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医学人工智能

人工智能在胰腺疾病新型诊疗模式中的应用及进展

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【摘要】基于临床资料、医学影像学、基因组学的计算机诊疗辅助系统在鉴别胰腺囊性疾病、诊断胰腺癌等方面显现出优于传统诊疗方法的潜力。本文综述人工智能在胰腺各类疾病的诊断、预后、预测治疗反应和指导治疗方面的作用,并为胰腺疾病精准医疗、改良目前的临床诊疗模式提供新的思路及方法。

【关键词】人工智能;机器学习;深度学习;胰腺疾病;胰腺炎;胰腺癌;精准医疗
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Application of artificial intelligence in new diagnostic and therapeutic pattern of pancreatic diseases and its advances

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Abstract: The computer-aided diagnosis and treatment system which is based on clinical data, medical imaging and genomics shows the potential to be superior to traditional diagnosis and treatment methods in identifying pancreatic cystic diseases and diagnosing pancreatic cancer. Herein the role of artificial intelligence in the diagnosis, prognosis, prediction of treatment response, and guidance for treatment of various pancreatic diseases are summarized, and some new ideas and methods are put forward for precision medicine for pancreatic diseases and improvement of the current clinical diagnostic and therapeutic pattern.

Keywords: artificial intelligence; machine learning; deep learning; pancreatic disease; pancreatitis; pancreatic cancer; precision medicine

前 言

胰腺是由外分泌组织与内分泌组织共同组成的器官,在消化与代谢中起到重要作用[1]。胰腺疾病主要包括胰腺炎症、胰腺恶性肿瘤以及胰腺囊性疾病等。急性胰腺炎(Acute Pancreatitis, AP)是最常见的急腹症之一,其病情变化多样,程度轻重不等,重症患者会出现各类并发症,甚至导致休克、死亡[2]。慢性胰腺炎症(Chronic Pancreatitis, CP)由于纤维化改变导致胰腺内外分泌功能紊乱,目前仍以对症治疗为主[1]。胰腺占位主要包括胰腺良性和交界性或低度恶性肿瘤[2-3],高度恶性的肿瘤则以胰腺导管上皮癌(Pancreatic Ductal Adenocarcinoma, PDAC)为主[4]。良性肿瘤及部分交界性肿瘤可以长期随访观察,恶性肿瘤与分化差的肿瘤则需要进一步治疗,术前合并症、肿瘤分型及是否R0切除、术后并发症对于患者的预后有重要影响[5-6]。

人工智能(Artificial Intelligence, AI)是一种通过建立数学模型对数据进行分析并解决实际问题的方法,可以自动学习并识别数据,主要应用于探究各类因素间的复杂非线性关系。医学问题正是多种因素相互影响的复杂问题,因此AI在分析医学问题方面大有前景[7-8]。AI主要通过机器学习(Machine Learning, ML)中的传统统计方法与深度学习(Deep Learning, DL)方法解决医疗领域的难题。ML是指系统通过输入数据而不涉及形成问题进行学习,医学方面常用的传统统计方法模型有:支持向量机

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(Support Vector Machines, SVM)、随机森林(Random Forests, RF)、Logistic回归、人工神经网络(Artificial Neural Network, ANN)等以最大似然法为基础的模型;DL则是利用模型、分析数据获得更高级别的特征,并根据特征分析得出结果,能够对数据中非常复杂的关系进行建模,最常用的DL方法是卷积神经网络(Convolutional Neural Networks, CNN)、生成对抗模型(Generative Adversarial Network, GAN)等[9-11]。虽然AI在胰腺疾病诊疗方面处于起步阶段,但已展现出在诊断、治疗、疾病预后等方面的广阔前景,并为精准医学发展、个体化治疗提供一条明确、可行的道路。本文将通过描述AI在胰腺疾病诊疗中的应用进展,为建立新型诊疗模式提供新思路。

1 AI与胰腺炎症

1.1 AI与AP

AP是一种常见的消化系统疾病,是由胆石症、高甘油三酯血症和饮酒等多种病因引发胰腺腺泡细胞内胰蛋白酶的过早激活,导致胰腺及周围组织自我消化,出现胰腺局部水肿、出血甚至坏死的炎症反应[12]。临床工作中关于AP的严重程度及病情转归预测包括Ranson评分、Glasgow评分、APACHEII评分等,但是这些评分系统的一个显著问题是它们会随着临床信息的变化而出现误差[13]。C反应蛋白、血尿淀粉酶、脂肪酶以及血细胞比容、尿液中胰蛋白酶原激活肽等标志物对于AP虽然有预测作用[14-15],但是与现有评分标准联系并不紧密。由于ANN以非线性方式工作,可以更好地利用现有数据描述风险因素之间的相互作用,因此它们是传统评分系统的良好的替代方案[16]。Pearce[13]使用ML模型同时纳入APACHEII评分系统数据与C反应蛋白数据,用于AP严重程度及病程预测。Andersson[17]首次纳入"到达急诊科前的疼痛持续时间"这一特征参数以及AP病人入院时基线资料建立ANN模型预测转归为重症的可能性,两者均证明与AI相结合预测模型效能优于传统评分。

1.2 AI与重症急性胰腺炎(Severe Acute Pancreatitis, SAP)

20%~25%的AP患者会进展为SAP。在SAP进展过程中,腹腔感染起着重要作用,而且也是决定患者预后的重要因素之一[18-20]。临床实践中AP患者是否并发腹腔感染常根据白细胞计数、中性粒细胞百分比和C反应蛋白等实验室检查判断,但是后者在SAP患者中普遍升高,很难将其用作确定是否存在腹腔内感染的指标[21]。Qiu等[22]通过分析炎症和凝血参数并使用Logistic回归模型(Logistic Regression Model, LRM)和ANN模型构建预测早期腹腔内感染的可靠且实用的模型,及时预测AP的严重程度与进展为SAP的可能。

约20%的SAP患者会出现器官功能衰竭(Organ Failure, OF),并且有30%的OF患者死亡,但是在OF发生之前,很难预测SAP的最终临床结局[23]。Xu等[24]通过收集多中心数据并使用6种不同ML模型对数据进行重复验证,不同模型之间进行内部验证并建立预测性能良好的多器官功能衰竭(Multiple Organ Failure, MOF)预测模型。

