

ORIGINAL ARTICLE

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HIGHLIGHTS

- Pancreatic ductal adenocarcinoma (PDAC) is an aggressive cancer with limited prognostic accuracy through traditional methods.
- Convolutional neural networks (CNNs) are being explored for prognostic models in PDAC.
- They can extract complex features from images, aiding PDAC prognostication.
- Further validation and optimization of CNN-based models are needed for better reliability and clinical utility in PDAC.

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Beyond traditional tools: exploring convolutional neural networks as innovative prognostic models in pancreatic ductal adenocarcinoma

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ABSTRACT – Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive and lethal form of cancer with limited prognostic accuracy using traditional factors. This has led to the exploration of innovative prognostic models, including convolutional neural networks (CNNs), in PDAC. CNNs, a type of artificial intelligence algorithm, have shown promise in various medical applications, including image analysis and pattern recognition. Their ability to extract complex features from medical images makes them suitable for improving prognostication in PDAC. However, implementing CNNs in clinical practice poses challenges, such as data availability and interpretability. Future research should focus on multi-center studies, integrating multiple data modalities, and combining CNN outputs with biomarker panels. Collaborative efforts and patient autonomy should be considered to ensure the ethical implementation of CNN-based prognostic models. Further validation and optimisation of CNN-based models are necessary to enhance their reliability and clinical utility in PDAC prognostication.

KEYWORDS – Pancreatic neoplasms, prognosis, convolutional neural networks, artificial intelligence, multimodal imaging.

INTRODUCTION

Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive and lethal form of cancer that arises from the cells lining the pancreatic ducts. It accounts for a significant number of cancer-related deaths worldwide, with a five-year survival rate of less than 10%. PDAC is often diagnosed at advanced stages, when treatment options are limited, contributing to its poor prognosis⁽¹⁾. Due to the aggressive nature of PDAC and the challenges associated with its early detection, accurate prognostic indicators are crucial for guiding treatment decisions and predicting patient outcomes. Traditional prognostic tools, such as tumour stage, histological grade, and lymph node involvement, have limitations in accurately predicting individual patient outcomes^(2,3). As a result, there is a pressing need for more robust and reliable prognostic indicators that can aid in personalised treatment strategies and improve patient outcomes.

Convolutional neural networks (CNNs) have demonstrated immense potential in the field of medical imaging and prognostication. Their ability to analyse complex patterns and extract meaningful features from medical images has opened up new possibilities for improving diagnosis, prognosis, and treatment planning⁽⁴⁾. In recent years, there has been growing interest in exploring the potential of CNNs, a type of artificial intelligence (AI) algorithm, as prognostic indicators in PDAC. CNNs have shown promising results in various medical applications, including image analysis and pattern recognition, and their ability to extract complex features from medical images and clinical data makes them an attractive tool for prognostication⁽⁵⁾.

When it comes to prognostication, CNNs can utilise not only imaging data but also incorporate other clinical variables to predict patient outcomes. By analysing a combination of imaging features, clinical data, and relevant biomarkers, CNNs can generate personalised prognostic models that provide valuable insights into disease progression, treatment response, and overall survival⁽⁶⁾. These models can aid clinicians in making informed decisions about treatment strategies, identifying patients at higher risk, and selecting appropriate therapeutic interventions. This commentary highlights the

challenges associated with prognostication in PDAC and emphasises the urgent need for more accurate and reliable prognostic indicators.

CHALLENGES ASSOCIATED WITH PROGNOSTICATION IN PDAC

Limitations of traditional prognostic factors

Traditional prognostic factors in PDAC have certain limitations that hinder their accuracy and reliability. These factors often fail to capture the complex biology and heterogeneity of PDAC, leading to limited prognostic accuracy. Associated limitations include:

Tumour stage and size: traditional staging systems, such as the TNM classification, rely on tumour size and extent of local invasion. However, these factors alone fail to capture the complex biology and heterogeneity of PDAC, resulting in limited prognostic accuracy⁽⁷⁾.

