

阿尔茨海默病连续疾病谱影像组学研究进展

刘聪聪¹, 宋莉^{2*}, 梁圆³, 韩志远¹, 盛灿²

¹济宁医学院临床医学院(附属医院), 山东 济宁

²济宁医学院附属医院神经内科, 山东 济宁

³黄河水利委员会黄河中心医院, 河南 郑州

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摘要

阿尔茨海默病(Alzheimer's disease, AD)是全球老龄化社会中的主要健康挑战之一, 伴随着认知功能的逐渐丧失, 严重影响患者的生活质量和社会功能。AD的发病机制复杂, 涉及多个病理阶段, 包括临床前期、轻度认知功能障碍(mild cognitive impairment, MCI)期以及AD痴呆阶段。早期识别AD, 尤其是MCI阶段, 对于疾病干预至关重要。近年来, 影像组学作为一种新兴的医学图像分析技术, 得到了广泛的应用与研究。通过对大量医学影像数据进行定量分析, 影像组学能够提取出细致的疾病影像特征, 提供潜在的生物标志物, 从而在AD的早期诊断、病情评估和预后预测等方面具有巨大的潜力。本文就阿尔茨海默病连续疾病谱影像组学研究进行综述。

关键词

阿尔茨海默病, 神经影像学, 影像组学, 磁共振成像, 氟脱氧葡萄糖正电子发射断层显像

Research Progress of Radiomics in the Continuous Disease Spectrum of Alzheimer's Disease

Congcong Liu¹, Li Song^{2*}, Yuan Liang³, Zhiyuan Han¹, Can Sheng²

¹Clinical Medical College (Affiliated Hospital), Jining Medical University, Jining Shandong

²Department of Neurology, Affiliated Hospital of Jining Medical University, Jining Shandong

³Yellow River Central Hospital of the Yellow River Conservancy Commission, Zhengzhou Henan

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*通讯作者。

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Abstract

Alzheimer's disease (AD) is one of the major health challenges in the global aging society. Accompanied by the gradual loss of cognitive function, it seriously impairs patients' quality of life and social functioning. The pathogenesis of AD is complex, involving multiple pathological stages, including the preclinical stage, mild cognitive impairment (MCI) stage, and AD dementia stage. Early identification of AD, especially in the MCI stage, is crucial for disease intervention. In recent years, radiomics, as an emerging medical image analysis technology, has been widely applied and studied. By quantitatively analyzing large amounts of medical imaging data, radiomics can extract detailed disease imaging features and provide potential biomarkers, thus holding great potential in the early diagnosis, disease assessment, and prognosis prediction of AD. This article provides a review of the research on the continuum of Alzheimer's disease within the framework of radiomics.

Keywords

Alzheimer's Disease, Neuroimaging, Radiomics, Magnetic Resonance Imaging, Fluorodeoxyglucose Positron Emission Tomography

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1. 引言

阿尔茨海默病(Alzheimer's disease, AD)是老龄化社会面临的主要挑战之一,它导致认知功能逐渐下降,进而引起独立生活、工作和参与社会的能力下降甚至丧失[1]。研究表明,AD是一个连续的病理生理学过程,包括AD临床前期、轻度认知功能障碍(mild cognitive impairment, MCI)期和AD痴呆阶段[2],MCI与临床前AD被认为是认知障碍的早期阶段,并且进展为AD的风险很高[3]。因此,要重视AD的早期诊治,尽早识别MCI。但因阿尔茨海默病的多因素病因和临床表现,使其成为早期诊断最具挑战性的神经退行性疾病之一[4]。使用磁共振成像,如结构MRI (structural MRI, sMRI)、功能MRI (functional MRI, fMRI)或正电子发射计算机断层显像(positron emission tomography, PET)进行神经影像学检查已成为诊断神经退行性疾病的标准工具,并显示出预后潜力[5]。

美国国家老龄化研究所-阿尔茨海默氏症协会的指南表明,MR成像是AD和MCI患者诊断检查中的支持性成像工具,在AD的诊断中起着重要作用[6] [7]。然而临床医师在MRI阅片中识别小病灶的能力有限,且带有一定主观性,可能无法准确判断疾病早期分期。因此2012年Lambin首次提出放射组学这一新兴的医学图像分析方法[8],基于大量的影像数据可以建立更为精确的统计模型,挖掘更多潜在的规律和信息。近年来,使用放射组学及人工智能来诊断及鉴别AD取得了迅速进展。利用海量的医学影像数据,影像组学可以从中提取大量定量的疾病影像特征,在疾病诊断、疗效评估和预后预测等方面具有极大的潜力[9]。有研究表明,在认知能力下降的前期,一些特定大脑区域的体积和形态指标会发生变化,包括海马、海马旁回、颞上回等区域[10]。而最近的纹理分析研究表明,海马体等结构的磁共振成像纹理比海马体积可以更早预测阿尔茨海默病的痴呆进展,并且它们预测从MCI过渡到痴呆的准确性要优于体积减少的准确性[11] [12]。此外,Leandrou等[13]也证实与内嗅皮层体积相比,内嗅皮层纹理特征能更好地预测AD的进展。由此可见基于医学影像特征进行分析研究,某些纹理特征能够准确反映病变组

