

· 心房颤动专题研究 ·

机器学习在心房颤动筛查和管理中的应用进展



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【摘要】 心房颤动是一种常见的心律失常类型, 随着年龄增长其发病率不断升高, 且其不规则的心脏节律会引起急性脑卒中等严重并发症。但心房颤动发作时多无明显症状, 患者常在发生栓塞事件后才会被首次确诊。近年来随着人工智能技术不断发展, 机器学习可以帮助临床医生识别心房颤动高危人群。本文主要综述了机器学习在心房颤动筛查和管理中的应用进展, 旨在提高临床医生对机器学习的认识。

【关键词】 心房颤动; 人工智能; 机器学习; 筛查; 疾病管理

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Application Progress of Machine Learning in Screening and Management of Atrial Fibrillation HUANG Yan¹, DENG Qi¹, CAO Liping¹, FAN Yongmei², XIAO Chunxia³

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【Abstract】 Atrial fibrillation is a common type of arrhythmia. Its incidence increases with age, and its irregular heart rhythm can cause serious complications such as acute stroke. However, there are no obvious symptoms when atrial fibrillation attacks, and patients are often diagnosed for the first time after embolization events. In recent years, with the development of artificial intelligence technology, machine learning can help clinicians identify people with high risk of atrial fibrillation. This article reviews the application progress of machine learning in screening and management of atrial fibrillation, in order to improve clinicians' understanding of machine learning.

【Key words】 Atrial fibrillation; Artificial intelligence; Machine learning; Screenin; Disease management

心房颤动 (atrial fibrillation, AF) 是临床最常见的心律失常类型, 其不规则的心脏节律可引起急性脑卒中等严重并发症。据估计, 在美国有近60万的AF未确诊, 医疗费用负担

约31亿美元, 且超过一半的患者存在卒中中高风险^[1]; 我国≥35岁居民AF患病率为0.7%, 其中新发AF约占34.0%^[2]。早期诊断并对有血栓栓塞危险因素的患者进行抗凝治疗可有效降低其急性卒中中发生风险。因此, 《2016欧洲心脏病学会心房颤动管理指南》建议, 年龄>65岁的患者均需要机会性筛查AF^[3]。尽管如此, 仍有许多患者在血栓栓塞事件发生后才被诊断为AF^[4-5]。

人工智能 (artificial intelligence, AI) 提出至今已有60多年历史^[6], 且过去10年其开始有了迅速发展。机器学习 (machine learning, ML) 是AI的一种方法, 近年随着AI进入医疗领域, ML在帮助医疗人员优化个性化治疗方案方面取得明显进展。研究表明, ML可以帮助临床医生识别AF高危人群, 进而减少血栓栓塞事件发生风险并改善患者预后^[7]。本文主要综述了ML在AF筛查和管理中的应用进展, 旨在提高临

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床医生对ML的认识。

1 ML方法

AI指通过计算机等技术独立处理数据并得出结论的能力,通常这些能力需要人类的认知功能^[8],且输入数据时要求机器可读,最好是高度结构化的形式。传统的AI方法(如监督ML)已经使用几十年,包括随机森林和支持向量机等算法。监督ML需要表格数据来检测参数的模式(如年龄、校正QT时间或心率变异性等),可以检测数据的线性和非线性关系,但其需要依赖人工操作员标记数据和选择输入变量。相反,无监督ML指在没有标记数据的情况下,基于数据样本间的相似性将其聚类为具有相似性的组。成功训练ML模型后,执行这些模型所需的计算能力就会明显降低。因此,既往经过培训和测试的ML模型可以集成到可穿戴技术和智能手机中。

深度学习(deep learning, DL)是利用神经网络独立识别输入数据的特征,从而检测未知的模式。神经网络是模仿生物神经系统(如人脑)的计算结构,其最基本的形式是将输入数据直接连接到输出层。更复杂的系统,如深度神经网络(deep neural network, DNN)包含多个层次,这些层次可以执行不同的任务,其连接强度由可训练和可调节的权值决定,而不是相邻层的节点均可以连接^[9]。根据输入数据,经过调整的网络结构显示出巨大的预测潜力,如用于图像、心电图或时间序列的卷积神经网络,这种特殊类型的神经网络是使用过滤器识别图像边缘或曲线等数据,并将其组合成特征图。

