ISSN 2644-3236 (online)

Artificial Intelligence in *Gastroenterology*

Artif Intell Gastroenterol 2023 December 8; 4(3): 48-71

Published by Baishideng Publishing Group Inc

AIG Artificial Intelligence in Gastroenterology

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Quarterly Volume 4 Number 3 December 8, 2023

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Artificial Intelligence in Gastroenterology

Quarterly Volume 4 Number 3 December 8, 2023

ABOUT COVER

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The primary aim of *Artificial Intelligence in Gastroenterology* (*AIG*, *Artif Intell Gastroenterol*) is to provide scholars and readers from various fields of artificial intelligence in gastroenterology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

AIG mainly publishes articles reporting research results obtained in the field of artificial intelligence in gastroenterology and covering a wide range of topics, including artificial intelligence in gastrointestinal cancer, liver cancer, pancreatic cancer, hepatitis B, hepatitis C, nonalcoholic fatty liver disease, inflammatory bowel disease, irritable bowel syndrome, and *Helicobacter pylori* infection.

INDEXING/ABSTRACTING

The *AIG* is now abstracted and indexed in Reference Citation Analysis, China Science and Technology Journal Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Si Zhao*; **Production Department Director:** *Xu Guo*; **Editorial Office Director:** *Jin-Lei Wang*.

NAME OF JOURNAL
Artificial Intelligence in Gastroenterology

ISSN
ISSN 2644-3236 (online)

LAUNCH DATE
July 28, 2020

FREQUENCY
Quarterly

EDITORS-IN-CHIEF
Rajvinder Singh, Ferruccio Bonino

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/2644-3236/editorialboard.htm

PUBLICATION DATE
December 8, 2023

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Artif Intell Gastroenterol 2023 December 8; 4(3): 48-63

DOI: 10.35712/aig.v4.i3.48

ISSN 2644-3236 (online)

REVIEW

Role of artificial intelligence in the characterization of indeterminate pancreatic head mass and its usefulness in preoperative diagnosis

Palash Rawlani, Nalini Kanta Ghosh, Ashok Kumar

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C, C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Cabezuelo AS, Spain

Received: July 27, 2023
Peer-review started: July 27, 2023
First decision: August 31, 2023
Revised: September 11, 2023
Accepted: October 8, 2023
Article in press: October 8, 2023
Published online: December 8, 2023

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Abstract

Artificial intelligence (AI) has been used in various fields of day-to-day life and its role in medicine is immense. Understanding of oncology has been improved with the introduction of AI which helps in diagnosis, treatment planning, management, prognosis, and follow-up. It also helps to identify high-risk groups who can be subjected to timely screening for early detection of malignant conditions. It is more important in pancreatic cancer as it is one of the major causes of cancer-related deaths worldwide and there are no specific early features (clinical and radiological) for diagnosis. With improvement in imaging modalities (computed tomography, magnetic resonance imaging, endoscopic ultrasound), most often clinicians were being challenged with lesions that were difficult to diagnose with human competence. AI has been used in various other branches of medicine to differentiate such indeterminate lesions including the thyroid gland, breast, lungs, liver, adrenal gland, kidney, *etc.* In the case of pancreatic cancer, the role of AI has been explored and is still ongoing. This review article will focus on how AI can be used to diagnose pancreatic cancer early or differentiate it from benign pancreatic lesions, therefore, management can be planned at an earlier stage.

Key Words: Artificial intelligence; Indeterminate pancreatic lesion; Imaging; Biomarkers; Diagnosis

Core Tip: Surgical management of a pancreatic head lesion usually requires pancreaticoduodenectomy, which is associated with significant morbidity and mortality. For a benign lesion it is unacceptable. The investigation modalities *i.e.* computed tomography, magnetic resonance imaging, endoscopic ultrasound, positron emission tomography, and biochemical markers are available today to distinguish benign from malignant lesions and have their limitations (human judgmental errors). The application of artificial intelligence (AI) algorithms can minimize human errors and improve the sensitivity and specificity of diagnostic yield. The AI can help with great precision in differentiating benign from malignant lesions, affecting the management strategy and minimizing post-operative complications.

Citation: Rawlani P, Ghosh NK, Kumar A. Role of artificial intelligence in the characterization of indeterminate pancreatic head mass and its usefulness in preoperative diagnosis. *Artif Intell Gastroenterol* 2023; 4(3): 48-63
URL: https://www.wjgnet.com/2644-3236/full/v4/i3/48.htm
DOI: https://dx.doi.org/10.35712/aig.v4.i3.48

INTRODUCTION

The concept of a machine that can think like a human being was proposed by Mr. Alan Turing in the year 1950 in his book entitled “Computing Machinery and Intelligence” and later, the term “artificial intelligence (AI)” was coined by John McCarthy[1,2]. The applicability of AI ranges from simple tasks to more complex tasks mimicking a human brain. There are six major sub-fields of AI: machine learning (ML), neural network, deep learning (DL), natural language processing (NLP), cognitive computing, and computer vision. ML can learn from data, recognize typical patterns, and make decisions with little or no human interference. A neural network is the field of AI that is inspired by the human brain, where a set of algorithms is used to derive a correlation. Most of the AI models in the medical field use ML and neural networks. NLP is a method where textual data has been used to search, analyze, and comprehend complex information. Computer vision understands visual inputs (radiological or pathological images, surgical videos) and derives desired information. There are many modifications of conventional sub-fields of AI which have been in use. The twentieth century has seen that AI has become an essential part of day-to-day life, including health tracking devices[3], automobiles[4], banking and finances (robo-traders)[5], surveillance, social media, entertainment, education, space exploration, and disaster management, *etc*[6,7].

AI has been used in various fields of medicine including online appointments and hospital check-ins, medical records digitalization, follow-up, drug dosage reminders, adverse effect warnings, *etc.* Moreover, its application in the field of oncology is paramount. AI can be useful in cancer detection, screening, diagnosis, classification, prognostication, new drug discovery, *etc*[8-11]. It has played its role in differentiating various indeterminate lesions in the thyroid gland[12,13], breast[14], lungs[15,16], liver[17], adrenal[18,19], kidneys[20], and indeterminate biliary strictures[21] (Table 1). Various authors have studied the role of AI algorithms to identify pancreatic lesions from imaging modalities computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasonography (EUS), positron emission tomography (PET) scan, *etc* and thus can differentiate malignant indeterminate pancreatic lesions (IPLs) from benign ones for better management at an early stage.

IPLs are those detected by imaging techniques performed for non-specific abdominal complaints or detected incidentally, otherwise known as pancreatic incidentaloma. With the increase in imaging modalities, the detection of such IPLs has increased[22]. These incidentalomas are mostly detected in other organs, *i.e.* the thyroid gland, pituitary gland, kidney, lungs, adrenal gland, *etc*. Though, the incidence of indeterminate lesions is less in the pancreas, however, most of them are malignant compared to other sites[23]. Identification of such lesions creates confusion in clinicians and anxiety among the patients. Moreover, early diagnosis of malignancy can provide reasonably early management and better overall outcomes. Therefore, it is necessary to diagnose such lesions for better patient management.

The overall prevalence of such lesions was reported to be 0.01%–0.6% in 2009, which may be less compared to its true incidence[24]. A review of a series of pancreatic resections shows an asymptomatic neoplastic lesion to be 6%-23% (24% to 50% of them are malignant, and 24% to 47% are considered potentially malignant or pre-malignant)[25,26]. A recently published Leopard-2 trial comparing laparoscopic and open pancreaticoduodenectomy has shown the incidence of benign or pre-malignant lesions to be 12%[27]. Frequently, cystic lesions of the pancreas are detected on MRI and their incidence is up to 20%[28] and recent series shows the incidence to be 49% in the general population[29]. The majority of cystic lesions are benign, however, approximately, 3% are malignant or potentially malignant[30].

The etiology of such lesions is diverse, benign adenoma to adenocarcinoma, borderline malignant tumors, mesenchymal tumors, neuroendocrine tumors, cysts, congenital changes, metastatic lesions, inflammatory masses *etc*[23]. These lesions may be broadly divided into benign, pre-malignant, or malignant lesions[24]. Figure 1 shows different pathologies of IPLs[31].