织的病理学信息,为 MCI 的诊断及预测提供了重要的影像学生物标志物。本文将重点探讨影像组学在 AD 连续疾病谱中的应用,分析不同影像学数据结合影像组学在 AD 早期诊断和进展预测中的作用。

2. 诊断

2.1. sMRI 影像组学与早期诊断

MRI 作为一种无创、无辐射、并广泛应用的影像学检查方法,可为 AD 临床诊断提供重要的支持证据[6]。有研究使用不同类型的交叉验证和机器学习技术,证明影像组学特征是 AD 稳健、可重复和可推广的成像特征[14]。Ding 等[15]基于 T1WI 提取海马影像组学特征开发了诊断模型,结果发现该模型在区分轻度认知障碍与痴呆方面表现出优异的性能。有研究利用区域放射组学相似性网络来识别 MCI 的亚型,为 MCI 患者的风险评估和精准早期干预提供了新的见解[16]。之前关于多参数磁共振成像的研究发现 MCI 及 AD 患者的额叶,尤其是额叶-皮质下回路和大脑白质的完整性已经受损[17][18],因此有研究从 3D-T1WI 图像中提取额叶白质的细微变化构建影像组学模型以区分 MCI 患者及正常人群,决策曲线分析证明该模型具有良好的临床预测价值[19]。

2.2. fMRI 影像组学与早期诊断

静息态功能磁共振成像(fMRI)作为一种先进的非侵入性神经影像学技术,是了解 aMCI 和早期 AD 神经退行性病程的重要影像学方式[20],已被广泛应用于检测脑部疾病的功能异常[21]。因此有研究将海马体在慢 5 频段的低频波动幅度纹理特征与结构 MRI 图像相结合,使用放射组学分析研究其对 AD 和 MCI 的鉴别性能,以此用来比较能否提高传统海马结构模型的诊断效能,结果发现,基于结构图像和低频波动幅度纹理特征组合的放射组学模型能更好的区分 AD 及 MCI,有助于 AD 的早期诊断[22]。

2.3. 多模态影像组学与早期诊断

主观认知能力下降(Subjective cognitive decline, SCD)被认为是阿尔茨海默病进展中的高危临床前阶段。有研究利用结构 MRI、功能 MRI 及扩散张量成像三种不同参数的磁共振提取放射组学特征,使用支持向量机构建 SCD 分类模型,结果表明,基于多参数磁共振成像的影像组学可以有效区分 SCD 与健康对照[23]。同样有研究结合多参数 ^{18}F -FDG PET/MRI 的海马放射组学探索其在早期阿尔茨海默病的诊断效用,发现多模态分类器有助于识别早期 AD,为临床提供潜在的生物标志物[24]。

3. 预测

3.1. 临床进展预测

由于 AD 存在较长的临床前阶段,且早期诊断困难,因此准确预测 AD 早期进展对疾病干预至关重要。有研究发现基于全脑影像组学的综合模型可以准确识别和预测可能进展为 AD 的 MCI 患者的高危人群[25]。为全面研究大脑结构变化,获得灵敏准确的神经变性生物标志物,Song 等[26]通过一项为期五年的随访研究建立了包含整个大脑皮层和深部核综合信息的放射组学模型,改进了阿尔茨海默病 ATN 分类方案来预测 MCI 患者的认知进展。有研究发现脑白质 PET 放射组学可作为 AD 的一种生物标志物,可以预测轻度认知障碍向阿尔茨海默病的进展[27]。Ding 等[28]也利用 $\text{A}\beta$ PET 图像提取放射组学用作 AD 神经影像学标志物及评估 MCI 患者的进展,分析表明, $\text{A}\beta$ PET 图像的放射组学特征可以作为临床应用的新的生物标志物,并为进一步预测 MCI 患者的进展提供了证据。近年来,有研究发现小脑损伤与学习障碍、注意力缺陷及记忆障碍等认知功能障碍有关[29],放射组学为研究小脑在认知障碍中的作用提供了一种新的工具。因此有研究通过构建小脑来源的放射组学和结构连接组模型来预测 AD 进展,结果发现小

