Application of imaging technology for the diagnosis of malignancy in the pancreaticobiliary duodenal junction (Review)

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Abstract. The pancreaticobiliary duodenal junction (PBDJ) is the connecting area of the pancreatic duct, bile duct and duodenum. In a broad sense, it refers to a region formed by the head of the pancreas, the pancreatic segment of the common bile duct and the intraduodenal segment, the descending and the horizontal part of the duodenum, and the soft tissue around the pancreatic head. In a narrow sense, it refers to the anatomical Vater ampulla. Due to its complex and variable anatomical features, and the diversity of pathological changes, it is challenging to make an early diagnosis of malignancy at the PBDJ and define the histological type. The unique anatomical structure of this area may be the basis for the occurrence of malignant tumors. Therefore, understanding and subclassifying the anatomical configuration of the PBDJ is of great significance for the prevention and treatment of malignant tumors at their source. The present review comprehensively discusses commonly used imaging techniques and other new technologies for diagnosing malignancy at the PBDJ, offering evidence for physicians and patients to select appropriate examination methods.

Contents

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1. Introduction

The pancreaticobiliary duodenal junction (PBDJ) is the area where the pancreatic duct (PD), bile duct and duodenum are connected, including the head of pancreas, the pancreatic segment of the common bile duct (CBD) and the intraduodenal segment, the descending and horizontal parts of duodenum, and the soft tissue around the pancreatic head (1). This site has a complex anatomical structure and an important physiological function. Digestive fluids such as bile, pancreatic juice and gastrointestinal fluid converge at the PBDJ, referred to as the 'confluence of three rivers' (2). The PBDJ is susceptible to a range of conditions, such as stones, inflammation and tumors, which can lead to obstructive jaundice, cholangitis and pancreatitis (3). Due to the intricate anatomy and diverse pathology of this area, early diagnosis and precise treatment of malignant tumors in the PBDJ are challenging. Additionally, the progression of these diseases may be associated with the unique anatomical basis of the region (4). Thus, understanding and delineating the anatomical configurations of the PBDJ is significant for preventing and treating such conditions at their source.

Despite the rapid advancements in medical imaging technologies providing a variety of high-precision methods for the diagnosis of malignant tumors at the PBDJ, numerous challenges and limitations remain. Firstly, the complex anatomical layout of this region complicates image interpretation, particularly in the early tumor stages where lesions are small and poorly defined, increasing the risk of missed or misdiagnosed cases (5). Secondly, the different imaging modalities have their advantages; for instance, computed tomography (CT) excels in demonstrating tumor morphology, density and relationships with surrounding structures but has limited soft tissue resolution (6). By contrast, magnetic resonance imaging (MRI) offers superior delineation of soft tissue details but requires longer examination times and notable patient cooperation (7).

Emerging artificial intelligence (AI)-assisted diagnostic tools and three-dimensional visualization technology (3DVT) show potential but are still in the early stages of development, necessitating further validation of their accuracy, stability and widespread applicability (8).

Furthermore, despite the application of several treatment approaches for malignant tumors of the PBDJ, such as surgical intervention, radiotherapy, chemotherapy, immunotherapy, targeted therapy and neoadjuvant therapy, which have yielded certain results (including enhanced surgical resection rates, diminished recurrence risks, specific inhibition of cancer cell proliferation and metastasis, and extended overall survival time for patients), numerous challenges remain (9-12). The complexity of the surgical procedures, the prevalence of complications and the slow postoperative recovery restrict treatment options for certain patients. Additionally, the efficacy of radiotherapy and chemotherapy may be limited by drug side effects or the emergence of tumor resistance (13). Therefore, tailoring personalized and precise therapeutic strategies based on individual patient differences continues to be one of primary focuses of current clinical research.

The diagnosis and treatment of malignant tumors at the PBDJ is a complex task which requires continuous investigation and innovation in order to overcome the limitations of current technologies, and enhance both the accuracy of diagnosis and the effectiveness of treatment. The present review aimed to comprehensively discuss the commonly used imaging techniques in the diagnosis of malignant tumors at this anatomical site, along with other novel methodologies, with the intention of providing a scientifically sound reference for clinicians and patients alike; thereby collectively advancing the standards of care in this field.

2. Preliminary study on the anatomy of the PBDJ

The pancreatic head is located within the concave surface of the duodenum, to the right of the midline. It is ~1 cm thick with its lower portion extending downward and leftward in a hook-like fashion encircling the posterior aspect of the mesenteric vessels (14). The pancreatic head is surrounded by the duodenum on its superior, inferior and right sides, with the area in contact with the duodenum slightly recessed inward (15). The anterior side of the pancreatic head is mostly adjacent to the beginning of the transverse colon and its mesentery; the superior portion is covered by the posterior wall of the omental sac, whilst the inferior portion is covered by the membrane extending from the transverse colon mesentery and is adjacent to the small intestine (16). The hepatic artery travels along the superior margin of the pancreas, directed rightwards. Posteriorly, the pancreatic head is adjacent to the medial border of the upper half of the right kidney, the right renal vessels, the inferior vena cava, the terminal section of the left renal vein and the right diaphragmatic foot (17). When a pancreatic head tumor is large, it may compress the inferior vena cava or the portal vein, resulting in lower limb edema or ascites.

The CBD begins at the junction of the cystic duct and the common hepatic duct, terminating at the major duodenal papilla, with a length range of 4-8 cm (18). It is divided into the supraduodenal, retroduodenal, pancreatic and intramural segments. During its descent, the CBD is initially positioned posterior to the pancreatic head, with its terminal part passing through the head, which is a common site for obstructive jaundice due to pancreatic head cancer (PHC) invasion (19). Prior to entering the duodenum, the CBD expands to form the ampullary structure, known as ampulla of Vater, where ampullary cancer (AC) may occur, representing another frequent site of lower segment obstruction of the CBD (20).

The duodenum, which is the initial section of the small intestine, connects superiorly to the stomach and inferiorly to the jejunum, measuring ~25 cm in length and forming a 'C' shape that encircles the pancreatic head (21). In PHC, this 'C'-shaped loop may become enlarged or distorted. The duodenum is divided into four parts: i) Superior; ii) descending; iii) horizontal; and iv) ascending, each with distinct clinical significance (22). The medial side of the descending part of the duodenum is closely associated with the pancreatic head, CBD and PD opening to the major duodenal papilla in the middle of its posterior medial side. With the development of duodenal surgery, variations of the duodenum are increasingly common (23). For instance, the horizontal part of the duodenum may be positioned anteriorly to the descending portion or ascend to the right side. The terminal portion may terminate on the right side or traverse behind the pancreas and mesenteric vessels to ultimately connect with the duodenojejunum flexure on the left side. Such variations arise due to abnormal rotation (24).