2 ML在AF筛查中的应用进展

2.1 基于智能手机的心电图设备在AF筛查中的应用 目前,心电图机自动诊断系统已在临床应用数十年,近年随着AI技术的不断发展,基于智能手机的心电图设备已被多家公司开发^[10],其中AliveCor Kardia公司开发的AF算法被多次进行科学研究,并证实其实诊断AF的特异性较高^[11-13]。YAN等^[14]研究证实,由TomTom Runner Cardio应用程序支持的智能手机可利用内置摄像头获得光容积描记测量值,结果显示,34.6%(75/217)的患者12导联心电图显示存在AF,阳性预测值、阴性预测值分别为92%〔95%CI(84%, 96%)〕、97%〔95%CI(93%, 99%)〕,预测价值较高。CHEN等^[15]研究表明,心电图和光电容积脉搏波描记法(photoplethysmography, PPG)预测AF的正确率分别为94.7%、93.2%,而二者联合预测AF的正确率更高,为97.5%。WASSERLAUF等^[16]比较了苹果手表和可插入循环记录器评估非卧床人群AF发作及持续时间的敏感性,共分析了24例患者的31 348.0 h的记录数据,结果表明,与可插入循环记录器相比,苹果手表对非卧床人群AF发作和持续时间的评估敏感度高。

目前,仅有两项基于AI技术进行AF筛查的大规模前瞻性研究,一项是“苹果心脏研究(The Apple Heart Study)”,该研究纳入的是居住在美国并使用苹果智能手表的419 000例参与者,其是利用光容积脉搏波传感器监测参与者心律,如果手表记录为可能的AF,则通过邮寄心电图贴片的形式进行

7 d的心电图筛查,结果显示,2 161例(0.52%)可能为AF的参与者中,450例(21%)参与者返回了心电图贴片,其中又有34%的参与者存在AF^[17]。另外一项是“华为心脏研究”,共纳入近19万名中国参与者,其是基于华为智能手表的光容积描记算法监测参与者心律,结果显示,424名(0.23%)受试者收到了疑似AF的信息,其中262名(62%)受试者接受了12导联或动态心电图随访,227名(87%)受试者确诊为AF^[18]。上述研究表明,基于人群的大型AI技术筛查项目具有可以接受的阳性预测值,但也存在大量参与者无法有效随访的局限,且由于研究设计本身原因无法报告假阴性率。

2.2 DNN在AF筛查中的应用 既往研究表明,与传统ML方法相比,DNN筛查AF的灵敏度和特异度均明显升高^[16, 19]。HANNUN等^[20]研究结果显示,DNN的平均F分数(即阳性预测值和灵敏度的调和平均值)为0.837,高于心脏病专家的平均F分数(0.780),表明DNN在单导联心电图可以对心律失常进行分类。RAMESH等^[21]研究报道了另外一种DNN,其在心电图检测AF的灵敏度为94.5%、特异度为96.0%、正确率为95.5%,其在光容积描记记录中检测AF的灵敏度为94.6%、特异度为95.2%、正确率为95.1%。此外,还有研究利用DNN估计高危人群(如慢性肾脏病^[22]或有缺血性卒中史的患者^[23])AF发生风险。ATTIA等^[24]在180 000例患者近650 000份心电图上测验DNN,结果显示,DNN检测AF的灵敏度为79.0%、特异度为79.5%;如果同时分析1例患者的多份心电图,DNN检测AF的灵敏度、特异度分别为82.3%、83.4%。

3 ML在AF患者管理中的应用进展

研究表明,与传统Holter监护仪相比,手持式心脏设备诊断导管消融术后AF复发的价值较高(灵敏度为100%,特异度为97%)^[25],且DNN能够通过分析12导联心电图估计Ⅲ类抗心律失常药物的血浆浓度^[26]。有研究者开发了诊断正确率高于既往风险评估和传统线性或逻辑算法的DNN,并用于评估导管消融^[27]或胸腔镜消融治疗^[28]后患者AF复发风险。在导管消融程序方面,有研究探索了用于消融过程中识别AF触发源的DNN^[29-30]。LI等^[31]评估了一种能检测与快速心室率和低体力活动相关的AF发作的算法,并证实该算法能够在AF发病前4.5 min内检测到AF发作,这有利于指导临床医生早期实施干预措施。

