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Early diagnosis of pancreatic cancer: current diagnostic methods and the role of primary care physicians in improving outcomes - a narrative review

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Abstract

Pancreatic cancer is one of the most aggressive malignancies and a leading cause of cancer-related mortality worldwide. Prognosis remains poor due to late diagnosis, as early-stage disease is usually asymptomatic or presents with non-specific symptoms, and the lack of effective screening results in most patients being diagnosed at an advanced stage. This review evaluates challenges in pancreatic cancer diagnosis, summarizes available diagnostic methods, and highlights the role of primary care physicians in early detection. Evidence published between 2015 and 2026 was analyzed. A structured literature search was conducted using PubMed and Google Scholar. Search terms included "pancreatic cancer", "early diagnosis", "screening", "biomarkers", "imaging", "liquid biopsy", "circulating tumor DNA", and "artificial intelligence". Original studies, reviews, and clinical guidelines were included. CT remains the primary imaging modality, though sensitivity decreases for small lesions. Endoscopic ultrasound improves detection and enables tissue sampling. CA 19-9 has limited early diagnostic value. Liquid biopsy methods show promise but remain under validation. Radiomics and AI may enhance detection of subtle imaging features. Primary care physicians are essential for recognizing suspicious symptoms and ensuring timely referral. Early diagnosis remains challenging due to non-specific symptoms, limited screening, and diagnostic shortcomings. A multimodal approach combining imaging, biomarkers, and emerging technologies is needed.

Greater awareness among primary care physicians and continued development of liquid biopsy and AI tools may improve outcomes.

Key words: pancreatic cancer; early diagnosis; screening; biomarkers; imaging; liquid biopsy; artificial intelligence; primary care; early detection

Introduction

Pancreatic cancer is one of the most aggressive and lethal malignancies worldwide, with a persistently poor prognosis and a 5-year survival rate remaining below 10% in most developed countries [1, 2, 3]. Despite advances in oncological treatment, the mortality closely mirrors incidence rates, largely due to late-stage diagnosis and the absence of effective population-based screening strategies [3].

Epidemiological data indicate a steady increase in both incidence and mortality of pancreatic cancer globally, with projections suggesting it may become the second leading cause of cancer-related deaths in the coming decades [3]. Established risk factors include older age, smoking, obesity, chronic pancreatitis, type 1 and type 2 diabetes mellitus and family history of pancreatic cancer. Genetic predispositions such as Lynch syndrome, Peutz–Jeghers syndrome, and BRCA1/2 mutations are also associated with elevated risk [4]. However, most cases arise sporadically, and the absence of clearly identifiable early clinical markers significantly limits opportunities for early detection.

Current diagnostic pathways rely primarily on imaging methods such as computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasound (EUS), and positron emission tomography (PET), complemented by serum biomarkers, most notably CA 19-9 [5]. Although CA 19-9 is the most widely used biomarker in clinical practice, its diagnostic utility is limited - with reported sensitivity of approximately 70–74% even in resectable, early-stage tumors - due to insufficient specificity and poor performance across disease stages [6].

In recent years, there has been growing interest in novel diagnostic strategies aimed at improving early detection. Liquid biopsy approaches, including circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and exosomes have demonstrated promising potential in identifying tumor-specific alterations at earlier disease stages [7]. Additionally, radiomics and artificial intelligence-based image analysis are emerging as supportive tools capable of detecting subtle radiological patterns not visible to the human eye [8]. However, most of these

techniques remain in experimental or early clinical validation phases and are not yet part of routine diagnostic algorithms.

The role of physicians, particularly those working in primary care facilities, is crucial in the early recognition of pancreatic cancer. Non-specific symptoms such as unexplained weight loss, epigastric pain, or jaundice should prompt further diagnostic evaluation, especially in high-risk individuals. Increased clinical awareness and timely referral for advanced imaging or specialist consultation may significantly improve the outcome.

Given the complexity of pancreatic cancer diagnosis and the lack of effective screening programs, a multidisciplinary approach integrating clinical vigilance, radiological expertise, novel biomarker, and the active involvement of primary care physicians research is essential. Understanding current diagnostic limitations and emerging opportunities is therefore critical to improving early detection and ultimately patient survival. This narrative review aims to summarize current diagnostic methods for pancreatic cancer, evaluate emerging technologies with potential for earlier detection, and highlight the essential role of physicians in improving outcomes.

