·综　述·

心房心肌病：心房颤动消融术后复发的结构性基础与评估策略

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［摘　要］　心房心肌病（atrial cardiomyopathy，ACM）是一种以心房结构重塑、电生理异常和纤维化为特征的病理状态，与心房颤动（atrial fibrillation，AF）消融术后复发密切相关。ACM导致的心房广泛纤维化和电重构形成致心律失常基础，不仅促进AF的发生与维持，更是消融后复发的重要结构性基础。研究表明，消融术仅能隔离肺静脉，而无法消除ACM的病理基础，使得纤维化区域持续存在非肺静脉触发灶和缓慢传导区，最终导致术后AF或房速复发。文章系统阐述ACM作为AF复发基础的病理机制，通过整合超声心动图、心脏磁共振及循环生物标志物等多模态无创技术，构建涵盖结构、功能与分子层面的综合评估体系。深入分析多维度无创参数联合评估价值，并提出ACM导向的围术期干预路径，为改善AF消融预后提供循证依据。

［关键词］　心房心肌病；房颤；复发；超声心动图；生物标志物

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Atrial cardiomyopathy：the role of non-invasive assessment in post-ablation atrial fibrillation recurrence

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［**Abstract**］　Atrial cardiomyopathy（ACM）is a pathological condition characterized by structural remodeling，electrophysiological abnormalities，and fibrosis of the atria. It is closely associated with atrial fibrillation（AF）recurrence following catheter ablation. Diffuse atrial fibrosis and electrical remodeling induced by ACM create a pro-arrhythmic substrate that not only perpetuates AF but also serves as a key structural determinant of post-ablation recurrence. Studies have indicated that while ablation effectively isolates pulmonary veins，it fails to eliminate the underlying ACM substrate. Consequently，residual fibrotic regions persist，harboring non-pulmonary vein triggers and zones of slow conduction，which ultimately lead to recurrent AF or atrial tachycardia. This review systematically elucidates the pathological mechanisms linking ACM to post-ablation recurrence. By integrating multimodal non-invasive technologies，including echocardiography，cardiac magnetic resonance，and circulating biomarkers，we establish a comprehensive assessment system encompassing structural，functional，and molecular dimensions. We evaluate the synergistic role of combining these multidimensional non-invasive parameters in risk prediction and propose an ACM-guided peri-procedural management strategy to optimize AF ablation outcomes.

［**Key words**］　atrial cardiomyopathy；atrial fibrillation；recurrence；echocardiography；biomarkers

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心房心肌病（atrial cardiomyopathy，ACM）作为一种复杂的心脏病理改变，其核心特征是心房结构重构、电生理异常和收缩功能障碍，这些改变可导致严重的临床后果[1]（图1）。近年来，随着对心房颤动（atrial fibrillation，AF）机制研究的深入，ACM在AF导管消融术后复发中的作用日益受到重视。

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大量临床证据表明，ACM与AF之间存在双向促进关系：一方面，ACM通过心房纤维化和电重构为AF的发生和维持提供基础[2]；另一方面，AF本身又会进一步加重心房重构，形成恶性循环[3-4]。研究发现，ACM患者消融术后复发率高，为20%~50%[5]，其中阵发性AF的单次手术后复发率24%~27%，非阵发性AF的单次手术后复发率40%~50%[6-7]。值得注意的是，ACM的严重程度直接影响导管消融的治疗效果。且复发风险与心房纤维化程度呈正相关[8]。尽管ACM在AF发生发展中的作用机制已取得研究进展，但仍缺乏以临床为导向的评估标准。传统的预测模型，如APPLE、CAAP-AF、CHA_2DS_2-VASc评分等，虽整合了年龄、性别、并发症等基线特点，但没有探索应变成像、心房纤维化程度等更直接的心房评估指标，只初步完成了对AF复发风险预测的量化评估，评估能力表现不足，且准确率及灵敏度有限[9]，不适合现阶段的临床应用。所以构建联合结构、功能与生物标志物等的分类体系，对准确评估疾病严重程度、预测临床结局和指导治疗决策至关重要。

文章将从ACM的病理机制出发，深入探讨其作为AF复发基础的核心作用，系统阐述多模态无创评估策略在ACM围术期管理中的应用价值，并据此提出ACM导向的精准干预路径，旨在为优化AF消融预后提供坚实的循证依据。

