Current Status and Future Directions for Screening Patients at High Risk for Pancreatic Cancer

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Abstract: It is well known that pancreatic ductal adenocarcinoma has a high mortality rate. Despite progress in understanding the biology and genetic basis of this disease, life expectancy has changed minimally in the last 50 years. This article highlights the importance of screening patients at high risk for developing pancreatic cancer and reviews current methods as well as methods in development for pancreatic cancer early detection and surveillance.

A total of 53,070 new cases of pancreatic cancer were expected for 2016, and 41,750 deaths were anticipated from the disease during the same year.[1] Several reasons have been postulated to explain the poor prognosis of pancreatic cancer, including aggressive biology and advanced stage at the time of diagnosis.[2,3] Pancreaticoduodenectomy, a surgery introduced in 1935 by Dr Allen Oldfather Whipple, remains the treatment of choice for patients with resectable pancreatic cancer. However, fewer than 20% of patients diagnosed with pancreatic cancer have resectable disease.[4] In recent decades, significant advances in surgical techniques have resulted in decreased perioperative morbidity and mortality rates following pancreatic resection[5]; however, this has only minimally impacted the median overall survival of patients with localized operable pancreatic cancer, highlighting the urgent need for implementation of early detection strategies. It should be noted that most chemotherapy and immunotherapy regimens have limited efficacy once a diagnosis is made in a symptomatic patient with nonresectable disease. Therefore, multiple national and international centers are focusing on screening asymptomatic patients. Given the overall lower incidence and prevalence of pancreatic cancer compared to other malignancies, it is not cost-effective to screen the general population. The International Cancer of the Pancreas Screening (CAPS) Consortium, which consists of worldwide experts, has thus advocated for both establishing guidelines to classify individuals as high risk based upon family history and genetic susceptibility and developing screening and surveillance programs for this population.[6-10]

Table 1. Current and Novel Biomarkers, Imaging Techniques, and Endoscopic Methods for Screening Patients at High Risk for PDAC

	Current Methods	Methods in Development
Biomarkers	Cancer antigen 19-9 Carcinoembryonic antigen Serum glucose Amylase and lipase	Plectin-1 Glypican-1 Three-biomarker panel in urine
Imaging Techniques	Computed tomography Magnetic resonance imaging Magnetic resonance cholangiopancreatography	Single-source, dual-energy, spectral MDCT Hybrid positron emission tomography–magnetic resonance imaging Iterative reconstruction algorithm on MDCT
Endoscopic Methods	Endoscopic ultrasound	Contrast-enhanced harmonic EUS EUS elastography EUS-guided fine-needle aspiration and pancreatic juice sampling Needle-based confocal laser endomicroscopy Duodenal spectroscopy

EUS, endoscopic ultrasound; MDCT, multidetector computed tomography; PDAC, pancreatic ductal adenocarcinoma.

Mathematical models indicate that several years could pass between the formation of a cell serving as the parental clone and the seeding for metastasis, highlighting a window of opportunity for early detection of pancreatic cancer.[11] This information, in addition to the lack of efficacy of most therapies used for pancreatic cancer treatment, strongly supports efforts for pancreatic cancer early detection. This article reviews current screening strategies used in patients at high risk for pancreatic ductal adenocarcinoma (PDAC) and discusses some of the methods in development to improve early detection (Table 1).

Goals of Surveillance

Fewer than 20% of patients with pancreatic cancer present with localized disease, approximately 30% present with regional disease, and more than 50% present with distant disease. Even though recent statistics have reported a 5-year overall survival rate of 7.7% for patients with pancreatic cancer, the few patients who present with stage IB have a 5-year survival rate of 12%, which increases to 14% for patients with stage IA.[1] It has been reported that patients with lesions smaller than 10 mm, or minute lesions, have a 5-year survival rate as high as 60%,[12] although the number of patients diagnosed with this tumor size is extremely low. These data indicate that early detection might have enormous importance in the disease prognosis. The goal of a surveillance program in asymptomatic patients should be the detection of stage I pancreatic cancer; ideally, the goal would be to detect premalignant lesions, which would dramatically increase survival rates. Novel imaging methods and biomarkers should evolve together, and the challenge is to increase the sensitivity and specificity of the detection methods to avoid unnecessary overtreatment of patients.