The PD is located within the substance of the pancreas, originating from the tail of the pancreas and traversing its entire length to the right edge of the pancreatic head (22). Typically, it merges with the CBD to form the ampulla of Vater, which subsequently opens into the major duodenal papilla, or the PD may have a separate opening (17). The diameter range of the PD near the duodenum is 2-3 mm. Occasionally, a small duct can be observed in the pancreatic head running above the PD, opening onto a smaller papilla adjacent to the major duodenal papilla, known as the accessory PD, which has an occurrence rate of ~50% (25). Among the abdominal organs, the PBDJ is regarded as the most intricate and delicate structure. This region involves three distinct organs: i) The biliary tract; ii) the pancreas; and iii) the intestines, which collectively receive precise regulation from the nervous and endocrine systems, justifying its consideration as a closely linked structural and functional entity (26). Lesions at the PBDJ can have varying origins, but their pathogenesis, pathological changes and clinical manifestations often interrelate, necessitating a comprehensive approach in diagnosis and treatment (3). Once the PBDJ is compromised, the leakage and mixing of bile and pancreatic juice can activate pancreatic enzymes, triggering a severe corrosive 'chain reaction' that leads to extensive erosion of surrounding tissues, and even hemorrhage, necrosis, infection and abscess formation in the abdominal cavity or retroperitoneal tissues, which can be life-threatening in severe cases (27,28).

3. Biological characteristics of PBDJ tumors

Common manifestations of malignant tumors at the PBDJ. Malignant tumors at the PBDJ encompass PHC, distal bile duct cancer (DBDC) and duodenal cancer (DC), which typically leads to biliary obstruction, dilation and gallbladder

enlargement. PHC may also manifest as localized PD destruction with distal dilation (29). Most patients present with a notable mass and often exhibit involvement of mesenteric vessels, lymph node or surrounding organ metastasis (30). Furthermore, levels of specific serological and secretory markers may significantly increase, triggered either by the tumor itself or due to biliopancreatic duct obstruction (31).

Biological characteristics of PHC. Based on an extensive analysis of pancreatic cancer cases, it has been shown that PHC primarily exhibits an invasive multifocal growth pattern (32-34). The risk factors for its development include, but are not limited to, age, smoking history, alcohol abuse, obesity, diabetes, genetic predisposition, dysbiosis of gut microbiota and chronic pancreatitis (35,36). As a highly malignant gastrointestinal tumor, PHC is characterized by its insidious onset, rapid progression, high postoperative recurrence rates and insensitivity to both chemotherapy and radiotherapy, leading to a low 5-year survival rate (37). The degree of tumor differentiation is inversely associated with its malignant potential, with poorly differentiated tumors being more prone to metastasis and vascular invasion.

The biological characteristics of PHC are manifested as follows: First, the pancreatic head itself lacks a capsule, which facilitates intraductal spread and invasion of adjacent organs and blood vessels (38), such as the celiac trunk, hepatic artery, superior mesenteric artery, splenic artery, abdominal aorta, portal venous system and inferior vena cava, resulting in tumors that are unresectable or inadequately resected. Electron microscopy has revealed that nerve fibers within the pancreas are predominantly unmyelinated, allowing cancer cells to easily disrupt the perineurium, nerve fibers and their synaptic membranes, leading to central-side neural metastasis and the formation of intra-pancreatic multicentric lesions. When the main (M)PD is obstructed, tumor cells can implant and grow retrogradely in the ducts (39,40). Second, lymphatic and hematogenous metastasis may be at early stages. Due to the abundance of peripancreatic lymphatic tissue, lymph node metastasis occurs early and has a high incidence (41,42). The complex mechanisms underlying lymph node metastasis are not fully understood; however, research has reported that microRNA-1231 in exosomes derived from bone marrow mesenchymal stem cells inhibit the invasion, metastasis and tumor microenvironment of PHC (43). Third, PHC exhibits neurotropic growth and the characteristic of invasive spread along perineural sheaths. Nerves are protected by three layers of connective tissue: i) The epineurium; ii) perineurium; and iii) endoneurium, with interstitial spaces between these layers providing pathways for cancer cell invasion. Selvaggi *et al* (44) and Wang *et al* (45) define neural infiltration as the presence of tumor cells in any layer of the three-layer nerve sheath or tumor cells surrounding >1/3 of the nerve tissue within a lesion. PHC demonstrates a neural invasion rate of 80-100%, which is a critical factor contributing to postoperative recurrence and poor prognosis, severely affecting the outcomes of curative surgeries (46-48).

Biological characteristics of DBDC. DBDC originates from bile duct epithelial cells and is classified as a primary malignant tumor of the biliary system, located in the extrahepatic bile duct region below the point where cystic duct merges with common hepatic duct. The incidence of bile duct cancer is relatively low, accounting for only ~3% of gastrointestinal malignancies, whilst DBDC represents 20-30% of bile duct cancers (49). Research has reported that DBDC is characterized by infiltrative multifocal growth and shares numerous biological features with PHC, including pathological findings that exhibit biliopancreatic morphological changes which contribute to its poor prognosis (50). However, the surgical resection rate and prognosis for DBDC are superior to those for PHC, potentially attributable to the following: i) The tendency for DBDC to cause biliary obstruction, with jaundice symptoms appearing early, facilitating early diagnosis and radical surgical intervention; and ii) its unique biological characteristics, such as differing mutation patterns of the KRAS, P16 and P53 genes compared with pancreatic cancer (51-53), higher tumor differentiation and less infiltration into the duodenum with lymph node metastasis tending to occur later with a migratory pattern distinctly different from that of PHC often confined to lymph nodes near the distal bile duct (54,55). Moreover, Kwon *et al* (56) reported that lymphovascular invasion and tumor (T)-node-metastasis staging are independent risk factors affecting patient prognosis.

The tumors in the ampullary region of Vater have diverse origins, with marked differences in biological characteristics, pathological features and prognosis among PHC, DBDC, AC and DC. Zheng-Pywell and Reddy (57) and Williams *et al* (58) reported that patients with PHC have the worst prognosis, followed by those with DBDC; AC prognosis is moderate, whilst patients with duodenal papilla cancer have the best prognosis, suggesting that the site of origin of the tumor is a critical factor affecting patient outcomes. Pathologically, DBDC can be categorized into sclerotic, nodular, papillary and infiltrative types (59). Early-stage cholangiocarcinoma is further subdivided into elevated, superficial and depressed types. Histologically, the main classifications include papillary adenocarcinoma, tubular adenocarcinoma, mucinous carcinoma, squamous cell carcinoma and undifferentiated carcinoma, with papillary adenocarcinoma and tubular adenocarcinoma accounting for >90% of cases (60). Although papillary adenocarcinoma has a relatively favorable prognosis, it tends to spread along the bile duct mucosal surface.