Methods

A narrative literature review was conducted using the PubMed and Google Scholar databases. The search covered publications from January 2015 to May 2026. Eligible sources included original research articles, systematic reviews, meta-analyses, clinical guidelines, and consensus statements relevant to the diagnosis of pancreatic cancer and the role of primary care physicians in early detection. Articles written in English were considered. References of retrieved articles were also manually screened to identify additional relevant sources.

Results

Epidemiology and stage at diagnosis

Pancreatic cancer is a growing public health challenge worldwide, with incidence and mortality rates continuing to rise. According to GLOBOCAN, the cumulative risk of developing pancreatic cancer in Europe is approximately 2.21% over a lifetime, corresponding to about 2 cases per 100 individuals [9]. Across Europe in 2020, pancreatic cancer was responsible for 132,134 deaths, with 140,116 new cases recorded annually, making it one of the most lethal malignancies on the continent. This statistics implies that almost 29% of all deaths recorded in Europe annually are due to pancreatic cancer [10].

The prognosis of pancreatic cancer is inextricably linked to the stage at which it is diagnosed. The majority of patients present with locally advanced or metastatic disease at diagnosis, with approximately 80–85% of cases being unresectable at presentation [2]. Approximately 15% of patients with pancreatic cancer are diagnosed at a localized stage, which corresponds to the subgroup potentially eligible for surgical resection [11].

Role of imaging in pancreatic cancer detection

Each available imaging technique carries distinct advantages and limitations, and their appropriate use depends on clinical context, lesion characteristics, and available resources.

Computed tomography (CT) remains the primary imaging modality in the diagnostic workup of suspected pancreatic cancer. CT is the preferred modality over MRI due to wider availability, greater consistency in image quality, and lower cost, with pancreatic cancer typically appearing as a hypoenhancing mass on arterial phase imaging, often associated with pancreatic duct dilatation and distal parenchymal atrophy [12]. Meta-analytic data report an overall sensitivity of 90%, specificity of 87% and diagnostic accuracy of 89% for CT in the diagnosis of pancreatic adenocarcinoma [13]. However, CT performs significantly worse for small lesions — approximately 40% of pancreatic tumors smaller than 2 cm are missed on CT, precisely at the stage when curative intervention remains most feasible [14].

Magnetic resonance imaging (MRI) combined with magnetic resonance cholangiopancreatography (MRCP) offers complementary value, particularly in the evaluation of cystic and indeterminate lesions. MRI with MRCP is considered the standard non-invasive modality for detecting and evaluating pancreatic cystic lesions, offering superior contrast resolution compared to CT for delineating cyst septations, mural nodules, and ductal communication [15]. MRI offers superior contrast resolution compared to CT, particularly in the detection of smaller and isoattenuating lesions that may be missed on CT, with reported sensitivity of 93% and specificity of 90%, though its clinical use remains limited by higher cost, longer acquisition time, and lower availability compared to CT [13].

Endoscopic ultrasound (EUS) represents the most sensitive modality for the detection of small pancreatic lesions and occupies a critical role in both diagnosis and tissue acquisition. EUS achieves an overall sensitivity of approximately 94% for detecting pancreatic tumors, consistently outperforming CT, and its high resolution enables detection of focal lesions as small as 2-5 mm [16]. EUS-guided fine needle aspiration (EUS-FNA) further allows tissue

sampling for histological confirmation. Despite these advantages, EUS is operator-dependent, resource-intensive, and still not widely available in primary care.

Positron emission tomography (PET) plays a supplementary rather than primary role in pancreatic cancer diagnosis. International guidelines do not currently recommend its routine use in initial diagnosis. It can play a role in detecting occult distant metastases and assessing resectability, particularly following neoadjuvant treatment [17]. When combined with serum CA 19-9 measurement, PET diagnostic sensitivity may increase substantially, suggesting potential utility in a multimodal diagnostic approach [18].

Transabdominal ultrasound, while widely available and commonly the first imaging investigation ordered in primary care, has significant limitations in pancreatic cancer detection. Its sensitivity ranges from 75% to 89%, with sub-optimal performance stemming from operator experience, large body habitus, the retroperitoneal location of the pancreas, and the presence of bowel gas [19]. It may identify large tumours, biliary dilatation, or main pancreatic duct dilatation, but cannot reliably exclude malignancy and should not be considered sufficient in high-risk patients with persistent symptoms [19].

Taken together, no single imaging modality offers sufficient sensitivity and specificity for routine population-based screening. A stepwise approach - beginning with CT or transabdominal ultrasound in primary care, followed by EUS or MRI/MRCP for indeterminate findings - represents current best practice and should be guided by clinical risk stratification [12].

