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REVIEW

Artificial intelligence in pancreatic cancer: diagnosis, limitations, and the future prospects—a narrative review

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Abstract

Purpose This review aims to explore the role of AI in the application of pancreatic cancer management and make recommendations to minimize the impact of the limitations to provide further benefits from AI use in the future.

Methods A comprehensive review of the literature was conducted using a combination of MeSH keywords, including "Artificial intelligence", "Pancreatic cancer", "Diagnosis", and "Limitations".

Results The beneficial implications of AI in the detection of biomarkers, diagnosis, and prognosis of pancreatic cancer have been explored. In addition, current drawbacks of AI use have been divided into subcategories encompassing statistical, training, and knowledge limitations; data handling, ethical and medicolegal aspects; and clinical integration and implementation.

Conclusion Artificial intelligence (AI) refers to computational machine systems that accomplish a set of given tasks by imitating human intelligence in an exponential learning pattern. AI in gastrointestinal oncology has continued to provide significant advancements in the clinical, molecular, and radiological diagnosis and intervention techniques required to improve the prognosis of many gastrointestinal cancer types, particularly pancreatic cancer.

Keywords Artificial intelligence · Pancreatic cancer · Gastrointestinal cancer · Machine learning · Limitations

Introduction

Artificial intelligence (AI) has caught the medical field by storm, and its applications are at the forefront of emerging medical science and innovation. In simple terms, AI refers to computational machine systems that mimic human intelligence to perform given tasks and improve themselves based on the information they collect. Machine learning (ML) is an AI subfield that allows the identification of patterns that can be used to analyze a particular situation (Kaul et al. 2020). ML can "learn" from the datasets provided and apply that information to similar scenarios in the future (Kaul et al. 2020). Another branch of AI, deep learning (DL), uses artificial neural networks called convolutional neural networks (CNN) that can continuously learn and make decisions on their own (Kaul et al. 2020). CNN is a mathematical computational model based on the behavior of biological neural networks in the human brain.

Since 1970, AI has been used in medicine for various purposes, including improving diagnostic effectiveness, facilitating treatment and disease monitoring, and improving overall patient outcomes (Kaul et al. 2020; Liu et al. 2020). Recently, AI has emerged in an array of wide application uses in gastroenterology, which relies heavily on endoscopy and radiological imaging for diagnosis and to guide treatment, and by extension, in pancreatic cancers.

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In 2022, an estimated 62,210 adults (32,970 men and 29,240 women) will be diagnosed with pancreatic cancer in the United States (US) (American Cancer Society 2022). The 5-year survival rate for all stages of pancreatic cancer combined is about 11% (Surveillance et al. 2020), with pancreatic ductal adenocarcinoma (PDAC) being the most common form of pancreatic cancer, representing approximately more than 90% of all pancreatic tumors (Kleeff et al. 2016). PDAC's dismal survival rates are due to several factors, including a lack of appropriate screening tests, delayed diagnosis, and suboptimal treatment options. As a result, changes in all these areas are urgently required.

The use of AI in the study of pancreatic cancers, especially PDAC, has been used to radiologically differentiate PDAC from normal pancreatic tissue in Computed Tomography (CT) images with a sensitivity and specificity as high as 100 and 98.5%, respectively, (Chu et al. 2019) and to assist in endoscopic ultrasound (EUS) and enhance its performance by aiding endosonography to distinguish PDAC from other lesions/normal tissue using a CNN model in real-time (Udriștoiu et al. 2021). Outside of radiomics, AI has also been used to develop risk scores for the development of PDAC based on urinary biomarkers (Blyuss et al. 2020); to predict clinical performance and response to celiac plexus neurolysis for pancreatic cancer patients (Facciorusso et al. 2019); to predict survival time (Osman 2018), and to identify genes associated with a poor prognosis in pancreatic ductal adenocarcinoma via a bioinformatics analysis (Zhou et al. 2019). In this literature review, we aim to summarize the use of AI and recent innovations related to AI in pancreatic cancers.