1 ACM的病理级联进程

ACM的病理机制是炎症反应、氧化应激、心房牵拉及神经激素信号异常（如血管紧张素Ⅱ和醛固酮升高），导致心房肌细胞功能障碍、结构重构与电生理特性改变，最终导致心律失常[10]。遗传（如心肌细胞发育相关基因突变）和年龄相关性退变（心肌细胞功能下降、细胞外基质改变）是重要促发因素[1,11]。ACM与心力衰竭、AF及代谢性疾病（如肥胖、糖尿病）形成恶性循环：心力衰竭时心室功能障碍导致心房压力持续升高，通过机械牵张激活转化生长因子（transforming growth factor，TGF）-β/Smad通路，驱动成纤维细胞增殖及胶原沉积，加速心房纤

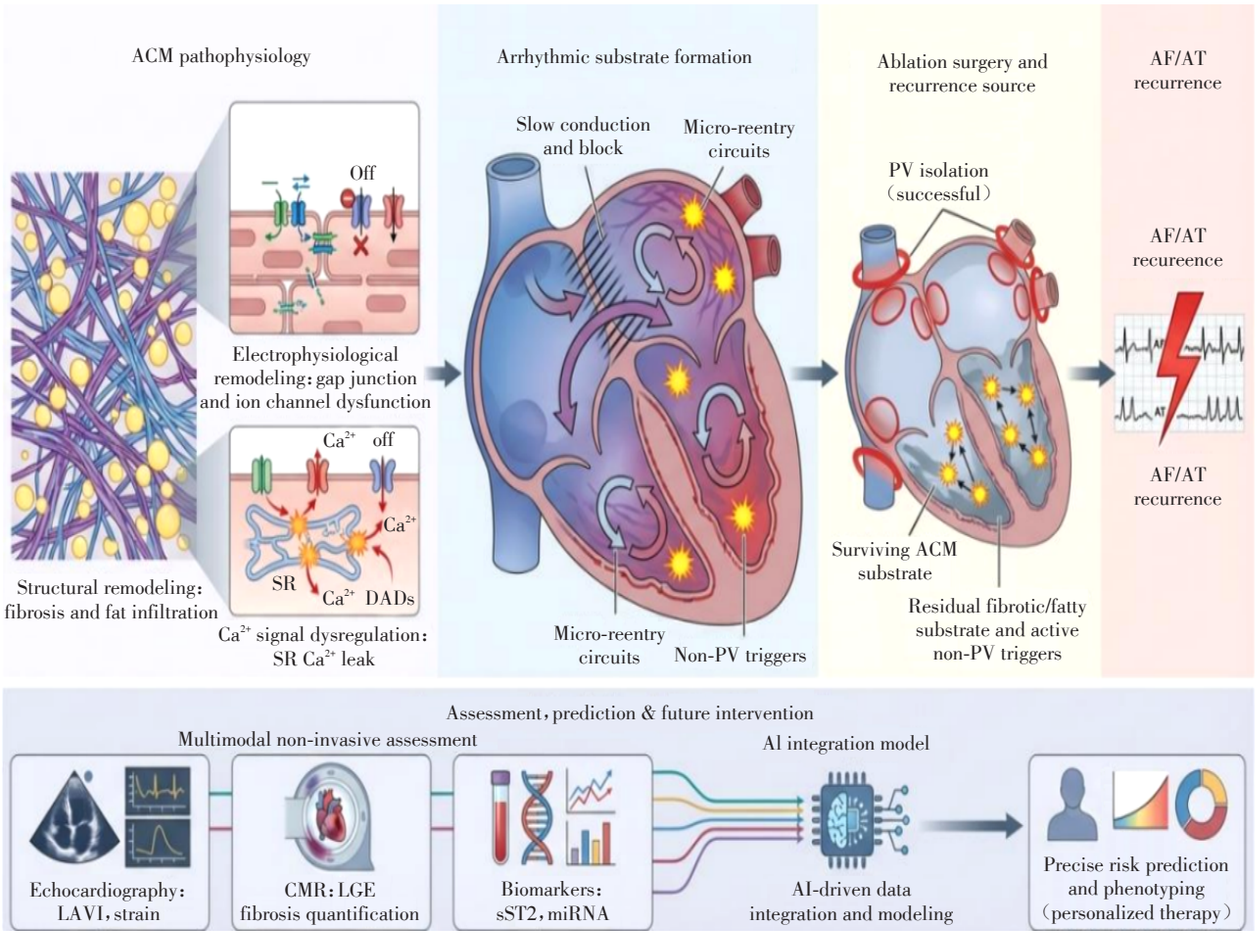

图1 ACM导致AF消融术后复发的机制与评估

Figure 1 Mechanisms and assessment of ACM in post-ablation AF recurrence

维化[12]；而AF的快速电激动（≥300次/min）诱发心肌细胞兰尼定受体2（ryanodine receptor 2，RyR2）过度磷酸化，导致舒张期钙泄漏和细胞内钙超载，进一步激活钙调磷酸酶-活化T细胞核因子（nuclear factor of activated T cell，NFAT）轴，使TGF-β表达升高，促进纤维化级联并损害心房收缩功能[13]。与此同时，代谢性疾病通过“脂肪-炎症轴”加剧病理进程，肥胖者内脏脂肪释放的瘦素和肿瘤坏死因子（tumor necrosis factor，TNF）-α激活Janus激酶2（Janus kinase-2，JAK2）/信号转导与转录激活因子3（signal transducer and activator of transcription 3，STAT3）通路刺激纤维化，高血糖则增强血管紧张素Ⅱ效应，共同导致心房脂肪浸润面积增加2.5倍[14]。

1.1　结构重塑的病理基础：纤维化、脂肪浸润与淀粉样沉积

ACM的结构重塑以纤维化为首要病理特征，其核心机制在于炎症因子[TGF-β、白介素（interleukin，IL）-6]和机械牵张持续激活心房成纤维细胞，促使细胞外基质中的Ⅰ/Ⅲ型胶原蛋白异常沉积，形成纤维网络[15]。这种纤维网络不仅破坏心肌细胞间连接蛋白，显著降低心房顺应性，更通过增加电阻抗使电传导速度下降40%~50%[16]，这种由纤维化导致的电传导改变，可以让AF风险升高3.2倍[17]。