There is a considerable overlap of imaging features of different benign and malignant pancreatic lesions. Cystic degeneration of solid tumors may masquerade as cystic lesions. Various modalities (ultrasonography, contrast-enhanced CT, MRI, EUS, PET, cytopathology, histopathology, and tumor markers) have been used to differentiate the possible etiology, however, there are limitations of each modality intrinsic to the investigation itself or on the operator. Recently, AI has been used to distinguish various indeterminate lesions in the breast, lungs, adrenal gland, kidney, *etc.* Thus, the use of AI in association with conventional imaging or diagnostic modalities can improve their overall diagnostic yield

Table 1 Studies on differentiation of indeterminate lesions using artificial intelligence

No.	Ref.	Number of patients	Organ of interest	Sub-type of AI	Outcome
1	Ippolito *et al*[12], 2004	453	Thyroid nodule (benign *vs* malignant)	ANN	Refinement of risk stratification of FNAB and clinical data
2	Daniels *et al*[13], 2020	121	Indeterminant thyroid nodule	ML	ML and ultrasonography can identify genetically high risk lesions
3	Becker *et al*[14], 2018	632	Breast lesion (benign *vs* malignant)	Generic DLS	Aids diagnosing cancer on breast ultrasound images with an accuracy comparable to radiologists
4	Scott *et al*[15], 2019	125	Lung GGO (benign *vs* malignant)	ANN	Improve diagnostic ability using CT scan, PET, and clinical data
5	Guo *et al*[16], 2022	20	Indeterminant small lung lesions	DNN	DNN based method may detect small lesions < 10 mm at an effective radiation dose < 0.1 mSv.
6	Yasaka *et al*[17], 2018	460	Liver mass (HCC *vs* others)	CNN	High diagnostic performance in differentiation of liver masses using dynamic CT
7	Moawad *et al*[18], 2021	40	Adrenal incidentaloma (benign *vs* malignant)	ML	Machine learning and CT texture analysis can differentiate between benign and malignant indeterminate adrenal tumors
8	Stanzione *et al* [19], 2021	55	Indeterminant solid adrenal lesions	ML	MRI handcrafted radiomics and ML can be used to different adrenal incidentalomas
9	Massa'a *et al*[20], 2022	160	Indeterminant solid renal mass (benign *vs* malignant)	ML	MRI-based radiomics and ML can be useful in differentiation
10	Saraiva *et al*[21], 2022	85	Indeterminant biliary strictures	CNN	CNN can accurately differentiate benign strictures from malignant ones

AI: Artificial intelligence; ANN: Artificial neural network; CNN: Convolutional neural network; CT: Computed tomography; DNN: Deep neural network; DLS: Deep learning software; FNAB: Fine needle aspiration biopsy; GGO: Ground glass opacities; HCC: Hepatocellular carcinoma; ML: Machine learning; MRI: Magnetic resonance imaging.

and therefore, more precise diagnosis and patient care.

This paper reviews the current status of AI in the differentiation of various IPLs and its future implications.

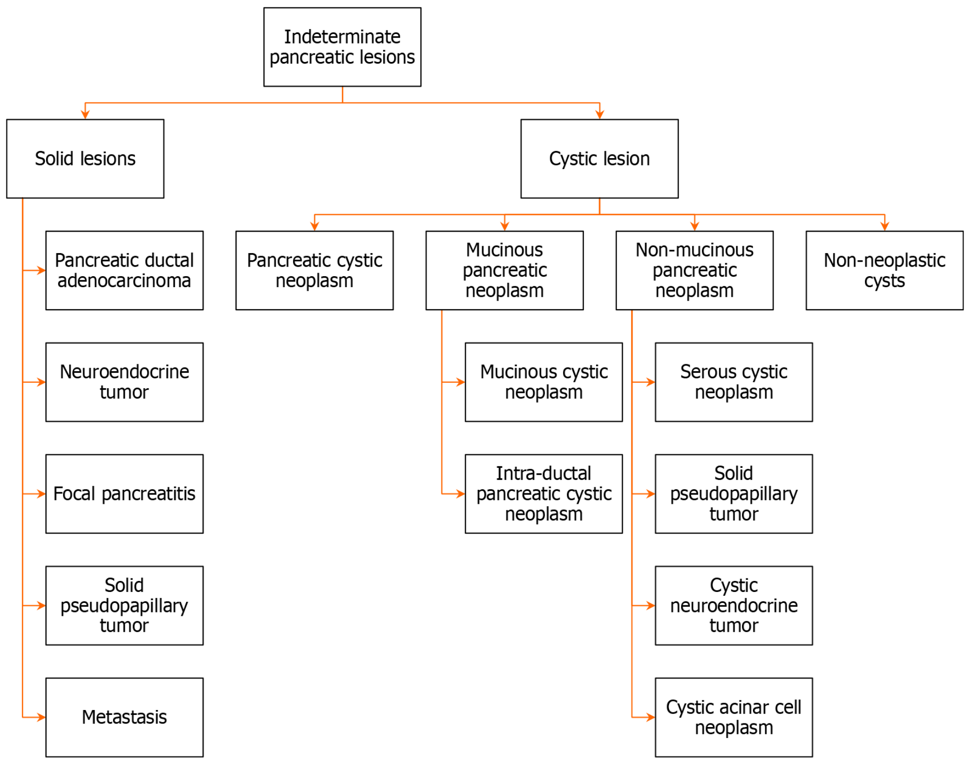
METHODS AND LITERATURE SEARCH

All the relevant articles were searched from PubMed and Google Scholar using the keywords, *i.e.* “artificial intelligence” AND “pancreatic lesions” OR “cystic lesions”, OR “CT”, OR “MRI”, OR “EUS”, OR “PET” OR “pathology”, OR “biomarkers” between 2005 and 2023, and only full articles were studied. Articles discussing the differentiation of different types of pancreatic lesions were included and screened by all authors. Abstracts and conference presentations were excluded. Studies discussing the differentiation of any pancreatic lesion (benign *vs.* malignant) were included in relevant sections for discussion. The study flow chart is shown in Figure 2.

Role of clinical parameters and AI on the identification of IPLs

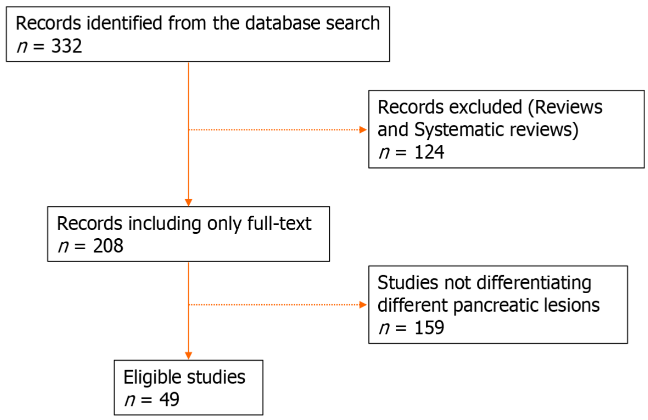
Pancreatic cancer is one of the leading causes of cancer-related death worldwide, thus early diagnosis is crucial for better management. Often, patients are asymptomatic to start with, so presentation is delayed leading to advanced disease at diagnosis. This delay in diagnosis can be minimized by the identification of high-risk groups and the introduction of targeted screening of high-risk populations. Any lesion identified in these patient groups can be subjected to further evaluation using an AI augmented imaging system (CT, MRI, PET, EUS), which will be discussed later. The proposed schema of patient evaluation and management is presented in Figure 3.

Several clinical parameters can be used to predict the future incidence of pancreatic cancer including, symptoms, hereditary factors (BRCA1, BRCA2, PALB2, Hereditary pancreatitis, and Peutz-Jeghers Syndrome), pre-existing clinical conditions (new-onset diabetes mellitus), lifestyle (smoking, alcohol, obesity, nutrient-poor diet), and demographic factors. Elevation of CA 19-9, CEA, and recently developed CEMIP (cell migration-inducing hyaluronan binding protein) can be considered as an early indicator of pancreatic cancer[32-34]. None of these parameters can confirm pancreatic cancer, however, a combined assessment can suggest a possible pancreatic cancer leading to screening of high-risk populations. In a retrospective study from Kaiser Permanente Southern California, an algorithm for risk stratification for pancreatic cancer was generated using imaging (CT/magnetic resonance) and clinical factors[35]. In this study, imaging features used were pancreatic duct dilatation as a predictor of malignancy and other features such as atrophy, calcification, pancreatic cyst, and irregular pancreatic duct. Multi-state prediction model showed a discriminatory index (c-index: 0.825–0.833) between normal individuals and individuals with pancreatic cancer. A study at the Biomedical



DOI: 10.35712/aig.v4.i3.48

Figure 1 Pathology of different indeterminate pancreatic lesions.



DOI: 10.35712/aig.v4.i3.48

Figure 2 Study flow chart.

Imaging Research Institute of Cedars Sinai Medical Center, Los Angeles used ML and CT-based radiomic features as an indicator of pancreatic ductal adenocarcinoma (PDAC)[36]. The scans were obtained in non-pancreatic cancer patients for different purposes, who later developed pancreatic cancer after 6 mo to 3 years. The AI model had an accuracy of 86% in the prediction of PDAC. As CT scans were performed frequently for different purposes, such AI models can identify patients having potential risk for future pancreatic malignancy.