Population Target for Pancreatic Cancer Early Detection Screening Programs

The risk for pancreatic cancer is multifactorial, consisting of both environmental and inherited causes. Hereditary factors appear to play a key role in the development of pancreatic cancer in approximately 5% to 10% of all cases, including in individuals with an underlying germline gene mutation (Table 2) and those with a strong family history of pancreatic cancer.[13,14] The International CAPS Consortium, after meeting in 2011, published consensus criteria for screening individuals based upon their genetic susceptibility or family history.[6] These criteria take into consideration the specific genetic mutations and the degree and number of relatives affected to determine the need for screening. The recommendations were established primarily in evidence of elevated risk rather than proven efficacy of screening.[6,15] Despite many controversies and a lack of consensus on issues such as when to start screening, the method and interval of follow-up surveillance after an initial examination, and when to consider surgery, there was agreement and support for endoscopic ultrasound (EUS) and magnetic resonance imaging (MRI) as the preferred modalities for initial screening compared with endoscopic retrograde cholangiopancreatography (ERCP) and computed tomography (CT). The risk of pancreatic cancer based upon family history can be determined using a Mendelian risk assessment tool called PancPRO (Johns Hopkins), which calculates the probability that an

Table 2. Genetic Mutations and Syndromes Associated With Increased Risk for Pancreatic Cancer

Genetic Mutations	Family Syndromes
BRCA1/*BRCA2*	Hereditary breast and ovarian cancer syndrome
PALB2	Hereditary syndrome related to *PALB2* mutation
MLH1, *MSH2*, *MSH6*, *PMS2*	Lynch syndrome
TP53	Li-Fraumeni syndrome
CDKN2A/*p16*	Familial atypical multiple mole melanoma syndrome
STK11	Peutz-Jeghers syndrome
PRSS1	Hereditary pancreatitis syndrome

individual carries a deleterious mutation in a pancreatic susceptibility gene.[15,16]

Current Methods for Screening

Biomarkers

Cancer Antigen 19-9 Cancer antigen 19-9 (CA 19-9), a sialylated Lewis blood group antigen discovered by Dr Hilary Koprowski in 1979, has been the standard serum tumor marker utilized for diagnosis, prognosis, and recurrence detection in patients with pancreatic cancer.[17] However, this biomarker has several limitations, such as reduced accuracy in pancreatic cancer diagnosis and in discriminating between pancreatic cancer, extrapancreatic malignancies, and benign hepatopancreaticobiliary conditions, which can also raise CA 19-9 levels. A meta-analysis reviewing more than 35 studies revealed a sensitivity of 78.2% and a specificity of 82.2%.[18] Additionally, approximately 6% of the white population and 22% of the African American population in the United States do not produce the specific sialyl antigen, which increases the number of false-negative results.[18,19]

Carcinoembryonic Antigen Carcinoembryonic antigen (CEA) is the second most common serum biomarker used in clinical practice for pancreatic cancer diagnosis. A systematic review of 13 studies encompassing 1323 cases using CEA showed a sensitivity of 54% and a specificity of 79% for discriminating between malignant and benign conditions.[20] Therefore, even though CEA is less accurate than CA 19-9 for malignant pancreatic cancer diagnosis, it has comparable specificity to CA 19-9 for identification of benign pancreatic conditions.[17,18,21]

Serum Glucose The association between diabetes and pancreatic cancer is complex. An important issue is whether diabetes in patients with pancreatic cancer represents a preexisting condition or if it is secondary to the cancer development.[22] Several studies have shown either no association or mild increased risk for pancreatic cancer in patients with long-standing diabetes.[23,24] Glucose levels improve following subtotal pancreatectomy for pancreatic cancer resection, suggesting that pancreatic cancer may lead to diabetes.[25] Recently, new-onset diabetes has been recognized as an early manifestation of pancreatic cancer, which could aid the diagnosis of asymptomatic patients with pancreatic cancer. Identification of new-onset diabetes could lead to diagnosis at an early resectable stage, as it may predate the diagnosis of pancreatic cancer by as much as 18 to 24 months.[26] However, long-standing type 2 diabetes is very prevalent in the general population, making screening of this group a difficult task. Therefore, discovery of novel biomarkers to be utilized in conjunction with glucose levels is imperative.

Amylase and Lipase Pancreatic enzymes such as amylase and lipase represent another group of tumor markers used for pancreatic cancer diagnosis and follow-up. Despite their reflection of pancreatic metabolic activity, the enzymes lack sufficient sensitivity and specificity to be clinically useful for diagnosing pancreatic cancer, except for the rare subtype known as acinar cell carcinoma.[21,27]

Imaging

Imaging methods currently used for pancreatic cancer screening include CT, MRI, and magnetic resonance cholangiopancreatography (MRCP).