Histopathological features: histological parameters, including tumour grade and histological subtype, provide important prognostic information but may not fully reflect the aggressive nature of PDAC. Additionally, inter-observer variability in histopathological interpretation poses challenges in standardising prognostic assessment⁽⁸⁾.

Serum biomarkers: several serum biomarkers, such as CA 19-9, have been used as prognostic indicators in PDAC. However, their utility is limited by variability in expression levels among patients and their inability to reliably predict individual patient outcomes⁽⁹⁾.

Incomplete representation of patient characteristics: traditional prognostic factors may not fully consider individual patient characteristics, such as age, comorbidities, performance status, and treatment response. These factors can significantly influence prognosis and treatment outcomes, but their integration into traditional prognostic models is often limited⁽¹⁰⁾.

Limitations of scoring systems

Scoring systems commonly used for prognostication in PDAC have their own limitations that affect their predictive power. These scoring systems often rely on a limited set of clinical and

pathological parameters, which may not fully capture the complexities and nuances of the disease. Associated limitations include:

AJCC staging system: While the American Joint Committee on Cancer (AJCC) staging system is widely used for PDAC prognostication, it has limitations in capturing the heterogeneity of the disease and providing personalised prognostic information⁽¹¹⁾.

Charlson Comorbidity Index (CCI): CCI is commonly used to assess comorbidities and predict overall survival in PDAC. However, it may not adequately account for the unique challenges and complexities associated with this aggressive malignancy⁽¹²⁾.

Performance status scales: performance status scales, such as the Eastern Cooperative Oncology Group (ECOG) performance status, are often used to evaluate patients' functional status. However, they may not fully capture the impact of PDAC-related symptoms and overall prognosis⁽¹³⁾.

The need for more accurate and reliable prognostic indicators

Despite advancements in prognostic tools and scoring systems, there is a pressing need for more accurate and reliable prognostic indicators in PDAC. The limitations of traditional factors and scoring systems underscore the necessity for improved prognostic approaches. The need for more accurate and reliable prognostic indicators in PDAC is driven by the following factors:

Enhanced risk stratification: PDAC is characterised by significant heterogeneity, both in terms of tumour biology and patient outcomes. More accurate prognostic indicators can help stratify patients into distinct risk groups, enabling personalised treatment strategies and improved clinical decision-making⁽¹⁴⁾.

Prediction of treatment response: reliable prognostic indicators can aid in predicting individual patient responses to specific treatment modalities. This can assist clinicians in tailoring therapies to maximise treatment efficacy and minimise unnecessary interventions for patients who are unlikely to benefit⁽¹⁵⁾.

Facilitating clinical trial design: accurate prognostic indicators are crucial in the design of clinical trials, especially for identifying patient subgroups that are

more likely to respond to investigational therapies. Such indicators can help optimise trial enrolment and improve the chances of successful outcomes⁽¹⁶⁾.

Patient counselling and support: prognostic information plays a crucial role in patient counselling and shared decision-making. More accurate prognostic indicators can provide patients and their families with a clearer understanding of their disease trajectory, enabling them to make informed choices regarding treatment options, supportive care, and end-of-life planning⁽¹⁷⁾.

Advancing precision medicine: precision medicine aims to deliver tailored therapies based on individual patient characteristics. Improved prognostic indicators can contribute to the development of precision medicine approaches in PDAC, allowing for targeted treatments and improved patient outcomes⁽³⁾.

Role of CNNs in PDAC prognostication

CNNs have emerged as powerful tools in medical image analysis and have shown promise in improving prognostication in PDAC. CNNs are deep learning algorithms specifically designed for analysing visual data, such as medical images, by automatically learning hierarchical representations and patterns. CNNs have several key features that make them suitable for prognostication in PDAC:

Feature extraction: CNNs excel at automatically extracting relevant features from medical images, capturing both local and global patterns. This capability is particularly valuable in PDAC, where tumour characteristics and their spatial distribution play a crucial role in prognosis⁽¹⁸⁾.

Nonlinear mapping: CNNs can capture complex nonlinear relationships between image features and clinical outcomes, which traditional prognostic factors may overlook. This nonlinear mapping ability allows for a more comprehensive and accurate assessment of prognostic information⁽¹⁶⁾.