Biomarker CA 19-9 in clinical practice

Carbohydrate antigen 19-9 (CA 19-9) remains the only widely used and regulatory-approved serum biomarker for pancreatic cancer, and has been the subject of extensive clinical investigation since its discovery. It is a carbohydrate antigen related to the Lewis blood group system, detectable in serum at concentrations above the standard clinical cutoff of 37 U/mL [5]. In symptomatic patients, CA 19-9 demonstrates a sensitivity of 79–81% and specificity of 82–90% for the diagnosis of pancreatic cancer, making it a useful adjunct to imaging in the clinical workup [5].

Despite its widespread use, CA 19-9 carries significant limitations that preclude its application as a population-based screening tool. False negative results occur in patients with Lewis-negative blood group phenotype, which accounts for approximately 5–10% of the Caucasian population, who entirely lack the enzyme required for CA 19-9 antigen production and therefore

do not express measurable serum levels regardless of tumour burden [5, 20]. Conversely, false positive elevations are observed in a range of benign conditions including obstructive jaundice, chronic pancreatitis, cholangitis, and diabetes mellitus. [5, 21]. Furthermore, CA 19-9 levels may remain within the normal range during the earliest and most treatable stages of disease, limiting its utility for early detection [6].

In current clinical practice, CA 19-9 is therefore not recommended for screening of asymptomatic individuals [21]. Its principal role lies in monitoring treatment response following surgical resection or systemic chemotherapy - a decrease of 20–50% or more from baseline following treatment is associated with improved survival outcomes - as well as in detecting postoperative recurrence [5, 21]. Carcinoembryonic antigen (CEA) is sometimes used as a secondary marker, particularly in CA 19-9-negative patients, though it demonstrates lower overall sensitivity and diagnostic accuracy compared to CA 19-9 [22].

These limitations highlight the urgent need for novel biomarkers capable of detecting pancreatic cancer at an earlier and more actionable stage.

Liquid biopsy approaches in pancreatic cancer detection

Liquid biopsy refers to the analysis of tumour-derived material circulating in peripheral blood or other body fluids, offering a minimally invasive alternative to tissue biopsy for tumour detection, molecular profiling, and disease monitoring. The principal components of liquid biopsy include circulating tumour cells (CTCs), circulating tumour DNA (ctDNA), extracellular vesicles including exosomes, microRNAs, and tumour-educated blood platelets, each providing distinct biological information about tumour presence and characteristics. Given the anatomical inaccessibility of the pancreas and the limitations of conventional biomarkers, liquid biopsy has attracted considerable interest as a potential tool for early detection of pancreatic cancer [7, 23].

Circulating tumour DNA (ctDNA) is the most extensively studied liquid biopsy component in pancreatic cancer. KRAS mutations, present in over 90% of pancreatic ductal adenocarcinomas, represent the primary target for ctDNA detection, as their identification in cell-free DNA provides tumour-specific evidence of malignancy detectable prior to radiological manifestation. Detection is performed using highly sensitive methods including droplet digital PCR (ddPCR) and next-generation sequencing (NGS). However, a significant challenge is the low concentration of ctDNA in plasma at early disease stages - ctDNA constitutes only a small fraction of total cell-free DNA, necessitating ultrasensitive detection techniques, and only approximately 31% of patients with stage I/II pancreatic cancer have detectable KRAS ctDNA

scores [24]. Despite this, ctDNA detected during postoperative follow-up predicted clinical recurrence with a sensitivity of 90% and specificity of 88%, suggesting particular utility in monitoring rather than primary screening [25].

Circulating tumour cells (CTCs) represent intact tumour cells shed into the bloodstream and carry prognostic significance in pancreatic cancer. Their detection is technically challenging due to the extremely low abundance of CTCs in peripheral blood relative to normal haematopoietic cells, requiring highly specialised enrichment and detection platforms [26]. Exosomes - small extracellular vesicles released by tumour cells - represent another promising avenue. Glypican-1 (GPC1), a cell surface proteoglycan overexpressed in pancreatic cancer-derived exosomes, has shown promise as a screening marker, with initial studies reporting absolute sensitivity and specificity in distinguishing pancreatic cancer patients from healthy controls and patients with benign pancreatic disease [27]. Furthermore, combining flow cytometry with microRNA expression patterns on pancreatic cancer cell exosomes has demonstrated screening sensitivity of 100% with a specificity of 80% in experimental settings [23]. However, these results require validation in large prospective cohorts before clinical adoption, as subsequent studies have been unable to consistently reproduce the original findings using alternative detection methods [27].

