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Research Article

Updates in The Role of MRI in Diagnosis and Staging of Pancreatic Cancer: A Systematic Review

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Abstract: Pancreatic cancer is the fourth leading cancer-related cause of death throughout the world. Magnetic resonance imaging (MRI) is typically capable of quickly differentiating cystic from noncystic tumours due to the good soft tissue contrast resolution. Cystic tumours are frequently simple to identify with an MRI; however, non-cystic non-adenocarcinoma tumours can exhibit a wide range of imaging characteristics that may be mistaken for ductal adenocarcinoma. An effective method for identifying pancreatic lesions is MRI. This study investigates the current and recent evidence concerning the role of MRI in the diagnosis and staging of pancreatic cancer. PubMed, Web of Science, Science Direct, EBSCO, and Cochrane library were searched. Study articles were screened by title and abstract using Rayyan QCRI then a full-text assessment was implemented. A total of 7 studies were included, with 618 pancreatic cancer patients with different histopathological types. Most studies reported the benefits of MRI in the diagnosis and staging of pancreatic cancer and in identifying extra-abdominal metastases. Only one study found that MRI under-staged the tumor size and did not detect the micro-infiltration of peri-pancreatic tissues. MRI has a significant role in diagnosing and staging pancreatic cancer. There have lately been substantial advancements in pancreatic imaging utilizing multiple imaging modalities, such as SG-KS-4D-MRI and DW imaging with traditional MR.

Keywords; Pancreatic Cancer, Adenocarcinoma, *MRI,* Imaging, Pancreas, Tumor, Malignancy

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1. INTRODUCTION

With an incidence rate that is equal to its mortality rate, pancreatic cancer is the fourth most prevalent cancer-related cause of death worldwide [1]. The prognosis for pancreatic cancer is still poor because the five-year survival rate is less than 5%, and the mortality rate has not decreased over the past few decades [2]. This is in contrast to other malignancies, such as colorectal cancer, breast cancer, and prostate cancer, where significant advances were made in the early detection and treatment of the disease. Therefore, it appears that pancreatic cancer will continue to be one of the biggest obstacles in the fight against cancer in the twenty-first century [3]. The difficulty in making an early diagnosis of pancreatic cancer is one of the key reasons for its poor prognosis. The proper screening and early identification of pancreatic cancer are fairly difficult due to the fact that it often develops with minimal symptoms in the early stages and that there are not many particular, well-known risk factors aside from smoking and family history [4]. As a result, only 10% to 20% of patients diagnosed have a chance for a successful resection and a potential cure, and even among those with resectable disease, the survival rate is only 23% [5]. Despite the multiple challenges listed above, efforts are still being made to detect pancreatic cancer early and choose the best surgical candidates [6]. Furthermore, the various imaging modalities currently available for pancreatic imaging, such as ultrasonography (US), computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and endoscopic ultrasonography (EUS), have a critical principle in the differentiation of focal pancreatic lesions, initial staging, surgical and therapeutic planning, and assessment of the treatment response [7]. Magnetic resonance imaging (MRI) is typically capable of quickly differentiating cystic from noncystic tumours due to the good soft tissue contrast resolution. Cystic tumours are frequently simple to identify with an MRI; however, non-cystic non-adenocarcinoma tumours can exhibit a wide range of imaging characteristics that may be mistaken for ductal adenocarcinoma. An effective method for identifying pancreatic lesions is MRI. [6] The image quality and diagnostic precision have improved as a result of the development of more advanced MRI scanners and imaging methods in recent years. Therefore, patients with pancreatic illness are currently using MRI with MRCP as a problem-solving technique [8]. There are several specific circumstances in which MRI is superior to CT: small tumors, hypertrophied pancreatic head, attenuating pancreatic cancer, and focal fatty infiltration of the parenchyma [9]. This is due to the greater soft-tissue contrast of MRI compared to that of CT. Consequently, it has been demonstrated that MRI is excellent for describing pancreatic masses. A great substitute for ERCP, MRCP is also a very effective and traditional MR technique for non-invasively defining the pancreatic ductal system [10]. The detection of modest ductal constriction that may point to the presence of a tiny mass is another important application of MRCP. As an additional source of biliary or pancreatic ductal dilatation, the presence of stones can be distinguished by MRCP extremely effectively [11]. Although MDCT now plays a significant role in PC assessment, MRI with MRCP enables more effective tumour detection at an early stage by enabling a thorough investigation of the pancreatic duct's and parenchyma's morphological alterations [12].