Muhammad *et al*[37], Placido *et al*[38], and Chen *et al*[39] used demographic and clinical parameters with artificial neural networks (ANNs) algorithms to predict pancreatic cancer. In the validation arm, the area under the curve (AUC) was 0.85, and the sensitivity and specificity of diagnosis were 80.7%. Malhotra *et al*[40] used ML principles to identify symptoms to predict pancreatic cancer. Their algorithm could detect 41.3% of patients with pancreatic cancer < 60 years of age, 20 mo earlier than diagnosis (AUC: 0.66), and 43.2% of patients with pancreatic cancer > 60 years of age, 17 mo earlier than diagnosis (AUC: 0.61). Appelbaum *et al*[41] used neural network algorithms to identify high-risk groups 1 year in advance. Thus, these AI techniques not only help to detect pancreatic cancer but also, earlier than conventional imaging.

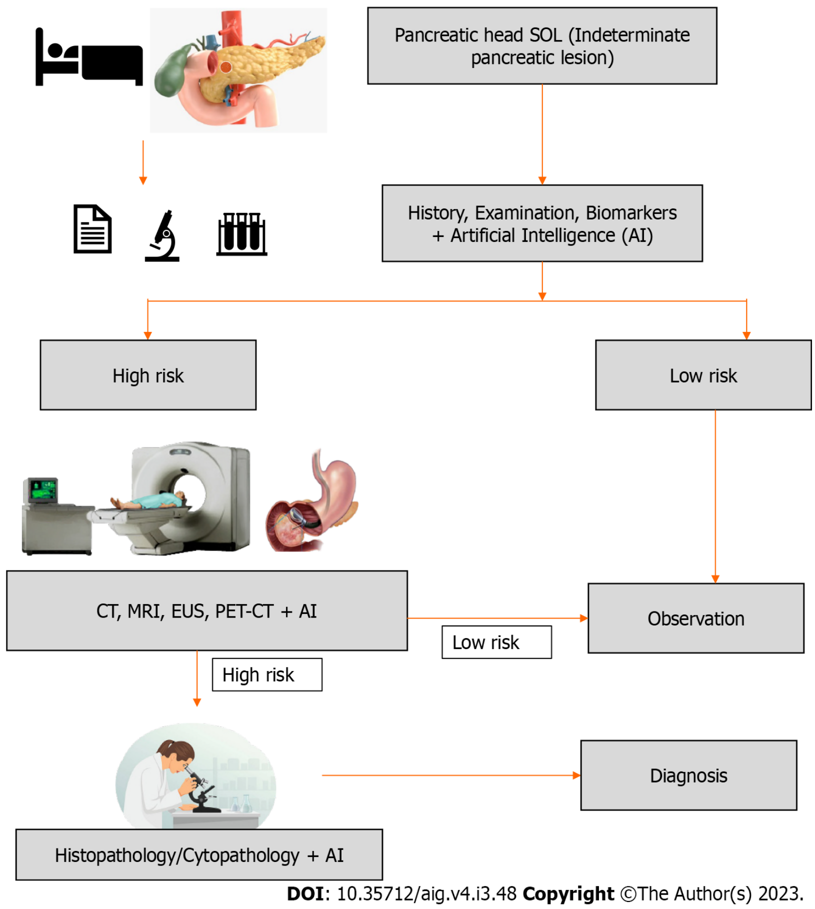


Figure 3 Schematic presentation of diagnosis of indeterminate pancreatic lesion using artificial intelligence. AI: Artificial intelligence; CT: Computed tomography; EUS: Endoscopic ultrasonography; MRI: Magnetic resonance imaging; PET: Positron emission tomography; SOL: Space occupying lesion.

Role of AI on CT scan imaging on detection of pancreatic lesions

If a mass lesion is detected in the pancreas, the possibility of neoplasm is kept as a differential diagnosis. The most common (85%–95%) among the lesions is pancreatic ductal adenocarcinoma (PDAC) and it has a poor prognosis[42,43]. Ill-defined hypovascular mass is the characteristic of PDAC in contrast-enhanced imaging[44]. Atypical imaging of a solid mass may harbor a malignancy, however, its mimic, an inflammatory mass, can have a better prognosis than PDAC, and management of both these conditions is different.

Among all the imaging modalities, CT is most commonly favored for the investigation of a pancreatic lesion, as it is widely available, quick to acquire, has a high spatial resolution, assesses relationship to vascular structures, and determines surgical planning. Recent advances in CT imaging in the form of multiplanar reformatted images, and three-dimensional (3D) techniques have improved sensitivity by up to 96% in tumor identification[45,46]. However, small tumors or tumors with atypical features may not be visible on CT scans or subtle changes may not be appreciable to the human eye and prone to errors. These limitations of conventional CT imaging can be overcome by the use of AI algorithms.

Differentiation of PDAC

Among all malignancies, PDAC has the worst overall survival[47]. It is because patients present late at an advanced stage due to late detection of asymptomatic subtle pancreatic lesions on imaging[40]. Zhu *et al*[48] and Liu *et al*[49] have used DL to detect pancreatic cancer and in the study by Liu *et al*[49], malignancy could be detected in just 3 s with an AUC of 0.96. Chu *et al*[50] could diagnose PDAC with an AUC of 99.9% using ML algorithms.

Differentiation of cystic lesions

With the increase in the frequency of cross-sectional imaging, the detection of cystic lesions of the pancreas has increased and it is aptly called “technopathies”. Management of these cystic lesions requires classification of the type of lesion and the risk of malignancy which is sub-optimal with present imaging modalities[51,52]. AI has been used to differentiate the types of cystic lesions into, intraductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasm (MCN), serous cystic neoplasia (SCN), solid pseudopapillary neoplasia, *etc*[53,54]. Dmitriev *et al*[53] used the convolutional neural network (CNN) model (contrast-enhanced CT and clinical data) to differentiate the types of cystic lesions with an accuracy of 84% which is better than radiologists which has an accuracy of less than 70%[53,55]. However, Li *et al*[54] used only CT images and AI (DL) to differentiate the cystic lesions with an accuracy of 73% compared to radiologists in their study which had an accuracy of only 48%. Differentiation of SCN from other cystic lesions is important as they have a rare chance of being malignant, thus, Wei *et al*[56] used an ML-based algorithm to distinguish SCN from others based on CT images. Yang *et al*[57] and Chen *et al*[58] have used AI algorithms to distinguish SCN from MCN. Chakraborty *et al*[59] and Polk *et al*[60] used the RF model to differentiate low-grade IPMN from high-grade IPMN which has management implications. Table 2 summarizes studies on the uses of AI along with CT images in the differentiation of pancreatic lesions.

Role of AI on MRI on the detection of pancreatic lesions

MRI is favored over CT scan due to superior soft tissue delineation and it also helps to detect small lesions, assessment of the vascular relationship, and relationship to the pancreatic duct, lymph node, or distant metastasis[43,61]. Detection of iso-attenuating pancreatic lesions on CT scan is challenging which is observed in approximately 10% of patients. In these situations, indirect evidence of malignancy is used for diagnosis, *i.e.* convex pancreatic contour, double duct sign, vascular involvement, mass effect, *etc*[42]. However, MRI can be helpful to diagnose such lesions. Recently, the use of AI algorithms has improved the diagnostic ability of MRI. Li *et al*[62] and Chen *et al*[63] used AI algorithms for the identification of PDAC on different phases of MRI (Table 3).

Management of cystic lesions depends upon the precise characterization, which indicates its clinical behavior[64]. However, overlapping imaging features make differentiation challenging[64]. The role of imaging is to differentiate benign from malignant cystic neoplasms. MRI uses T2 images to identify ductal communication and post-contrast images to characterize the lesion. It is limited in the detection of calcifications which is better appreciated on a CT image. MRI can differentiate benign from malignant lesions with an accuracy of 73% to 81% compared to a CT scan which has an accuracy of 75% to 78%[52,65,66].

The use of AI has enabled MRI to detect high-grade dysplasia or malignancy in IPMN with a sensitivity and specificity of 75% and 78%, respectively[67]. Corral *et al*[67] used 3D CNN to classify IPMN into different types with an accuracy of 58%. Interestingly, Cheng *et al*[68] compared radiomics features of CT and MRI using AL algorithms [LASSO, LR, support vector machine (SVM)] and found out that, the MRI-based model(AUC: 0.940) had better diagnostic ability than the CT based model(AUC: 0.864). Studies on the use of AI with MRI to detect the type of cystic or solid pancreatic lesions are presented in Table 3.

Role of AI on EUS in the detection of pancreatic lesions

EUS uses a high-frequency transducer at the tip of an endoscope. It helps to obtain high-resolution images of the pancreas through the esophagus, stomach, or duodenum. Various modalities of EUS including contrast-enhanced EUS, EUS-guided fine needle aspiration (FNA), and EUS elastography have been used for the evaluation of pancreatic cancer, detection of small lesions, differentiation of solid from cystic tumors, and assessment of resectability[69]. Most importantly, it helps to obtain tissue for cytopathology or histopathology[70,71]. The main drawback is operator dependency, which may reduce the diagnostic yield[72,73]. AI algorithms have been used in association with EUS to detect pancreatic cancers and to differentiate from other lesions (Table 4). Mass-forming chronic pancreatitis may masquerade as pancreatic malignancy, EUS based AI algorithms can be used to distinguish pancreatic cancer from chronic pancreatitis.