MicroRNA panels represent a further emerging approach, with specific miRNA signatures shown to distinguish pancreatic cancer patients from healthy controls and patients with chronic pancreatitis [28]. Liquid biopsy components including cell-free nucleic acids, CTCs, metabolome compounds, exosomes, and platelets have all demonstrated potential clinical relevance for diagnosis, prognosis, stratification, and treatment follow-up in pancreatic cancer, though most remain at the stage of research or early clinical validation [29].

Taken together, liquid biopsy approaches hold considerable promise for improving early detection of pancreatic cancer, particularly as complementary tools alongside conventional imaging and CA 19-9. Nevertheless, the transition from experimental to routine clinical use requires standardisation of detection platforms, large-scale prospective validation, and demonstration of clinical utility in improving patient outcomes [7, 23]

Emerging role of artificial intelligence in diagnosis

Artificial intelligence (AI), encompassing machine learning (ML) and deep learning (DL), is rapidly emerging as a transformative tool in oncological diagnostics, including pancreatic cancer detection. By analysing vast quantities of imaging data and identifying subtle patterns beyond the capacity of human visual perception, AI-based systems hold considerable promise

for improving early detection of pancreatic ductal adenocarcinoma [30, 31].

Radiomics - the automated extraction of quantitative imaging features from cross-sectional imaging - represents one of the most clinically advanced AI applications in this field. A key study demonstrated that quantitative radiomic features derived from CT imaging can predict pancreatic cancer up to 36 months before clinical diagnosis, with sensitivity ranging from 88% to 91%, specificity from 96% to 98%, and area under the curve (AUC) of 0.98–0.99 for patients without chronic pancreatitis [8]. These findings suggest that radiomics-based algorithms may be capable of identifying precancerous imaging signatures at a stage when curative intervention remains feasible, representing a significant advance over conventional visual CT interpretation.

Deep learning models applied to CT imaging have also demonstrated strong diagnostic performance. A nationwide population-based study utilising deep learning for pancreatic cancer detection on CT scans reported high accuracy, with the model outperforming radiologist assessment in identifying early-stage lesions [14]. AI has further been applied to endoscopic ultrasound (EUS) image analysis, where convolutional neural networks have demonstrated improved differentiation of pancreatic masses from surrounding tissue, potentially reducing operator dependency - one of the key limitations of conventional EUS [30].

Beyond imaging, machine learning approaches have been explored for mining electronic health records (EHR) to identify patients at elevated risk of pancreatic cancer based on combinations of diagnosis codes, laboratory values, and demographic data - an application with direct relevance to primary care practice. Machine learning and deep learning algorithms analysing CT images have shown the ability to compare identified changes characteristic of pancreatic cancer against reference datasets, offering a promising complement to conventional diagnostic pathways [32].

Despite these advances, significant barriers to clinical implementation remain. Current limitations include the lack of large, prospectively validated, multicentre datasets; the so-called "black box" problem of algorithmic interpretability; absence of regulatory approval for most AI diagnostic tools; and insufficient integration into existing clinical workflows [30, 31]. Most AI applications in pancreatic cancer diagnosis remain at the research or early validation stage and are not yet part of routine practice. Nevertheless, the convergence of radiomics, deep learning, and EHR-based risk stratification represents one of the most promising frontiers in improving early pancreatic cancer detection.

Role of primary care physicians in early detection

Primary care physicians occupy a uniquely pivotal position in the early detection of pancreatic cancer, as they represent the first point of contact for the vast majority of patients presenting with symptoms. Early diagnosis remains particularly challenging due to the non-specific and often subtle clinical presentation of pancreatic cancer, with symptoms frequently overlapping with common benign gastrointestinal conditions [33]. Several studies have demonstrated that patients commonly attend multiple primary care consultations before receiving a diagnosis of pancreatic cancer, contributing to significant diagnostic delays [33, 34] Symptoms that should raise clinical suspicion include unexplained weight loss, persistent epigastric or back pain, painless jaundice, and new-onset diabetes mellitus, particularly in individuals over 50 years of age [35, 36].

New-onset diabetes mellitus deserves particular attention as a potential early manifestation of pancreatic cancer. Population-based studies have shown that adults over 50 years old with newly diagnosed diabetes have a significantly increased risk of pancreatic cancer compared with the general population [36]. The coexistence of new-onset diabetes and unexplained weight loss should therefore be considered a red flag warranting urgent diagnostic evaluation, including abdominal imaging and laboratory assessment [35, 36].

