Review Article

Risk factors, biomarker and imaging techniques used for pancreatic cancer screening

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Abstract: Pancreatic cancer (PC) is one of the most lethal epithelial malignancies. There have been many attempts aimed at improving survival rates; however, the fatality of PC has been attributed to its few, nonspecific and diverse symptoms that delay diagnosis, rapid metastatic progression and overall treatment resistance. The aggressive nature of PC has stimulated interest in detecting smaller asymptomatic cancers or precursor lesions that are more likely to be curable. This review discusses potential risk factors including lifestyle and genetic variables that are believed to be the most important in contributing to the development of PC. In addition, we focus our review on emerging literature to compare and contrast current screening strategies including biomarkers and imaging modalities with regards to detecting early PC. It is hoped that in the future, biomarker development will be supported by novel techniques in medical imaging that are currently being developed and tested to ultimately lead to earlier detection and increased cure for this fatal disease.

Keywords: Pancreatic cancer (PC); tumor markers; magnetic resonance imaging (MRI); multidetector computed tomography (MDCT); positron emission tomography (PET)

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Introduction

Pancreatic cancer (PC) is the fourth leading cause of cancer related deaths worldwide and remains one of the most fatal malignancies (1). There have been minimal improvements in survival rates over the last few decades despite advances in risk factor identification, imaging, surgical technique and chemotherapy (1-3). In contrast to the death rates of other common malignancies—lung, colorectal, breast and prostate—which have declined since 2003, the death rate from pancreatic adenocarcinoma has increased during that same time period (4). The few and diverse symptoms of this disease lead to delays in diagnosis, which is in part why most patients with PC present with late stages of the disease (4). Prognosis for PC is poor with 5-year survival rate less than 10% with only 10–20% of patients having a chance of successful resection and possible cure (3). One of the main causes of its poor prognosis is difficulty in early diagnosis (5). Median survival time for patients with metastatic PC is 5–8 months (6). PC develops with few symptoms in its early stages and although there are not many well-known risk factors, some accepted risk factors including smoking, a family history of PC and specific inherited genetic syndromes (7).

Given the poor prognosis of PC, there has been intense interest to detect precursor lesions or small asymptomatic cancers that are more likely to be curable (8). Widespread screening may not be cost-effective or feasible at this time due to a lack of inexpensive, non-invasive and accurate diagnostic tests for early lesions; however, screening may be beneficial in a selected population that is at high-risk for developing PC (8). This article will discuss various risk factors that have been associated with PC and focus specifically on diagnostic screening methodologies which include currently available and anticipated tumor markers and their limitations. In addition, our review will investigate current and possible future advances in imaging that may contribute to effective screening for early PC.

Risk factors

Tobacco

Tobacco—most commonly in the form of cigarette smoking—has been identified as a risk factor for PC. Smoking tobacco increases risk of PC and in particular, one-quarter of PC risk might be attributable to smoking (6). There are many chemicals that have been identified as carcinogenic in cigarette smoke. Nicotine is absorbed in the upper aerodigestive tract and predisposes to PC by causing genetic mutations in pancreatic cells (9). A study by Treviño *et al.* revealed that ligation of nicotine to its receptor stimulated metastasis and chemoresistance in PC through the Src pathway (9). In addition, a prospective study by Delitto *et al.* demonstrated that the microenvironment-dependent paracrine signaling mechanism is adversely affected by nicotine exposure, ultimately promoting the growth and metastasis of PC (10). Interestingly, there is an increased risk in smokers who follow a paternal inheritance pattern of hereditary pancreatitis by approximately 2-fold and decreased age at onset of PC by approximately 20 years (8).

Diabetes

PC is more commonly found in people with diabetes; however, an exact link between the two conditions remains inconsistent in the literature. It has been shown that patients with long-term diabetes have a 1.5- to 2-fold increased risk of PC (11,12). Mean age of developing PC in these patients was significantly older than patients with new-onset diabetes (12). Investigation of the association between diabetes mellitus and intraductal papillary mucinous neoplasms (IPMNs) showed a significantly higher risk (6.9 fold) of high grade dysplasia and invasive carcinoma in patients with recent onset diabetes mellitus (12). Due to the strong correlation between diabetes and PC, the use of Metformin as a potential therapeutic for PC patients was investigated in a retrospective study of patients with both diabetes and PC with results showing significantly longer survival (15.4 months in the metformin group *vs.* 11.1 months in the control group)—specifically in those with nonmetastatic disease (13).