Computed Tomography A study led by Gangi and colleagues[28] was conducted to test the value of imaging in early diagnosis of pancreatic cancer. For the study, 2 radiologists blindly interpreted 62 CT scans performed before a pancreatic cancer clinical diagnosis was made, and both radiologists agreed that suspicious findings were present in 50% of CT scans performed within 18 months prior to pancreatic cancer diagnosis. However, only 7% of CT scans performed more than 18 months prior to diagnosis showed suspicious lesions.[28] The main early signs detected in the CT scans are pancreatic ductal dilation and cutoff.[29,30] However, it should be noted that many patients had normal CT scans even 6 months before diagnosis, highlighting the importance of further developing novel imaging methods to detect smaller lesions. CT has a threshold for lesion detection of 0.3 to 0.5 cm. High-resolution, fast CT scanners with less than a 1-mm slice thickness are now available, although their role in screening noninvasive precursor lesions

(pancreatic intraepithelial neoplasias, panINs) or early pancreatic cancer remains to be established.[29,31,32]

The main disadvantage of CT scans for pancreatic cancer screening is the ionizing radiation that this method delivers, particularly in individuals with impaired DNA mismatch repair gene function and chromosomal instability. Thus, the majority of current pancreatic cancer screening programs have replaced CT with MRI.

Magnetic Resonance Imaging and Magnetic Resonance Cholangiopancreatography MRI examination of the pancreas is performed with intravenous administration of gadolinium as a contrast material. Given the characteristic hypovascularity, pancreatic cancer is usually hypointense in T1-weighted images compared to the pancreatic parenchyma.[33] A study comparing MRI with CT scans showed no significant differences, with similar sensitivities of 84% and 86%, respectively.[34]

MRCP utilizes magnetic resonance technology to create a 3-dimensional image of the hepaticpancreaticobiliary area, providing optimal anatomic visualization of the biliary and pancreatic ducts.[33] In particular, MRCP imaging is superior to CT scans or MRI in distinguishing inflammatory, nonmalignant pancreatic masses from pancreatic cancer.[35]

Endoscopic Screening for Pancreatic Cancer

The only endoscopic method that is clinically used for pancreatic cancer screening is EUS, commonly performed in combination with cross-sectional imaging modalities such as MRI. A number of studies have looked at the efficacy of EUS for the early detection of pancreatic dysplasia and other precursor lesions in high-risk individuals (HRIs).[6,9,36-42] Brentnall and colleagues prospectively studied 14 patients who had 2 or more family members in more than 2 generations with a history of pancreatic cancer.[36] Patients were assessed with EUS, ERCP, CEA, and CA 19-9. Seven of 14 patients had abnormal, albeit nonspecific, findings on EUS and ERCP. These 7 patients underwent pancreatic resections, which showed evidence of intraductal dysplasia in all specimens. CT scans and tumor markers were unable to detect any changes.[36]

Rulyak and colleagues studied 35 patients from 13 familial pancreatic cancer kindreds.[37] EUS was the initial test of choice followed by ERCP in cases of symptomatic individuals or patients with abnormalities on EUS. Twelve of 35 patients had abnormalities on both EUS and ERCP and underwent pancreatectomy, with histology showing pancreatic dysplasia on all 12 cases. Follow-up of the 35 patients varied from 1 to 48 months, and none had pancreatic cancer at follow-up.

Langer and colleagues studied 76 HRIs from families with familial pancreatic cancer and enrolled them in a prospective screening program,[39] which included clinical examination, EUS, MRI, MRCP, and magnetic resonance angiography. Twenty-eight patients were found to have abnormalities, and pancreatic resections were performed in 6 patients, with results showing serous adenoma (n=3), early panIN (n=1), more advanced panIN (n=1), and intraductal papillary mucinous neoplasm (IPMN; n=1).

Poley and colleagues studied 44 individuals, 13 with familial atypical multiple mole melanoma syndrome, 21 with familial pancreatic cancer, 2 with hereditary pancreatitis, 2 with Peutz-Jeghers syndrome, 1 with Li-Fraumeni syndrome, 3 with *BRCA1* mutations, and 2 with *BRCA2* mutations; EUS and abnormal studies were further followed up with CT scans and/or MRI.[38] EUS detected mass lesions on 3 patients, all of whom had cancer found on resection. EUS also showed IPMN in 7 patients.