Risk assessment and clinical decision-support tools may improve the identification of high-risk patients in primary care settings. Several tools, including QCancer, electronic risk assessment tools (eRATs), Future Health Today, and C the Signs have demonstrated potential utility in supporting earlier recognition of pancreatic cancer symptoms in primary care, though no tool has been developed for pancreatic cancer alone [37]. The QCancer algorithm, derived and validated using primary care electronic health records, incorporates symptoms and risk factors to calculate individualised cancer risk scores and has been integrated into GP software systems in several healthcare settings [38].

Barriers to early diagnosis in primary care are well recognised and include the low prior probability of pancreatic cancer in the general population - a GP may see only one patient with the disease every five years - as well as the non-specific nature of early symptoms [33, 39]. Addressing these barriers requires a multifaceted approach: targeted education of primary care physicians regarding red flag symptom combinations, development and implementation of validated risk stratification tools, improved direct access pathways to CT and EUS, and clearly defined referral protocols for high-risk patients [37, 39].

Discussion

This narrative review summarizes current evidence on the diagnosis of pancreatic cancer, with particular focus on the role of primary care physicians in improving early detection outcomes. The collected data highlight the persistent and multifaceted challenge of diagnosing pancreatic cancer at a stage when curative intervention remains feasible.

Interpretation of main findings

The epidemiological data confirm that pancreatic cancer continues to carry one of the worst prognoses of any malignancy, with the majority of patients diagnosed at an advanced, unresectable stage. The survival difference between localized and metastatic disease underscores that stage at diagnosis is the single most decisive determinant of outcome [1, 11].

Among imaging modalities, CT remains the cornerstone of diagnosis and staging, though its limited sensitivity for lesions smaller than 2 cm represents a critical bottleneck in early detection [12, 14]. EUS demonstrates superior sensitivity for small lesions and tissue acquisition, but its resource intensity and operator dependency limit widespread availability [16]. The stepwise approach combining multiple modalities according to clinical risk remains the standard of care, though no single modality is adequate for population-level screening.

CA 19-9 remains the only routinely used serum biomarker but is compromised by well-documented limitations including false negatives in Lewis-negative patients and insufficient sensitivity in early-stage tumours [5, 6]. Liquid biopsy approaches - particularly ctDNA and exosome-based markers - show promise but remain largely in the research and early validation phase, with sensitivity for early-stage disease still insufficient for routine clinical implementation [24, 25, 27].

Artificial intelligence and radiomics represent genuinely promising developments, with radiomic CT features demonstrating the ability to predict pancreatic cancer up to 36 months before clinical diagnosis, and deep learning models showing strong performance in both imaging analysis and EHR-based risk stratification [8, 14, 32].

Primary care physicians emerge as a critical determinant of diagnostic timeliness, with clinical decision-support tools such as QCancer and eRATs offering practical support - though no tool has yet been validated specifically for pancreatic cancer alone [37].

Clinical significance and practical implications

These findings emphasise the need for a multidisciplinary and integrated approach to pancreatic cancer diagnosis. Primary care physicians should maintain heightened awareness of red flag

symptom combinations - particularly new-onset diabetes over age 50, unexplained weight loss, and epigastric or back pain - and ensure timely referral for imaging and CA 19-9 measurement [35, 36, 39]. Integration of AI-based risk stratification into primary care electronic health records and incorporation of liquid biopsy into multimodal diagnostic panels represent the most promising near-future directions. Targeted education of primary care physicians and structured referral protocols remain as a priority [37, 38].

Limitations and future research directions

The current evidence base is characterised by predominantly single-centre, retrospective studies with heterogeneous designs, limiting generalisability. Liquid biopsy approaches lack standardised detection platforms and large prospective validation datasets [23, 25]. Furthermore, most AI diagnostic models have been developed and validated in highly specialised academic centres, and their performance in real-world clinical settings - including primary care - remains to be established.

Future research should prioritise multicentre prospective validation of emerging diagnostic tools, with particular focus on early-stage disease detection. The development of pancreatic cancer-specific risk assessment instruments for primary care represents an important clinical need [37]. Combining imaging, biomarker, and clinical risk data into integrated multimodal diagnostic algorithms - supported by AI - offers the greatest potential for meaningful improvement in early detection rates and, ultimately, patient survival.