Authors have used ML algorithms to differentiate normal pancreatic tissue from PDAC with more than 93% accuracy [74-76]. Two studies have used AI to distinguish chronic pancreatitis from PDAC on EUS images with an accuracy of more than 80%[77,78]. Săftoiu *et al*[79] demonstrated better diagnostic ability of contrast-enhanced EUS (94.6% and a specificity of 94.4%) compared to EUS-FNA (87.5% and 92.7%) in differentiating CP from PDAC using AI.

Recently, EUS elastography has been used to diagnose focal pancreatic lesions. Using ANN, it can differentiate benign from malignant lesions with an accuracy of 95%[80]. In another multicenter prospective study using ANN, they demonstrated that EUS elastography (sensitivity (87.6%) and specificity (82.9%)) had better diagnostic ability than two experienced endoscopists combined (sensitivity 80.0%, specificity 50.0%)[81]. Udriştoiu *et al*[82] used ML principles to distinguish focal pancreatitis from pancreatic mass (neuroendocrine tumor or PDAC) with an accuracy of 98.26%. Differentiation of benign IPMN from malignant IPMN has management implications, Kuwahara *et al*[83] studied to detect malignant IPMN using CNN (ResNet-50).

Role of AI on PET imaging on the detection of pancreatic lesions

PET is a functional imaging technique used for staging malignant lesions and is based on the physiological characteristics of tumor cells[84,85]. However, inflammation may mimic a malignant lesion due to high metabolic activity giving rise to false positive results, conversely, in patients with hyperglycemia, it can give a false negative result[86,87]. PET CT is also useful in the assessment of tumor response to therapy[43]. Li *et al*[88] used a hybrid feedback-SVM-random forest model to detect pancreatic cancer from a normal pancreas with an accuracy of 96.47%. Liu *et al*[89] studied the role of dual time PET/CT and SVM model to differentiate PDAC from AIP with an AUC of 0.96 similarly, Xing *et al*[90] showed a diagnostic performance of 0.93 of AUC.

Role of AI in pathological examination on detection of pancreatic lesions

Often, imaging cannot achieve an accurate diagnosis, requiring a tissue diagnosis-cytology or histology[91,92]. AI can be applied to hematoxylin-eosin-stained slides for the detection of pancreatic cancer[93]. Song *et al*[94] used AI algorithms to segment epithelial cell nuclei on slide images and extract morphological features and could differentiate SCN from MCN and grading of PDAC[95]. The CNN was used by Kriegsmann *et al*[96] to localize pancreatic intra-epithelial neoplasm or PDAC in a slide. Niazi *et al*[97] used DL to detect neuroendocrine tumors from normal tissues on Ki-67 stained biopsy

Table 2 Studies on differentiation of indeterminate lesions using artificial intelligence algorithms on computed tomography images

No.	Ref.	Number of patients	Primary objective	Sub-type of AI used	Outcome
1	Qureshi *et al*[36], 2022	108	Identification of PDAC	ML	Accuracy: 86%
2	Ebrahimian *et al*[121], 2022	103	Differentiation of benign *vs* malignant pancreatic lesions	RF	AUC: 0.94
3	Chakraborty *et al*[59], 2018	103	High risk *vs* low risk IPMN	RF, SVM	AUC: 0.81
4	Polk *et al*[60], 2020	29	High risk *vs* low risk IPMN	LR	AUC: 0.90
5	Ikeda *et al*[122], 1997	71	PDAC *vs* pancreatitis	NN	AUC: 0.916
6	Chen *et al*[58], 2021	100	SCN *vs* MCN	LASSO and RFE_Linear SVC	AUC: 0.932
7	Yang *et al*[57], 2019	53	SCN *vs* MCN	LASSO	AUC: 0.66
8	Yang *et al*[123], 2022	63	SCN *vs* MCN	MMRF-ResNet	AUC: 0.98
9	Ren *et al*[124], 2020	112	PDAC *vs* pancreatic adenosquamous carcinoma	RF	AUC: 0.98
10	Xie *et al*[125], 2021	226	MCN *vs* ASCN	RF	AUC: 0.734
11	Ziegelmayer *et al*[126], 2020	86	AIP *vs* PDAC	CNN, ML	AUC: 0.90
12	Li *et al*[62], 2022	97	Focal-type AIP *vs* PDAC	LASSO regression	AUC: 0.97
13	Gao *et al*[127], 2021	170	MCN *vs* SCN	mRMR + LASSO	AUC: 0.91
14	Dmitriev *et al*[53], 2017	134	Classification of pancreatic cyst	RF, CNN	Accuracy: 83.6%
15	Li *et al*[54], 2019	206	Classification of pancreatic cysts	DNN (Dense-Net)	Accuracy: 72.8%
16	Wei *et al*[56], 2019	260	SCN *vs* other cystic neoplasms	ML	AUC: 0.767

AI: Artificial intelligence; AIP: Autoimmune pancreatitis; ASCN: Atypical serous cystic neoplasm; AUC: Area under the curve; CNN: Convolutional neural network; DNN; Deep neural network; IPMN: Intraductal papillary mucinous neoplasm; LASSO: Least absolute shrinkage and selection operator; LR: Logistic regression; MCN: Mucinous cystic neoplasm; ML: Machine learning; PDAC: Pancreatic ductal adenocarcinoma; RFE: Recursive feature elimination; RF: Random forest; SCN: Serous cystic neoplasm; SVM: Support vector machine; NN: Neural network; mRMR: Minimum redundancy maximum relevance; SVC: Support vector classifier; MMRF: Multi-channel-multiclassifier-random forest.

Table 3 Studies on differentiation of indeterminate lesions using artificial intelligence algorithms on magnetic resonance images

No.	Ref.	Number of patients	Primary objective	Sub-type of AI used	Outcome
1	Li *et al*[62], 2022	267	PDAC detection	UDA + meta learning + GCN	DSC (62.08%, T1), (61.35%, T2), (61.88%, DWI), (60.43%, AP)
2	Chen *et al*[63], 2022	73	PDAC detection	Spiral-ResUNet	DSC: 65.60%, Jaccard index: 49.64%
3	Liang Y *et al*[128], 2020	56	PDAC detection	CNN	DSC: 71%
5	Cui *et al*[129], 2021	202	Grading-BD IPMN	LASSO	AUC: 0.903
6	Corral *et al*[67], 2019	139	Classification of IPMN	CNN	AUC: 0.783
7	Cheng *et al*[68], 2022	60	Malignant IPMN	LR, SVM	MRI + SVM: AUC: 0.940, CT + SVM: AUC: 0.864
8	Hussein *et al*[130], 2019	171	Classification of IPMN	SVM, RF, 3D, CNN	Accuracy 84.22%

AI: Artificial intelligence; AP: Arterial phase; AUC: Area under the curve; CT: Computed tomography; CNN: Convoluted neural network; DSC: Dice similarity coefficient; DWI: Diffusion weighted image; GCN: Graph convolutional network; IPMN: Intraductal papillary mucinous neoplasm; LASSO: Least absolute shrinkage and selection operator; LR: Logistic regression; MRI: Magnetic resonance and imaging; PDAC: Pancreatic ductal adenocarcinoma; RF: Random forest; SVM: Support vector machine; UDA: Unsupervised data augmentation.

Table 4 Studies on differentiation of indeterminate lesions using artificial intelligence algorithms on endoscopic ultrasonography images

No.	Ref.	Number of patients	Primary outcome	Sub type of AI used	Outcome
1	Zhu *et al*[78], 2013	262	PDAC *vs* CP	SVM	Accuracy: 94.2%
2	Zhu *et al*[131], 2015	100	AIP *vs* CP	SVM	Accuracy: 89.3%
3	Zhang *et al*[74], 2010	216	Normal pancreas *vs* PDAC	SVM	Accuracy: 97.98%
4	Ozkan *et al*[76], 2016	332	Recognition of pancreatic cancer amongst various age group	ANN	Accuracy: Average: 87.5% (all ages), Min: 88.46% (40-60 yr), Max: 92% (< 40 yr)
5	Kuwahara *et al*[83], 2019	50	Benign *vs* malignant IPMN	CNN	Accuracy: 94%
6	Das *et al*[75], 2008	56	PDAC *vs* normal pancreas *vs* CP	ANN	AUC: 0.93
7	Săftoiu *et al*[80], 2008	68	Benign *vs* malignant pancreatic lesion	ANN	Accuracy: 89.7%
8	Tonozuka *et al*[132], 2021	139	PDAC *vs* CP	CNN	AUC: 0.94
9	Marya *et al*[133], 2021	583	PDAC *vs* benign causes of pancreatic SOL	CNN	AUC: 0.976
10.	Xu *et al*[134], 2013	Systemic Analysis of 6 studies	Benign *vs* malignant pancreatic lesion	-	AUC: 0.962

AI: Artificial intelligence; AIP: Autoimmune pancreatitis; ANN: Artificial neural network; CNN: Convoluted neural network; CP: Chronic pancreatitis; IPMN: Intraductal papillary mucinous neoplasm; PDAC: Pancreatic ductal adenocarcinoma; SOL: Space occupying lesion; SVM: Support vector machine.

images with a 97.8% sensitivity and 88.8% specificity. Momeni-Boroujeni *et al*[98] could differentiate benign from malignant pathology using a K-means clustering algorithm from FNA-based slides with an accuracy of 100%. Naito e*t al* [99] used CNN in FNB-based slides to assess PDAC with an AUC of 0.984. Cyst fluid analysis is an essential part of the diagnosis of pancreatic cystic lesions. Kurita *et al*[100] used a neural network to differentiate benign from malignant cysts taking into consideration biomarkers in cyst fluid, cytology and clinical parameters.