1.1 Typical Imaging Features Of Pancreatic Cancer

Pancreatic cancer often shows up as hypointense on fat-suppressed, T1-weighted imaging (Figure 3) and on pancreatic parenchymal phase, dynamically enhanced, fat-suppressed, T1-weighted sequences, although it can show up in a variety of ways on T2-weighted images [9]. Diffusion-weighted imaging displays for pancreatic cancer can vary. 80 patients participated in a recent study, and of those, 38 had pancreatic tumours that were hyperintense, 12 were isointense, and 4 were hypointense [10].

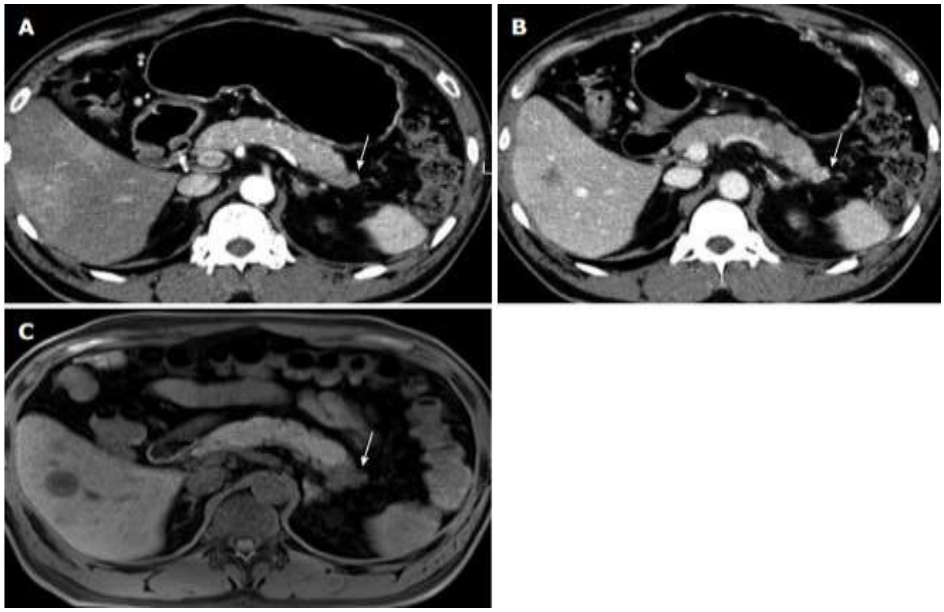

Fig 3 A 64-year-old male with biopsy-proven pancreatic adenocarcinoma with liver metastasis. A, B: On MDCT, the pancreatic tail mass (arrow) shows isoattenuation, causing distal parenchyma atrophy; C: On pre-contrast, T1–weighted, gradient-echo sequence MRI,

The pancreatic tail mass (arrow) is clearly depicted, as well as the liver metastasis, owing to the increased soft-tissue contrast of MR compared with that of CT. MRI: Magnetic resonance imaging; MDCT: Multi-detector computed tomography.[9,10] The review aims to explore the current and recent evidence concerning the role of MRI in the diagnosis and staging of pancreatic cancer.

2. METHODOLOGY

A systematic search of the literature was conducted to identify studies examining the incremental accuracy of MRI in local staging and the detection of pancreatic cancer. Criteria for inclusion Studies were considered for inclusion only if they presented clear individualised results with respect to index tumour or MRI-detected pancreatic lesions not seen on conventional tests. The gold standard for evaluating the validity of MRI was histopathological confirmation or follow-up. Studies also had to have confirmed at least the positive MRI results, both true positives and false positives.

4.1 Search strategy

An experienced reference librarian conducted the electronic search to identify all the primary studies published in journals indexed in the databases EMBASE and. The reference lists of selected articles and reviews were also examined.