Conclusion

Pancreatic cancer remains one of the most lethal malignancies, with prognosis predominantly determined by stage at diagnosis. Despite advances in imaging, biomarker research, and artificial intelligence, the majority of patients continue to be diagnosed at an advanced, unresectable stage, and effective population-based screening programmes do not yet exist. Current diagnostic pathways rely on a multimodal approach combining CT, MRI, EUS, and CA 19-9, each with distinct strengths and limitations. Emerging technologies - including liquid biopsy, radiomics, and deep learning - hold considerable promise for improving early detection, but require further prospective validation before routine clinical implementation.

Primary care physicians occupy a uniquely important position in this diagnostic landscape, as the first point of contact for the vast majority of patients. Heightened clinical awareness of red

flag symptom combinations, timely referral, and the use of validated risk stratification tools are essential components of an effective early detection strategy. Addressing the barriers to timely diagnosis in primary care - through education, improved access to imaging, and integration of clinical decision-support tools - represents one of the most actionable and immediate opportunities to improve outcomes for patients with pancreatic cancer.

Disclosures

Author's contribution:

Conceptualization: MS, PC, AP;

Methodology: MS, WK, PC;

Formal analysis: MS, MK, MSl;

Investigation: MS, WK, IG;

Resources: AA, MSz;

Data curation: AA, KC**;**

Writing – original draft: MS, PC;

Writing – review & editing: AP, MSl;

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Supervision: MS;

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References:

1. Siegel RL, Giaquinto AN, Jemal A.: Cancer statistics, 2024. CA: A Cancer Journal for Clinician. 2024;74(1):17–48. https://doi.org/10.3322/caac.21820
2. McGuigan A, Kelly P, Turkington RC, Jones C, Coleman HG, McCain RS.: Pancreatic cancer: A review of clinical diagnosis, epidemiology, treatment and outcomes. World Journal of Gastroenterology. 2018;24(43):4846–4861. https://doi.org/10.3748/wjg.v24.i43.4846
3. Rawla P, Sunkara T, Gaduputi V.: Epidemiology of pancreatic cancer: Global trends, etiology and risk factors. World Journal of Oncology. 2019;10(1):10–27. https://doi.org/10.14740/wjon1166
4. Ilic M, Ilic I.: Epidemiology of pancreatic cancer. World Journal of Gastroenterology. 2016;22(44):9694–9705. http://doi.org/10.3748/wjg.v22.i44.9694
5. Ballehaninna U, Chamberlain R.: Serum CA 19-9 as a biomarker for pancreatic cancer - A comprehensive review. Indian Journal of Surgical Oncology. 2011;2(2):88–100.https://doi.org/10.1007/s13193-011-0042-1
6. Haab BB, Huang Y, Balasenthil S, Partyka K, Tang H, Anderson M, et al.: Definitive Characterization of CA 19-9 in Resectable Pancreatic Cancer Using a Reference Set of Serum and Plasma Specimens. *PLoS One.* 2015;10(10):e0139049. https://doi.org/10.1371/journal.pone.0139049
7. Wang K, Wang X, Pan Q, Zhao B.: Liquid biopsy techniques and pancreatic cancer: diagnosis, monitoring, and evaluation. Molecular Cancer. 2023;22:167. https://doi.org/10.1186/s12943-023-01870-3