Verna and colleagues enrolled 51 patients from 43 families at high risk for pancreatic cancer in a screening program that included genetic testing.[10] EUS, MRI, or both were offered based on each patient's individual risk; 31 patients underwent EUS and 33 underwent MRI. EUS revealed 2 pancreatic cancers (1 resectable and 1 metastatic), 5 IPMNs, 7 cysts, and 6 parenchymal changes suggestive of chronic pancreatitis. Overall, 6 of the 51 patients (12%) had neoplastic lesions of the pancreas. The authors concluded that screening HRIs for pancreatic cancer with a comprehensive strategy of genetics and imaging was effective in detecting curable neoplasms.

Zubarik and colleagues enrolled 546 patients in a study to determine if early pancreatic neoplasia could be detected by elevated CA 19-9 levels and EUS.[42] All patients included in this study were tested for CA 19-9, and those with elevated CA 19-9 levels (27/546) were further evaluated with EUS. Neoplastic findings were detected in 5 patients and cancer in 1. The authors concluded that potentially curative pancreatic cancer could be detected by this protocol.

In a multicenter, prospective, cohort study led by Canto and colleagues,[43] 225 asymptomatic HRIs were screened at 5 academic medical centers in the United States using CT scan, MRI, and EUS. Ninety-two of 216 HRIs (42%) had evidence of 1 pancreatic mass (84 cystic, 3 solid) or dilated pancreatic duct (n=5). CT scan, MRI, and EUS detected a pancreatic abnormality in 11.0%, 33.3%, and 42.6% of HRIs, respectively. Among these abnormalities, neoplasms were identified in 85 HRIs (82 IPMNs, 3 pancreatic endocrine tumors). Five patients underwent surgery, and 3 of them had high-grade dysplasia in IPMNs (<3 cm) and multiple intraepithelial neoplasms. The authors concluded that screening of asymptomatic HRIs could detect curable, noninvasive,

high-grade lesions alongside the detection of multiple cystic lesions. EUS and MRI were superior to CT scans for the screening of HRIs.

The diagnostic yield of EUS ranges from 10% to 50%.[44] The yield of EUS is variable depending upon the underlying high-risk condition; therefore, criteria for screening through EUS should be carefully assessed.

Future Directions

There is a need for the development of novel methods for early detection of pancreatic cancer at the earliest stages and for premalignant lesions. Biomarker development should run in parallel to the development of novel imaging instruments so that both independent methods could validate each other. Below is a review of methods that are currently undergoing validation and that may become part of the standard care for pancreatic cancer screening in the future.

Novel Biomarkers

Plectin-1 Plectin-1 is a high molecular weight–protein normally expressed in several tissues, including skin, muscle, and brain,[45] and plays an important role in the cytoskeleton network organization, contributing to the maintenance of mechanical integrity and viscoelasticity properties of tissues.[46] Studies using engineered mouse models that mimic molecular features of human PDAC have demonstrated that plectin-1, which is normally expressed in the cytoplasm, is overexpressed in the cell membrane of PDAC cells compared to normal pancreatic ductal cells.[3,4] Plectin-1 has been initially identified as a specific PDAC biomarker. Probes designed with magneto-fluorescent nanoparticles were used to detect plectin-1 in preclinical models of PDAC by MRI. This method has allowed for the detection of small PDAC precursor lesions as well as micrometastatic lesions in liver and lymph nodes.[5,6] The ability of this probe to detect small PDAC but also premalignant lesions is a sign of its potential future utility for early detection in high-risk populations.

Glypican-1 Glypican-1 is a cell membrane proteoglycan, essential as a coreceptor for heparin-binding growth factors, and implicated in the control of cellular growth and differentiation. Glypican-1 has been reported to be expressed in breast and pancreatic cancer–derived exosomes.[47] Melo and colleagues analyzed exosomes from 190 patients with pancreatic cancer vs 18 patients with pancreatitis, 8 patients with serous cystadenoma, and 5 patients with IPMN (discovery cohort).[48] The authors then analyzed 56 patients with pancreatic cancer, 6 with pancreatitis, and 20 healthy donors (validation cohort), and demonstrated that exosomes from pancreatic cancer patients express higher levels of glypican-1 than healthy subjects with a sensitivity and specificity of 100% for both parameters. Regarding precursor lesion detection, the levels of glypican-1 in exosomes in the patients with IPMN were higher than the levels in the healthy donors and in the patients with benign pancreatic disorders, suggesting a potential use of this biomarker for early detection of precursor lesions. Of note, this study used mainly higher-stage pancreatic cancer samples and was limited to relatively smaller numbers of cases, underscoring the need for validation studies in larger blinded cohorts.