SAP同样会导致多种并发症,这些并发症大多会导致严重后果,因此预测并发症的发生也是AI与临床实践结合的重点[25]。门静脉血栓形成(Portal Vein Thrombosis, PVT)是AP的血管并发症之一,PVT可以累及所有门脉分支[26],并产生局限性门静脉高压,导致胃或食管静脉曲张出血。它还可能导致患者肝衰竭、腹水、住院时间延长、死亡率升高[27]。Fei[28-29]分别通过径向基函数(Radical Basis Function, RBF)模型与反向传播(Back Propagation, BP)模型预测PVT,并证明两者效能均优于传统Logistic回归分析。SAP患者在入院早期死亡率的预测一直未进行深入研究,应用单因素及多因素Logistic回归分析及ANN模型结合后构建仅有4个危险因素的AP早期死亡率的预测模型,其预测效能不劣于具有14个危险因素的APACHEII评分[30]。Keogan等[31]通过CT图像特征、临床数据及实验室检查训练新的ANN模型预测AP患者严重程度,该模型在预测受试者是否会超过平均住院时间方面优于传统评分系统。AI与临床数据相结合会提升关于AP患者疾病严重程度、并发症发生率和死亡率的预测效率,然而一些研究显示出相互矛盾的结果,并且大多数算法仅与现有评分系统或模型之间进行效能对比,而没有在外部数据集上得到验证,因此,建立具有外部验证数据集的新型AI模型是进一步研究的重点[13, 17, 32-33]。

1.3 AI与自身免疫性胰腺炎(Autoimmune Pancreatitis, AIP)

AIP是一种自身免疫性疾病,以淋巴细胞浸润与纤维化为主,临床表现上会出现无痛性黄疸,影像学上也会出现"血管侵犯"的表现[34-35],通过血清学以及影像学仅能鉴别出70%的AIP患者,仅在57.7%的AIP患者可以通过超声内镜引导下的细针穿刺活检(Endoscopic Ultrasonography-Fine Needle Aspiration, EUS-FNA)明确诊断。如何诊断AIP并与PDAC等恶性疾病相鉴别一直是临床实践的重点及难点[36]。现代CNN通过使用AIP、PDAC、正常胰腺、CP的EUS图像进行分析并辅助鉴别诊断,不仅防止PDAC

的漏诊与误诊，而且及时指导医师应用免疫抑制剂或激素治疗阻止AIP进展为CP[37]。

1.4 AI与复发性急性胰腺炎（Recurrent Acute Pancreatitis, RAP）

RAP是指AP两次或两次以上发作，发作之间疾病接近或完全缓解。17%~22%诊断为AP的患者将来会复发，高达36%的RAP患者最终会进展为CP[38-40]。目前的干预措施并未证明能有效减少复发，因此准确预测RAP的发病并将其与其他腹部疾病进行鉴别，避免其进展为CP尤为重要[41-43]。通过将CT影像特征纳入等距特征映射方法（ISOMAP）SVM训练，成功将功能性腹痛、RAP与CP三者鉴别[32]。Chen等[44]选择将AP患者影像组学中的特征像素按照7∶3随机分配到训练集及验证集中，使用Logistic回归分析及SVM预测AP的复发率及相关的危险因素。AI适用于解决胰腺炎症中各种非线性的复杂问题，不仅提高了原先诊疗模式下的准确度，降低误诊率，同时也为胰腺炎症新型诊疗模式的建立提供新思路。

2 AI与胰腺肿瘤

2.1 AI与胰腺囊性肿瘤（Pancreatic Cystic Neoplasms, PCN）

PCN主要包括导管内乳头状黏液瘤（Intraductal Papillary Mucinous Neoplasm, IPMN）、浆液性囊腺瘤（Serous Cystic Neoplasm, SCN）和黏液性囊腺瘤（Mucinous Cystic Neoplasm, MCN）、实性假乳头肿瘤（Solid Papillary Neoplasm, SPN）4类[2]，IPMN、SPN、MCN是胰腺恶性肿瘤的癌前病变[45]，其中以侵犯主胰管的IPMN恶变率最高，达70%[46]，因此Kuwahara[47]将已确诊IPMN患者的EUS图像输入CNN进行训练，预测模型准确率达94%，远远优于人为诊断与传统Logistic回归分析，做到及时、精确诊断癌前病变，避免其进展为恶性肿瘤。许多研究利用PCN的CT、MR影像学特征或放射组学数据，通过ML算法建立出具有优异的鉴别、预测效能的模型，展现出AI在诊断囊性肿瘤方面优于传统诊断方法的准确性以及很大的潜力，不仅可以鉴别囊性病变的性质，同时也可以鉴别出不同亚型，根据这些结果选择手术，或密切随访，制定出适合每一位患者的治疗措施[3, 48-54]。Kruita等[2]将手术及EUS-FNA获得的囊液进行肿瘤标志物以及淀粉酶检测，通过DL模型进行学习、验证，并最终与现实结果进行对比，证明AI诊断模型对恶性和良性囊性病变高度敏感，可用于排除恶性胰腺囊性病变。

AI算法不仅可以处理临床资料或影像学数据，也可以将两种数据结合，进一步提升ML模型的适用范围及准确性。最近的研究表明生物标志物微小核糖核酸（miRNA）具有区分良性与高风险PCN的潜力[55-56]，因此可以将肿瘤的影像学特征与miRNA相结合预测囊性肿瘤如IPMN的恶性潜能，对术后患者的血浆及组织进行全基因组miRNA分析，根据术后诊断筛选出特异性miRNA，并分组收集组内不同患者的CT影像学特征，两类变量相结合预测IPMN的恶变风险，及时进行手术治疗，避免其进展为恶性肿瘤[57]。