脑模型在早期识别和预测 AD 临床前阶段进展方面优于海马模型[30]。而另一项回顾性多中心研究同样发现小脑 MRI 影像组学模型在识别认知障碍和 MCI 方面表现出与海马模型相当的诊断准确性[31]。另外,有研究发现,使用影像组学-临床-实验室模型和多预测因子列线图可以准确地预测从 MCI 到 AD 的个体进展时间[32]。同样,为准确预测 AD 的进展, Lin 等[33]基于 T1WI 构建了一种临床-放射学综合模型,以预测临床前 AD 的进展时间和疾病风险分层。Zhou 等[34]发现放射组学分析和 Cox 模型分析相结合可以有效地用于生存数据分析,显著提高了 MCI 转换为 AD 的预测准确性。

3.2. 淀粉样蛋白病理预测

淀粉样斑块作为阿尔茨海默病的特征,是 AD 最重要的神经病理学标志之一[35],有研究发现基于正电子发射断层扫描(PET)图像区分 AD 和正常对照的分类分析性能已达到约 80%~90%的准确率[36]。因此有研究使用放射组学方法从 FDG-PET 图像中无创地预测淀粉样蛋白阳性,结果显示,其所提出的方法具有更高的精度[37]。同样有研究[38]利用影像组学方法开发了 MCI 患者淀粉样蛋白阳性的预测模型,并与皮质厚度和非成像预测因子相结合,显著提高了其预测性能。有研究结合临床谱系,探讨 MCI 海马体放射组学对脑脊液 A β 42 状态的预测,其开发了基于放射组模型、基于临床特征的临床模型以及基于放射学和临床特征的综合模型,结果表明,综合模型在预测脑脊液淀粉样蛋白阳性方面表现最好, AUC 为 0.823 [39]。

4. 结论与展望

目前 AD 影像组学研究最可靠的核心发现集中在以下两方面:一是海马亚区纹理特征在 MCI 向 AD 转化预测中的优势。海马作为阿尔茨海默病病理进程中的关键脑区,其亚区的纹理特征在疾病预测领域展现出独特价值。相较于传统基于形态学的海马体积测量方法,纹理分析能够捕捉到海马微观结构的细微改变。并且在多中心临床队列研究中,这些纹理特征的预测效能得到充分验证。二是多模态影像组学提升临床前 AD 预测与诊断效能。阿尔茨海默病病理机制复杂,随着 AD 研究的深入,单一模态影像难以全面解析其病理机制。多模态影像技术通过整合 sMRI、fMRI、以及 PET 等不同影像技术的优势,从多角度构建更全面的 AD 信息图谱,不仅提升临床前 AD 的诊断灵敏度,而且通过 ATN 生物标志物框架优化了 AD 亚型分型精度。

随着影像组学技术的不断发展,未来其在阿尔茨海默病的临床应用将呈现出更加广泛的前景。首先,多模态影像数据的联合应用将成为趋势,结合不同影像技术的优势,以提高对疾病的早期诊断和预后评估能力。其次,随着人工智能算法的不断进步,将进一步提高影像组学特征提取、分析和预测的效率和准确性,实现对 AD 的早期筛查和精准诊断。最后,随着大数据的积累和数据库的完善,影像组学的个体化应用将成为一个新的研究方向。目前,影像组学主要集中在 MCI 到 AD 的转化预测,但未来可能会扩展到更多的亚型识别、AD 早期认知功能损伤的检测以及治疗效果的长期评估。

尽管影像组学在阿尔茨海默病的诊断与研究中取得了显著进展,但仍面临一些挑战和不足。首先,目前影像组学的研究样本量普遍较小,且大多数研究集中于单中心数据。未来需要进行多中心、大规模的研究,以验证影像组学特征的可靠性和稳定性。其次,虽然影像组学能够提取出大量的定量特征,但如何将这些特征与临床病理数据有效结合,形成可靠的预测模型仍是一个挑战。此外,影像组学技术也面临着标准化问题。不同医院和设备之间的成像标准差异可能导致影像数据的不一致性,从而影响研究结果的准确性。如何实现影像数据的标准化,确保影像组学的可重复性和可靠性,是未来研究的重要方向。尽管现阶段的影像组学研究仍然面临着样本量、标准化等问题,但仍为阿尔茨海默病的早期诊断和病情评估提供了新的方向。

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