Biological characteristics of DC. Primary DC specifically refers to malignant tumors originating from the epithelial cells of the duodenum and confined to several parts of the duodenum excluding the pancreatic head, the distal CBD and the ampulla of Vater. Such tumors are relatively rare in clinical practice, accounting for ~0.3% of gastrointestinal tumors and 30-45% of small intestine malignancies (61,62). Due to their mild and non-specific clinical manifestations, early diagnosis is challenging, leading to missed and misdiagnosed cases. However, advances in endoscopic detection and imaging technologies have improved the early diagnosis rates of primary duodenal tumors (63).

Zhao *et al* (64) performed a retrospective analysis of clinical data from 94 cases of primary duodenal malignancies between January 2014 and December 2019, which included 60 cases of adenocarcinoma (63.8%), 32 cases of stromal tumors (34.1%) and two cases of lymphoma (2.1%). To identify

factors associated with prognosis, the authors performed a Kaplan-Meier analysis and reported that pancreatic invasion is associated with the prognosis of patients with adenocarcinoma. By contrast, the location of the tumor, complications, depth of infiltration, and the distance from the mesangial side of the tumor to the duodenal papilla are not associated with patient prognosis.

From a pathological perspective, the macroscopic morphology of DC is diverse, with the polypoid type being the most common, followed by the ulcerative, constrictive and diffuse infiltrative types. The pathological types of adenocarcinoma are varied, encompassing poorly differentiated adenocarcinoma, well-differentiated adenocarcinoma, papillary adenocarcinoma and mucinous adenocarcinoma (65). Depending on the relative position of the tumor to major duodenal papilla, cancers around the papilla often present as infiltrative ulcerative or polypoid types, whilst tumors above the papilla predominantly exhibit polypoid forms. Those below tend to be constrictive. The pathogenic factors and mechanisms of DC remain unclear, but they may be associated with bile acid forming carcinogenic cholanthracene and methylcholanthracene under the influence of intestinal bacteria, as well as with abnormalities in bile and pancreatic secretions and imbalances in the acid-base levels of duodenal fluids leading to mucosal damage (66). Certain studies have suggested dietary factors, such as refined carbohydrates, lack of dietary fiber and diets high in sugar and fat, especially those with excessive red meat consumption and insufficient fruit and vegetable intake, may be risk factors for the occurrence of DC, similar to those associated with colorectal cancer (67,68). Research by Kakushima *et al* (69) further emphasized smoking and *Helicobacter pylori* infection as common high-risk factors among male and female patients.

4. Imaging diagnosis of PBDJ tumors

Ultrasound (US). US diagnostic technology encompasses surface US and endoscopic (E)US. As tumors at the PBDJ often display no characteristic manifestations in the early stages, most clinical cases commonly present with progressive jaundice, significant weight loss, abdominal distension and dull pain, typically indicating middle-to-late-stage disease (70). Therefore, it is essential to focus on relevant clinical signs while remaining vigilant for this condition, employing auxiliary examination methods for timely and accurate diagnosis. This approach is crucial for minimizing misdiagnosed and missed cases, formulating precision treatment plans, enhancing the rate of radical resection and improving prognosis (71). As a widely used preliminary screening tool, US has the advantages of being non-invasive, rapid, cost-effective and easy to perform. However, its imaging quality is frequently compromised by intestinal gas interference, which limits clear visualization of the PBDJ (6). Despite these limitations, US remains the preferred examination for patients with a high suspicion of tumors at the PBDJ, as it can initially reveal tumor location, size and degree of dilatation in the bile and PD. Color Doppler flow imaging further enhances diagnostic capability by demonstrating the relationship between the tumor and adjacent blood vessels, thereby assisting in the preoperative assessment of tumor resectability (60). Water window ultrasonography using patient-ingested water to fill the gastrointestinal tract, serving as an acoustic window that effectively reduces gas interference and enhances the delineation of mass boundaries, size and involvement of neighboring organs, thus improving diagnostic accuracy and tumor staging abilities (72,73). Double contrast-enhanced ultrasonography (DCEUS) uses oral or injected gastrointestinal echogenic agents alongside intravenous US contrast agents. This method not only clearly depicts the morphology, size and boundaries of lesions and their relationships with surrounding tissues, but also reveals the vascular supply characteristics of tumors improving the detection rate of tumors at the PBDJ (5,74,75). Research data indicate that DCEUS markedly enhances the visibility of lesions compared with conventional US and gastroduodenal water window ultrasonography (76,77). However, the application of DCEUS and the water-window technique is relatively limited given the convenience of the clinical operation and diagnostic accuracy offered by CT and MRI.

EUS leverages its probe to establish close contact with lesions through the intestinal wall within the gastrointestinal cavity, thus overcoming the limitations of conventional US which is often hindered by intestinal gas. This modality offers enhanced soft tissue resolution, enabling the clear visualization of the relationship between tumors at the PBDJ and adjacent structures, which is beneficial for preoperative tumor staging assessment (78,79). The sensitivity of EUS in T staging surpasses that of both US and CT (80,81), making it a crucial tool for guiding fine-needle (FN) aspiration (FNA) and FN biopsy (FNB) to achieve cytological and histological diagnoses (82). Research has indicated that the sensitivity for diagnosing pancreatic malignancies using EUS-FNA and -FNB is 71 and 82%, respectively, with both techniques achieving a specificity of 100% (83). In evaluating the etiology of biliary strictures, the overall diagnostic accuracy of EUS-guided tissue sampling exceeds that of endoscopic retrograde cholangiopancreatography (ERCP)-guided tissue sampling, particularly for strictures caused by pancreatic lesions; however, in the case of primary malignant biliary obstruction, the difference between the two methods is not significant as confirmed by multiple studies (82,84-86).

The advantage of EUS lies in its ability to visualize the intestinal cavity and the duodenal papilla directly, facilitating procedures such as biopsies and fluid collections, thereby providing a wealth of information for comprehensive diagnostics (79). In areas that are challenging to access endoscopically, percutaneous FNA cytology can serve as a supplementary method to obtain qualitative diagnostic evidence of malignant cells. Ultimately, a definitive diagnosis often necessitates surgical exploration to thoroughly assess the lesion nature and extent, the involvement of surrounding organs and distant lymph node metastasis, providing critical information for surgical decision-making and technique selection.