Scalability and generalisability: CNNs can be trained on large datasets, enabling the analysis of diverse patient populations and accounting for the heterogeneity of PDAC. Once trained, CNN models can generalise their learning to new cases, facilitating the application of prognostic models in clinical practice⁽⁴⁾.

In a recent study by Liu et al., the diagnostic performance of CNNs in detecting pancreatic

cancer on computed tomography (CT) imaging was evaluated⁽¹⁹⁾. The findings demonstrated promising results for CNN-based analysis. In the local test sets, the CNN achieved high sensitivity, specificity, and accuracy, with an area under the curve (AUC) close to 1. The CNN outperformed radiologists in terms of sensitivity, particularly for tumours smaller than 2 cm. Notably, the CNN correctly classified the majority of pancreatic cancers missed by radiologists.

Ma et al., utilised a dataset of CT images obtained from patients with pathologically confirmed pancreatic cancer and patients with normal pancreas⁽²⁰⁾. The approach was evaluated using binary classification (cancer or not) and ternary classification (no cancer, cancer at tail/body, cancer at head/neck). The overall diagnostic accuracy of the binary classifier was high, ranging from 95.15% to 95.76%, across the different image phases. The sensitivity scores were also favorable, with no significant differences among the phases. The plain phase showed comparable sensitivity, easier accessibility, and lower radiation compared to the arterial and venous phases, making it more suitable for the binary classifier. Furthermore, the CNN classifier achieved higher accuracies than trainee gastroenterologists on plain scan diagnosis. Although there was no significant difference between the CNN and board-certified gastroenterologists, the CNN's performance suggests its potential as a reliable diagnostic tool. In the ternary classifier, the CNN achieved satisfactory diagnostic accuracy across the image phases. The sensitivity scores for detecting cancers in the tail and head varied among the phases, with the arterial phase demonstrating the highest sensitivity for cancers in the head.

Similarly, Tonozuka et al., conducted a study aiming to develop a computer-assisted diagnosis (CAD) system using deep learning analysis of endoscopic ultrasound (EUS) images for the detection of PDAC⁽²¹⁾. The results demonstrated the efficacy of the EUS-CAD system for detecting PDAC. The areas under the receiver operating characteristic curve were 0.924 and 0.940 in the validation and test settings, respectively, indicating good discriminative ability. In the analysis of misdirection, no factors were identified on univariate analysis among PDAC cases. However, in non-PDAC cases, mass formation was found to be associated with over-diagnosis of

tumors on multivariate analysis. The findings from Tonozuka et al. pilot study highlight the potential of the EUS-CAD system for PDAC detection. The deep learning-based CAD system achieved high accuracy in distinguishing PDAC from control images, including those from patients with chronic pancreatitis and normal pancreas. This technology has the potential to assist endoscopists in early detection and diagnosis of PDAC, enabling timely intervention and improved patient outcomes.

The application of CNNs and deep learning techniques in pancreatic cancer detection shows great promise. These studies highlight the potential for these technologies to assist in early detection, improve diagnostic accuracy, and ultimately contribute to better patient outcomes. However, further research is needed to address the limitations and challenges associated with these approaches, such as dataset biases, model interpretability, and real-world implementation.

ADVANTAGES AND LIMITATIONS OF CNNs AS PROGNOSTIC MODELS

Advantages of CNNs as prognostic indicators:

Ability to capture complex patterns: CNNs excel at capturing intricate patterns and features in images, including medical images. They can automatically learn and extract relevant features from input data, allowing them to identify subtle details and relationships that may not be easily discernible to human observers. This capability makes CNNs well-suited for analysing complex medical images, such as CT scans or histopathological slides⁽¹⁶⁾.

Improved accuracy and reliability: CNNs have demonstrated superior accuracy and reliability compared to traditional prognostic tools in various medical applications. Their ability to analyse large amounts of data and extract meaningful information leads to more precise and consistent predictions. By leveraging deep learning algorithms, CNNs can identify and consider a broader range of prognostic factors, potentially leading to more accurate prognostic assessments⁽²²⁾.