2.2 AI与胰腺神经内分泌肿瘤（Pancreatic Neuroendocrine Tumors, pNETs）

pNETs占整个消化道神经内分泌肿瘤的12%[58]。肿瘤的分级取决于Ki67指数和有丝分裂计数。为了帮助病理学家捕捉可能遗漏的切片中肿瘤组织位点，Niazi等[59-60]将Ki67抗体染色的活检的图像标记为像素点通过CNN模型区别为肿瘤区域和非肿瘤区域，利用转移学习强化模型区分切片中肿瘤和非肿瘤区域的能力，减少病理科医师的工作量并避免漏诊。不同分级的pNETs在临床实践中的处理原则截然不同，其中G1/2组可以进行胰腺部分切除术，而G3组为了改善预后，常进行包括根治性手术切除和系统化疗在内的综合治疗策略[61-62]。Luo等[63]分别使用DL算法中的CNN模型与传统ML模型学习不同分级患者术前的增强CT图像，并进行训练、验证、对比，证明CNN模型在术前判断肿瘤分级及预后方面均更加吻合于临床真实情况。Gao等[64]利用GAN训练不同分级肿瘤的核磁图像，并在扩充训练集中加入CNN模型，有效避免了CNN模型过度拟合的问题，最后进行交叉验证提高CNN模型的准确度。

pNETs在影像学上多表现为血管富集状态，这一发现表明肿瘤具有丰富的毛细血管网，并且最近的研究表明微血管密度与肿瘤预后密切相关[65-66]。Chen等[67]利用EUS图像描述不同患者的血管富集情况，通过多种ML模型学习训练，进而设计一个具有预测肿瘤分级与预后的血管结构分析模式。手术切除是彻底治疗pNETs的唯一方式，但是不同分级肿瘤术后复发率不同，术后整体复发率高，术后监测方面几乎没有共识。目前国际上大多数指南建议在根治性手术后的前3~5年进行合理的强化随访，并至少随访7年[68-70]。因此，Song等[71]收集患者术前CT影像学资料并使用深度学习放射组学（Deep Learning Radiomics, DLR）模型提取特征进行验证，并将临床指标添加到优化模型中再次进行交叉验证，成功预测患者术后的复发率并制定个体化的随访计划。

2.3 AI与胰腺癌(Pancreatic Cancer, PC)

PC是预后最差的癌症之一[72]。在中国,PC是死亡率最高的恶性肿瘤,早期发现是增加生存机会最有希望的方法[73]。如何早期诊断PC一直是胰腺外科的重点与难点,尤其是当患者不存在或者仅有轻微症状,影像学仅发现细微病变时。目前已经有很多通过改良影像学技术以提升PC检出率的研究[74-76],但是将AI与CT图像相结合辅助诊断的研究还比较少。目前主要采用的研究方式是首先获得CT图像中具有诊断意义的区域,使用纹理分析方法提取定量特征,考虑到总体样本量较小,因此Qiu[77]选用线性SVM模型进行交叉验证并训练,Si[78]则选用深度残差网络模型(ResNet)进行训练验证,Liu等[79]在CNN模型学习训练的基础上与临床资料、手术资料相结合,使得后者的诊断效能优于前两者,Liu的参数训练集较前两者更为丰富,虽然SVM是一种有效的小样本学习方法,但并不适合用于线性关系的分析。PC的发病情况在既往研究中证明与年龄有密切关系,随着年龄增长,发病率也逐渐增高[72]。Rajan等[80]通过前瞻性收集不同年龄阶段人群EUS图像,证明随着年龄增长,胰腺形态越容易发生变化。Ozkan[81]进一步分年龄段收集PDAC患者与正常人群的EUS图像并提取合适特征,使用ANN模型进行学习训练,其准确性及特异性均优于将年龄统一对比的模型。因此,根据年龄分组训练可以提高诊断模型整体的性能,也更符合临床诊疗的思路。在使用EUS诊断PC时,操作者的经验和主观因素对EUS诊断结果有较大影响[82],尤其是在并发CP的PC患者中。Zhu等[83]利用SVM系统具有良好泛化能力并适合管理有限样本量简单分类问题的特点,将PC患者与CP患者EUS图像按2:1纳入样本并采集特异区域,通过SVM进行学习验证并建立鉴别CP与PC的预测模型,Zhang[82]通过将正常人群、CP患者、PC患者EUS图像同时纳入样本并进行SVM学习训练,虽然样本总量小于前者,但其模型的敏感度与特异性均优于前者,证明预测模型的效能会随分组增多而提升。Das[84]通过ANN模型分组训练NP、CP、PC的EUS图像数据,虽然样本量大于Zhang的研究,但是其预测模型效能仅与Zhu的模型相当,说明SVM的泛化能力优于ANN模型,更适于对小样本数据进行诊断鉴别。

AI除了通过与影像学相结合提升诊断准确率,也可以通过血清学检验指标提高恶性肿瘤的诊断能力。既往关于多种血清学标记物联合诊断的研究结果表明虽然联合诊断灵敏性升高,但是特异性会降低[85-86],与计算机算法结合后会有效避免这类情况的发生。Yang等[87]利用多种PC特异血清学标记物通过ANN分组进行训练验证,证明ANN模型在敏感性、特异性和准确率方面均优于传统Logistics回归模型。随着细胞外小泡(Extracellular Vehicles,EVs)研究的深入,发现EVs中的长链RNA(EV long RNAs,exLRs)与肿瘤进展、肿瘤分型有关,并在癌细胞中富集[88-91],但是与PC的关系尚未明确。Yu等[92]收集PDAC患者、CP患者以及正常人群血浆进行exLRs测序及通路分析,显示exLRs在mTOR信号通路和VEGF信号通路等与PC密切相关的通路中富集,选取特异的exLR标记作为算法数据集并使用SVM算法学习训练,分别进行内部及外部验证,最终得出以特异型exLR为数据变量的诊断模型,可用于早期预测PDAC并进行鉴别诊断。