CT. Multi detector (MD)CT is a crucial imaging technique for diagnosing tumors at the PBDJ due to its rapid scanning speed, and superior spatial and density resolution. Through post-processing technologies such as multi planar reconstruction and curved planar reformation, MDCT can provide a more intuitive and stereoscopic visualization of tumors and the surrounding anatomy, enhancing the detection rates

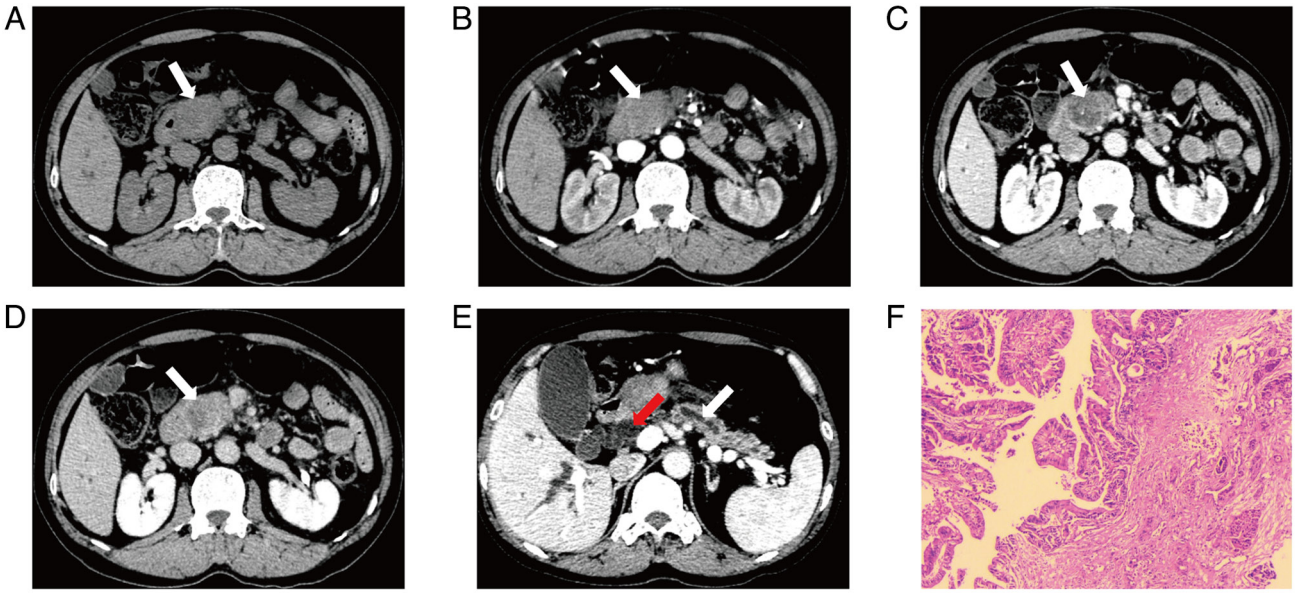

Figure 1. Highly differentiated papillary adenocarcinoma of the pancreatic head. (A) Computed tomography plain scan demonstrates an isodensity mass in the head of pancreas with an unclear boundary. (B) Arterial and (C) venous phases reveals low enhancement of the mass. (D) Delayed period demonstrates delayed enhancement of the mass. (E) Venous phase reveals distal pancreatic atrophy, a dilated pancreatic duct (white arrow) and bile duct (red arrow). (F) Hematoxylin and eosin staining of the lesion demonstrates intraductal papillary gland hyperplasia with atypia and infiltration. Magnification, x100. The images were obtained from the Department of Radiology, Affiliated Nanhua Hospital, University of South China, with the consent of both the involved patient and the institution, for the purpose of this review.

and diagnostic accuracy of lesions (87). Research has reported a sensitivity of 100% for MDCT in assessing the resectability of tumors at the PBDJ, with an overall accuracy of 84.4%, thereby solidifying its core position in this domain (88). Moreover, the introduction of spectral CT technology, which not only reflects the anatomical structure of lesions, but also reveals their functional characteristics, provides new directions for the diagnosis and differential diagnosis of tumors.

Liang *et al* (89) reported that low kilovolt monoenergetic images from dual-energy CT markedly improves both the subjective and objective quality of images in patients with pancreatic cancer as well as the consistency in tumor measurements, whilst combining iodine maps enhances the detectability of isodense pancreatic cancers. However, it is noteworthy that despite its promising prospects, in-depth research on the application of spectral CT in the diagnosis and differential diagnosis of tumors at the PBDJ is currently lacking. Therefore, there is an urgent need for more exploratory studies in the future to fully uncover its potential clinical applications.

Direct CT signs of tumors at the PBDJ include soft tissue density masses in the ampulla, thickening of the duodenal wall or intraluminal soft tissue shadows, and thickening of the wall or intraluminal soft tissue shadows at the end of CBD (90). Indirect signs manifest as atrophy of the distal pancreatic parenchyma, dilation of PD, dilation of the intrahepatic and extrahepatic bile ducts, and enlargement of the gallbladder (91). When the lesions are large and extensive, it becomes challenging to identify the origin of primary lesions, and certain CT signs can have auxiliary diagnostic significance.

Zhao *et al* (92) reported the imaging differences between PHC, cholangiocarcinoma, AC and benign lesions through MDCT image analysis. Cholangiocarcinoma is characterized by small lesions with significant wall thickening, markedly dilated intrahepatic and extrahepatic bile ducts and gallbladder along with significant delayed enhancement; PHC typically presents as large lesions with high necrosis rates, extensive invasion, notable double-duct signs and mild early enhancement in the arterial phase, with enhancement less than that of normal pancreas; and AC shows intermediate enhancement, whilst benign lesions generally exhibit no significant enhancement. Moreover, key points for differentiating pancreatic cancer also include patient age >50 years, ill-defined tumor borders and pancreatic atrophy (Fig. 1) (93). For AC, the presence of a mass in the ampullary region, asymmetric narrowing of the distal CBD, dilation of the intrahepatic bile duct, dilation of the PD, thickening of the duodenal wall and delayed enhancement, are indicative of diagnosis (94). Early-stage DBDC may present with bile duct obstruction symptoms and simple bile duct dilation without PD dilation. The degree of bile duct wall thickening and morphological analysis assist in distinguishing between cholangitis and cholangiocarcinoma (95): Dilation of the CBD due to inflammatory narrowing often appears tapered, with wall thickening of <1.5 mm, whilst exceeding this threshold suggests a neoplastic condition.