4.2 Selection of dedicated studies

The 4-member team of clinicians and methodologists formed six pairs to review potential articles. Each eligible study was assessed for possible inclusion by one pair of evaluators, with a third evaluator in a different pair responsible for resolving disagreements. The title and abstract of articles located in the initial search were first reviewed to select those potentially eligible for full review. The full text of potentially relevant articles was then read to decide if they would finally be included.

4.3 Assessment of study quality

The methodological quality of the studies included was assessed using a subset of items from the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) scale, adapted for this review. We assessed the following criteria: type of study design, patient selection by diagnostic protocol or referred for MRI, consecutive recruitment, confirmation using the same gold standard, for positive and negative cases for index test, complete verification of all cases with a gold standard, prospective data collection, adequate description of the test evaluated and definitions of multifocality and multicentricity.

4.4 Data extraction

Data extraction was performed by two investigators working independently, and disagreements were resolved by consensus. If no agreement was reached, a third evaluator was called. The pairs extracted in duplicate the information on clinical characteristics, methodologies, and the validity results. Authors independently extracted information on the technical characteristics of the MRI devices used. Data from primary studies were extracted using an ad hoc form that included information on the study design and methodological characteristics, clinical and demographic characteristics of the patients included, characteristics of the diagnostic test and results of the study.

3. STATISTICAL ANALYSIS

For studies in which it was possible to extract information on all cells, therefore, to confirm both the positive and negative MRI results with a reference standard, the indices of sensitivity/specificity were estimated with 95% confidence intervals (CIs). The data analysis was carried out through the constant comparative method from Glaser and Strauss' grounded theory. First, a complete reading of the results and conclusions of the different studies was carried out. Subsequently, the information corresponding to the objective of this review was identified, using the authors' interpretations and textual quotes. Finally, categories and subcategories emerged, whose origin was the main topic of the study, which can be found in the Results section. To provide a qualitative overview of the included research aspects and outcome data, summary tables were presented, including the collected details from the eligible studies. After finishing the data extraction in this systematic review, decisions were made on how to maximize the use of the available data of the included study articles. Studies that met the full-text inclusion requirements but did not provide any data on the MRI's role in the detection of pancreatic cancer were excluded.

4. RESULTS

4.5 Search results

A total of 560 study articles were extracted from the systematic search, and then 63 duplicates were removed. Title and abstract screening were conducted on 497 studies, and 352 studies were excluded. 145 reports were sought for retrieval, and only 10 articles were not retrieved. Finally, 135 studies were screened for full-text assessment; 79 were excluded for wrong study outcomes, 21 for unavailable data on the role of MRI on pancreatic cancer, and 28 for the wrong population type. Seven eligible study articles were included in this systematic review. A summary of the study selection process is illustrated in Figure 1.