既往研究表明未经治疗的PC患者中位生存期约为3.5个月,5年生存率仅为10%[72]。针对PC预后的预测,Walczak[6]通过基于ANN算法的模型,用于各种治疗决策,包括观察、辅助治疗、切除和切除联合辅助治疗,尽可能使患者获益。Chakraborty[93]利用从治疗前CT扫描中提取的纹理图像特征进行最小冗余最大相关性以及朴素贝叶斯算法提取纹理特征并进行交叉验证,以预测PC患者的2年生存率,优化患者治疗方案选择。淋巴结阳性率一直是临床实践中关于肿瘤预后的一个很重要的判断因素[94]。淋巴结比率(Lymph Node Ratio,LNR)是指阳性淋巴结除以检验的淋巴结总数,在食管癌、胃癌、结肠癌、乳腺癌、PC等肿瘤预后预测方面具有重要作用[95-97]。Smith[98]由此设计两个使用交互式贝叶斯算法的模型,即通过术后患者的肿瘤病理与TM分级预测LNR,并根据术后病理验证模型准确性,再利用前者的样本结合患者基线资料与肿瘤病理、是否行放射治疗等数据预测患者预后并取得优异的预测效能。虽然仅通过实验室检查、术后的病理情况[99]或影像学资料[100]可以设计出优秀的预测模型,但是纳入多种类型的数据进行分析或许能有效提高模型的准确性。Kaissis[101]回顾性收集PDAC患者的MRI图像特征与临床数据,并与实验室检查相结合,通过RF算法监督学习,最终模型预测生存曲线与患者的实际生存时间几乎完全重叠,说明多种类型数据与正确的算法相结合可以极大提高模型效能。

胰腺术后并发症一直是临床治疗的重点和难点,权威机构的临床指南仍是各大医疗中心通过不断地总结治疗经验,归纳各类风险预测评分并进行改良,但是其准确性会随着临床治疗而产生变化[102],而将AI应用于术后并发症预测则体现出很大的研究潜力。术后手术部位的感染(Surgical Site Infections,

SSIs)不仅影响胰腺术后患者的恢复,同时也是所有外科医生共同面对的问题。目前,多项研究使用ML算法模型进行数据分析学习,术前数据作为算法输入,术后治疗方案用于确定是否发生术后感染,最后通过单一算法或多种算法结合构建新的算法模型预测术后感染发生率[103, 104]。胰腺术后并发症以术后胰瘘(Postoperative Pancreatic Fistula, POFF)最为危险,并且是导致术后死亡的最大危险因素[102, 105],预防POFF也是外科医生术后优先关注的问题。Han等[106]回顾1 769位进行过胰十二指肠切除术的病人并提取出38个临床变量,通过PF和ANN算法分别学习与训练,最后两种算法模型结合设计了临床决策工具预测POFF。既往的研究表明胰腺组织的弹性模量与POFF关系密切[107-110]。Kambakamba[111-112]将胰瘘患者与无胰瘘患者1:1纳入研究,将这些患者术前的胰腺影像学纹理特征与胰瘘风险评分(Fistula Risk Score, FRS)相结合,通过ML算法分析验证建议预测模型。Mu等[113]则是将所有的胰腺术后患者各项临床数据及CT图像纳入研究,通过DL训练,设计出胰瘘风险预测模型。两个研究得出的预测模型效能均优于FRS评分。

交界性可切除与不可切除PC患者得到R0切除的比例随着新辅助治疗、MDT模式概念的提出越来越高。目前AI已应用于多种肿瘤新辅助治疗,评估治疗疗效并预测预后[114-117]。De Geus与Sharma[118-119]均通过决策分析方法证明基于新辅助治疗的管理改善了交界可切除PC患者的预后,但是这些决策分析由于整体样本量很少,纳入的变量有限,其效能值得怀疑,因此需要大量数据与AI相结合,制定效能优良的预测模型,并在临床实践中为每一位患者制定个体化的化疗方案及手术选择。

3 总结与展望

在过去的10年里,AI在普外科领域取得了巨大进展,本文主要概述了AI在胰腺疾病方面的应用。过去虽然取得了重大进步,但是为了实现胰腺疾病精准医疗,还有许多困难需要解决。需要临床医生充分发挥各个学科优势,通过收集和处理临床资料,建立稳定准确的数据库。临床实践及诊疗思路不是简单的从数据到结果的过程,这就要求研究人员提出与医生临床思维类似、具有更强的可解释性的算法。同时,AI应该与研究人员及科学家的工作相结合,利用AI技术处理生物医学领域问题,将宏观与微观相结合,将临床资料与组学资料相结合。AI技术并不能代替医生进行决策,但是可以在减少医疗繁琐工作的同时改进目前的诊疗模式,以实现个性化医疗。

【参考文献】

[1] Greenhalf W, Levy P, Gress T, et al. International consensus guidelines on surveillance for pancreatic cancer in chronic pancreatitis. Recommendations from the working group for the international consensus guidelines for chronic pancreatitis in collaboration with the International Association of Pancreatology, the American Pancreatic Association, the Japan Pancreas Society, and European Pancreatic Club [J]. Pancreatology, 2020, 20(5): 910-918.

[2] Kurita Y, Kuwahara T, Hara K, et al. Diagnostic ability of artificial intelligence using deep learning analysis of cyst fluid in differentiating malignant from benign pancreatic cystic lesions[J]. Sci Rep, 2019, 9 (1): 6893.

[3] Dalal V, Carmicheal J, Dhaliwal A, et al. Radiomics in stratification of pancreatic cystic lesions: Machine learning in action[J]. Cancer Lett, 2020, 469: 228-237.

[4] Pancreatic Cancer Committeeof Chinese Anticancer. A comprehensive guidelines for the diagnosis and treatment of pancreatic cancer (2020 version)[J]. Chinese Journal of Surgery, 2021, 59(2): 81-100.

[5] Pereira SP, Oldfield L, Ney A, et al. Early detection of pancreatic cancer [J]. Lancet Gastroenterol Hepatol, 2020, 5(7): 698-710.

[6] Walczak S, Velanovich V. An evaluation of artificial neural networks in predicting pancreatic cancer survival[J]. J Gastrointest Surg, 2017, 21(10): 1606-1612.

[7] Cai J, Lu L, Zhang Z, et al. Pancreas segmentation in MRI using graph-based decision fusion on convolutional neural networks[J]. Med Image Comput Comput Assist Interv, 2016, 9901: 442-450.

[8] Goyal H, Mann R, Gandhi Z, et al. Application of artificial intelligence in pancreaticobiliary diseases[J]. Ther Adv Gastrointest Endosc, 2021, 14: 2631774521993059.

[9] Waldrop MM. News feature: What are the limits of deep learning?[J]. Proc Natl Acad Sci USA, 2019, 116(4): 1074-1077.