Discussion

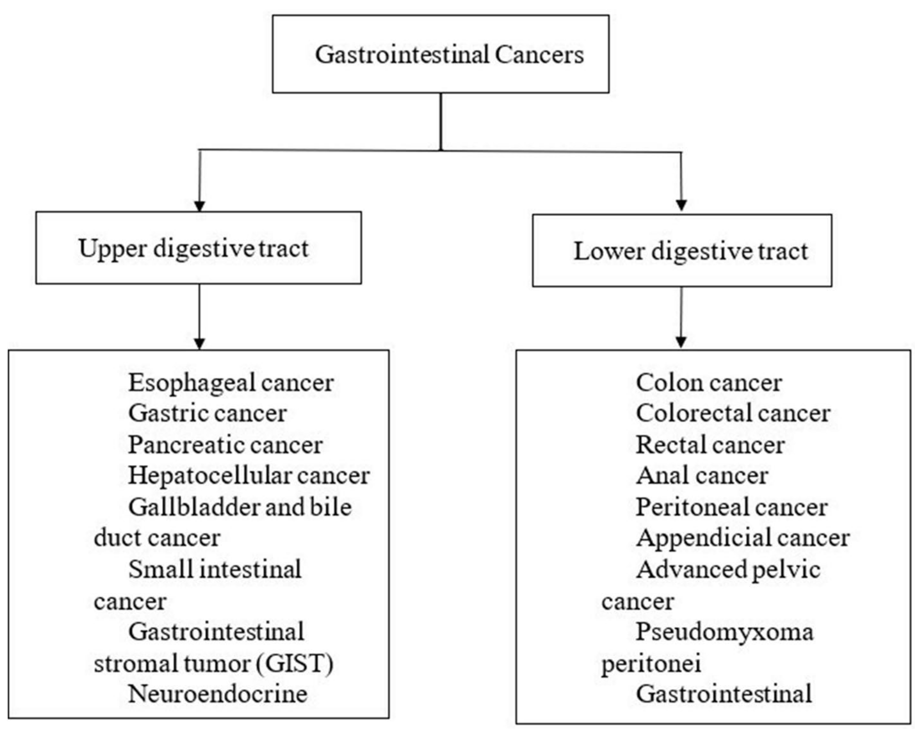
Overview of gastrointestinal cancers

Presently, the detection of various gastrointestinal cancers is primarily based on radiologists' interpretative analysis of radiographic scans and endoscopists' evaluation of endoscopic images. The broad classification of gastrointestinal malignancies has been summarized in Fig. 1. By effectively interpreting diagnostic clinical imaging, finding therapeutic targets, and processing vast datasets, AI may be helpful in screening, diagnosing, and treating different malignancies. The use of AI in endoscopic treatments represents a major advancement in modern medicine. Despite significant improvements in diagnostic accuracy, AI systems are not fully autonomous. AI-assisted techniques will become a critical tool in the management of these cancer patients soon.

Overview of pancreatic ductal adenocarcinoma

PDAC is a deadly malignancy that accounts for more than 90% of pancreatic cancer patients (Adamska et al. 1338;

Fig. 1 Types of gastrointestinal cancers



Nolen et al. 2014; Almeida et al. 2020). PDAC is the third largest cause of cancer death in the United States (Kamisawa et al. 2016) and ranks seventh worldwide (Bray et al. 2018). All diagnosed patients have a five-year survival rate of less than 10%, with metastatic cancer having a survival rate of only 3% (Siegel et al. 2019; Young et al. 2020). PDAC's dismal survival rates are due to several factors, including a lack of appropriate screening tests, delayed diagnosis, and suboptimal treatment options. As a result, changes in all of these areas are urgently required.