Role of AI in biomarkers on detection of pancreatic lesions

Biomarkers act as an adjunct in diagnosis, prognosis, and screening for recurrence and they can be used for early diagnosis of tumors. However, in the case of pancreatic cancer, it lacks sensitivity and specificity for routine clinical practice[91,101,102]. Liquid biopsy is one of the recent developments in oncology, developed with the intent of detecting tumor cells from blood when biopsy cannot be obtained, or to assess tumor response to therapy (surgery or chemoradio-therapy) and assess genetic mutation. It includes three types of sampling of biological materials; which are circulating tumor cells (CTCs), circulating tumor DNA, and exosomes. CTCs have faced difficulties for years because of very low concentrations in many studies, which is 1–10 cells per 10-mL of blood (much lower than billions of hematopoietic cells) and short half-life (approximately from 1 to 2.4 h) in blood which poses difficulty in further study. AI can be used in the detection of disease from these biomarkers and various studies have explored AI algorithms for biomarkers for diagnosis [91,103]. Studies used exosomes[104-106], cell-free DNA[107], extracellular vesicles long RNA[108], proteins[109-112], and circulating microRNA[113] in association with AI for diagnosis of pancreatic cancer. Table 5 shows studies on the role of biomarkers and AI in the differentiation of pancreatic lesions.

This review has shown that AI can be used in routine investigation modalities (CT, MRI, EUS, PET, biomarkers) to improve diagnostic and differentiating potential; however, it is still in progress. In the beginning, studies have trained and validated AI algorithms, in the future it is a challenge to implement such studies at different geographical locations, ethnicity, genetic makeup, *etc*. The majority of studies have explored the potential to differentiate, chronic pancreatitis from pancreatic ductal adenocarcinoma, SCN from MCN, and high-risk *vs*. low-risk IPMN, however, there can be other differential diagnoses in a clinical scenario.

DISCUSSION

Surgery for malignant pancreatic head lesions was standardized by Whipple *et al*[114] which is acceptable worldwide. It includes a complex single-stage procedure of pancreaticoduodenectomy, which is associated with morbidity (25%) and mortality (0%-9.3%) even in high-volume centers[115-117]. Professor Whipple[118] reported a mortality of 29.2% in his series of patients who underwent pancreaticoduodenectomy. Though, recent series have reported reduced mortality following pancreaticoduodenectomy, morbidity of the procedure continues to be high. Recently, many modifications have been made to reduce morbidity, however, none of the measures appeared to be successful. Are *et al*[119] reported a

Table 5 Studies on differentiation of indeterminate lesions using artificial intelligence algorithms on different biomarkers

No.	Ref.	Number of samples	Type of biomarker used	Sub-type of AI used	Conclusion
1	Chen *et al*[104], 2019	28	Exosomes	LDA	Accuracy: 100%
2	Zheng *et al*[105], 2022	220	Exosomes	ANN	AUC: 0.86
3	Ko *et al*[106], 2017	28	Exosomes	LDA	Accuracy: 100%
4	Cristiano *et al*[107], 2019	34	Cell-free DNA	GBM	AUC: 0.86
5	Yu *et al*[108], 2020	501	extracellular vesicles long RNA	SVM	AUC: 0.96
6	Gao *et al*[109], 2012	199	Proteomes	SVM, KNN, ANN	AUC: 0.971
7	Yu *et al*[110], 2005	100	Proteomes	DT	Sensitivity: 88.9%, specificity: 74.1%
8	Qiao *et al*[112], 2022	136	Proteomes	CNN	Accuracy: 87.63%
9	Alizadeh *et al*[113], 2020	671	Circulating micro RNA	ANN	Accuracy: 0.86

AI: Artificial intelligence; ANN: Artificial neural network; CNN: Convoluted neural network; DT: Digital transformation; KNN: K-nearest neighbor; GBM: Gradient boosting machine; LDA: Linear discriminant analysis; SVM: Support vector machine.

historical perspective where 7 out of 37 pancreaticoduodenectomies performed by Prof Whipple AO turned out to be chronic pancreatitis (18.9%), where such a morbid procedure could have been avoided. Recent series have also supported these findings of incidence of benign pathology following pancreaticoduodenectomy in the range of 5%-10%[117,120]. Hence, there is an unmet need to differentiate benign pancreatic lesions from malignant ones. Multiple imaging modalities have been used to distinguish benign from malignant lesions, however, each investigation modality has its limitations which are compounded by human errors. The application of AI has minimized those errors and can make diagnoses earlier. Table 6 shows how AI increases the yield of different imaging modalities for predicting a malignant pancreatic head lesion. We have proposed an algorithm for the diagnosis of such entities. Whenever a patient presents to a clinician, history and clinical examination precede imaging. Hence, AI can be used to develop algorithms to predict malignancy[32-34]. In a patient with a high risk of pancreatic malignancy, a pancreatic indeterminate lesion should be investigated further with imaging or biopsy to rule out malignancy. Studies have reported the usefulness of biomarkers in the diagnosis of pancreatic cancer[107-110]. Hence, all non-invasive markers (clinical, biochemical) can be used to develop an algorithm that can predict pancreatic cancer before imaging has been performed and it can differentiate malignant pancreatic lesions. As shown in Table 6, AI has an added advantage over conventional imaging in differentiating pancreatic cancer from benign conditions. So, those high-risk patients marked on non-invasive pancreatic cancer detection models can be subjected to AI-enhanced imaging for better diagnosis. Further in line, to clarify the final tissue diagnosis, AI can help to detect subtle markers that can be ignored by human error. Therefore, AI can be used in every step of the diagnosis of an indeterminate pancreatic head mass, to detect malignant lesions early thus, availing proper oncological management.

Pancreatic incidentalomas or indeterminate lesions are on the rise due to the plethora of cross-sectional imaging performed to diagnose non-specific abdominal complaints. Though plenty of studies have been made in the fields of breast cancer, lung cancer, hepatocellular carcinoma, renal cell carcinoma, and adrenal tumors, there is a dearth of literature discussing how to differentiate benign pancreatic lesions from benign ones. The current literature included studies comparing individual pancreatic lesions, *i.e.* serous cystadenoma *vs.* mucinous cystadenoma, autoimmune pancreatitis *vs.* pancreatic adenocarcinoma, low-grade *vs.* high-grade IPMN, *etc*. However, a comprehensive review discussing how to differentiate various malignant pancreatic lesions (both cystic and solid) from benign lesions with the help of AI is lacking. Hence, in this review, we have discussed how to differentiate different pancreatic lesions encountered in day-to-day clinical practice using different algorithms of AI. We have discussed individually about different diagnostic modalities and different types of pancreatic lesions. There are more studies available in the field of radiological investigations and fewer studies available for the histopathological diagnosis or intra-operative differentiation of malignant from benign lesions. As the understanding of the usefulness of AI is increasing, these limitations can be curtailed in the near future.