[10] Hosny A, Parmar C, Quackenbush J, et al. Artificial intelligence in radiology[J]. Nat Rev Cancer, 2018, 18(8): 500-510.

[11] Gorris M, Hoogenboom SA, Wallace MB, et al. Artificial intelligence for the management of pancreatic diseases[J]. Dig Endosc, 2021, 33 (2): 231-241.

[12] Lee PJ, Papachristou GI. New insights into acute pancreatitis[J]. Nat Rev Gastroenterol Hepatol, 2019, 16(8): 479-496.

[13] Pearce CB, Gunn SR, Ahmed A, et al. Machine learning can improve prediction of severity in acute pancreatitis using admission values of APACHE II score and C-reactive protein[J]. Pancreatology, 2006, 6 (1-2): 123-131.

[14] Crockett SD, Wani S, Gardner TB, et al. American gastroenterological association institute guideline on initial management of acute pancreatitis[J]. Gastroenterology, 2018, 154(4): 1096-1101.

[15] Fei Y, Liu XQ, Gao K, et al. Analysis of influencing factors of severity in acute pancreatitis using big data mining[J]. Rev Assoc Med Bras, 2018, 64(5): 454-461.

[16] Bartosch-Harlid A, Andersson B, Aho U, et al. Artificial neural networks in pancreatic disease[J]. Br J Surg, 2008, 95(7): 817-826.

[17] Andersson B, Andersson R, Ohlsson M, et al. Prediction of severe acute pancreatitis at admission to hospital using artificial neural networks[J]. Pancreatology, 2011, 11(3): 328-335.

[18] Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus[J]. Gut, 2013, 62(1): 102-111.

[19] Hackert T, Buchler MW. Decision making in necrotizing pancreatitis [J]. Dig Dis, 2016, 34(5): 517-524.

[20] Van Brunschot S, Van Grinsven J, Van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial[J]. Lancet, 2018, 391(10115): 51-58.

[21] Neoptolemos JP, Kemppainen EA, Mayer JM, et al. Early prediction of severity in acute pancreatitis by urinary trypsinogen activation peptide: a multicentre study[J]. Lancet, 2000, 355(9219): 1955-1960.

[22] Qiu Q, Nian YJ, Tang L, et al. Artificial neural networks accurately predict intra-abdominal infection in moderately severe and severe acute pancreatitis[J]. J Dig Dis, 2019, 20(9): 486-494.

[23] Schepers NJ, Bakker OJ, Besselink MG, et al. Impact of characteristics of organ failure and infected necrosis on mortality in necrotising pancreatitis[J]. Gut, 2019, 68(6): 1044-1051.

[24] Xu F, Chen X, Li C, et al. Prediction of multiple organ failure complicated by moderately severe or severe acute pancreatitis based