Overview of pancreatic cancer biomarkers

CA19-9 (Carbohydrate antigen 19-9) is presently the most reliable and frequently used biomarker for pancreatic cancer (Humphris et al. 2012). CA19-9 has a median diagnostic sensitivity of 79 percent and a median specificity of roughly 80 percent, limiting its value in pancreatic cancer screening (Goonetilleke and Siriwardena 2007). Because PDAC is extremely rare (Bray et al. 2018), screening the public at large is neither practical nor recommended due to the high risk of false positives (Kenner et al. 2015), potentially leading to unnecessary interventions (Young et al. 2020). Screening of people identified as having a more significant risk for developing PDAC, such as positive family history, which accounts for around 10% of cases (Franck et al. 2020), patients with cystic pancreatic lesions, and individuals over 50 years old who are recently diagnosed with type 2 diabetes (Klapman and Malafa 2008; Pereira et al. 2020), could help to determine precursor lesions while they are still potentially reversible. Prevalence rises with age (Midha et al. 2016) and is linked to comorbidities such as smoking, diabetes, and obesity (GBD 2017).

Application of AI in the diagnosis of pancreatic cancer

An alternate solution to extending survival is to diagnose PDAC early by utilizing tissue and blood biomarkers in combination with AI. In the age of precision medicine, AI can assist in more easily converting extensive data into required functionality perception, reducing inevitable errors to increase diagnostic accuracy and making real-time predictions (Koumakis et al. 2016; Zhu et al. 2020). The early recognition of PDAC via radiological data is a promising application of AI technology.

Most AI studies to date have focused on classifying malignant lesions and healthy pancreas pictures using CT scans, which is the conventional diagnostic technique for diagnosing PDAC (Zhao et al. 2019). CT is the most broadly adopted method for the initial evaluation of suspected PDAC, with a detection sensitivity ranging from 76 to 96% (Chu et al. 2017).

The characteristics of early PDAC could be delicate and established retrospectively up to 34 months well before the confirmed diagnosis of PDAC (Gonoi et al. 2017). An AI-powered diagnostic tool could help to reduce oversight. As a result, there is an increasing need for AI-based models for reliable pancreatic tumor diagnosis. An AI can examine thousands of photos on a pixel-by-pixel basis and is not prone to human error. Another AI advantage is the rapid diagnosis, which takes less than a minute in each case from when the original CT picture is entered to when a diagnosis is obtained.

The study of CT images of malignant tumors consists of three significant steps: detection, characterization, and time-dependent monitoring of change (Hosny et al. 2018). The majority of existing research has concentrated on the AI-assisted characterization of lesions. Three studies (Chu et al. 2019; Fu et al. 2018; Liu et al. 2019) used AI to analyze CT images in PDAC for diagnostic reasons. Fu et al. (Fu et al. 2018) stated that their algorithm obtained an overall sensitivity of 76% in a small sample of 15 healthy individuals and 44 with diverse pancreatic tumors. (Chu et al. 2019) showed a 99 percent accuracy in their computer-derived method in a retrospective case–control study of 380 individuals (190 cases and 190 controls). Meanwhile, Liu et al. (Liu et al. 2019) found a 76 percent accuracy rate in a prospective trial.

EUS and EUS-fine-needle aspiration (EUS-FNA) has become primary diagnostic tools for PDAC, with diagnostic accuracies of up to 85 percent, which is significantly higher than the 50 percent accuracy in CT-assisted diagnosis. The sensitivity of diagnosis of pancreatic tumors 3 cm in diameter with EUS was found to be 93 percent, which was higher than CT (53 percent) and MRI (67 percent) (Müller et al. 1994). A meta-analysis found that CT and EUS had equivalent sensitivity and specificity in identifying the resectability of PDAC (Rahman et al. 2020).

Application of AI in the prognosis of pancreatic cancer

One of the critical reasons for PDAC's high death rate is a lack of understanding of its malignant activity and an uncertain therapeutic response rate. The AI-assisted genetic and molecular profiling of PDAC has significantly increased our knowledge of these factors (Sinkala et al. 2020).

The Alliance of Pancreatic Cancer Consortium Imaging Working Group is now conducting a study (Young et al. 2020). Their purpose is to extract pre-and post-diagnosis CT, MRI, and transabdominal ultrasound images from individuals who are eventually identified with PDAC. These photos will be used to build a repository that can be shared and examined later. The project's ultimate goal is to create AI models that can forecast the advent of PDAC and diagnose it in its early stages.