Family history of PC

Family history of PC has consistently been associated with increased risk of PC. Results from previous studies suggest a family history of selected cancers (ovarian, breast and colorectal) could also be associated with increased risk of PC (14). Jacobs *et al.* pooled data from several prospective cohort studies and one case-control study and found that a family history of PC in a parent, sibling or child was associated with increased risk of PC (14). Even when the analysis was adjusted for non-genetic pancreatic risk factors (obesity, diabetes and smoking), the association between family history of PC and risk of PC was not attenuated (14). Furthermore, case control studies done in Ontario and Quebec found a 12.3% lifetime risk of PC in first degree relatives of multiple patients who were diagnosed with PC, thus revealing that the risk of association was higher in immediate family members (15).

Chronic pancreatitis

Chronic pancreatitis is a clearly identified and strong risk factor for PC (16). During the course of inflammation, many pro- and anti-inflammatory mediators (cytokines, reactive oxygen species and cyclooxygenase-2) are released from the pancreas promoting genomic damage and cellular proliferation, possibly leading to pancreatic malignancy (17). Furthermore, as tumor associated macrophages (TAMs) are within inflammatory infiltrates, high concentration of TAMs may be associated with carcinogenesis and metastasis (6,17).

Alcohol

Epidemiologic evidence suggest that alcohol consumption is associated with PC (6). During metabolism of alcohol in humans, acetaldehyde and fatty acid ethyl esters produce pancreatitis-like injury (6). A meta-analysis conducted by Wang *et al.* found that high alcohol intake is associated with increased risk of PC (18). It is also important to note that chronic pancreatitis—a known risk factor for PC—is associated with heavy alcohol consumption (18).

Obesity

Obesity has been identified as a risk factor for PC. Bracci *et al.* reviewed pooled data and meta-analyses that examined the effect of obesity/high body mass index (BMI) on increased risk of PC (19). They found that obesity increased risk of PC through the effects of adipose on insulin and insulin resistance, release of hormones, cytokines, chemokines and environmental exposure to carcinogens

in foods (19-22). Although significant evidence indicates that obesity increases risk of PC, additional hypotheses and further study of adiposity and obesity related factors will increase our understanding of the mechanisms relevant to pancreatogenesis and the onset of PC (23,24).

Inherited genetic syndromes

Hereditary breast and ovarian cancer (HBOC) syndrome
Hereditary breast-ovarian cancer syndrome is an autosomal dominant inherited syndrome associated with mutations in *BRCA1* and *BRCA2*—tumor suppressors involved in the repair of damaged DNA (8). Germline *BRCA1* mutation is associated with a 2.3- to 3.6-fold increase in PC whereas *BRCA2* mutation is associated with a 3- to 10-fold increase in PC risk (25,26). Approximately 1% of the general Ashkenazi Jewish population carries each of the *BRCA1* and *BRCA2* founder mutations (27). Studies focused on this population has revealed that a germline *BRCA2* mutation is found in 5.5–10% of patients with pancreatic adenocarcinoma (27-29). In addition, recent studies suggest that *BRCA* mutations may be a predictive treatment biomarker in PC since those with BRCA related PC may benefit from the addition of platinum agents to standard chemotherapy (30).

Hereditary pancreatitis
Hereditary pancreatitis is an inherited disorder characterized by recurrent attacks of acute pancreatitis in childhood or early adolescence followed by the development of chronic pancreatitis in late adolescence or early adulthood (31). This condition is inherited through an autosomal dominant pattern with incomplete penetrance (31). The majority of bona fide cases of hereditary pancreatitis are due to germline mutations in the cationic trypsinogen gene (*PRSS1*) (32). Mutations in this gene cause premature trypsin activation and ineffective autodegradation of active trypsin mutants leading to autodigestion and acute pancreatitis (33-35). Hereditary pancreatitis is associated with one of the highest estimated lifetime risks for developing PC among the inherited PC syndromes, approaching 40% (34,35). In particular, those with a paternal inheritance pattern have a cumulative risk of approximately 75% for developing PC (36).