on machine learning: amulticenter Cohort study[J]. Mediators Inflamm, 2021, 2021: 5525118.
[25] Fei Y, Gao K, Li WQ. Artificial neural network algorithm model as powerful tool to predict acute lung injury following to severe acute pancreatitis[J]. Pancreatology, 2018, 18(8): 892-899.
[26] Butler JR, Eckert GJ, Zyromski NJ, et al. Natural history of pancreatitis-induced splenic vein thrombosis: a systematic review and meta-analysis of its incidence and rate of gastrointestinal bleeding[J]. HPB (Oxford), 2011, 13(12): 839-845.
[27] Tripodi A, Legnani C, Palareti G. The risk of a first and a recurrent venous thrombosis associated with an elevated D-dimer level and an elevated thrombin potential: results of the THE-VTE study: comment [J]. J Thromb Haemost, 2015, 13(12): 2283-2286.
[28] Fei Y, Hu J, Gao K, et al. Risk prediction for portal vein thrombosis in acute pancreatitis using radial basis function[J]. Ann Vasc Surg, 2018, 47: 78-84.
[29] Fei Y, Hu J, Li WQ, et al. Artificial neural networks predict the incidence of portosplenomesenteric venous thrombosis in patients with acute pancreatitis[J]. J Thromb Haemost, 2017, 15(3): 439-445.
[30] Halonen KI, Leppaniemi AK, Lundin JE, et al. Predicting fatal outcome in the early phase of severe acute pancreatitis by using novel prognostic models[J]. Pancreatology, 2003, 3(4): 309-315.
[31] Keogan MT, Lo JY, Freed KS, et al. Outcome analysis of patients with acute pancreatitis by using an artificial neural network[J]. Acad Radiol, 2002, 9(4): 410-419.
[32] Mashayekhi R, Parekh VS, Faghih M, et al. Radiomic features of the pancreas on CT imaging accurately differentiate functional abdominal pain, recurrent acute pancreatitis, and chronic pancreatitis[J]. Eur J Radiol, 2020, 123: 108778.
[33] Mofidi R, Duff MD, Madhavan KK, et al. Identification of severe acute pancreatitis using an artificial neural network[J]. Surgery, 2007, 141 (1): 59-66.
[34] Majumder S, Takahashi N, Chari ST. Autoimmune pancreatitis[J]. Dig Dis Sci, 2017, 62(7): 1762-1769.
[35] Madhani K, Farrell JJ. Autoimmune pancreatitis: an update on diagnosis and management [J]. Gastroenterol Clin North Am, 2016, 45(1): 29-43.
[36] Janssen J, Schlorer E, Greiner L. EUS elastography of the pancreas: feasibility and pattern description of the normal pancreas, chronic pancreatitis, and focal pancreatic lesions[J]. Gastrointest Endosc, 2007, 65(7): 971-978.
[37] Marya NB, Powers PD, Chari ST, et al. Utilisation of artificial intelligence for the development of an EUS-convolutional neural network model trained to enhance the diagnosis of autoimmune pancreatitis[J]. Gut, 2021, 70(7): 1335-1344.
[38] Testoni PA. Acute recurrent pancreatitis: Etiopathogenesis, diagnosis and treatment[J]. World J Gastroenterol, 2014, 20(45): 16891-16901.
[39] Sankaran SJ, Xiao AY, Wu LM, et al. Frequency of progression from acute to chronic pancreatitis and risk factors: a meta-analysis[J]. Gastroenterology, 2015, 149(6): 1490-1500.
[40] Ahmed Ali U, Issa Y, Hagenaars JC, et al. Risk of recurrent pancreatitis and progression to chronic pancreatitis after a first episode of acute pancreatitis[J]. Clin Gastroenterol Hepatol, 2016, 14(5): 738-746.
[41] Cote GA, Imperiale TF, Schmidt SE, et al. Similar efficacies of biliary, with or without pancreatic, sphincterotomy in treatment of idiopathic recurrent acute pancreatitis[J]. Gastroenterology, 2012, 143(6): 1502-1509.
[42] Wilcox CM, Seay T, Kim H, et al. Prospective endoscopic ultrasound-based approach to the evaluation of idiopathic pancreatitis: causes, response to therapy, and long-term outcome[J]. Am J Gastroenterol, 2016, 111(9): 1339-1348.
[43] Cote GA, Yadav D, Abberbock JA, et al. Recurrent acute pancreatitis significantly reduces quality of life even in the absence of overt chronic pancreatitis[J]. Am J Gastroenterol, 2018, 113(6): 906-912.
[44] Chen Y, Chen TW, Wu CQ, et al. Radiomics model of contrast-enhanced computed tomography for predicting the recurrence of acute pancreatitis[J]. Eur Radiol, 2019, 29(8): 4408-4417.
[45] Malleo G, Bassi C, Rossini R, et al. Growth pattern of serous cystic neoplasms of the pancreas: observational study with long-term magnetic resonance surveillance and recommendations for treatment [J]. Gut, 2012, 61(5): 746-751.
[46] Tanaka M, Chari S, Adsay V, et al. International consensus guidelines for management of intraductal papillary mucinous neoplasms and mucinous cystic neoplasms of the pancreas[J]. Pancreatology, 2006, 6(1-2): 17-32.
[47] Kuwahara T, Hara K, Mizuno N, et al. Usefulness of deep learning analysis for the diagnosis of malignancy in intraductal papillary mucinous neoplasms of the pancreas[J]. Clin Transl Gastroenterol, 2019, 10(5): 1-8.
[48] Han X, Yang J, Luo J, et al. Application of CT-based radiomics in discriminating pancreatic cystadenomas from pancreatic neuroendocrine tumors using machine learning methods[J]. Front Oncol, 2021, 11: 606677.
[49] Medical Image Computing and Computer Assisted Intervention-MICCAI 2017[M]. 2017.
[50] Yang J, Guo X, Ou X, et al. Discrimination of pancreatic serous cystadenomas from mucinous cystadenomas with CT textural features: based on machine learning[J]. Front Oncol, 2019, 9: 494.
[51] Wei R, Lin K, Yan W, et al. Computer-aided diagnosis of pancreas serous cystic neoplasms: A radiomics method on preoperative MDCT images[J]. Technol Cancer Res Treat, 2019, 18: 1533033818824339.
[52] Sahani DV, Sainani NI, Blake MA, et al. Prospective evaluation of reader performance on MDCT in characterization of cystic pancreatic lesions and prediction of cyst biologic aggressiveness[J]. AJR Am J Roentgenol, 2011, 197(1): W53-W61.
[53] Corral JE, Hussein S, Kandel P, et al. Deep learning to classify intraductal papillary mucinous neoplasms using magnetic resonance imaging[J]. Pancreas, 2019, 48(6): 805-810.
[54] Li H, Shi K, Reichert M, et al. Differential diagnosis for pancreatic cysts in CT scans using densely-connected convolutional networks[J]. Annu Int Conf IEEE Eng Med Biol Soc, 2019, 2019: 2095-2098.
[55] Henry JC, Bassi C, Giovinazzo F, et al. MicroRNA from pancreatic duct aspirate differentiates cystic lesions of the pancreas[J]. Ann Surg Oncol, 2013, 20(Suppl 3): S661-S666.
[56] Utomo WK, Looijenga LH, Bruno MJ, et al. A MicroRNA panel in pancreatic cyst fluid for the risk stratification of pancreatic cysts in a prospective Cohort[J]. Mol Ther Nucleic Acids, 2016, 5: e350.
[57] Permuth JB, Choi J, Balarunathan Y, et al. Combining radiomic features with a miRNA classifier may improve prediction of malignant pathology for pancreatic intraductal papillary mucinous neoplasms[J]. Oncotarget, 2016, 7(52): 85785-85797.
[58] Klimstra DS, Modlin IR, Coppola D, et al. The pathologic classification of neuroendocrine tumors: a review of nomenclature, grading, and staging systems[J]. Pancreas, 2010, 39(6): 707-712.
[59] Niazi MK, Tavolara TE, Arole V, et al. Identifying tumor in pancreatic neuroendocrine neoplasms from Ki67 images using transfer learning [J]. PLoS One, 2018, 13(4): e0195621.
[60] Xing F, Xie Y, Yang L. An automatic learning-based framework for robust nucleus segmentation[J]. IEEE Trans Med Imaging, 2016, 35 (2): 550-566.
[61] Vaghaiwalla T, Keutgen XM. Surgical management of pancreatic neuroendocrine tumors[J]. Surg Oncol Clin N Am, 2020, 29(2): 243-252.
[62] Crippa S, Zerbi A, Boninsegna L, et al. Surgical management of insulinomas: short- and long-term outcomes after enucleations and pancreatic resections[J]. Arch Surg, 2012, 147(3): 261-266.
[63] Luo Y, Chen X, Chen J, et al. Preoperative prediction of pancreatic neuroendocrine neoplasms grading based on enhanced computed tomography imaging: validation of deep learning with a convolutional neural network[J]. Neuroendocrinology, 2020, 110(5): 338-350.
[64] Gao X, Wang X. Deep learning for World Health Organization grades of pancreatic neuroendocrine tumors on contrast-enhanced magnetic resonance images: a preliminary study[J]. Int J Comput Assist Radiol Surg, 2019, 14(11): 1981-1991.
[65] Takahashi Y, Akishima-Fukasawa Y, Kobayashi N, et al. Prognostic value of tumor architecture, tumor-associated vascular characteristics, and expression of angiogenic molecules in pancreatic endocrine tumors [J]. Clin Cancer Res, 2007, 13(1): 187-196.
[66] Lewis RB, Lattin GE, Paal E. Pancreatic endocrine tumors: radiologic-clinicopathologic correlation[J]. Radiographics, 2010, 30(6): 1445-1464.
[67] Chen K, Zhang W, Zhang Z, et al. Simple vascular architecture classification in predicting pancreatic neuroendocrine tumor grade and prognosis[J]. Dig Dis Sci, 2018, 63(11): 3147-3152.