Reduced subjectivity: traditional prognostic tools often rely on manual interpretation and subjective judgment, which can introduce variability and

bias. In contrast, CNNs provide an objective and standardised approach to prognostication. They follow predefined algorithms and rules, reducing the influence of personal interpretations and increasing the reproducibility of results⁽⁴⁾.

Scalability and efficiency: once trained, CNNs can analyse large volumes of data rapidly, making them scalable for high-throughput analysis. This efficiency is particularly advantageous when dealing with large datasets or time-sensitive prognostic assessments. CNNs can process images and generate prognostic predictions in a timely manner, potentially improving patient care and treatment decision-making⁽²³⁾.

Adaptability and continuous learning: CNNs have the ability to continuously learn and adapt based on new data. As more patient data becomes available, the CNN model can be updated and refined, incorporating the latest knowledge and improving its prognostic capabilities over time. This adaptability is crucial in the rapidly evolving field of medicine, where new prognostic factors and biomarkers are constantly being discovered^(16,23).

Limitations and challenges in implementing CNNs in clinical practice:

Data availability and quality: CNNs require large amounts of high-quality labeled data for training. However, obtaining such datasets, especially for rare diseases or specific subtypes, can be challenging. The availability of comprehensive and diverse datasets is crucial for developing accurate and reliable prognostic CNN models.

Interpretability and explainability: CNNs are often considered black-box models, meaning that their decision-making process is not easily interpretable or explainable. Understanding the underlying reasons for the CNN's predictions can be difficult, which may limit their acceptance and trust in clinical settings. Efforts are underway to develop techniques for interpreting and explaining CNN decisions, which would enhance their clinical utility⁽²⁰⁾.

Generalisability: CNNs trained on specific datasets may exhibit limitations in generalising their predictions to new or different patient populations. The performance of CNN models may vary across different imaging modalities, institutions, or demographic groups. Validation on diverse

datasets and populations is essential to ensure the generalisability of CNN-based prognostic models.

Integration into clinical workflows: incorporating CNN-based prognostic tools into routine clinical workflows presents practical challenges. Integration with existing electronic health record systems, data management, and interoperability need to be considered. Clinician acceptance, training, and understanding of the limitations and appropriate use of CNN-based prognostic tools are also critical factors.

Ethical and legal considerations: the use of CNNs in clinical practice raises ethical and legal concerns related to patient privacy, data security, and potential biases in the data or algorithmic decision-making. Ensuring data privacy, informed consent, transparency, and addressing biases are crucial aspects that need to be carefully managed.

FUTURE DIRECTIONS AND IMPLICATIONS

Opportunities for future research:

Multi-center studies: conducting multi-centre studies with larger and more diverse patient cohorts can enhance the generalisability and robustness of CNN-based prognostic models. Collaborative efforts involving multiple institutions and international collaborations can provide more comprehensive insights into the performance and applicability of these models across different populations and healthcare settings.

Prospective studies: prospective studies are needed to validate the performance of CNN-based prognostic models in real-time clinical practice. Prospective data collection allows for the evaluation of the models' effectiveness in guiding treatment decisions, monitoring patient outcomes, and assessing their impact on patient management and overall healthcare outcomes.

Longitudinal studies: longitudinal studies can provide valuable insights into the temporal dynamics of prognostic indicators. By analysing sequential imaging data or serial biomarker measurements over time, CNN-based models can potentially capture disease progression, treatment response, and long-term prognostic trends, allowing for more personalised and dynamic prognostication.

External validation and comparison studies: it is crucial to externally validate CNN-based prognostic models on independent datasets from different populations and clinical settings. Comparing the performance of CNN models with established prognostic tools and incorporating them into existing prognostic algorithms can help assess their incremental value and potential integration into clinical practice⁽²⁴⁾.

Integration of CNNs with other clinical and molecular factors:

Multi-modal data fusion: integrating CNN-based image analysis with other clinical data, such as patient demographics, clinical history, laboratory results, and genetic/molecular information, can enhance the accuracy and comprehensive nature of prognostic models. Combining multiple data modalities may provide a more holistic understanding of disease prognosis and enable personalised prognostication.