The study of real-world clinical records using ML approaches is another potential platform for applying ML to the problem of early identification of pancreatic cancer (Santus et al. 2020). Such documents can be investigated for various characteristics, including environmental conditions, personal history, the impact of therapeutic intervention, and disease codes.

Current limitations and possible solutions

Statistical limitations

Though AI models are making progress, there are significant setbacks in their application in clinical practice; the retrospective pattern of study, incapability outside the trained domain, bias, false positive (FP) and false negative (FN) detections, bias, unintended confounding, and gullibility.

Some studies define FP detection as any false activation and FN detection as any missed detection (regardless of the number of frames) (Esteva et al. 2017). FP detections significantly burden healthcare, resulting in many biopsies, overtreatment, and unnecessary consumption of money and time. An essential drawback in dealing with FP detections is that there is no evident cause for FP detections to improve model capabilities (Winkler et al. 2019). Reasons for FN detection include small or flat lesions (challenging to identify), rare cancers (low availability of data sets) (Lui et al. 2020), and low quality of images (missed lesions). The lack of common standards for false detection is a significant impediment.

Since all reported different inventors designed Computed Assisted Diagnosis (CAD) systems, there is a high risk of inventor bias. Moreover, images used for training algorithms might have been selectively chosen, reflecting a possible selection bias.

Machine learning algorithms will exploit whatever signals are available to obtain the highest potential performance in the data set, resulting in unidentified confounding (Yoon et al. 1310; Ueyama et al. 2021), limiting the algorithm's performance. For example, in a study conducted in 2018, rather than learning the features of pneumonia on chest x-rays, the algorithm learned a relationship between a portable x-ray machine and pneumonia (Hassan et al. 2020).

Research must be well-designed, prospective, tested in real-time, and rely on massive data sets obtained from different institutions and geographic locations to mitigate the above flaws. Currently, limited literature is available, making it challenging to draw tangible conclusions.

Priorities and challenges in the training of AI models

Size of the input data

The AI models are usually trained on small datasets, and the algorithm approach varies in each medical center. Small data sets cause measurement errors and overfitting (good performance while testing but uncertain results during validation) (Hassan et al. 2020). Hence, these results are unreliable in different settings. To minimize overfitting and to optimize the performance of AI systems in various domains, future research studies should include data from multiple geographical regions (Chu et al. 2017), with larger data sets from different centers for fewer errors and more accuracy.

Quality of the input data

1. Images

In medicine, AI models are progressing well, but the accuracy of the outcomes is mainly dependent on the quality of the data used to train them. As a result, additional attention must be paid to the quality of photos and videos utilized in model training. Low-resolution, blurry, motionless photos, noise, and unwanted objects are some pesky traits. Initially, most AI experiments employed high-resolution still photos (Cabitza et al. 2017), with low-resolution images being excluded from most of the investigations (Narla et al. 2018). This led to AI models misdiagnosing (Topol 2019) when given low-quality photos or videos, resulting in model overfitting. To enhance the outputs of these models, it is vital to provide various forms of data, such as high and low-quality still photos, videos, and real-time perspective training. In addition, even enhancement techniques can be used for low-quality images.

However, there are several real-time constraints when using images as input data. These include the quantity of insufflation (for example, over-insufflation can flatten a lesion), post-biopsy hemorrhage, mucus, specificity of bowel preparation, exposure duration, and processing time. Therefore, steps should be taken to use videos rather than images, to develop appropriate standards by organizations and societies (Bortsova et al. 2021) for dealing with variables, and to reduce processing time.

2. Noise

Noise is one of the several limitations that significantly influence model accuracy. Hence, AI models must be trained to recognize and screen out noise using localization and segmentation (Chang et al. 2018) to increase the quality of the input data. However, the outcome is uncertain, and training may not represent reality.

Black box

AI-based approaches to medicine have had some noteworthy practical triumphs, but their complexity and inefficacy hamper their usefulness in 'explaining' their decision-making or predictions. This issue of limited knowledge about AI's internal workings, algorithms, and why it makes a specific decision is called the "black box" (Beg et al. 2017). For clinicians to adopt and trust AI models in regular clinical care, they must be reliable, interpretable, explainable, and not just a well-performing approach. Recent advances and the rise of several "explainable AI" methodologies are addressing the challenge mentioned above, yet there is presently no explicit agreement on the preferred methods.