[68] Falconi M, Eriksson B, Kaltsas G, et al. ENETS consensus guidelines update for the management of patients with functional pancreatic neuroendocrine tumors and non-functional pancreatic neuroendocrine tumors[J]. Neuroendocrinology, 2016, 103(2): 153-171.
[69] Delle Fave G, O'toole D, Sundin A, et al. ENETS consensus guidelines update for gastroduodenal neuroendocrine neoplasms [J]. Neuroendocrinology, 2016, 103(2): 119-124.
[70] Niederle B, Pape UF, Costa F, et al. ENETS consensus guidelines update for neuroendocrine neoplasms of the jejunum and ileum[J]. Neuroendocrinology, 2016, 103(2): 125-138.
[71] Song C, Wang M, Luo Y, et al. Predicting the recurrence risk of pancreatic neuroendocrine neoplasms after radical resection using deep learning radiomics with preoperative computed tomography images[J]. Ann Transl Med, 2021, 9(10): 833.
[72] Siegel RL, Miller KD, Fuchs HE, et al. Cancer statistics, 2021[J]. CA Cancer J Clin, 2021, 71(1): 7-33.
[73] Chen W, Zheng R, Baade PD, et al. Cancer statistics in China, 2015[J]. CA Cancer J Clin, 2016, 66(2): 115-132.
[74] Cassinotto C, Chong J, Zogopoulos G, et al. Resectable pancreatic adenocarcinoma: Role of CT quantitative imaging biomarkers for predicting pathology and patient outcomes[J]. Eur J Radiol, 2017, 90: 152-158.
[75] Duan H, Baratto L, Iagaru A. The role of PET/CT in the imaging of pancreatic neoplasms[J]. Semin Ultrasound CT MR, 2019, 40(6): 500-508.
[76] Schima W, Bohm G, Rosch CS, et al. Mass-forming pancreatitis *versus* pancreatic ductal adenocarcinoma: CT and MR imaging for differentiation[J]. Cancer Imaging, 2020, 20(1): 52.
[77] Qiu JJ, Yin J, Qian W, et al. A novel multiresolution-statistical texture analysis architecture: Radiomics-aided diagnosis of PDAC based on plain CT images[J]. IEEE Trans Med Imaging, 2021, 40(1): 12-25.
[78] Si K, Xue Y, Yu X, et al. Fully end-to-end deep-learning-based diagnosis of pancreatic tumors[J]. Theranostics, 2021, 11(4): 1982-1990.
[79] Liu SL, Li S, Guo YT, et al. Establishment and application of an artificial intelligence diagnosis system for pancreatic cancer with a faster region-based convolutional neural network[J]. Chin Med J (Engl), 2019, 132(23): 2795-2803.
[80] Rajan E, Clain JE, Levy MJ, et al. Age-related changes in the pancreas identified by EUS: a prospective evaluation[J]. Gastrointest Endosc, 2005, 61(3): 401-406.
[81] Ozkan M, Cakiroglu M, Kocaman O, et al. Age-based computer-aided diagnosis approach for pancreatic cancer on endoscopic ultrasound images[J]. Endosc Ultrasound, 2016, 5(2): 101-107.
[82] Zhang MM, Yang H, Jin ZD, et al. Differential diagnosis of pancreatic cancer from normal tissue with digital imaging processing and pattern recognition based on a support vector machine of EUS images[J]. Gastrointest Endosc, 2010, 72(5): 978-985.
[83] Zhu M, Xu C, Yu J, et al. Differentiation of pancreatic cancer and chronic pancreatitis using computer-aided diagnosis of endoscopic ultrasound (EUS) images: a diagnostic test[J]. PLoS One, 2013, 8(5): e63820.
[84] Das A, Nguyen CC, Li F, et al. Digital image analysis of EUS images accurately differentiates pancreatic cancer from chronic pancreatitis and normal tissue[J]. Gastrointest Endosc, 2008, 67(6): 861-867.
[85] Silsirivanit A, Araki N, Wongkham C, et al. A novel serum carbohydrate marker on mucin 5AC: values for diagnostic and prognostic indicators for cholangiocarcinoma [J]. Cancer, 2011, 117(15): 3393-3403.
[86] Alizadeh M, Safarzadeh A, Beyranvand F, et al. The potential role of miR-29 in health and cancer diagnosis, prognosis, and therapy[J]. J Cell Physiol, 2019, 234(11): 19280-19297.
[87] Yang Y, Chen H, Wang D, et al. Diagnosis of pancreatic carcinoma based on combined measurement of multiple serum tumor markers using artificial neural network analysis[J]. Chin Med J (Engl), 2014, 127(10): 1891-1896.
[88] Huarte M. The emerging role of lncRNAs in cancer[J]. Nat Med, 2015, 21(11): 1253-1261.
[89] Batista PJ, Chang HY. Long noncoding RNAs: cellular address codes in development and disease[J]. Cell, 2013, 152(6): 1298-1307.
[90] Kristensen LS, Andersen MS, Stagsted LV, et al. The biogenesis, biology and characterization of circular RNAs[J]. Nat Rev Genet, 2019, 20(11): 675-691.
[91] Chen S, Zhu X, Huang S. Clinical applications of extracellular vesicle long RNAs[J]. Crit Rev Clin Lab Sci, 2020, 57(8): 508-521.
[92] Yu S, Li Y, Liao Z, et al. Plasma extracellular vesicle long RNA profiling identifies a diagnostic signature for the detection of pancreatic ductal adenocarcinoma[J]. Gut, 2020, 69(3): 540-550.
[93] Chakraborty J, Langdon-Embry L, Cunanan KM, et al. Preliminary study of tumor heterogeneity in imaging predicts two year survival in pancreatic cancer patients[J]. PLoS One, 2017, 12(12): e0188022.
[94] Aoki S, Mizuma M, Hayashi H, et al. Prognostic impact of intraoperative peritoneal cytology after neoadjuvant therapy for potentially resectable pancreatic cancer[J]. Pancreatology, 2020, 20 (8): 1711-1717.
[95] Singh D, Mandal A. The prognostic value of lymph node ratio in survival of non-metastatic breast carcinoma patients[J]. Breast Cancer Res Treat, 2020, 184(3): 839-848.
[96] Zhu X, Tian X, Yu C, et al. A long non-coding RNA signature to improve prognosis prediction of gastric cancer[J]. Mol Cancer, 2016, 15(1): 60.
[97] Osterman E, Mezheyeuski A, Sjoblom T, et al. Beyond the NCCN risk factors in colon cancer: An evaluation in a Swedish population-based Cohort[J]. Ann Surg Oncol, 2020, 27(4): 1036-1045.
[98] Smith BJ, Mezhir JJ. An interactive Bayesian model for prediction of lymph node ratio and survival in pancreatic cancer patients[J]. J Am Med Inform Assoc, 2014, 21(e2): e203-e211.
[99] Ansari D, Nilsson J, Andersson R, et al. Artificial neural networks predict survival from pancreatic cancer after radical surgery[J]. Am J Surg, 2013, 205(1): 1-7.
[100] Zhang Y, Lobo-Mueller EM, Karanicolas P, et al. CNN-based survival model for pancreatic ductal adenocarcinoma in medical imaging[J]. BMC Med Imaging, 2020, 20(1): 11.
[101] Kaissis G, Ziegelmayer S, Lohofer F, et al. A machine learning model for the prediction of survival and tumor subtype in pancreatic ductal adenocarcinoma from preoperative diffusion-weighted imaging[J]. Eur Radiol Exp, 2019, 3(1): 41.
[102] Lyu Y, Li T, Wang B, et al. Selection of pancreaticojejunostomy technique after pancreaticoduodenectomy: duct-to-mucosa anastomosis is not better than invagination anastomosis: A meta-analysis[J]. Medicine, 2018, 97(40): e12621.
[103] Da Silva DA, Ten Caten CS, Dos Santos RP, et al. Predicting the occurrence of surgical site infections using text mining and machine learning[J]. PLoS One, 2019, 14(12): e0226272.
[104] Brennan M, Puri S, Ozrazgat-Baslanti T, et al. Comparing clinical judgment with the MySurgeryRisk algorithm for preoperative risk assessment: A pilot usability study[J]. Surgery, 2019, 165(5): 1035-1045.
[105] Garg PK, Sharma J, Jakhetiya A, et al. The role of prophylactic octreotide following pancreaticoduodenectomy to prevent postoperative pancreatic fistula: A meta-analysis of the randomized controlled trials[J]. Surg J (N Y), 2018, 4(4): e182-e187.
[106] Han IW, Cho K, Ryu Y, et al. Risk prediction platform for pancreatic fistula after pancreatoduodenectomy using artificial intelligence[J]. World J Gastroenterol, 2020, 26(30): 4453-4464.
[107] Callery MP, Pratt WB, Kent TS, et al. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy[J]. J Am Coll Surg, 2013, 216(1): 1-14.
[108] Mungroop TH, Van Rijssen LB, Van Klaveren D, et al. Alternative fistula risk score for pancreatoduodenectomy (a-FRS): design and international external validation[J]. Ann Surg, 2019, 269(5): 937-943.
[109] Gaujoux S, Cortes A, Couvelard A, et al. Fatty pancreas and increased body mass index are risk factors of pancreatic fistula after pancreaticoduodenectomy[J]. Surgery, 2010, 148(1): 15-23.
[110] Wellner UF, Kayser G, Lapshyn H, et al. A simple scoring system based on clinical factors related to pancreatic texture predicts postoperative pancreatic fistula preoperatively[J]. HPB (Oxford), 2010, 12(10): 696-702.
[111] Kambakamba P, Mannil M, Herrera PE, et al. The potential of machine learning to predict postoperative pancreatic fistula based on preoperative, non-contrast-enhanced CT: A proof-of-principle study [J]. Surgery, 2020, 167(2): 448-454.
[112] Bassi C, Dervenis C, Butturini G, et al. Postoperative pancreatic fistula: an international study group (ISGPF) definition[J]. Surgery,