Peutz-Jeghers syndrome (PJS)
PJS is an autosomal dominant polyposis syndrome with a reported frequency of 1 in 8,300 to 280,000 (37). PJS is characterized by hamartomatous polyps in the gastrointestinal (GI) tract and mucocutaneous pigmentation (38). This genetic syndrome is caused by a germline mutation of the *STK11/LKB1* tumor suppressor gene (38). Patients with PJS have a significantly increased lifetime risk of multiple GI cancers, including esophageal, stomach, small intestinal and colon (39). In addition to these cancers, patients with PJS have reported the occurrence of IPMNs, pancreatic adenocarcinomas with a one Dutch study reporting a 26% cumulative risk of PC at 70 years for those with PJS (40,41).

Familial atypical multiple mole melanoma (FAMMM)
FAMMM is an autosomal dominant disease with variable penetrance. It is characterized by familial occurrences of benign melanocytic nevi, dysplastic nevi and melanoma (42). FAMMM is caused by germline mutations in *p16/CDKN2A*—a major tumor suppressor gene (43,44). This syndrome has been associated with an increased risk of sarcomas, endometrial, breast and lung cancers (45,46). An approximately 13- to 22-fold increase in PC has been reported in these patients compared to the general population (46,47).

Lynch syndrome
Lynch syndrome is caused by mutations in DNA mismatch repair genes (*MLH1*, *MSH2*, *MSH6* and *PSM2*) (48). Lynch syndrome is characterized by early onset of colorectal cancer and patients with this condition are prone to developing other types of cancer including endometrial, gastric, renal, ureter and small intestinal (48). Patients with Lynch syndrome have a 3.7% lifetime risk of developing PC up to the age of 70—an 8.6-fold increased risk compared to that of the general population (49).

Targets for screening

A useful strategy towards screening for PC would target high-grade benign non-invasive precursor neoplastic lesions—such as pancreatic intraepithelial neoplasms (PanINs) or IPMNs (50,51). Ideally, these lesions should be detected prior to malignant transformation or at an early stage that would allow curative resection. IPMNs are usually detected as cystic lesions, a dilated main pancreatic duct or both (8). Alternatively, PanINs are small branch ducts less than 5 mm in size which are often microscopic in size and not visualized by clinical imaging tests (8). For this reason, the best and potentially most reliable strategy for the early detection of PC may involve biomarker tests—testing for tumor markers naturally found in the body—

alone or in combination with imaging techniques.

Carbohydrate antigen 19-9 (CA19-9)

CA19-9 is an epitope of sialylated Lewis blood group antigen on Mucin 1 (MUC-1)—a surface glycoprotein expressed by PC cells (52). CA19-9 is also found on normal pancreatic, biliary duct, gastric, colonic, endometrial and salivary epithelia. The antigen is not expressed in approximately 4–15% of the general population and lacks sufficient sensitivity and specificity for detection of early PC as the marker is only elevated in 50% of pancreatic adenocarcinomas (53-55). Chronic inflammation or acute injury may promote CA19-9 synthesis and serum measurement is not useful in differentiating between PC and chronic pancreatitis (6). CA19-9 serum levels are useful for monitoring responses to therapy in patients already diagnosed with cancer rather than early diagnosis (6). Although CA19-9 remains a widely used serum biomarker for monitoring treatment response and post-treatment surveillance, The American Society of Clinical Oncology 2016 guidelines do not recommend its use for PC screening (56).

Carcinoembryonic antigen (CEA)

CEA is normally found in the tissue of the developing fetus and blood levels decrease after birth (6). Levels of CEA have been found to significantly correlate with tumor size, tumor differentiation and lymphatic and liver metastasis in PC (6). Studies have shown elevated levels of CEA in pancreatic juice of patients with PC compared to benign pancreatic disease suggesting its use as a tumor marker (57-60).

PAM4

PAM4 is an anti-MUC-1 monoclonal antibody that detects the MUC-1 antigen expressed by PC more specifically than that of other cancers (breast/ovarian) (61). Levels of PAM4 have been shown to be a better predictor than CA19-9 for discriminating between PC and chronic pancreatitis since it has a higher sensitivity and specificity (62). PAM4 is expressed on 89% of PanINs and 86% of IPMNs (63). Further investigation is needed to determine its use as an effective screening tool.

Pancreatic juice biomarkers

Pancreatic juice provides a rich medium for genetic and epigenetic marker analysis (8). Samples are typically obtained either during endoscopic ultrasound (EUS) or endoscopic retrograde cholangiopancreatography [duodenal aspirate (64) or pancreatic juice (65)]. *KRAS* mutations are present in 90% of pancreatic adenocarcinomas (65). Unfortunately, *KRAS* mutation detection in pancreatic juice is associated with poor sensitivity (38–62%) and is of poor diagnostic value because these mutations can be found in chronic pancreatitis and PanINs without PC (65,66).