FUTURE PERSPECTIVES

There is a surge in the number of medical imaging for different indications leading to the identification of many indeterminate pancreatic lesions (IPLs), which help to diagnose a disease earlier or can lead to a plethora of other investigations, psychological stress, clinical dilemmas, *etc*. Human judgment is prone to errors as subtle differences in these small or atypical lesions are challenging to discern leading to inter-observer and intra-observer variations which can be

Table 6 Studies demonstrating impact of artificial intelligence on increasing efficacy of diagnostic modalities

No.	Ref.	Objective	Modality	Sensitivity	Specificity	Accuracy
1	Corral *et al*[67], 2019	Differentiate cystic SOL of pancreas	Fukuoka guideline	62%	77	77.5%
			Deep learning	75%	78%	78.3%
2	Kuwahara *et al*[83], 2019	Detection of malignant IPMN	Human pre-operative diagnosis (Clinical + lab + imaging)	95.7%	22.2%	56%
			Artificial intelligence	95.7%	92.66	94%
3	Gao *et al*[135], 2020	Ability to differentiate pancreatic disease	CE-MR	NA	NA	83.93%
			GAN	NA	NA	76.79%
4	Rigiroli *et al*[136], 2021	Detection of pancreatic cancer and SMA involvement	CT scan	NA	NA	71%
			Artificial intelligence	62%	77%	54%
5	Chen *et al*[137], 2023	Detection of pancreatic cancer	CT scan	89.9%	95.9%	AUC: 0.96
			CNN	90%	93%	NA
6	Tang *et al*[138], 2023	Pancreatic mass diagnosis	EUS FNA	81.6%	100%	87.9%
			CE EUS Master-guided FNA	90.9%	100%	93.8%

CE-MR: Contrast enhanced-magnetic resonance; CT: Computed tomography; CNN: Convoluted neural network; EUS: Endoscopic ultrasound; FNA: Fine needle aspiration; GAN: Generative adversarial network; IPMN: Intraductal papillary mucinous neoplasm; NA: Not available; SMA: Superior mesenteric artery; SOL: Space occupying lesion.

minimized with the use of AI.

CONCLUSION

AI is an evolving technical advancement in the field of medicine and can play a significant role in differentiating IPLs into benign or malignant, by enhancing the diagnostic yield of conventional imaging (CT, MRI, PET), EUS, tissue diagnosis (cytopathology, histopathology), and biomarkers (liquid biopsy). An early and accurate diagnosis may lead to timely intervention, thereby improving the patient outcome. The current literature on this is still limited and sparse, therefore, more studies are required to reach a standard approach for the application of AI in IPLs.

FOOTNOTES

Author contributions: Kumar A designed the concept, corrected, and finalized the manuscript; Ghosh NK and Palash R wrote the manuscript and reviewed the literature; All authors have read and approved the final manuscript.

Conflict-of-interest statement: Dr. Kumar has nothing to disclose.

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S-Editor: Lin C
L-Editor: Filipodia
P-Editor: Zhao S

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Artificial Intelligence in Gastroenterology

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Artif Intell Gastroenterol 2023 December 8; 4(3): 64-71

DOI: 10.35712/aig.v4.i3.64

ISSN 2644-3236 (online)

SYSTEMATIC REVIEWS

Use of artificial intelligence in total mesorectal excision in rectal cancer surgery: State of the art and perspectives

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Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Ma X, China

Received: July 27, 2023
Peer-review started: July 27, 2023
First decision: August 31, 2023
Revised: September 13, 2023
Accepted: October 23, 2023
Article in press: October 23, 2023
Published online: December 8, 2023

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Abstract

BACKGROUND

Colorectal cancer is a major public health problem, with 1.9 million new cases and 953000 deaths worldwide in 2020. Total mesorectal excision (TME) is the standard of care for the treatment of rectal cancer and is crucial to prevent local recurrence, but it is a technically challenging surgery. The use of artificial intelligence (AI) could help improve the performance and safety of TME surgery.

AIM

To review the literature on the use of AI and machine learning in rectal surgery and potential future developments.

METHODS

Online scientific databases were searched for articles on the use of AI in rectal cancer surgery between 2020 and 2023.

RESULTS

The literature search yielded 876 results, and only 13 studies were selected for review. The use of AI in rectal cancer surgery and specifically in TME is a rapidly evolving field. There are a number of different AI algorithms that have been developed for use in TME, including algorithms for instrument detection, anatomical structure identification, and image-guided navigation systems.

CONCLUSION

AI has the potential to revolutionize TME surgery by providing real-time surgical guidance, preventing complications, and improving training. However, further research is needed to fully understand the benefits and risks of AI in TME surgery.

Key Words: Artificial intelligence; Machine learning; Rectal cancer; Total mesorectal excision; Colorectal surgery

Core Tip: This review provided an overview of the current use of artificial intelligence methods in surgery and the latest findings on their use during total mesorectal excision dissection in rectal cancer procedures. It also discussed the main limitations of artificial intelligence in surgery and that it is still not used in clinical settings.

Citation: Mosca V, Fuschillo G, Sciaudone G, Sahnan K, Selvaggi F, Pellino G. Use of artificial intelligence in total mesorectal excision in rectal cancer surgery: State of the art and perspectives. *Artif Intell Gastroenterol* 2023; 4(3): 64-71

URL: https://www.wjgnet.com/2644-3236/full/v4/i3/64.htm

DOI: https://dx.doi.org/10.35712/aig.v4.i3.64

INTRODUCTION

Colorectal cancer is a significant public health concern, with 1.9 million new cases and 953000 deaths worldwide in 2020. It is the third most common cancer and the second leading cause of cancer-related deaths globally, according to GLOBOCAN data[1]. Despite advances in non-surgical treatment of colorectal cancer, oncological radical surgical excision of the primary tumor and locoregional lymph nodes represents the predominant aspect of curative treatment. Total mesorectal excision (TME) is a surgical technique that has become the standard of care for the treatment of rectal cancer and involves the complete removal of the rectum and surrounding tissues, including the mesorectum, the fatty tissue that surrounds the rectum. The technique was first introduced in the 1980s and has since been shown to improve local control of the disease and reduce the risk of recurrence, leading to better long-term outcomes for patients[2]. This surgery requires skill and expertise to achieve both oncological radicality and preservation of the presacral nerves responsible for continence and sexual function.

Incomplete TME is directly linked to local tumor recurrence and decreased overall survival. Curtis *et al*[3] demonstrated that surgeons in the top skill quartile consistently achieved superior-quality histopathological TME specimens, resulting in improved patient outcomes. Many countries are considering centralizing rectal cancer treatment for this reason. The application of adjunctive measures such as artificial intelligence (AI) could aid surgeons in performing an adequate TME. The effect is likely to be more pronounced in surgeons who are still at the beginning of their learning curve but may also be useful to orientate more experienced surgeons in challenging cases, such as cases of recurrent rectal cancer and patients who have previously received neoadjuvant treatment.

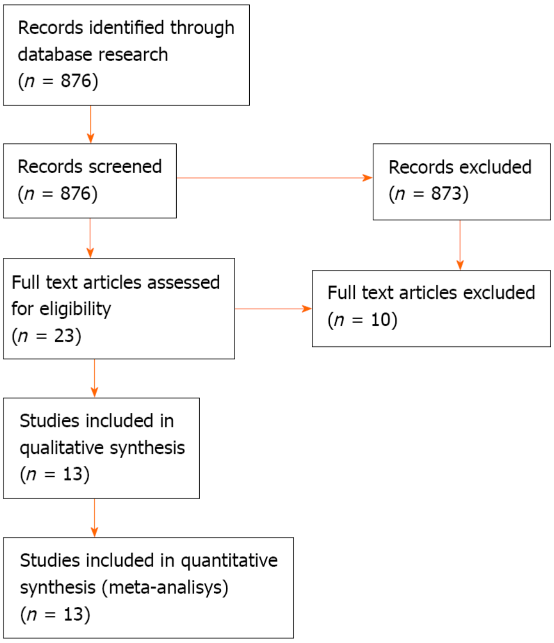
This review provided an overview of the current state of knowledge on the use of AI, specifically in the performance of a TME dissection, focusing on the scientific evidence that supports its use in the management of rectal cancer.

MATERIALS AND METHODS

A comprehensive literature search was conducted to identify relevant studies for this review. The search was performed using the PubMed electronic database, using the following search terms: “TME” OR “Total Mesorectal Excision” OR “Rectal Cancer Surgery” AND “Artificial Intelligence” OR “Machine Learning” OR “Deep Learning.” The search was limited to studies published between 2020 and 2023. Only articles published in English were included. Only studies addressing the use of AI in rectal cancer surgery and specifically in TME were selected.

RESULTS

The literature search yielded 876 results. Thirteen studies met our inclusion criteria. The selection flowchart is illustrated in Figure 1. In an initial screening, only the title and abstract of the papers were analyzed until we obtained 26 results. After reading the full text, only 13 studies were selected for review.



DOI: 10.35712/aig.v4.i3.64

Figure 1 Study selection flowchart.

Overview of AI in medicine

AI is a technology that today encompasses several approaches, such as machine learning (ML), a complex set of mathematical algorithms that allow computers to learn through experience[4], deep learning (DL), or computer vision (CV). The concept of ML is to identify patterns and optimize their parameters to better solve a specific problem by analyzing large-scale datasets[5]. ML has shown encouraging results in the analysis of data such as texts, images, and videos. DL is a subfield of ML that uses multilayer artificial neural networks to draw pattern-based conclusions from input data[6]. In medicine, a large amount of data is visualized in the form of images, and CV is another subfield of ML, which trains machines to extract valuable information from images (*e.g.*, radiological and histopathological) and videos (*e.g.*, endoscopic and surgical videos)[7].