2005, 138(1): 8-13.
[113]Mu W, Liu C, Gao F, et al. Prediction of clinically relevant pancreatico-enteric anastomotic fistulas after pancreatoduodenectomy using deep learning of preoperative computed tomography[J]. Theranostics, 2020, 10(21): 9779-9788.
[114]Shu Z, Fang S, Ye Q, et al. Prediction of efficacy of neoadjuvant chemoradiotherapy for rectal cancer: the value of texture analysis of magnetic resonance images[J]. Abdom Radiol (NY), 2019, 44(11): 3775-3784.
[115]Cain EH, Saha A, Harowicz MR, et al. Multivariate machine learning models for prediction of pathologic response to neoadjuvant therapy in breast cancer using MRI features: a study using an independent validation set[J]. Breast Cancer Res Treat, 2019, 173(2): 455-463.
[116]Ferrari R, Mancini-Terracciano C, Voena C, et al. MR-based artificial intelligence model to assess response to therapy in locally advanced rectal cancer[J]. Eur J Radiol, 2019, 118: 1-9.
[117]Jeong SY, Kim W, Byun BH, et al. Prediction of chemotherapy response of osteosarcoma using baseline (18)F-FDG textural features machine learning approaches with PCA[J]. Contrast Media Mol Imaging, 2019, 2019: 3515080.
[118]Sharma G, Whang EE, Ruan DT, et al. Efficacy of neoadjuvant *versus* adjuvant therapy for resectable pancreatic adenocarcinoma: a decision analysis[J]. Ann Surg Oncol, 2015, 22(Suppl 3): S1229-S1237.
[119]De Geus SW, Evans DB, Bliss LA, et al. Neoadjuvant therapy *versus* upfront surgical strategies in resectable pancreatic cancer: A Markov decision analysis[J]. Eur J Surg Oncol, 2016, 42(10): 1552-1560.

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