Other biomarkers currently under investigation are DNA promoter methylation alterations. A number of candidate markers were studied including p16 and cyclin D2—a member of the cyclin family of regulators that play a role in mitotic coordination within cells and interact with tumor suppressor proteins (67). DNA promoter hypermethylation status was confirmed in these genes in pancreatic juice samples obtained from patients with PCs, IPMN, chronic pancreatitis, patients with no known pancreatic disease and those from high-risk cohorts (68). DNA promoter methylation markers are associated with a high sensitivity (82%) and specificity (100%) in identifying patients with PC. Mutations in mitochondrial DNA (mDNA) are also under investigation (69). mDNA mutations are found in multiple colorectal cancer cell lines and initial studies suggest that mDNA mutations are detectable in pancreatic juice samples from patients with PC (51,69,70). Finally, circulating microRNAs (miRNAs) are being investigated as a possible pancreatic juice marker. Studies profiling miRNAs were conducted and validated and a marked difference in the profiles of four specific miRNAs (miR-205, miR-210, miR-492 and miR-1427) was found in samples collected from patients with PC compared to those without pancreatic disease (71). Elevated levels of circulating miRNAs were associated with decreased overall survival and importantly, elevated levels of the four specific miRNAs described above, together with serum CA19-9, predicted PC with a high sensitivity (91%) and specificity (100%) (72).

Mesothelin

Mesothelin is a 40-kDa protein present on normal mesothelial cells (73). It is consistently elevated in human tumors including mesothelioma, ovarian cancer and PC (73). Studies report the overexpression of mesothelin in human PC cells and silencing of mesothelin decreased cell proliferation and promoted apoptosis in PC cells *in vitro* and inhibited tumor growth *in vivo* (72,73). These findings

suggest that mesothelin is important in PC growth and it may be useful as a potential target for monoclonal antibody therapy and/or as an assay to detect levels in blood, pancreatic fluid or stool.

Glypican-1 (GPC-1)

GPC-1 is a cell surface proteoglycan specifically enriched in cancer-cell derived exomes—extracellular vesicles that contain proteins and nucleic acids (74). Flow cytometry experiments showed that GPC-1 circulating exosomes (crExos) were detected in the serum of patients with PC which distinguished them from healthy subjects (17). GPC-1 crExos correlated with tumor burden and survival of pre- and post-surgical patients and are found in pancreatic intraepithelial lesions in mice (74). These investigations suggest that GPC1 crExos could serve as a non-invasive diagnostic and screening marker to detect early stages of PC.

Serum thrombospondin-1 (TSP-1)

TSP-1 is a multifunctional matricellular glycoprotein that can activate transforming growth factor-β—an important profibrotic cytokine involved in various fibrotic diseases (8). In terms of pancreatic pathology, studies found a significant reduction in levels of TSP-1 up to 24 months prior to the diagnosis of PC (75). Levels were decreased in PC compared to healthy subjects and low levels correlated with worse survival pre- and at clinical diagnosis. In addition, reduced TSP-1 was also more frequently observed in those with confirmed diabetes mellitus (75).

Serum osteopontin (OPN)

Serum OPN is a highly phosphorylated sialoprotein found in osteoblasts (8). Proinflammatory cytokines such as TNAα and angiotensin II upregulate the expression of OPN (8). Elevated levels of OPN were found in various cancers including lung, stomach and pancreatic (8). Findings from several investigations infer that OPN is believed to promote cancer metastasis through the ligand-receptor interaction with the CD44 receptor family (76). Importantly, a meta-analysis done recently showed the significance of OPN as a serum biomarker for early stage PC (77). Given these findings, it is likely that serum OPN may be useful as a screening marker for the early detection of PC; however, further investigation must be done into assessing its efficacy and accuracy.

Fecal markers

Several fecal markers including methylated bone morphogenetic protein 3 (mBMP3) and adnab-9 have been studied for their roles as tumor markers (61). Stool from patients with PC showed significantly higher mBMP3 than a control population (7). The presence of the fecal biomarker adnab-9 was associated with PC precursor lesions with a sensitivity of 80% and specificity of 87% (61,78). The advantages of using stool DNA testing is that it is non-invasive, the colon does not need to be prepared and no dietary restrictions are needed (8).