值得注意的是，DECAAF研究证实当纤维化体积占左房心肌20%以上时，AF消融失败率骤增至80%[18]。此外，心肌纤维化还与卒中等并发症相关，近期研究表明，在尚未发生AF的心房纤维化患者中，卒中发生风险仍可提高2.1倍[19]，该研究揭示了纤维化诱导的内皮功能障碍在血栓栓塞事件中也扮演着重要角色。

在心房纤维化基础上，脂肪浸润能够进一步加剧AF的病理进程。心外膜脂肪组织（epicardial adipose tissue，EAT）不仅通过机械压迫心肌微结构侵袭心房肌层，还能通过释放促炎脂肪因子（瘦素、TNF-α）和促纤维化因子[TGF-β、结缔组织生长因子（connective tissue growth factor，CTGF）]，激活JAK2/STAT3通路形成心肌结构毁损的恶性循环[20]。被脂肪包绕的心房区，因电传导各向异性增加导致局部传导延迟（>15 ms），成为微折返的病理基础。临床研究数据显示：EAT的厚度每增加1 mm，AF复发风险就会上升18%[21]。

此外，淀粉样沉积亦会构成老年性ACM的特异性损伤。异常折叠的转甲状腺素蛋白（transthyretin，TTR）或轻链蛋白（amyloid light-chain，AL）沉积于心房间质，破坏肌原纤维排列并挤压毛细血管，导致心肌细胞能量代谢衰竭[22]。这不仅引起心房僵硬度显著增加和收缩功能丧失，淀粉样蛋白更能够直接结合钠离子通道（voltage-gated sodium channel，Nav）1.5干扰电信号，诱发传导阻滞及早期后除极，使室上性心律失常发生率上升至67%[23]。纤维化、脂肪浸润和淀粉样沉积三者协同作用，最终形成不可逆的致心律失常网络。

1.2　电生理重构的核心机制：离子通道异常与缝隙连接紊乱

ACM的电生理重构起始于离子通道功能障碍[24]。其中，钾通道异常（如I_k、I_{to}电流减弱）会引发复极延迟以及有效不应期延长，显著提升早期后除极的风险[25]；而钠通道（Nav1.5）表达下调会降低动作电位的上升速度与幅度，致使电传导速度下降≥40%[26]，成为折返性AF发生的基础。ACM患者心房组织中的缝隙连接蛋白（connexin，Cx）43若发生类泛素化修饰驱动的“侧化位移”（即从细胞端端连接转变为侧侧分布），则会导致电信号由快速纵向传播转变为缓慢横向扩散[27]。这种结构改变使传导的各向异性比扩大（>2∶1），进而形成局部缓慢传导区，直接促进微折返环路的形成。