8. Chen W, Zhou Y, Asadpour V, Parker R, Puttock E, Lustigova E, Wu B.: Quantitative radiomic features from computed tomography can predict pancreatic cancer up to 36 months before diagnosis. Clinical and Translational Gastroenterology. 2023;14(1):e00548. https://doi.org/10.14309/ctg.0000000000000548
9. Ferlay J, Ervik M, Lam F, Colombet M, Mery L, Piñeros M, et al.: Global Cancer Observatory: Cancer Today. International Agency for Research on Cancer (IARC). Available from: https://gco.iarc.who.int/today (accessed 10 May 2026).
10. Partyka O, Pajewska M, Kwaśniewska D, Czerw AI, Deptała A, Budzik M, et al.: Overview of pancreatic cancer epidemiology in Europe and recommendations for screening in high-risk populations. Cancers. 2023;15(14):3634. https://doi.org/10.3390/cancers15143634
11. Surveillance, Epidemiology, and End Results (SEER) Program. Pancreatic Cancer-Cancer Stat Facts. National Cancer Institute. Available from: https://seer.cancer.gov/statfacts/html/pancreas.html (accessed 12 May 2026).
12. Chu LC, Fishman EK.: Pancreatic ductal adenocarcinoma staging: a narrative review of radiologic techniques and advances. International Journal of Surgery. 2024;110(10):6052–6063. http://doi.org/10.1097/JS9.0000000000000899
13. Hussain A, Weimer D, Mani N.: Diagnosing pancreatic adenocarcinoma with contrast-enhanced ultrasonography: a literature review of research in Europe and Asia. Cureus. 2022;14(2):e22592. http://doi.org/10.7759/cureus.22080
14. Chen PT, Wu T, Wang P, et al..: Pancreatic cancer detection on CT scans with deep learning: a nationwide population-based study. Radiology. 2023;306(1):172–182. https://doi.org/10.1148/radiol.220152
15. Quingalahua E, Al-Hawary MM, Machicado JD.: The role of magnetic resonance imaging (MRI) in the diagnosis of pancreatic cystic lesions (PCLs). Diagnostics. 2023;13(4):585; https://doi.org/10.3390/diagnostics13040585
16. Yoshida T, Yamashita Y, Kitano M.: Endoscopic ultrasound for early diagnosis of pancreatic cancer. Diagnostics. 2019;9(3):81. https://doi.org/10.3390/diagnostics9030081
17. Ghidini M, Vuozzo M, Galassi B, Mapelli P, Ceccarossi V, Caccamo L, Picchio M, Dondossola D.: The role of positron emission tomography/CT for staging and disease response assessment in localized and locally advanced pancreatic cancer. Cancers. 2021;13(16):4155. https://doi.org/10.3390/cancers13164155

18. Huang S, Chong H, Sun X, Wu Z, Jia Q, Zhang Y, Lan X.: The value of 18F-FDG PET/CT in diagnosing pancreatic lesions: comparison with CA19-9, enhanced CT or enhanced MR. Frontiers in Medicine. 2021;8:668697. http://doi.org/10.3389/fmed.2021.668697
19. Ashida R, Tanaka S, Yamanaka H, et al.: The role of transabdominal ultrasound in the diagnosis of early stage pancreatic cancer: review and single-center experience. Diagnostics. 2019;9(1):2. http://doi.org/10.3390/diagnostics9010002
20. Hasan S, Jacob R, Manne U, Paluri R.: Advances in pancreatic cancer biomarkers. Oncology Reviews. 2019;13(1):410. http://doi.org/10.4081/oncol.2019.410
21. Azizian A, Rühlmann F, Krause T, Bernhardt M, Jo P, Ghadimi M, Gaedcke J.: CA19-9 for detecting recurrence of pancreatic cancer. Scientific Reports. 2020;10:1332. http://doi.org/10.1038/s41598-020-57930-x
22. Balaban DV, Marin FS, Manucu G, Zoican A, Ciochina M, Mina V, Patoni C, Vladut C, Bucurica S, Costache RS, Ionita-Radu F, Jinga M.: Clinical characteristics and outcomes in carbohydrate antigen 19-9 negative pancreatic cancer. World Journal of Clinical Oncology. 2022;13(7):630–640. http://doi.org/10.5306/wjco.v13.i7.630
23. Ramírez-Maldonado E, López Gordo S, Major Branco RP, Pavel MC, Estalella L, Llàcer-Millán E, Guerrero MA, López-Gordo E, Memba R, Jorba R.: Clinical application of liquid biopsy in pancreatic cancer: a narrative review. International Journal of Molecular Sciences. 2024;25(3):1640. http://doi.org/10.3390/ijms25031640
24. Macgregor-Das A, Yu J, Tamura K, Abe T, Suenaga M, Shindo K, Borges M, Koi C, Kohi S, Sadakari Y, Dal Molin M, Almario JA, Ford M, Chuidian M, Burkhart R, He J, Hruban RH, Eshleman JR, Klein AP, Wolfgang CL, Canto MI, Goggins M.: Detection of circulating tumor DNA in patients with pancreatic cancer using digital next-generation sequencing. Journal of Molecular Diagnostics. 2020;22(6):748–756. http://doi.org/10.1016/j.jmoldx.2020.02.010
25. Groot VP, Mosier S, Javed AA, Teinor JA, Gemenetzis G, Ding D, Haley LM, Yu J, Burkhart RA, Hasanain A, Debeljak M, Kamiyama H, Narang A, Laheru DA, Zheng L, Lin MT, Gocke CD, Fishman EK, Hruban RH, Goggins MG, Molenaar IQ, Cameron JL, Weiss MJ, Velculescu VE, He J, Wolfgang CL, Eshleman JR.: Circulating tumor DNA as a clinical test in resected pancreatic cancer. Clinical Cancer Research. 2019;25(16):4973–4984. http://doi.org/10.1158/1078-0432.CCR-19-0197