Imaging techniques

Transabdominal ultrasound (US)

Transabdominal US methods allow the imaging of hypoechoic masses, dilatation of pancreatic ducts and dilatation of the bile duct—features of pancreatic head tumors (78). Body and tail cancers are hard to visualize in the presence of gas in the stomach and transverse colon due to posterior shadowing (78). Difficulty can occur in the differentiation between PC from other focal lesions (chronic pancreatitis/neuroendocrine tumors) without contrast as they show the same features (9).

Multidetector computed tomography (MDCT)

MDCT is the current abdominal imaging test of choice for pancreatic disease—specifically, it is useful in diagnosing solid tumors and staging PC (79). Despite its high accuracy for detecting and staging PC, its sensitivity is not high as MDCT misses' lesions in screenings for early pancreatic neoplasia (80,81). MDCT provides good spatial and temporal resolution with wide anatomic coverage allowing local and distant disease assessment during a single session (82). This technique is also regarded for its best performance for evaluation of vascular involvement—an important factor for predicting tumor resectability (82-84). The reported positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity for predicting resectability of PC with MDCT are 89%, 78%, 100% and 72% respectively (85). Although it is the current imaging test of choice for PC, MDCT has its disadvantages. MDCT poses a theoretical concern for radiation exposure particularly for people with impaired DNA repair gene function due to mutations in the *BRCA1*, *BRCA2* or *PALB2* genes and thus, this imaging modality

is not ideal for high risk groups (86). Additionally, this technique may not reliably identify metastasis to the liver, peritoneum or a primary pancreatic tumor showing isoattenuation (86).

Magnetic resonance imaging (MRI)/magnetic resonance cholangiopancreatography (MRCP)

MRI and MRCP are non-invasive screening techniques used for high risk individuals because it allows imaging of the entire abdomen and pelvis without radiation exposure (8). This form of imaging is performed using a 1.5- or 3-Tesla coil gradient system. Several sequences can be obtained to visualize the PC; however, the process is time consuming and susceptible to motion artifacts (16). Typical imaging includes T1 and T2 weighted sequences followed by gadolinium enhanced dynamic sequences at 20, 60, 120 and 180 seconds (16). On T2 and diffusion weighted images in particular, the tumor would have a high signal because sequencing with fat suppression is helpful in assessing vessel structure (16).

MRI can image pancreatic ductal anatomy noninvasively and small cystic lesions such as IPMNs. Preliminary data from high-risk patients that underwent resection suggest that MRI/MRCP imaging is superior to CT, particularly for the detection of IPMNs (87). MRI/MRCP offers better soft-tissue contrast compared with CT and therefore, provides better imaging of small tumors, hypertrophied pancreatic head, isoattenuating PC and focal fatty infiltration of the parenchyma (87). In addition, this technique is useful for detection of subtle ductal narrowing that may suggest the presence of a small mass—a possible advantage for the early identification of PC (82).

EUS

Contrast enhanced EUS (CED-EUS) is a modified version of EUS that uses the injection of contrast material to examine the intensity of blood flow to differentiate between vascular-rich and hypovascularized patterns with clarity using a power Doppler (88). With the administration of micro-bubble agents, the diagnostic accuracy of EUS can be as high as 82% for PC (89). PC is characterized by reduced contrast enhancement compared to that of the surrounding tissue. Alternatively, E-EUS is a non-invasive method that measures tissue elasticity in real time using a dedicated probe (90,91). Studies have shown good results for the use of E-EUS for diagnosing pancreatic focal lesions (92,93). Studies comparing CED-EUS and E-EUS for differentiating solid pancreatic lesions showed no statistical significance concerning sensitivity and specificity (94-96). EUS-FNA provides the unique ability to obtain specimens for histopathological analysis and has shown to be highly accurate for the diagnosis of pancreatic masses and pancreaticobiliary disorders (97). The accuracy of EUS-FNA for detecting pancreatic malignancy usually exceeds 90% (98,99). Although these variations of EUS help to identify early changes in the pancreas, EUS-based screening may overcall suspicious findings potentially leading to unnecessary surgical intervention (100).