Radiomics, a cutting-edge technology at the forefront of the integration of AI and medical imaging, is capable of extracting rich and quantifiable features from raw imaging data and linking them to potential biological behaviors. By analyzing these features through AI algorithms, it provides critical information for precise diagnosis and prognostic evaluation (96). Lee *et al* (95) combined contrast-enhanced CT imaging with clinical presentations to construct a predictive nomogram using indicators such as ampullary masses, enhancement characteristics and the degree of bile duct dilation and jaundice, thus effectively distinguishing between

benign and malignant ampullary strictures and enhancing clinical decision support. The authors focused on the imaging assessment of MPD truncation and related abnormalities, combining the abnormal parenchyma outline of MPD truncation, the location of truncation (head or neck), the presence of acute pancreatitis and elevated cancer antigen 19-9 (CA 19-9) levels to develop a novel nomogram for early diagnosis of occult pancreatic malignancies (97). Jang *et al* (98) identified independent predictive factors for ampullary tumor lesions, including Vater ampulla mass, Vater ampulla size >12 mm, total bilirubin >1.2 mg/dl and age ≤63 years. The nomogram developed based on these factors demonstrates a diagnostic accuracy of 93.9%. Histogram parameter analysis of MDCT during arteriovenous phases revealed the optimal performance of venous phase percentiles in differentiating between PHC and DC, with whole focus CT histogram analysis notably enhancing diagnostic capabilities for tumors at the PBDJ (99).

Based on histological characteristics, PBDJ tumors are classified into intestinal-type and pancreatobiliary-type, with most studies indicating that intestinal-type tumors have a better prognosis (100,101). Ivanovic *et al* (102) made marked strides in the differential diagnosis of intestinal-type and pancreatobiliary-type AC using MDCT technology, achieving high sensitivity (85.7%), specificity (83.3%) and accuracy (84.4%). The study findings suggested that the features of intestinal-type AC include nodular morphology, duodenal papilla bulging, free duodenopancreatic groove appearance and no involvement of the pancreaticoduodenal artery. The pancreatobiliary-type tends to exhibit infiltrative growth, retraction of papilla, invasion of the CBD and MPD, fixed duodenopancreatic groove appearance and involvement of the pancreaticoduodenal artery. These characteristics are particularly evident under conditions of marked duodenal distension, highlighting the unique advantages of MDCT in distinguishing histological subtypes of AC. Bi *et al* (103), through a meticulous CT radiomics analysis combined with logistic regression algorithm models, precisely differentiated between intestinal- and pancreatobiliary-type malignant tumors at the PBDJ, exhibiting exceptional model performance [sensitivity, 90%; specificity, 93%; accuracy, 88%; area under the curve (AUC), 0.96], highlighting the potential application of preoperative CT radiomics in differentiation and the differences in enhancement patterns between the two types.

Enhanced CT is a crucial technology for diagnosing tumors at the PBDJ, demonstrating superior efficacy compared with that of US, and it also allows for assessment of distant metastases. However, for cases of missed microlesions or lesions of uncertain origin, it is necessary to combine it with enhanced MRI or biopsy pathology to refine the diagnosis.

MRI. MRI has been firmly established as a conventional imaging diagnostic tool, with its non-invasive and radiation-free characteristics revolutionizing medical diagnostics. However, patients with intra-body metallic foreign objects or implants need to avoid MRI to prevent interference or risks (91). For tumors at the PBDJ, non-invasive screening modalities such as US, CT and MRI are preferred, as these technologies can visually demonstrate biliary and PD obstruction and dilation (104). Diffusion weighted imaging (DWI) indirectly reflects cell density and tissue microstructural characteristics by quantifying the diffusion of water molecules, with tumors at the PBDJ often showing restricted diffusion (105).

Currently, enhanced MRI in conjunction with magnetic resonance cholangiopancreatography (MRCP) and DWI are primarily used for diagnosing and assessing PBDJ tumors (106). MRCP uses the long T2 relaxation time characteristics of the bile and pancreatic juice to highlight the biliary and PD systems through a heavily T2-weighted imaging technique, creating images similar to ERCP, facilitating observation of lesions (107). Research has validated that MRCP and ERCP exhibit comparable efficacy in distinguishing biliary strictures (108). Long-segment asymmetrical strictures with irregular margins suggest cholangiocarcinoma, whilst the opposite points towards benign conditions (108). The double duct sign, the degree of biliary dilation and gradual tapering or sudden narrowing of the duct are challenges for differential diagnosis, consistent with findings by Suthar *et al* (109). Further emphasis on the combined application of MRCP and CT has been presented by Wang *et al* (110), who proposed a scoring model based on the length of stricture, angle of distal biliary stricture, double duct sign and low density in the arterial phase, enhancing the diagnostic accuracy for benign and malignant distal biliary strictures.

Quantitative MRI analysis also demonstrates proficiency in differentiating PHC, intrapancreatic cholangiocarcinoma and AC. For instance, AC often shows the narrowest confluence angle of the pancreaticobiliary duct and the minimal distance between the terminus of the dilated pancreaticobiliary duct and the major duodenal papilla (111). MRI findings for PHC include enlargement of the pancreatic head, extraluminal mass in the biliary duct, ductal dilation above the lesion, a large confluence angle of the pancreaticobiliary duct and mild delayed enhancement post-contrast (3,112). DBDC typically presents with thickening of the bile duct wall, intraluminal small masses and 'rat tail' type narrowing (113). Additionally, DC and AC exhibit unique MRI manifestations, such as small masses in the duodenal lumen, blunt dilation at the end of the bile duct and thickening of the ampullary duct wall with a beak shape of the distal bile duct (Fig. 2) (114,115). Enhanced MRI combined with analysis of minimum apparent diffusion coefficient (ADC) demonstrate good diagnostic efficacy in distinguishing between intestinal- and pancreatobiliary-type cancers. As indicated by Bi *et al* (105), its sensitivity, specificity and AUC values are 70.4%, 78.6%, and 0.807, respectively. Furthermore, Nalbant *et al* (106) reported the application value of MRI and MRCP in a preliminary diagnosis of a mass at the PBDJ, highlighting that oval filling defects suggest the likelihood of intestinal-type tumors, whilst progressive enhancement of the mass, irregular narrowing of the distal CBD, PD truncation, involvement of the gastroduodenal artery, lymphadenopathy, and a low ADC value are more indicative of pancreatcobiliary-type. When utilizing MRI for the evaluation of tumors at the PBDJ, a multi-sequence and -phenomenon assessment is necessary, considering the pathophysiological characteristics of the different tumor types, inferring potential signs that may arise and providing as much imaging diagnostic information as possible to aid clinical decision-making in treatment strategies.