此外，交感神经过度激活使去甲肾上腺素释放量增加2倍以上，并通过β1-肾上腺素能受体（β1-adrenergic receptor，β1-AR）-环腺苷单磷酸（cyclic adenosine monophosphate，cAMP）通路增强钙时钟活性，从而提高起搏细胞的自律性[28]。组织学分析表明，ACM患者心房交感神经密度增加65%，且与术中记录的局灶触发灶数量呈强相关性[29]。离子通道紊乱、传导延迟和自主神经触发三者相互协同，最终导致持续性AF的不可逆维持。

1.3　钙信号失调的恶性循环：从心肌细胞功能障碍到触发活动增强

ACM的电生理失调起始于RyR2的过度磷酸化，此过程主要由持续激活的蛋白激酶A（protein kinase A，PKA）以及钙/钙调素依赖性蛋白激酶Ⅱ（Ca^{2+}/calmodulin-dependent protein kinase Ⅱ，CaMKⅡ）驱动。这会使舒张期钙离子从肌浆网异常泄漏，进而引发细胞内钙超载。这种钙稳态的破坏会触发双重病理级联反应：一方面，胞质内高钙水平激活钙调磷酸酶，进而激活NFAT转录通路，显著上调TGF-β的表达，有力地推动成纤维细胞向过度分泌胶原的肌成纤维细胞转化[30]；另一方面，钙超载直接延长心肌细胞动作电位时程，并大幅增加肌浆网自发

钙释放事件，为早期后除极和延迟后除极创造了条件，成为AF发生的直接电触发机制[31]。

钙信号紊乱与AF之间形成了紧密的双向恶性循环[32]。ACM自身固有的病理环境，如活性氧水平成倍增加以及TNF-α等炎症因子水平升高，持续促进RyR2磷酸化，加剧钙泄漏[33]。与此同时，一旦AF发作，其快速的心房电激动（≥300次/min）通过钠钙交换体的反向模式运转，使胞质钙浓度进一步升高40%[34]。这激活了钙依赖性蛋白酶Calpain-1，导致肌原纤维结构受损和细胞凋亡。这种钙失衡、结构重塑与AF之间的相互作用最终形成了一个难以逆转的病理三角。钙超载介导的心肌细胞凋亡持续扩大纤维化区域，形成的纤维瘢痕组织阻碍电传导的同步性，为AF的维持提供了稳定的基础。反之，持续存在的AF通过快速电激动增加L型钙通道的内流，不断加重钙超载，进一步耗尽肌浆网钙储备。

2 ACM作为AF消融术后复发的病理核心

2.1 结构异质性引发传导延迟与折返

ACM所形成的结构异质性，是决定AF导管消融术后不能维持窦性心律的关键病理条件[35]。与基础结构重塑不同，结构异质性并不单纯等于纤维化或脂肪浸润，而是指心房内正常心肌与病变心肌交错分布、电传导特性空间差异显著的病理状态，这一特征是单纯肺静脉隔离术后复发的核心基础[36]。

这种空间上的电生理不均一性，会在心房内制造出缓慢传导区、传导阻滞线、各向异性传导增强区，即使完成肺静脉电隔离，仍可独立形成微折返、大折返及局部转子，成为术后房速、房扑及AF复发的解剖基础[37]，同时结构异质性区域也是术后电重构持续存在、无法逆转的关键部位，可进一步降低折返波长、维持心律失常，显著削弱消融效果。多项研究均表示，结构异质性的程度越高，心房内残留致心律失常基质越丰富，术后复发风险越高[35]，也正是这一病理特征决定了仅行肺静脉隔离难以长期根治AF。

2.2 非肺静脉（non-pulmonary vein，NPV）触发灶的激活

ACM是介导NPV触发灶形成并导致AF消融术后复发的核心病理基础[38]。ACM引发的心房纤维化、电重构及自主神经重构，可直接导致心肌自律性异常升高与触发活动的出现。进而促使潜在异位灶兴奋性增高、阈值下降，最终形成具有致心律失常活性的肺静脉外的异位触发灶[39-40]。此类触发灶与心房纤维化区域具有高度空间关联性，若术中未能彻底消融，将直接构成术后复发的重要来源。

临床证据表明，NPV触发灶是AF消融术后复发的主要预测因子。在亚洲人群中，上腔静脉来源的触发更为常见，术中对其进行经验性隔离可显著降低术后复发率[41]。同时，10%~20%的AF术后复发由NPV触发灶介导，其常见部位包括上腔静脉、冠状窦、终末嵴、左房后壁及Marshall韧带等区域[42]。术中对上述位点进行精准识别与靶向消融，可有效提升AF消融的长期成功率。