Studies have demonstrated that exosomes released by pancreatic cancer may have an important biological role in the progression of metastatic disease because they are selectively taken up by the liver Kupffer cells, causing activation of fibrotic pathways and establishing a proinflammatory niche that can ultimately support metastases.[49,50] In addition to accurately indicating pancreatic cancer diagnosis, the quantities of glypican-1 circulating exosomes correlate with tumor burden and could be used to assess prognosis and pancreatic cancer recurrence.[51]

Identification of cancer-specific exosomes in body fluids could enable early monitoring and therapy. Future prospective studies are needed to provide the validation required to move this marker into clinical practice.

Three-Biomarker Panel in Urine As urine is an ultrafiltrate of the blood, it might be expected that biologic markers could be found at higher concentrations in urine than in blood. Urinary metabolomics studies offer an opportunity to identify tumor-associated perturbations of cellular metabolism reflecting changes that occur in the tumor micro- and macroenvironment.[52] Such is the case with 3 proteins recently reported to be useful as pancreatic cancer biomarkers: REG1A, TFF1, and LYVE1.[53] REG1A is a regeneration glycoprotein that is expressed in pancreatic acinar cells, acts as an autocrine and paracrine growth factor, and increases during islet regeneration and maintenance of the exocrine phenotype. TFF1 is a family of gastrointestinal secretory peptides that interacts with mucin, increases during repair of mucosal injury, and has antiapoptotic effects over epithelial cells. LYVE1 is the lymphatic vessel endothelial hyaluronan receptor and binds to an extracellular mucopolysaccharide, mostly in the context of lymphangiogenesis.[53]

The 3 markers have been found to be increased in urine samples from patients with pancreatic cancer compared with healthy controls. When the 3 markers are combined, their accuracy for pancreatic cancer diagnosis increases to 90%, particularly in stage I to II, which indicates their potential utility for diagnosis at early stages of disease.[53]

Novel Imaging Methods

Single-Source, Dual-Energy, Spectral Multidetector Computed Tomography Pancreatic cancers are commonly hypoattenuating lesions on CT images. Kim and colleagues[54] have found that 27% of pancreatic adenocarcinomas smaller than 2 cm were isoattenuating by multidetector CT (MDCT), which results in lesions potentially being missed. The single-source, dual-energy system utilizes a single radiograph beam source that switches energy between 80 and 140 kVp at submillisecond-intervals during a single helical acquisition, permitting photon energies to exploit differences in material composition and attenuation.[55]

Single-source, dual-energy, spectral MDCT offers the ability to detect hypovascular pancreatic cancers at lower viewing energy levels, diminishing the number of isoattenuating early-stage tumors.[56] This technique can now be used routinely in abdominal imaging and early detection of different types of gastrointestinal malignancies, including early detection of pancreatic cancer.[57]

Hybrid Positron Emission Tomography–Magnetic Resonance Imaging Fusioned imaging studies have demonstrated an improved quality of differentiation of pancreatic cancer from benign lesions; MRI provides useful structural and functional tumor information that is complementary to the information supplied by positron emission tomography (PET), an effective predictor of staging and prognosis in cancer patients.[58] A study has demonstrated that hybrid PET-MRI is significantly more accurate (96.6%) than PET-CT (86.6%) in terms of performing a diagnosis of solid tumors such as pancreatic cancer.[59] Additionally, PET-MRI offers lower radiation exposure and higher soft tissue contrast as well as multiparametric imaging.[60] PET-MRI fusion also offers information such as involvement of the main pancreatic duct or collateral veins, involvement of the peripancreatic anatomic borders, and compromise of the superior mesenteric artery or celiac artery, both of which are important predictive factors for resectability. This technique provides qualitative information regarding the tissue such as necrosis, cystic degeneration, or fibrotic changes.[61] PET-MRI fusion scanners are being developed and may offer a powerful multimodality diagnostic tool.