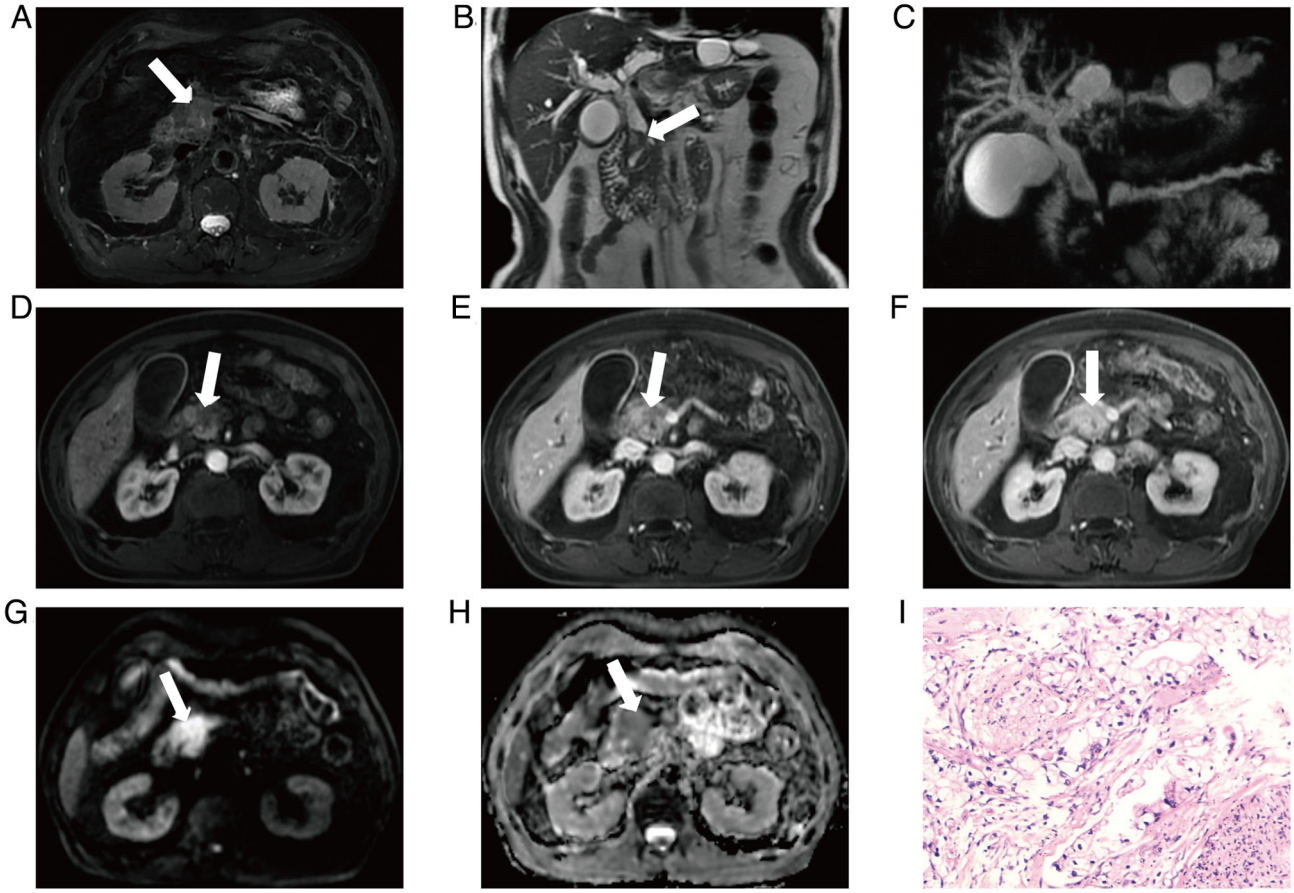

Figure 2. Ampullary carcinoma. (A) Axial T2W reveals high signal lesions around the ampulla. (B) Coronal T2W and (C) a magnetic resonance cholangiopancreatography postprocessing image demonstrates irregular thickening and stricture of the distal common bile duct in a beak shape with dilation of the bile duct and pancreatic duct above it. (D) Arterial phase, (E) venous phase and (F) delayed phase shows progressive enhancement of the mass. (G) Diffusion weighted imaging (B value, 1,000) demonstrates a high signal of the mass. (H) Low signal on apparent diffusion coefficient. (I) Hematoxylin and eosin staining of the lesion. Magnification, x200. T2W, T2 weighted image. The images were obtained from the Department of Radiology, Affiliated Nanhua Hospital, University of South China, with the consent of both the involved patient and the institution, for the purpose of this review.

ERCP. ERCP allows for direct visualization of lesions on the medial walls of the duodenum and the ampullary region through the injection of contrast agents (116). It facilitates the examination of pancreatic and bile duct structures, and it enables biopsy collection for pathological evaluation. Furthermore, it can be utilized for interventional treatments such as stent placement to alleviate jaundice in patients with advanced and inoperable conditions (85). When tumors are small and undetectable by other imaging modalities, ERCP is particularly effective for early diagnosis. The preferred method for diagnosing duodenal tumors is endoscopy, which not only allows for visual assessment of the tumor size, location and morphological characteristics, but facilitates biopsy for histopathological confirmation (117). A study indicated that the accuracy of endoscopic biopsy for diagnosing ampullary tumors is 81.9% (118). However, it may be challenging to identify tumors located in the horizontal and ascending portions, often necessitating the use of duodenal double contrast barium studies to enhance diagnostic rates. Notably, ERCP exhibits a diagnostic accuracy of ≤100% for ampullary tumors, notably surpassing that of US, CT and MRCP (104). Nevertheless, due to its limitations in assessing the spatial relationships of tumors to adjacent tissues and the extent of invasion into surrounding structures, additional imaging studies are needed for a comprehensive evaluation to ensure diagnostic completeness and accuracy (119).