研究表明,DNN有利于AF相关卒中患者全因死亡风险^[32]和神经系统^[33]的评估。一项基于神经网络的变分自动编码器和分层聚类分析9项评估 β -受体阻滞剂治疗心力衰竭效果的双盲、随机、安慰剂对照试验结果显示,基于神经网络的变分自动编码器和分层聚类能区分心力衰竭和低左心室射血分数(left ventricular ejection fraction, LVEF)患者的预后和 β -受体阻滞剂的治疗效果^[34]。此外,DNN还对卒中风险进行分层和细化口服抗凝药物的治疗决策。LIP等^[35]基于3 000多例AF患者(包括71例卒中患者)的植入心脏设备数据,开发了三种不同的AF特征监督ML模型(随机森林、CNN和L1正则化逻辑回归),结果显示,随机森林预测卒中风险的AUC为0.66、CNN为0.60、L1正则化逻辑回归为0.56。目前,临床应用最广泛的卒中风险预测模型是CHA₂DS₂-VASc评

分量表,其预测卒中风险的AUC为0.52,其与随机森林、CNN联合预测卒中风险的AUC为0.63^[35-36],表明CHA₂DS₂-VASc评分量表与传统风险评估工具联合可以提高卒中风险的预测效能。而结合临床病史、影像学检查和生物标志物等其他信息可以进一步完善疾病风险分层。ORBIT-AF注册研究对约10 000例AF患者进行无监督聚类分析,包括患者的特异性临床数据、药物、实验室检查指标、心电图和影像学检查数据,共确定了四种AF临床相关表型,且每种表型均与临床结果相关^[37]。

4 存在的问题

目前,包括传统ML在内的移动卫生设备和可穿戴技术正在用于临床实践。但由于多数检测AF的算法依赖绝对不规则的R-R间期,故极有可能导致心房扑动的漏诊。与AF相比,心房扑动症状通常是因心室快速反应所致,故更有可能通过传统方法进行诊断。心房颤动和心房扑动具有相似的血栓栓塞发生风险,且自动算法对其诊断效能不足,进而削弱了人们使用自动算法的信心。为此,有研究者训练DNN,以正确鉴别AF和三尖瓣峡部依赖性心房扑动^[38]。

此外,DNN在临床实践中存在的主要问题是透明,即该算法可以为医生提供信息,但如何解释这些信息尚不清楚。TISON等^[39]结合不同ML方法创建了个性化的心电图矢量轮廓,其能够估计左心室质量和e速度等,同时标注重要的心电图部分,以协助临床医生做出更准确的判断。MOUSAVI等^[40]研究表明,DNN能根据心电图中心电图中相关区域来区分AF和窦性心律。但与缺乏透明度且更复杂的ML方法相比^[41],易于解释的DNN仅提供了较少的临床益处。

一项大型研究评估了循环记录仪筛查AF的效果,结果显示,AF的检出率增加了3倍,但其对血栓栓塞事件的预防无明显作用^[42]。通过光电容积描记法(photo plethysmography, PPG)连续监测节律或基于DNN自动风险评估发现的AF患者可能比通过传统方法诊断的AF患者的血栓栓塞发生风险更低^[15],这可能需要重新评估AF患者的抗凝治疗策略。

5 小结及展望

虽然ML和人工神经网络已用于临床实践,但尚缺乏大型前瞻性研究来评估这些技术对临床终点事件(如血栓栓塞事件或死亡率)的影响。目前,DNN的另外一个具体应用可能是优化卫生系统的工作环境和评估初级保健水平^[43]。虽然传统的超声心动图和磁共振图像是由人工获取和解释的,但最近研究表明,AI引导的图像获取^[44]和自动解释^[45]具有可行性,且可以极大地提高检查速度^[46]。未来AI有可能改变整个医疗实践,尤其是AF患者的筛查和管理。但目前,AI还存在神经网络不透明及缺乏临床实践等问题,仍需在未来研究中进一步解决。

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