Several groups have developed radiological image processing algorithms to enable faster diagnoses, improve the visualization of pathologies, and recognize emergency situations[8-12]. Recent examples include DL-based algorithms to achieve accurate carotid artery stenosis detection and plaque classification using computed tomography angiography [11], 3D convolutional neural networks to automate tumor volumes using positron emission tomography computed tomography and magnetic resonance images[12], automatic detection of lymph node metastases in colon and head-and-neck cancer[13,14], and DL models for automatic classification of thyroid biopsies based on microscope images taken with a smartphone[15].

AI in surgery

Surgical data science describes an emerging field of research concerned with the collection and analysis of surgical data [16]. The application of AI technology in surgery was first studied by Gunn[17] in 1976, when he explored the possibility of diagnosing acute abdominal pain using computer analysis. Over the last two decades, interest in the application of AI in general and in colorectal surgery has increased. AI methods have been applied in multiple areas of colorectal surgery, preoperatively, intraoperatively, and postoperatively[18]. Preoperatively, AI can help diagnose and clinically classify patients as accurately as possible and offer a personalized treatment plan. Postoperatively, it can integrate the pathway to better recovery after surgery, automate pathology assessment, and support research. All these elements contribute to improved patient outcomes and provide promising results.

Intraoperatively, it could help improve the surgeon’s skills during laparoscopic and robotic procedures. The development of AI-based systems could support anatomy detection and trigger alerts, providing surgical guidance on dangerous actions at crucial stages and improving surgeons’ decision-making. ML algorithms have been used to identify surgical instruments as they enter the surgical field and the identification of anatomical landmarks such as vascular and nervous structures and organs[19]. This is achieved using methods that first assess the presence and second analyze the movement pattern of surgical instruments and/or by automatic assessment of surgical phases[20]. In 2022, the work of Mascagni *et al*[21] developed a DL model that automatically segments the hepatocystic triangle and automatically determines compliance with the critical view of safety criteria during laparoscopic cholecystectomy, with the aim of reducing bile duct injuries.

Although this is an evolving field, it is important to point out that AI-based assistance during surgery is still at an embryonic stage, and its developments, such as video segmentation and automatic detection of instruments, have so far shown little benefit, as no AI algorithm has yet been approved for clinical use.

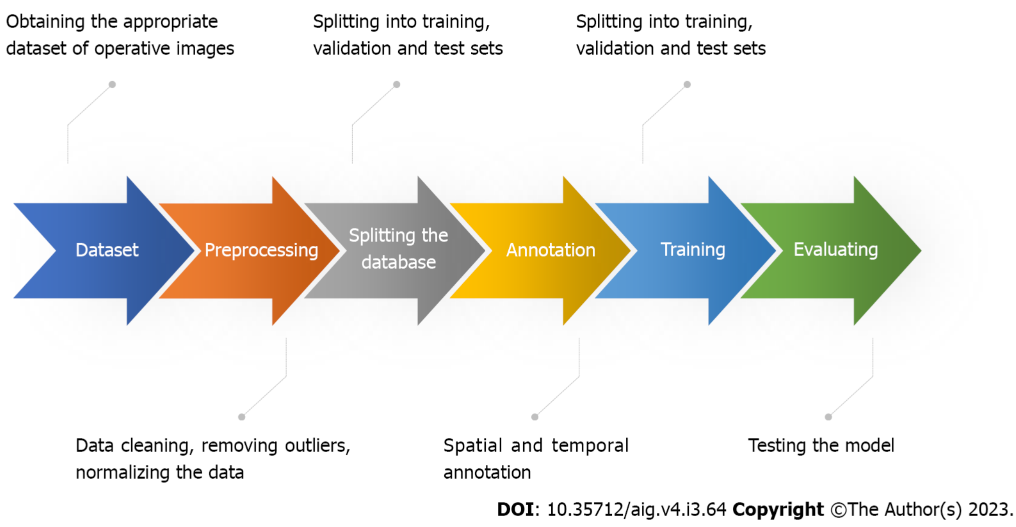


Figure 2 Machine learning pipeline.

AI in surgery focuses on training neural networks. This process starts with splitting the data into two main parts: the training data and the test data. The training data is a predetermined part of the overall data from which the network learns most of its information. The test data is used to see how well the network can apply what it has learned to new, unseen data. The neural network is then fine-tuned through a validation dataset, evaluating various hyperparameters so that the network can estimate the spectrum of data that it may receive.

The DL task can be divided into three categories depending on the type of output expected from the network: (1) Classification. The task of categorizing a given input into two or more possible classes. For example, a classification model could be used to identify the type of tissue in a medical image; (2) Detection. The task of identifying and localizing an object of interest in an image. For example, a detection model could be used to identify and track the surgical tools in a video; and (3) Segmentation. The task of assigning a label to each pixel in an image. For example, a segmentation model could be used to identify the different organs in a medical image. Surgical phase and tool detection models are two early examples of DL for surgical applications[20]. These models have been used to improve the accuracy and efficiency of surgical procedures.

The ML process used in surgical applications can be generally outlined with the following steps (Figure 2): (1) Obtaining an appropriate dataset. The dataset should contain surgical images linked to clinical outcomes. In some cases, a simple and effective way to verify that the data is sufficiently informative is to ask an expert to look at the data and perform the same task proposed for the model. People without medical education could correctly annotate the presence or absence of tools in images. However, the same cannot be said for annotating surgical phases, as this requires surgical understanding and a common definition of what exactly defines and delineates phases; (2) Pre-processing of data. This may include cleaning the data, removing outliers, and normalizing the data; (3) Splitting the dataset. The database is split into training, testing, and validation sets. It is good scientific practice to keep these sets as independent from each other as possible, as the network may develop biases; (4) Annotation. Data labeling is a crucial step in the ML pipeline, as it enables supervised training for ML models. Annotations can be temporal or spatial. Temporal annotations are useful when we need to determine surgical phases during an operation. Spatial annotations are used to identify surgical instruments in the surgical scene or anatomical structures (*e.g.*, tool detection); (5) Training the model. This involves feeding the data into the model and allowing it to learn the patterns in the data. The training process can be computationally expensive, depending on the size of the dataset and the complexity of the model; (6) Evaluation of the model. This involves testing the model on a verified dataset and evaluating its performance. This ensures that the model is not overfitted to the training data; and (7) Deployment of the model. This means making the model available for use in real-world applications.

As mentioned in the annotation description, phase recognition is the process of classifying frames in a video or image sequence according to a predetermined surgical phase. It is a CV task in which visual data is analyzed to identify and understand different phases or actions. The goal is to recognize the sequence of frames in a video or image sequence to identify specific actions or events that occur at different points in time. This can be done by observing characteristic visual cues, such as motion, changes in shape, or object interactions, to differentiate between different phases.

In semantic segmentation, an image is divided into meaningful regions or segments, and each segment is assigned a semantic label. The goal is to understand what the different parts of an image represent. To accomplish this task, an algorithm analyzes the image at the pixel level and assigns each pixel a label indicating which object or category it belongs to. By observing patterns and features in the training data, the algorithm can generalize its understanding to detect and classify new images.

In the context of surgical applications, semantic segmentation can be used to identify different anatomical structures, such as organs, tissues, and blood vessels. This information can be used to guide surgeons during surgery and to improve the accuracy and safety of the procedure. Examples of semantic segmentation in surgical applications include identification of the tumor and surrounding tissue in cancer surgery, localization of the surgical target in minimally invasive

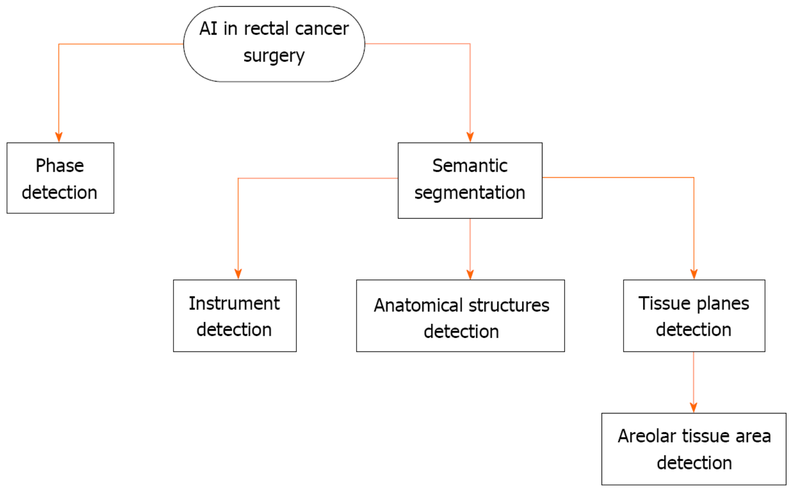


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Figure 3 Role of artificial intelligence in rectal cancer surgery. AI: Artificial intelligence.

surgery, tracking the movement of organs and tissues during surgery, detecting and removing blood clots, and preventing accidental injury to surrounding tissue.