Positron emission tomography (PET)/CT. 18F-Fluorodeoxyglucose (18F-FDG) PET/CT is a diagnostic technique that integrates functional metabolism with anatomical structure imaging. It effectively distinguishes between benign and malignant lesions by capturing the glycolytic activity of malignant cells, demonstrating efficacy particularly in the diagnosis of pancreatic malignancies (120). In this process, 18F-FDG, a glucose analogue, is transported into the cells via glucose transporters, where it is phosphorylated into 18F-FDG-6-phosphate by hexokinase. Due to the high expression of transporters and kinases in malignant tumor cells, 18F-FDG tends to be retained within the cells, resulting in high metabolic hotspots on PET/CT. Whilst PET/CT cannot replace pancreatic CT or MRI as the first-line examination, it serves as an advantageous adjunct, especially in the exclusion and detection of distant metastases, particularly in cases with larger primary lesions, suspected regional lymph node metastases and notably elevated CA 19-9 levels (121,122).

Chronic mass pancreatitis is a specific type of chronic pancreatitis characterized by long-term inflammation leading to damage of the pancreatic parenchyma and fibrotic tissue

proliferation, potentially forming a mass in the pancreatic head (123). Currently, CT is widely used as a routine imaging modality for anatomical assessment and tumor staging; however, its capacity for differential diagnosis is limited when faced with the highly similar clinical presentations and imaging characteristics of chronic mass pancreatitis and pancreatic cancer (124). The standardized uptake value (SUV) is an important semi-quantitative indicator for diagnosing pancreatic cancer, with SUV values being markedly higher in patients with pancreatic cancer compared with those in patients with chronic pancreatitis (125). Notably, although 18F-FDG PET/CT exhibits high sensitivity in diagnosing pancreatic cancer, it also encounters issues with false positives, such as in cases of active pancreatitis, peritoneal fibrosis and lymphocytic infiltration, and false negatives such as in low-density cancer cells and tumors with high fluid content. Therefore, it is necessary to conduct a comprehensive evaluation incorporating clinical manifestations, laboratory tests and other factors (126).

Overall, PET/CT demonstrates superior diagnostic efficacy compared with enhanced CT in the differential diagnosis of pancreatic cancer and chronic mass pancreatitis, providing a richer and more accurate imaging basis for clinical decision-making.

5. 3DVT imaging diagnosis

Tumors at the PBDJ, regardless of their benign or malignant nature, should be primarily treated with surgical intervention once diagnosed. Formulating a surgical plan necessitates a comprehensive consideration of the tumor location, size, infiltration range, vascular relationships, metastasis and the physical condition of the patient (127). Due to the unique anatomical positioning of these tumors, surgical complexity tends to be high, making preoperative assessment critically important. Traditional two-dimensional imaging techniques such as US, MDCT and MRI can provide information about the lesion and adjacent structures; however, due to the relatively sparse blood supply to the pancreas and distal bile duct, imaging clarity is often limited, possibly leading to errors in assessing tumor resectability (128,129).

To overcome the limitations of two-dimensional imaging, 3DVT has emerged and is gradually being applied in the diagnosis and treatment of tumors at the PBDJ. This technology relies on a 3D visualization system for abdominal medical imaging, allowing for a comprehensive evaluation of the tumor morphology, position, the state of pancreatobiliary duct obstruction and its spatial relationships with surrounding major blood vessels. Current research focuses on the consistency between 3D assessment results and intraoperative realities, aiming to optimize surgical planning, shorten operative duration and reduce the risk of injury to major vessels during surgery, which holds significant clinical importance (130). 3D imaging not only provides a clear depiction of anatomical structures, but also integrates dynamic simulation and real-time interactive functionalities, substantially enhancing diagnostic accuracy and the scientific rigor of surgical planning (131-133). In the field of oncology, 3DVT is particularly vital, granting physicians the precision to closely examine tumors and their surrounding environments (134,135). Specifically, this technology reconstructs two-dimensional CT images into 3D models that closely match the structures of the abdominal organs of the patient, allowing for an intuitive, spatial and comprehensive separation of the tumor in 3D images. This facilitates a swift and accurate assessment of the relationships between the pancreatic head, distal bile duct or ampullary tumors and vasculature, providing robust support for surgeons in evaluating tumor resectability and formulating personalized treatment strategies (136,137).

The resection of tumors located in the head and body-tail of the pancreas is recognized as one of the most complex procedures in upper gastrointestinal surgery, often facing challenges related to vascular variations during surgery, particularly those involving the portal vein and the hepatic artery (138). Research indicates that 3D visualization systems are effective in demonstrating the origins and branches of vessels, as well as the relationships between tumors, organs and vessels, achieving a diagnostic sensitivity, specificity and accuracy of 100% for identifying hepatic artery variations. The clarity of the images produced rivals that of angiography, thereby providing individualized preoperative guidance for patients with hepatic artery anomalies undergoing pancreaticoduodenectomy (139). Miyamoto *et al* (140) further expanded the application scope of 3DVT, using it to clearly present anatomical variations of peripancreatic vessels and changes induced by tumors, thus minimizing surgical trauma and shortening the operation time through preoperative simulations. Addressing one of the severe complications associated with pancreaticoduodenectomy, pancreatic fistulas, Miyamoto *et al* (141) proposed that preoperative measurement of the residual pancreatic volume using 3DVT can predict the risk of fistula occurrence, offering a scientific basis for preventing complications. Furthermore, the cinematic rendering technique, an advanced post-processing technology within 3D visualization, leverages unique illumination models to generate higher quality images, significantly enhancing detail representation (142). This technology exhibits distinctive advantages in depicting tumor location, adjacent relationships, modes of enhancement and internal characteristics such as necrosis and cystic changes. It is also able to simulate endoscopic views, thereby providing positive support for the qualitative diagnosis of lesions and planning of therapeutic strategies (143).

The blood supply to the lower segment of the CBD primarily originates from the right hepatic artery and the pancreaticoduodenal artery. Inadequate vascular management can markedly increase the risks of complications such as bleeding and anastomotic leaks. The application of 3DVT in surgical procedures for tumors at the PBDJ markedly enhances the visualization of lesion structures, facilitates precise surgical planning and ensures smoother handling of complex cases, ultimately improving the R0 resection rate (144,145). Furthermore, 3D pancreaticobiliary duct models demonstrate considerable potential in accurately assessing complex pathological anatomy, aiding differential diagnoses, and informing surgical planning by overcoming the limitations of traditional CT and MRCP techniques, particularly for patients with tumors at the PBDJ (146,147).

In the realm of diagnosis and treatment of hepatobiliary diseases, 3DVT also serves a crucial role (8,148-150). Zhang *et al* (151) reported that this technology has a notably

Table I. Evaluation and value of imaging techniques in the diagnosis of malignant tumors at the pancreaticobiliary duodenal junction.