Positron emission tomography (PET)

PET with fluorine 18-fluorodeoxyglucose (PET-FDG) is a nuclear medicine derived, functional imaging technique that uses a glucose analogue to observe metabolic processes in the body (101). This modality is more sensitive for treatment monitoring following chemotherapy/radiation and is useful for depicting tumor recurrence after resection compared to MDCT (102-104). PET-FDG provides wide anatomic coverage allowing the depiction of metabolic metastases throughout the whole body (105). PET imaging is advantageous due to its ability to produce functional images; however, low spatial resolution and false positive results caused by normal physiologic FDG uptake are among its disadvantages (106). In addition, PET is performed without iodinated contrast which limits its role in staging PC (107,108). Ideally, contrast enhanced imaging is preferred over non-contrast enhanced PET/CT for staging PC (88% *vs.* 76%) as it performs well in locally enhanced PC and aids in detecting unsuspected metastasis (101,106-108).

Confocal laser endomicroscopy (CLE)

CLE is another technique used for the imaging of PC where a confocal probe is passed into the duct through the working channel of a duodenoscope (78). The procedure involves intravenous injection of fluorescein (a synthetic organic fluorescent tracer) which is followed by a low power laser that focuses light onto a single point on the mucosa providing "real time histology" (78). A recent study showed that the sensitivity, specificity, PPV and NPV were 100%, 71%, 91% and 100% respectively (109). Another approach is needle-based CLE which can be specifically used in

the pancreas to image cysts and solid masses providing a potential imaging technique for pancreatic lesions (110).

New techniques in pancreatic imaging

Dual-energy CT and low tube voltage techniques

Although MDCT has been highly regarded for its use in PC imaging and its excellent performance regarding diagnosis and staging, the detection of small PCs (<2 cm in diameter) or otherwise isoattenuating tumors is still unreliable (111,112). Dual-energy CT and low tube voltage imaging is a useful technique for the diagnosis and staging detection of small PCs. Low tube voltage CT increases X-ray absorption of iodine by increasing the gap between mean effective energy of the X-ray spectrum and the K edge of iodine (113). This results in improved contrast enhancement of normal pancreatic parenchyma to maximize contrast to typically poorly vascularized cancers (113).

Iterative reconstruction algorithm on MDCT

The iterative reconstruction algorithm on MDCT allows the preservation and enhancement of the diagnostic capability of CT with reduced radiation doses (114). This is done by decreasing the image noise during the reconstruction process (114). By reducing the image noise, these techniques could be used for high spatial resolution pancreatic CT imaging—characterized by high quality 1–2 mm, thin slice CT images (114).

Dynamic contrast enhanced-MRI (DCE-MRI) and diffusion weighted imaging (DWI)

DCE-MRI is an imaging method that has been shown to provide enhancement patterns and perfusion parameters which are objective and helpful for the evaluation of malignant disease regarding both diagnosis and treatment monitoring (115). This technique is useful for differentiating PC from pancreatic neuroendocrine tumors (116). DWI on the other hand, characterizes pancreatic lesions of various pathological entities including cystic lesion, pancreatitis and malignant tumors (117-119). Advantages of DWI include its excellent soft tissue contrast for focal lesion detection and the fact that it may allow earlier detection of pancreatic adenocarcinomas since these neoplasms have increased signal intensity (119). Conversely, a disadvantage of this technique is that small or non-contour deforming pancreatic adenocarcinomas may lack classic imaging features, thus not being detectable on conventional MRI (120).

Hybrid PET/MRI

Integrated PET and MRI scanners have recently been available for use in humans. This combined method is known for its superior soft tissue contrast resolution, multiplanar imaging acquisition and functional imaging (121). PET/MRIs are used for staging in patients with locally advanced PCs and tumor response in those undergoing neoadjuvant chemo-radiation. The use of this technique is still in its developmental stages and further studies are required to confirm its effectiveness and uniqueness for the screening of PC in comparison to the other imaging techniques that are currently available.

Conclusions

As PC remains one of the leading causes of cancer related deaths worldwide with a high fatality, it is important to identify a method of screening for early detection. This review investigated the known and likely risk factors associated with PC and investigates the current research devoted to identifying screening markers to detect PC. Among the numerous tumor markers that may be affiliated with pancreatic neoplasms, the most predominant ones discussed in the literature have been reviewed here, identifying the pros and cons of their use in PC screening. In addition, notable improvements in pancreatic imaging have been seen in a variety of modalities. Each of these techniques has its own advantages and disadvantages for the diagnosis, treatment and follow-up of PC. Similarly, rapidly developing, new imaging techniques which include dual energy, low tube voltage CT, information retrieval (IR) algorithms, DCE-MRI, DWI and hybrid PET/MRI are expected to provide improved results for PC imaging in the future.

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Footnote

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