Deeper models with numerous layers and smaller kernels are now favored for AI performance over single and larger kernels. Still, many hidden layers result in unexpected consequences (Cimpoi et al. 2016) and substantial confounding (Kiener 2021). Recent improvements in data visualization tools have allowed clinicians, mathematicians, and data scientists to comprehend the logic that happens within the hidden layers of AI, which might improve performance, unintended consequences, and widespread acceptance.

Inefficient data handling

Another severe challenge of AI in medicine is properly handling information, especially data privacy and security (). AI demands a considerable volume of de-identified, traceable, and shareable data. Different models have been developed for sharing data in AI, each with its benefits and drawbacks (Lovis 2019; O'Sullivan et al. 2019).

Currently, centralized models exist for data sharing, in which all data is housed on a single central server, which is vulnerable to adversarial attacks (Yu et al. 2018). One effective solution might be decentralization (federated data sets), where data is stored on multiple servers (Abadir et al. 2020). The decentralized data must be re-identifiable and traceable, so medical practitioners can access it and make required bedside judgments. However, a viable technology solution to address the difficulty of maintaining data privacy while meeting the growing need for massive datasets is bleak (Robertson et al. 2021).

Ethical and legal aspects

To date, AI-assisted image analysis and machine-learning neural networks in illness diagnosis and prediction have only provided an "opinion", as the presiding doctor retains complete authority over the decisions to be made. Scientists and engineers are making tremendous progress in AI use in their fields, progressing to task autonomy or conditional autonomy, and may eventually complete automation. In the context of these fields, the liable party remains unclear if an algorithm makes an error with potentially fatal consequences. On the other hand, in many clinical negligence and malpractice cases, the principal defendant facing the ramifications of the law is the attending physician. According to a previous study, AI and associated autonomous performances have three legal elements: accountability, liability, and culpability (Bernal et al. 2017). Documentation might determine accountability, but culpability (related to punishment) is the component with the least clarity right now.

Although some progress has been made in that direction (Chassagnon and Dohan 2020), the path ahead remains uncertain. Results of AI algorithms lack explainability and so such results are hard to be certified as legal evidence. Prospective randomized clinical trials (RCTs) and transparent workflow are essential for providing solid evidence that might place AI within the range of legal and ethical concerns (Wang et al. 2018). One thing is certain; legislation, regulation, and clinical practice will all face challenges.

Inadequate standardization, validation, and reporting protocols

In the clinical setting, AI has great potential, yet its integration into routine clinical practice will be challenging because of the current lack of adequate frameworks for standardization, validation, and reporting.

Different AI technologies require different types of data and are trained in different environments, which may not reflect the real-world patients encountered at community hospitals (Gong et al. 2020). Therefore, it is necessary to design and define uniform processes for data collection, processing, storage, replication, and analysis. Moreover, experts from different institutions in different geographical locations should collaborate to analyze the data to establish "gold standards" for AI diagnosis. So far, only a small number of such standardizations have been established. A five-step process suggested by Robertson et al. (2021) (Lee et al. 1964) may help AI integration into clinical practice. Although possible, framing such universal protocols will be expensive and laborious due to unique challenges like the fast pace of innovation and the fluid nature of models.

Unique challenges exist not only with standardization but also regarding the validation of AI/CAD systems due to different regulations in different nations and a lack of a proper legal framework. Yet, few approvals have taken place, with the first AI system being approved in April 2018 by the Food and Drug Administration (FDA) for diabetic retinopathy (Zhang et al. 2020). However, worldwide utilization of AI systems is nowhere near complete, and future approvals might require substantially stronger evidence, post-market surveillance, and periodic safety update reports.

Developing guidelines to standardize the reporting of data obtained using AI models are necessary to make this tool a reliable source in clinical practice. AI extensions are plugged in for this purpose and a global effort has been taken to build AI extensions to both the CONSORT (Consolidated Standards of Reporting Trials) and SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) guidelines (). Such AI extensions for standardized guidelines will solve this drawback in using AI models.