2.3 ACM的病理负荷与复发风险的等级关联

术前评估的ACM病理负荷严重程度与AF消融术后的复发风险存在显著且具有临床指导意义的等级关联。这种负荷可通过超声心动图参数、生物标志物以及电生理特征等进行综合量化评估[43]。轻度负荷：左心房容积指数（left atrial volume index，LAVI）<34 mL/m^2，心脏磁共振成像晚期钆增强（late gadolinium enhancement cardiac magnetic resonance，LGE-CMR）显示纤维化范围<10%，左心房储备期应变（left atrial reservoir strain，LASr）>23%。此类患者消融术后复发风险相对较低（通常<20%）。中度负荷：LAVI 34~40 mL/m^2，纤维化范围10%~20%，LASr显著降低至15%~23%。此组患者面临中等复发风险（20%~40%）。重度负荷：LAVI >40 mL/m^2，纤维化范围>20%，LASr严重受损（<15%）。此组患者复发风险最高（>50%）。

大型临床研究（如DECAAF研究）为该观点提供了有力证据，研究显示心房纤维化程度每提升1%，术后复发风险相应升高约6%[44]。因此，术前借助影像学技术（如心脏磁共振或超声心动图）精确评估ACM的病理负荷，对于筛选适宜消融的患者、预测复发风险以及制定个体化手术策略具有关键意义。

3 ACM导向的无创评估体系构建

3.1 超声心动图

LAVI≥34 mL/m^{2}已被共识指南确立为ACM的诊断阈值[43]，这一指标能够直接反映心房结构扩张程度，且与CMR测量的纤维化范围呈显著正相关。值得注意的是，LAVI每增加5 mL/m^2，卒中风险相应升高15%，更凸显其对于AF复发的预测价值。此外，左心房应变能够通过斑点追踪技术评估心房机械功能，其灵敏度优于传统结构参数[45]。尤为重要的是，应变异常常早于LAVI的显著变化，为早期识别亚临床ACM提供了时间窗[46]。

3.2 心脏磁共振成像

LGE-CMR技术是当前量化心房纤维化的金标准[47]。其价值不仅体现在纤维化范围的精确测量[18]，更在于识别特征性空间分布模式：融合型（左房后壁弥漫性强化）提示广泛基质病变，斑片型（局灶性强化）多与NPV触发灶相关，而心内膜下型则代表了电传导屏障的形成，其构成了折返性心律失常的发生基础。

3.3 体表心电信号解析

体表心电图检测P波弥散度>150 ms提示心房内传导延迟，其延长程度与LGE-CMR所显示的纤维化范围呈独立相关性[48]。滤过后P波电位分析借助增强微伏级信号检测，能够识别传统心电图难以察觉的传导异常[49]。

3.4 血清生物标志物与微小核糖核酸（microRNA，miRNA）谱

在血清标志物方面，可溶性生长刺激表达基因2蛋白（soluble suppression of tumorigenicity 2，sST2）水平高于35 ng/mL时，能够特异性地提示心肌纤维化处于活跃状态[50]，其在预测AF消融术后复发的效能上，显著优于传统标志物B型利钠肽[51]；半乳糖凝集素（galectin，Gal）-3水平高于17.8 ng/mL时，可通过促进成纤维细胞活化直接推动心脏结构重塑[52]，且与LAVI增大呈现同步变化趋势[53]；高敏C反应蛋白水平高于3 mg/L作为炎症激活的关键指标，其可通过介导内皮间质转化加速心房重构，经证实是ACM进展的独立预测因子。在表观遗传调控层面，miRNA谱能够揭示更深层次的病理机制[54]：miRNA-21表达上调可通过激活TGF-β信号通路促进纤维化[55]，其血清水平与心脏磁共振成像量化的纤维化程度呈剂量依赖性正相关；miRNA-29b表达下调会减弱对胶原合成的抑制作用，其降低速率与左心房应变恶化显著相关[56]。尤为关键的是，联合miRNA-21、miRNA-29b及miRNA-133a构建的整合诊断模型能够在分子水平实现ACM轻、中、重度的精准分型，为个体化干预提供靶向依据[57]。