Iterative Reconstruction Algorithm on Multidetector Computed Tomography Iterative reconstruction algorithm on MDCT is a promising technique that provides quality CT images at significantly reduced radiation doses. This method is used to reconstruct 2- and 3-dimensional images from a series of object projections. The advantages of this method are tissue attenuation, scatter and partial volume effect, and better delineation of objects with better resolution. This method also provides information on other tissue abnormalities such as plastic, waxy, or blotchy pixilated texture.[32]

This technique could be used to obtain high spatial resolution of pancreatic tissue[62] and provide very thin slices of high-quality CT images, as it has been previously utilized for the diagnosis of hypervascular hepatocellular carcinomas.[32,63] It is not widely used in commercial scanners because of its high cost; however, as it becomes more accessible, its use may increase.

Novel Endoscopic Ultrasound Techniques

In the future, other enhanced endoscopic methods may help provide better screening yield for pancreatic cancer, especially for precursor lesions or prediction of which precursor lesions are likely to behave in an aggressive manner. Some of these techniques are briefly described below.

Contrast-Enhanced Harmonic Endoscopic Ultrasound This relatively new technique, based on the detection of signals from microbubbles in vessels, can visualize both parenchymal perfusion and microvasculature in the pancreas without the artifacts secondary to Doppler ultrasound.[64] In a recent systematic review, Fusaroli and colleagues[65] analyzed 210 articles in which contrast-enhanced harmonic EUS (CH-EUS) was used and concluded that, for pancreatic solid lesions, the pooled sensitivity and specificity in the diagnosis of pancreatic carcinoma are very high. The main application of CH-EUS is the differential diagnosis between benign and malignant pancreatic lesions. For pancreatic cystic lesions, identification of neoplastic solid components as hyperenhanced lesions represents a promising application of CH-EUS.

Endoscopic Ultrasound Elastography Elastography is a relatively new technique applied to EUS imaging to distinguish different tissues based on their elastic properties. Cancerous tissue is known to be stiffer than corresponding healthy tissue. EUS elastography is able to differentiate chronic pancreatitis and focal lesions from normal pancreas but cannot differentiate chronic pancreatitis from pancreatic tumors.[66] Therefore, further work needs to be done using this methodology to prove potential clinical utility.

Endoscopic Ultrasound–Guided Fine-Needle Aspiration and Pancreatic Juice Sampling Combining EUS-guided fine-needle aspiration cytopathology analysis with *KRAS* mutation assay increased the sensitivity, negative predictive value, and accuracy of cytopathology alone in the diagnosis of pancreatic cancer in situ.[67] Detection of *TP53* mutations in secretin-stimulated pancreatic juice

samples is another highly specific indicator of invasive pancreatic cancer or high-grade dysplasia.[68]

Needle-Based Confocal Laser Endomicroscopy Needle-based confocal laser endomicroscopy (nCLE) is a newly developed endomicroscopic technique that enables imaging of the mucosal layer at a subcellular level of resolution. nCLE has been developed for the evaluation of pancreatic cystic tumors, solid tumors, and lymph nodes. The presence of epithelial villous structures on nCLE has been associated with IPMN, providing a sensitivity of 59%, specificity of 100%, positive predictive value of 100%, and negative predictive value of 50%.[68] A superficial vascular pattern on nCLE was identified in serous cystadenomas.[69] In pancreatic cancer, nCLE found vascular leakage with irregular vessels and leakage of fluorescein into the tumor.[70]

Duodenal Spectroscopy The periampullary duodenal mucosa shares the genetic and environmental milieu of the pancreas. Using the concept of field carcinogenesis, Mutyal and colleagues conducted a case-control study to evaluate low-coherence–enhanced backscattering spectroscopy to predict the probability of pancreatic cancer by analyzing the duodenal mucosa.[71] This approach enables minimally invasive detection of ultrastructural consequences of pancreatic field carcinogenesis. The authors found that the low-coherence–enhanced backscattering spectroscopy parameters and optical properties were significantly altered in patients with cancer (including early stage) as compared to healthy controls. Study results showed a sensitivity of 78%, specificity of 85%, and accuracy of 81%.[71]

Conclusion

As we strive to decrease the mortality rate of pancreatic cancer, we have made a good beginning by identifying the target population that would benefit from screening and have reached some agreement on the use of currently available imaging modalities. However, there is still a need for consensus on many issues, including when to start screening, the ideal method and interval of follow-up, and the optimal time to consider surgery. The impact that screening programs have on the rate of survival remains to be seen. Several potential novel biomarkers and imaging techniques are under evaluation for detecting premalignant and early malignant changes in the pancreas. Further advancement and progress in these techniques will help in identifying precursor lesions while they are still resectable.

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