Fusion of CNN outputs with biomarker panels: CNN-based image analysis can be combined with molecular biomarker panels to develop composite prognostic models. By integrating imaging features captured by CNNs with genetic, proteomic, or transcriptomic markers, more accurate and comprehensive prognostic assessments can be achieved, potentially leading to personalised treatment strategies⁽²⁵⁾.

Ethical considerations and potential pitfalls of relying solely on CNN-based prognostication:

Bias and fairness: CNNs are susceptible to biases present in the training data, which may lead to biased predictions and unequal treatment recommendations. Care should be taken to address and mitigate biases related to demographics, race, gender, or socioeconomic factors. Regular monitoring and evaluation of the model's fairness and bias should be conducted to ensure equitable and unbiased prognostication.

Lack of human expertise: relying solely on CNN-based prognostication may overlook the valuable clinical expertise and judgment of healthcare professionals. Human interpretation and clinical context are essential for understanding the individual patient's unique circumstances, considering

comorbidities, and making informed treatment decisions. CNN-based models should be used as decision support tools, augmenting rather than replacing human expertise.

Patient autonomy and informed consent: patients should be adequately informed about the utilization of CNN-based prognostic models and their implications. Transparency in the limitations, uncertainties, and potential risks of using these models should be ensured. Respecting patient autonomy and preferences is crucial, and decisions should be made collaboratively between healthcare professionals and patients, taking into account individual values and preferences.

Legal and regulatory considerations: implementation of CNN-based prognostic models in clinical practice necessitates compliance with relevant legal and regulatory frameworks. Data privacy, security, and compliance with regulations governing medical device usage should be carefully addressed. Ethical guidelines and standards specific to the development, deployment, and maintenance of AI-based prognostic models should be adhered to.

CONCLUSION

In conclusion, the use of CNNs as prognostic indicators in PDAC shows great promise. CNNs offer advantages over traditional tools by accurately distinguishing pancreatic cancer from benign tissue in CT images and providing objective assessments of tumor characteristics and prognosis. However, challenges remain, and further research is needed to validate and optimize CNN-based prognostic models, ensuring their reliability across diverse patient populations. Integrating CNNs with other clinical and molecular factors could enhance prognostication accuracy and personalization. Ethical considerations surrounding data privacy and responsible AI use must be addressed. Despite these challenges, CNNs have the potential to revolutionise PDAC prognostication, leading to improved patient outcomes and more effective treatment strategies.

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Ahmed HS. Além das ferramentas tradicionais: explorando redes neurais convolucionais como modelos prognósticos inovadores no adenocarcinoma ductal pancreático. *Arq gastroenterol.* 2024;61:e23107.

RESUMO – Contexto – O adenocarcinoma ductal pancreático (ACDP) é uma forma de câncer altamente agressiva e letal com precisão prognóstica limitada usando fatores tradicionais. Isso levou à exploração de modelos prognósticos inovadores, incluindo redes neurais convolucionais (CNNs), no ACDP. As CNNs, um tipo de algoritmo de inteligência artificial, mostraram promessa em várias aplicações médicas, incluindo análise de imagem e reconhecimento de padrões. Sua capacidade de extrair características complexas de imagens médicas as torna adequadas para melhorar o prognóstico no ACDP. No entanto, a implementação de CNNs na prática clínica apresenta desafios, como a disponibilidade de dados e a interpretabilidade. Pesquisas futuras devem se concentrar em estudos multicêntricos, integrando múltiplas modalidades de dados e combinando saídas de CNN com painéis de biomarcadores. Esforços colaborativos e autonomia do paciente devem ser considerados para garantir a implementação ética de modelos prognósticos baseados em CNN. Mais validação e otimização de modelos baseados em CNN são necessárias para aumentar sua confiabilidade e utilidade clínica na prognóstico do ACDP.

Palavras-chave – Neoplasias pancreáticas, prognóstico, redes neurais convolucionais, inteligência artificial, imagem multimodal.

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