的解释。（3）目前对EAT的定量检测方法多种多样，尚无统一的方法及金标准，且指标受测量方式、图像质量及操作者人为干扰较大。今后，需建立相关房颤动物模型，观察房颤前后EATV、厚度和密度等相关指标的变化情况，并提取动物的EAT进行房颤相关分子机制方面研究，这对探讨EAT与房颤的关系，明确二者关系的机制将更有意义；也需进一步进行大样本量的多中心研究来确定EAT相关指标的定量及阈值标准，EAT指标与房颤的其他指标相比是否存在优势等；此外，EAT密度是否可作为更为敏感的房颤标志物，其与房颤的并发症和预后是否具有相关性尚需进一步研究；同时更应着重关注EAT指标在临床中的实用性，从而更好地服务于临床，为诊断和治疗提供便利。随着影像设备的发展，未来可能会产生更精确和更新的EAT定量测量指标，为研究房颤的发生、发展、治疗策略及预后提供新的思路。

参 考 文 献

[1] Klein C,Brunereau J,Lacroix D,et al. Left atrial epicardial adipose tissue radiodensity is associated with electrophysiological properties of atrial myocardium in patients with atrial fibrillation[J]. Eur Radiol,2019,29(6):3027-3035.

[2] Pouwels S,Topal B,Knook MT,et al. Interaction of obesity and atrial fibrillation:an overview of pathophysiology and clinical management[J]. Expert Rev Cardiovasc Ther,2019,17(3):209-223.

[3] Wong CX,Ganesan AN,Selvanayagam JB. Epicardial fat and atrial fibrillation:current evidence,potential mechanisms,clinical implications,and future directions[J]. Eur Heart J,2017,38(17):1294-1302.

[4] le Jemtel TH,Samson R,Ayinapudi K,et al. Epicardial adipose tissue and cardiovascular disease[J]. Curr Hypertens Rep,2019,21(5):36.

[5] Ansaldo AM,Montecucco F,Sahebkar A,et al. Epicardial adipose tissue and cardiovascular diseases[J]. Int J Cardiol,2019,278:254-260.

[6] Venteclef N,Guglielmi V,Balse E,et al. Human epicardial adipose tissue induces fibrosis of the atrial myocardium through the secretion of adipo-fibrokines[J]. Eur Heart J,2015,36(13):795-805a.

[7] Vyas V,Lambiase P. Obesity and atrial fibrillation:epidemiology, pathophysiology and novel therapeutic opportunities[J]. Arrhythm Electrophysiol Rev,2019,8(1):28-36.

[8] 陈丽雯, 孙丽杰, 崔鸣. 脂肪因子在心房颤动诊治中的研究进展[J]. 心血管病学进展, 2018,39(4):525-527.

[9] 孙静美, 尹德春, 曲秀芬. 炎症信号与心房颤动[J]. 心血管病学进展, 2020,41(1):31-34.

[10] Liu Q,Zhang F,Yang M,et al. Increasing level of interleukin-1beta in epicardial adipose tissue is associated with persistent atrial fibrillation[J]. J Interferon Cytokine Res,2020,40(1):64-69.

[11] Mazurek T,Kiliszek M,Kobylecka M,et al. Relation of proinflammatory activity of epicardial adipose tissue to the occurrence of atrial fibrillation[J]. Am J Cardiol,2014,113(9):1505-1508.

[12] Packer M. Drugs that ameliorate epicardial adipose tissue inflammation may have discordant effects in heart failure with a preserved ejection fraction as compared with a reduced ejection fraction[J]. J Card Fail,2019,25(12):986-1003.

[13] Couselo-Seijas M,Lopez-Canoa JN,Agra-Bermejo RM,et al. Cholinergic activity regulates the secretome of epicardial adipose tissue:association with atrial fibrillation[J]. J Cell Physiol,2019,234(7):10512-10522.

[14] Higuchi K,Akkaya M,Koopmann M,et al. The effect of fat pad modification during ablation of atrial fibrillation:late gadolinium enhancement MRI analysis[J]. Pacing Clin Electrophysiol,2013,36(4):467-476.

[15] Oba K,Maeda M,Maimaituxun G,et al. Effect of the epicardial adipose tissue

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[17] Baartscheer A,Schumacher CA,W ü st RCI,et al. Empagliflozin decreases myocardial cytoplasmic Na^+ through inhibition of the cardiac Na^+/H^+ exchanger in rats and rabbits[J]. Diabetologia,2017,60(3):568-573.

[18] Uthman L,Baartscheer A,Bleijlevens B,et al. Class effects of SGLT2 inhibitors in mouse cardiomyocytes and hearts:inhibition of Na^+/H^+ exchanger,lowering of cytosolic Na^+ and vasodilation[J]. Diabetologia,2018,61(3):722-726.

[19] Packer M,Anker SD,Butler J,et al. Effects of sodium-glucose cotransporter 2 inhibitors for the treatment of patients with heart failure:proposal of a novel mechanism of action[J]. JAMA Cardiol,2017,2(9):1025-1029.

[20] Fedak PW,Verma S,Weisel RD,et al. Cardiac remodeling and failure from molecules to man (part Ⅱ)[J]. Cardiovasc Pathol,2005,14(2):49-60.