4 转化医学与智能诊疗：ACM精准干预的新范式

4.1 ACM靶向干预现状与瓶颈

当前治疗手段难以精准靶向致心律失常性心肌病的核心病理环节。抗纤维化药物在临床转化方面成效欠佳：吡非尼酮虽具备抑制成纤维细胞增殖的作用，但缺乏心房组织特异性，在Ⅲ期临床试验（REVERSE-AF）中，心房纤维化逆转率仅达9%[58]。炎症调控策略也存在一定局限性，秋水仙碱虽可降低C反应蛋白水平，但未能显著改善心房机械功能[59]，这表明全身性抗炎治疗无法有效阻断心房局部炎症级联反应。此外，针对电重构的干预措施尚属空白，钙通道调控药物（如维拉帕米）可能加重心力衰竭[60]，且并无证据显示其可修复ACM相关的传导异质性。这些都提示，当前的靶向性治疗尚不足以阻断ACM的进展。

针对ACM特异性病理通路的创新疗法也是未来干预的核心方向。在免疫调控领域，靶向Gal-3的单克隆抗体[改性柑橘果胶（modified citrus pectin，MCP）]能够通过抑制炎症和心肌纤维化来改善心脏功能[61]；小分子拮抗剂Anakinra通过阻断IL-1受体通路，显著抑制巨噬细胞浸润，使心肌局部TNF-α水平下降[62]。表观遗传干预策略方面同样展现了巨大的潜力：基于CRISPR技术抑制自噬关键基因7表达，减轻了由快速起搏引起的AF易感性[63]。

4.2 人工智能驱动的心房纤维化精准评估与个体化诊疗

人工智能技术为解决心房纤维化评估缺乏统一标准的临床瓶颈提供了全新思路与技术路径。深度学习算法可显著提升心房结构与电生理参数分析的准确性及可重复性：基于神经网络构建的人工智能超声自动应变分析系统[64]，能够实现左心房心肌力学指标的自动化、标准化测量，将测量变异度由15%降至5%[65]，并可与心脏磁共振纤维化成像实现空间配准与联合解读。多模态数据融合模型进一步优化了消融术后复发风险评估效能，多维度心房纤维化风险人工智能预测模型通过整合LAVI、心房复杂碎裂电位及miRNA-21等多组学指标，使其对AF消融术后复发的预测效能较单一指标提升22%[66]。在治疗监测方面，基于人工智能的动态分析平台可实时整合生物标志物演变趋势（如sST2下降速率）与影像学功能改善程度（如左心房应变变化），实现抗纤维化治疗的精准化、个体化调整，为ACM的全程管理提供客观、量化的决策支持。

5 小结与展望

当前证据确证ACM是AF导管消融术后复发的核心病理基础，其结构性重塑（弥漫性纤维化、脂肪浸润及淀粉样沉积）与电生理重构（钙信号失调、缝隙连接蛋白侧化位移及自主神经失衡）协同形成持续性致心律失常基础，并通过激活NPV触发灶导致术后复发率显著升高。面对这一困境，文章论证了建立多模态无创评估体系（超声LAVI/应变、LGE-CMR纤

维化定量、血清sST2/Gal-3及miRNA谱）结合人工智能整合模型可精准分层ACM负荷并预测复发风险的必要性，该体系突破传统预测模型的局限性，以临床为导向，构建多维度预测模型，提高术后复发预测的准确性。然而临床转化仍面临双重瓶颈：评估标准化缺失（如左房应变测量变异度高达15%）与靶向治疗不足（全身抗纤维化药物心房逆转率仅9%）。

这一转化困境深刻反映了ACM在临床认知与管理体系上的历史局限。以2016年专家共识为代表的纯病理形态学分型[43]，虽极具基础研究价值，但因依赖有创活检且难以关联临床进程，适用性受限。2024年更新的共识提出了重要的范式转变，构建了基于临床表现、生物标志物与影像特征的轻、中、重3级临床分型[1]，旨在提升临床操作性。然而，这一更优分型体系的真正落地，恰恰有赖于克服上述瓶颈——它迫切需要标准化的评估工具为其提供客观、可重复的分型依据，并需要有效的干预手段以实现分型指导下的精准治疗。

为突破现状，未来必须构建一个连贯的转化路径。首先需要在技术层面推动标准化，并利用人工智能算法减少变异。在此基础上，应积极通过多中心临床试验验证新型评估模型。最终，需推动这些成果向临床实施转化，通过贯通从“技术标准化”、“证据生成”到“临床实施”的完整链条，最终构建起从“精准评估”到“靶向干预”的ACM全程管理路径，从根本上提升AF治疗的远期疗效。

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