Other real-time challenges: implementation, deployment, and quality assurance

Organizational limitations in AI development and its application in medicine include large data storage, a continual input of information, computational equipment, access to technologies, cooperation between various fields, timely hardware and software upgrades, and maintenance of systems. Another key issue to be considered for both patients and governments is the applicable medical costs. Therefore, all these challenges should be addressed in a cost and time-effective manner (Bernal et al. 2017).

To incorporate AI into daily practice, clinicians must be able to comprehend how the suggested algorithms and related software will affect patient care. On that basis, medical students and practicing doctors should be given access to an openly available AI curriculum with vast public image databases to train and evaluate the software for better comprehension and adoption (Qian et al. 2019).

Because AI implementation needs physicians who participate in clinical application and engineers (hardware and software), the study's outcomes and design may vary based on the study's conductors (Hoerter et al. 2020) which also affects the quality assurance (QA) of the model. So, it is advised that a specialized multidisciplinary team of experts in the area is engaged ahead of clinical deployment to ensure safe, secure, and clinically relevant use. Certain recommendations like performing risk analysis using methods such as the Failure model and Effect analysis are proposed for easy implementation of the AI model and to improve QA (Vandewinckele et al. 2020).

Future directions

Gastroenterology is a discipline where AI has the potential to make a substantial difference because the diagnosis of gastrointestinal disorders mostly relies on image-based examinations like endoscopy and radiology. Currently, AI is being utilized in diagnostics as precision medicine (Wang et al. 2018), but the clinical reasoning of the physician still dominates this arena. However, further developments are necessary to use AI in the screening, treatment, and prediction of diseases. More research needs to be done before drawing any conclusions on its accuracy, as there are considerable obstacles to overcome, such as scalability, explainability, patient safety, ethics, legislation, government permission, and cost-effectiveness.

Although premature, a research study revealed how broad AI's application field might be (Gong et al. 2020) and its need for more technological development to eventually become mainstream in clinical practice. This level of integration necessitates time to calibrate and create systems that are not only precise but also user-friendly and accessible. Shortly, it might be possible to integrate AI models with mobile phones and smart watches too. Real-time data transfer might help physicians in two different countries connect and communicate with each other to arrive at the best possible option for a patient.

By incorporating complex and heterogeneous data, AI's intrinsic potential for evaluating parallel streams of information may be leveraged to pave the way for better tailored and precision medicine. Converging AI models with 'multi-omics' (genomics, epigenomics, transcriptomics, proteomics, and metabolomics) and 'non-omics' (clinical history, disease endemicity, current medications, risk factors) data could aid in the accurate detection, characterization, and monitoring of diseases and personalized patient care (Zhang et al. 2020; Li et al. 2018).

An AI-based surgical instrument tracking algorithm has shown that the DL algorithm was able to learn the precise steps of surgery by closely watching the instruments during robotic surgery and was able to quantitatively assess the physicians' performance (Lee et al. 1964). Further research might produce semi-autonomous models which can help decrease the workload on clinicians, increase clinicians' productivity, or even complete autonomous models.

Conclusion

The recent emergence of AI in the field of gastrointestinal oncology has provided significant strides in diagnosis and treatment interventions, particularly in the case of pancreatic cancer. Pancreatic cancer is highly malignant with low survival rates, so its prompt detection and management is imperative to alter the disease course. Although AI has been recognized to provide genetic, molecular, and early radiological detection of pancreatic cancer through its implementation, potential setbacks in its utilization, including statistical, organizational, and knowledge limitations in algorithmic approaches involving AI, ethical and medico-legal implications of its application, as well as the challenges of integration into clinical practice, to name a few, must be addressed.

In this review, recommendations have been made to overcome these obstacles and facilitate the process of effective and beneficial adoption of the use of AI in the diagnosis and management of pancreatic cancer.

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Data availability The authors declare that data supporting the findings of this study are available within the article.

Declarations

Conflict of interest None.

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