One of the challenges in semantic segmentation for surgical applications is the complexity of the images. Surgical images are often cluttered with noise and artifacts, which can make it difficult for the algorithm to accurately segment the different objects. Another challenge is the variability of surgical procedures. Each procedure is unique, and the objects and tissues involved can differ from patient to patient. This makes it difficult to train a single algorithm that can be used for all surgical procedures. Recent advances in DL have made it possible to develop more accurate and robust semantic segmentation algorithms for surgical applications. These algorithms can learn the complex patterns in surgical images and generalize their understanding to new datasets[22].

The role of AI in TME surgery

In anterior rectal resection and TME, studies to date have focused on the development of DL-based phase, act, and tool recognition[22] as well as DL-based image-guided navigation systems for areolar tissue at the level of TME[23].

As mentioned earlier, TME is a complex surgical procedure in rectal cancer surgery consisting of the complete resection of the mesorectal envelope, which requires that the resection is performed in the correct plane and preserves vulnerable anatomical structures, such as the autonomic nerve plexus. An injury of this type could cause major issues such as postoperative incontinence and sexual dysfunction. Robotic-assisted surgery is particularly useful in TME surgery, although the authors acknowledge that no substantial clinical benefit over laparoscopic surgery has been demonstrated[24]. It does, however, offer advantages in terms of acquiring high-quality image data due to the benefits of 3D vision and a more stable camera platform. An additional advantage is that the system recognizes when a new instrument has been connected to the console, making it easy to compare instrument recognition algorithms.

In this context, AI could provide surgical guidance by identifying anatomical structures and helping to improve surgical quality, reduce differences between surgeons, and provide better clinical results. To date, efforts have been made to develop image recognition algorithms using minimally invasive video data, with a particular focus on automated instrument detection, which has only indirect surgical benefits[20,25]. Significant results have also been achieved in the recognition of relevant anatomical structures during less complex surgical procedures such as cholecystectomy[21,26].

The 2022 work by Kolbinger *et al*[22] (republished in 2023) was based on 57 robot-assisted rectal resections and focused on developing an algorithm for automatic detection of surgical phases and identification of determined anatomical structures. In particular, the algorithm achieved the best results in detecting the mesocolon, mesorectum, Gerota's fascia, abdominal wall, and dissection planes during mesorectal excision.

In 2022, Igaki *et al*[23] relied on the idea of the "holy plane," first proposed by Heald[27] in the 1980s when describing TME dissection. The holy plane lies between the mesorectal fascia and the parietal pelvic fascia through fibroareolar tissue and is an important landmark to follow an avascular pathway, ensuring that TME can be performed safely and effectively. Igaki *et al*[23] developed a DL algorithm to automatically detect areolar tissue using the open-source DeepLabv3plus software (Figure 3).

One limitation of the studies was the uncertainty of detection. According to the experience of Kolbinger *et al*[22], automatic recognition of thin and small structures is more difficult, *e.g.*, the recognition of the exact position of the dissection line in mesorectal excision. Furthermore, in TME, patient-related aspects such as individual anatomical variations and the history of neoadjuvant (radio) therapy can lead to the dissection lines being very different throughout the dataset and therefore difficult to detect automatically. These limitations could be overcome by technical improvements, *e.g.*, by displaying the detection uncertainty of the target structures using Bayesian calculation methods, which would increase acceptance among surgeons. Another improvement could be real-time display by minimizing the computational delay, which is currently 4 s[22].

The essential points for the integration of the above improvements and in general for the development of better algorithms for automatic recognition are the availability of data, the creation of publicly available datasets for complex surgical procedures, and the creation of multicenter studies for these applications.

DISCUSSION

In TME, identification of embryonic tissue planes and the closely associated line of dissection at the mesorectal fascia can be challenging because of significant variation due to neoadjuvant (radio) therapy and individual factors such as body composition. AI algorithms can improve intraoperative identification and highlight important parts of the anatomy involved in TME, such as the fibroareolar tissue plane and vascular and neural structures.

In robotic surgery, the use of visual aids could be considered more important than in laparoscopic surgery due to the lack of haptic feedback, *i.e.*, the sense of touch and force feedback that surgeons rely on in traditional open or laparoscopic surgery. To compensate for the lack of haptic feedback, visual augmentation plays a crucial role. In addition, advanced technologies such as fluorescence and near-infrared imaging are frequently used in robotic surgery. These techniques allow visualization of blood flow, tissue perfusion, and identification of vital structures that are not readily visible under normal lighting conditions. Combined with AI-assisted visual enhancements, the surgeon's ability to make critical decisions and perform delicate maneuvers such as TME with the required precision is improved.

Studies on AI-powered surgical guidance, which uses context-aware ML algorithms to automatically identify anatomical structures, surgical instruments, and surgical phases in complex abdominal surgery, require the creation of publicly available datasets and multicenter studies. This is because the datasets need to be large and diverse enough to train AI algorithms that can be generalized to new patients. Additionally, multicenter studies are necessary to ensure that the results are valid and reproducible.

CONCLUSION

The use of AI in TME is still in its infancy, but it has the potential to revolutionize the procedure. For example, AI algorithms can be used to identify and highlight key anatomical structures such as the mesorectal fascia, the vascular bundle, and the autonomic nervous structure. This could provide real-time identification of surgical structures and allow surgeons to perform complex procedures more accurately and safely, even in cases where the anatomy is challenging.

AI algorithms can also be used to track the movement of instruments, tissues, and organs during surgery. This can help prevent complications, such as accidental injury to surrounding tissue. For example, AI algorithms can track the movement of the rectum during dissection to prevent accidental perforation. AI algorithms can also be used to improve surgeons' training and help them become familiar with the complex anatomy of the pelvis and the techniques of TME.

While studies have shown that DL-based algorithms in TME are able to identify fibroareolar tissue and several other anatomical structures, these models have not related the results to postoperative outcomes. This may be due to experienced surgeons evaluating the algorithms, and the true effect is most apparent in those surgeons who are still in the learning phase.

The use of AI in TME is a promising area of research that has the potential to improve the safety and effectiveness of this important surgical procedure. However, more research is needed to fully understand the benefits and risks of this technology, including issues of safety, privacy, and ownership of sensitive data.

ARTICLE HIGHLIGHTS

Research background

Colorectal cancer is a major public health problem, with 1.9 million new cases and 953000 deaths worldwide in 2020. Total mesorectal excision (TME) is the standard of care for the treatment of rectal cancer, but it is a technically challenging surgery. Artificial intelligence (AI) has the potential to improve the performance of TME surgery, especially for surgeons who are still at the beginning of their learning curve.

Research motivation

AI in surgery is a rapidly evolving field with applications in the preoperative, intraoperative, and postoperative settings. In colorectal surgery, AI has been used to automate tasks such as instrument detection and anatomical structure identification. AI has also been used to develop image-guided navigation systems for TME surgery. One of the challenges of AI in surgery is the complexity of the images. Another challenge is the variability of surgical procedures. Recent advances in deep learning have made it possible to develop more accurate and robust AI algorithms for surgical applications.

Research objectives

To investigate the potential of AI in surgery, particularly in colorectal surgery, and the current state of the art. To describe AI algorithms for surgical applications, such as instrument detection, anatomical structure identification, and image-guided navigation systems. To describe their limitations and future developments, such as AI algorithms that can be used in real time. To propose the evaluation of the safety and efficacy of AI in surgery through clinical trials.

Research methods

A literature search was conducted to identify relevant studies on the use of AI in rectal cancer surgery and specifically in TME. The search was performed using the PubMed electronic database and was limited to studies published between 2020 and 2023. Only articles published in English were included.

Research results

The use of AI in rectal cancer surgery and specifically in TME is a rapidly evolving field. There are a number of different AI algorithms that have been developed for use in TME, including algorithms for instrument detection, anatomical structure identification, and image-guided navigation systems.

Research conclusions

The results of these studies are promising, but more research is needed to fully evaluate the safety and efficacy of AI in TME. Challenges that need to be overcome before AI can be widely adopted in TME include the need for large datasets of labeled images to train AI algorithms, the need to develop AI algorithms that can be used in real-time, and the need to address the ethical concerns raised by the use of AI in surgery.

Research perspectives

AI has the potential to revolutionize TME by providing real-time surgical guidance, preventing complications, and improving training. However, more research is needed to fully understand the benefits and risks of AI in TME.

FOOTNOTES

Author contributions: Mosca V and Pellino G conceived and presented the idea; Mosca V and Fuschillo G wrote the manuscript with the support of Sahnan K and Pellino G; Sciaudone G, Sahnan K, and Selvaggi F supervised the results of this work; Pellino G oversaw the process and was responsible for the overall planning and management; All authors discussed the results and contributed to the final manuscript.

Conflict-of-interest statement: Dr. Pellino has nothing to disclose. The other authors make no declarations regarding their potential conflicts of interest.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

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S-Editor: Lin C
L-Editor: Filipodia
P-Editor: Lin C

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