26. Yeo D, Bastian A, Strauss H, Saxena P, Grimison P, Rasko JEJ.: Exploring the clinical utility of pancreatic cancer circulating tumor cells. International Journal of Molecular Sciences. 2022;23(3):1671. http://doi.org/10.3390/ijms23031671
27. Herreros-Villanueva M, Bujanda L.: Glypican-1 in exosomes as biomarker for early detection of pancreatic cancer. Annals of Translational Medicine. 2016;4(4):64. http://doi.org/10.3978/j.issn.2305-5839.2015.10.39
28. Cao Z, Liu C, Xu J, You L, Wang C, Lou W, Sun B, Miao Y, Liu X, Wang X, Zhang T, Zhao Y.: Plasma microRNA panels to diagnose pancreatic cancer: results from a multicenter study. Oncotarget. 2016;7(26):41575–41583. http://doi.org/10.18632/oncotarget.9491
29. Buscail E, Maulat C, Muscari F, Chiche L, Cordelier P, Dabernat S, Alix-Panabières C, Buscail L.: Liquid biopsy approach for pancreatic ductal adenocarcinoma. Cancers. 2019;11(6):852. http://doi.org/10.3390/cancers11060852
30. Kumar V, Gaddam M, Moustafa A, Iqbal R, Gala D, Shah M, Gayam VR, Bandaru P, Reddy M, Gadaputi V.: The utility of artificial intelligence in the diagnosis and management of pancreatic cancer. Cureus. 2023;15(11):e49560. http://doi.org/10.7759/cureus.49560
31. Shahul Hameed B, Krishnan UM.: Artificial intelligence-driven diagnosis of pancreatic cancer. Cancers. 2022;14(21):5382. http://doi.org/10.3390/cancers14215382
32. Placido D, Yuan B, Hjaltelin JX, Bhatt DL, Preisler L, Bjørnsson ES, Johansen JS, Tjønnfjord GE, Agerschou ED, Reinholt FP, Kvale D, Fagerberg T, Lund-Andersen H, Christoffersen T, Larsen SJ, Brunak S.: A deep learning algorithm to predict risk of pancreatic cancer from disease trajectories. Nature Medicine. 2023;29(5):1113–1122. http://doi.org/10.1038/s41591-023-02332-5
33. Lyratzopoulos G, Vedsted P, Singh H.: Understanding missed opportunities for more timely diagnosis of cancer in symptomatic patients after presentation. British Journal of Cancer. 2015;112:S84–S91. https://doi.org/10.1038/bjc.2015.47
34. Stapley S, Peters TJ, Neal RD, Hamilton W.: The risk of pancreatic cancer in symptomatic patients in primary care: a large case-control study using electronic records. British Journal of Cancer. 2012;106(12):1940–1944. https://doi.org/10.1038/bjc.2012.190
35. Sharma A, Smyrk TC, Levy MJ, Topazian MA, Chari ST.: Fasting blood glucose levels provide estimate of duration and progression of pancreatic cancer before diagnosis. Gastroenterology. 2018;155(2):490–500.e2. https://doi.org/10.1053/j.gastro.2018.04.025

36. Chari ST, Leibson CL, Rabe KG, et al.: Pancreatic cancer–associated diabetes mellitus: prevalence and temporal association with diagnosis of cancer. Gastroenterology. 2008;134(1):95–101. https://doi.org/10.1053/j.gastro.2007.10.040
37. Claridge H, Cooke EA, Thomas SA, Greenwood N, Lemanska A.: Pancreatic cancer risk assessment tools in primary care: a mixed methods systematic review. Journal of Gastrointestinal Cancer. 2025;56(1):128. http://doi.org/10.1007/s12029-025-01229-5
38. Hippisley-Cox J, Coupland C.: Identifying patients with suspected pancreatic cancer in primary care: derivation and validation of an algorithm. British Journal of General Practice. 2012;62(594):e38–e45. https://doi.org/10.3399/bjgp12X616355
39. Pereira SP, Oldfield L, Ney A, Hart PA, Keane MG, Pandol SJ, Li D, Greenhalf W, Jeon CY, Koay EJ, Almario CV, Halloran C, Lennon AM, Costello E.: Early detection of pancreatic cancer. Lancet Gastroenterology and Hepatology. 2020;5(7):698–710. http://doi.org/10.1016/S2468-1253(19)30416-9