First author/s, year	Technique	Advantages	Disadvantages	Possible directions for improvement	(Refs.)
Zhang *et al*, 2016 and Swaraj *et al*, 2023	US	Non-invasive, convenience, real-time observation capabilities of lesions and low economic cost.	Susceptible to gastrointestinal gas interference, limited detection rates for small tumors and high operator dependence.	Develop DCEUS technology to improve small lesion detection. Integrate with CT and MRI for advanced multimodal imaging Enhance training for US diagnosticians.	(75,155)
Trikudanathan *et al*, 2014 and Oppong *et al*, 2020	EUS	High-resolution imaging, reduction of interference actors, real-time fguidance for puncture biopsies and assessment of tumor resectability.	The technical operational difficulty is high, with associated risks of complications, prolonged examination times and reliance on the operator's expertise.	Developing higher frequency US probes and new image processing techniques to improve image quality and diagnostic accuracy, multi-modal integration and optimizing patient preparation.	(78,83)
Liang *et al*, 2022 and Bi *et al*, 2022	CT	High-resolution imaging, multi-stage scanning technologies and extensive post-processing capabilities with broad applicability.	Radiation exposure risks, limited detection rates for small lesions and insufficient soft tissue contrast.	Develop low-dose scanning technologies, apply spectral CT and promote multimodal integration alongside AI-assisted diagnostics, such as radiomics.	(89,103)
Chen *et al*, 2019 and Nalbant *et al*, 2023	MRI	No radiation, high soft tissue resolution, multi-sequence imaging, advantages of MRCP and functional imaging capabilities.	Spatial resolution is limited, examination durations are lengthy, motion artifacts may affect results, costs are relatively high and contraindications for examinations.	Improvements in MRI hardware and software, development of new imaging technologies and sequences, promotion of multimodal integration and applications of radiomics.	(7,106)
Chen *et al*, 2008 and Park *et al*, 2004	ERCP	Intuitive visualization of the pancreaticobiliary anatomy allows simultaneous biliary drainage or biopsy.	The invasive nature of the procedure incurs a higher risk of complications and is limited to certain patient populations	It is necessary to elevate technical levels, optimize the materials of devices, integrate other examination methods and enhance posto-perative.management.	(104,108)
Reddy *et al*, 2022 and Wen *et al*, 2020	PET/CT	Comprehensive assessment of systemic tumor metastasis and effective differentiation between benign and malignant tumors.	Costs are high, radiation exposure is significant, sensitivity to certain low-metabolism tumors is lacking and detection of lesions in hollow organs has blind spots.	Solutions include reducing radiation doses, integrating other examination methods and developing specific tracers.	(156,157)
Barat *et al*, 2024 and Zhao *et al*, 2018	3DVT	Provides intuitive three-dimensional data on tumor morphology, location and relationship with surrounding structures enhance diagnostic precision, and assists in surgical planning and treatment.	High-quality raw imaging data required, high technical costs, complex processing workflows, and further data required to validate its effectiveness and reliability.	Need to lower costs, simplify operational processes, integrate with other imaging technologies, pursue ongoing research and innovation such as exploring new three-dimensional visualization algorithms and reconstruction techniques, along with performing more clinical studies.	(143,153)

US, ultrasound; DCEUS, double contrast-enhanced ultrasonography; EUS, endoscopic ultrasound; CT, computed tomography; MRI, magnetic resonance imaging; AI, artificial intelligence; MRCP, magnetic resonance cholangiopancreatography; ERCP, endoscopic retrograde cholangiopancreatography; PET/CT, positron emission tomography/CT; 3DVT, three-dimensional visualization technology.

higher positive predictive value for diagnosing portal vein invasion in hilar cholangiocarcinoma compared with subjective assessments based on CT scans; this provides a quantitative basis for the preoperative determination of resection extent and the surgical approach. Guo *et al* (152) explored the efficacy of 3DVT in guiding hepatic resection for complex intrahepatic stones, reporting that 3DVT offers a precise preoperative diagnosis of complex intrahepatic bile duct stones, demonstrating improved safety, feasibility and effectiveness compared with conventional imaging modalities. Zhao *et al* (153) performed a comparative study between two-dimensional medical imaging and 3DVT in evaluating tumor resectability, reporting accuracy rates of 85.9% for conventional imaging and 97.2% for 3DVT. This indicated that 3DVT predicts tumor resectability more accurately in preoperative evaluations. Moreover. 3DVT effectively addresses the limitations of two-dimensional imaging in abdominal CT, particularly in showcasing intricate details of the surgical area when dealing with affected organs and their surrounding complex structures, allowing surgeons to assess the relationships fully and spatially between tumors and adjacent blood vessels and lymph nodes, thereby optimizing surgical strategy selection. However, it is noteworthy that this technology is currently limited to spatial configuration reconstruction and does not yet provide the functional information necessary for differential diagnoses (154).

The present review systematically summarized and analyzed the advantages and limitations of several imaging techniques in the diagnosis of tumors at the PBDJ. Additionally, based on current advancements, the present review made forward-looking predictions and outlooks on future trends. This is presented in Table I (7,75,78,83,89,103,104,106,108, 143,153,155-157).

6. Conclusions

In summary, due to its complex anatomical structure and significant physiological functions, the PBDJ serves as a convergence point for several digestive fluids such as bile, pancreatic juice and gastrointestinal secretions, which results in it being a high-incidence area for malignant tumors and a key pathological basis. However, the etiological factors and specific mechanisms underlying tumors in this region remain to be elucidated, and there are numerous challenges in clinical diagnosis. Given the low sensitivity of PBDJ tumors to radiotherapy, chemotherapy, immunotherapy and targeted therapy, surgical intervention has become the preferred treatment strategy (158-161). Several imaging diagnostic methods each have their advantages and disadvantages when evaluating tumors at the PBDJ. Therefore, the judicious selection and combination of these techniques are crucial for enhancing tumor detection rates and diagnostic accuracy. Currently, accurately distinguishing the tissue origin of tumors at this junction, whether intestinal type or biliary-pancreatic type, using technologies such as US, MDCT, MRI, ERCP and PET-CT remains challenging, with limited differentiation capability. Consequently, there is a need for in-depth exploration and validation of radiomics and 3DVT to optimize the diagnostic and assessment strategies for tumors in this region.

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Authors' contributions

WYY participated in gathering and arranging the literature and drafting the paper. PSH conducted the analysis for Figs. 1 and 2 and contributed to the manuscript revisions. CHZ offered guidance and revised the manuscript throughout the entire process. All authors have read and approved the final manuscript. Data authentication is not applicable.

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Competing interests

The authors declare that they have no competing interests.

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