[21] Lee TM,Chang NC,Lin SZ. Dapagliflozin,a selective SGLT2 inhibitor, attenuated cardiac fibrosis by regulating the macrophage polarization via STAT3 signaling in infarcted rat hearts[J]. Free Radic Biol Med,2017,104:298-310.

[22] Kang S,Verma S,Hassanabad AF,et al. Direct effects of empagliflozin on extracellular matrix remodelling in human cardiac myofibroblasts:novel translational clues to explain EMPA-REG OUTCOME results[J]. Can J Cardiol,2020,36(4):543-553.

[23] Shi L,Zhu D,Wang S,et al. Dapagliflozin attenuates cardiac remodeling in mice model of cardiac pressure overload[J]. Am J Hypertens,2019,32(5):452-459.

[24] Packer M. Do sodium-glucose co-transporter-2 inhibitors prevent heart failure with a preserved ejection fraction by counterbalancing the effects of leptin?A novel hypothesis[J]. Diabetes Obes Metab,2018,20(6):1361-1366.

[25] Garvey WT,van Gaal L,Leiter LA,et al. Effects of canagliflozin versus glimepiride on adipokines and inflammatory biomarkers in type 2 diabetes[J]. Metabolism,2018,85:32-37.

[26] Sato T,Aizawa Y,Yuasa S,et al. The effect of dapagliflozin treatment on epicardial adipose tissue volume[J]. Cardiovasc Diabetol,2018,17(1):6.

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volume on the prevalence of paroxysmal and persistent atrial fibrillation[J]. Circ J,2018,82(7):1778-1787.

[16] Wong CX,Sun MT,Odutayo A,et al. Associations of epicardial,abdominal,and overall adiposity with atrial fibrillation[J]. Circ Arrhythm Electrophysiol,2016,9(12):e004378.

[17] Kogo H,Sezai A,Osaka S,et al. Does epicardial adipose tissue influence postoperative atrial fibrillation?[J]. Ann Thorac Cardiovasc Surg,2019,25(3):149-157.

[18] Maeda M,Oba K,Yamaguchi S,et al. Usefulness of epicardial adipose tissue volume to predict recurrent atrial fibrillation after radiofrequency catheter ablation[J]. Am J Cardiol,2018,122(10):1694-1700.

[19] Sepehri Shamloo A,Dagres N,Dinov B,et al. Is epicardial fat tissue associated with atrial fibrillation recurrence after ablation? A systematic review and meta-analysis[J]. Int J Cardiol Heart Vasc,2019,22:132-138.

[20] Vroomen M,Olsthoorn JR,Maesen B,et al. Quantification of epicardial adipose tissue in patients undergoing hybrid ablation for atrial fibrillation[J]. Eur J Cardiothorac Surg,2019,56(1):79-86.

[21] Ahn J,Shin SY,Shim J,et al. Association between epicardial adipose tissue and embolic stroke after catheter ablation of atrial fibrillation[J]. J Cardiovasc Electrophysiol,2019,30(11):2209-2216.

[22] Tsao HM,Hu WC,Tsai PH,et al. The abundance of epicardial adipose tissue surrounding left atrium is associated with the occurrence of stroke in patients with atrial fibrillation[J]. Medicine(Baltimore),2016,95(14):e3260.

[23] Yorgun H,Canpolat U,Aytemir K,et al. Association of epicardial and peri-atrial adiposity with the presence and severity of non-valvular atrial fibrillation[J]. Int J Cardiovasc Imaging,2015,31(3):649-657.

[24] Monno K,Okumura Y,Saito Y,et al. Effect of epicardial fat and metabolic syndrome on reverse atrial remodeling after ablation for atrial fibrillation[J]. J Arrhythm,2018,34(6):607-616.

[25] Mirolo A,Viart G,Savoure A,et al. Epicardial fat thickness predicts atrial fibrillation recurrence after a first pulmonary vein isolation procedure using a second-generation cryoballoon[J]. Arch Cardiovasc Dis,2019,112(5):314-322.

[26] Dereli S,Bayramoglu A,Yontar OC,et al. Epicardial fat thickness:a new predictor of successful electrical cardioversion and atrial fibrillation recurrence[J]. Echocardiography,2018,35(12):1926-1931.

[27] Cho KI,Kim BJ,Cho SH,et al. Epicardial fat thickness and free fatty acid level are predictors of acute ischemic stroke with atrial fibrillation[J]. J Cardiovasc Imaging,2018,26(2):65-74.

[28] Franssens BT,Nathoe HM,Leiner T,et al. Relation between cardiovascular disease risk factors and epicardial adipose tissue density on cardiac computed tomography in patients at high risk of cardiovascular events[J]. Eur J Prev Cardiol,2017,24(6):660-670.

[29] Liu Z,Wang S,Wang Y,et al. Association of epicardial adipose tissue attenuation with coronary atherosclerosis in patients with a high risk of coronary artery disease[J]. Atherosclerosis,2019,284(5):230-236.

[30] Kusayama T,Furusho H,Kashiwagi H,et al. Inflammation of left atrial epicardial adipose tissue is associated with paroxysmal atrial fibrillation[J]. J Cardiol,2016,68(5):406-411.

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