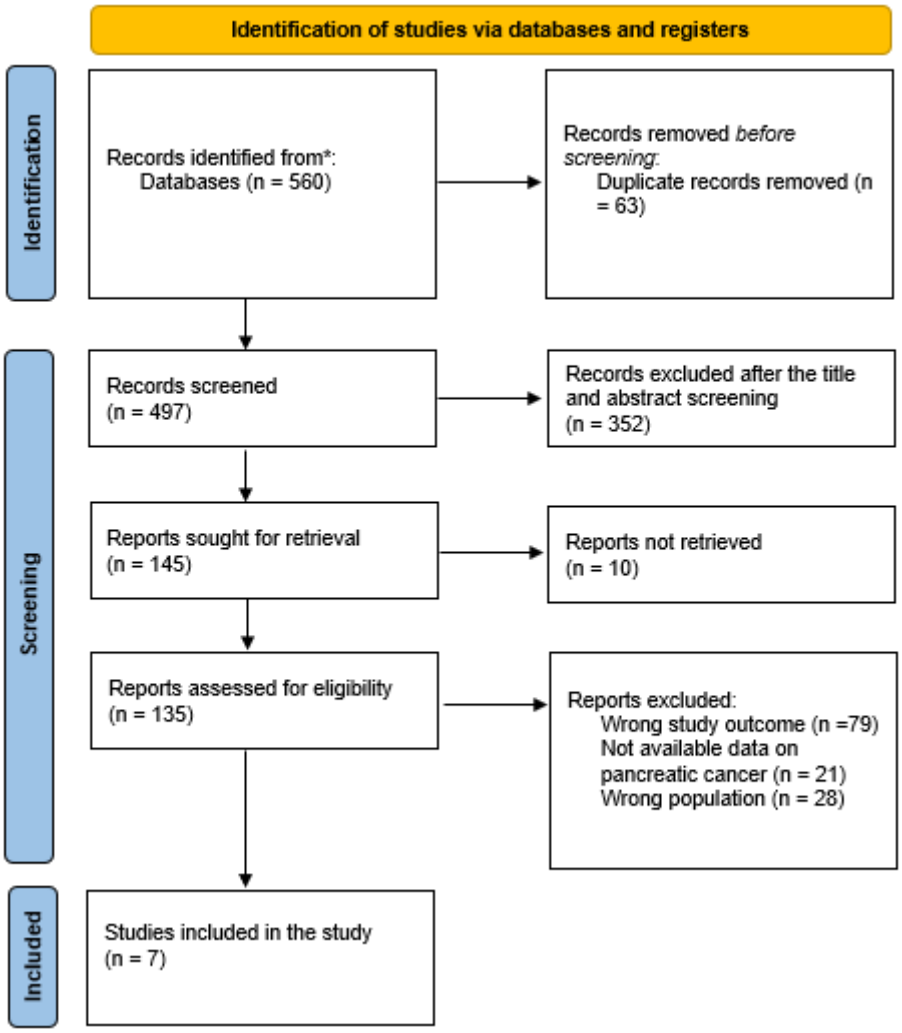

Fig (1): PRISMA flow chart presenting the study selection results.

4.6 Demographic patient

The review population revealed that the majority of patients(618 patients) affected by pancreatic cancer were over 35 years old. However, pancreatic cancer in the younger ages was not uncommon. Typically, pancreatic cancer has a peak onset of 35-65 years and affects males more. a prospective cohort study reported that the presentation of pancreatic cancer were associated with high morbidity and high mortality rate. Further observational studies will aid further understanding of the association of pancreatic cancer disease and the role of MRI in diagnosis.

4.7 Characteristics of the included studies

A total of 7 studies were included in this review, with 618 pancreatic cancer patients with different histopathological types. Four studies were conducted in China [15-17, 19], one in Japan [18], one in Romania [20], one in the USA [21], one in Korea [22], and one in Germany [14]. All studies were retrospective in nature. Three studies [15, 18, 19] reported the benefits of MRI in the early diagnosis of pancreatic cancer. Two studies [16, 17] reported that using MRI to detect the staging of pancreatic cancer was clinically significant. One study [23] found that MRI under-staged the tumor size and did not detect the micro-infiltration of peri-pancreatic tissues. One study [20] found that MRI is a significant tool for identifying extra-abdominal metastases in cases of pancreatic cancer. One study used the novel practicality of a self-gating k-space sorted 4-dimensional MRI (SG-KS-4D-MRI) method that combines self-gating-based k-space sorting with 3-dimensional (3D) radial sampling to produce respiratory phase-resolved 3D-MRI images to assess the motion of the pancreatic tumor. They found that the average motion pattern produced by SG-KS-4D-MRI is significantly better than single-instance data and may be a better indicator of the anticipated breathing motion. It also produces significantly increased spatial resolution and voxel isotropy [21] as illustrated in (Table

Table (1): Summary of characteristics of the included studies.

Study	Study design (data collection)	Country	Total Participants	Male (%)	Mean age (y)	Key findings	ROBINS-I	Patient selection	Complete varifiction
Yu et al., 2021 [15]	Retrospective study	China	160	97 (60.6)	47.52±11.43	MRI has a high detection rate of pancreatic cancer and provides information about the treatment plan. The sensitivity, specificity, and accuracy of the early diagnosis can be considerably increased by an MRI scan.	High	Diagnostice protocol	Yes
Yang et al., 2018 [16]	Retrospective study	China	31	21 (67.7)	40-75	Preoperative staging and respectability evaluation of pancreatic cancer using MRI was clinically significant. The postoperative pathological staging and the MRI staging were consistent.	High	Diagnostice protocol	Yes
Deng et al., 2020 [17]	Retrospective study	China	132	87 (65.9)	58	For the preoperative staging and respectability assessment of pancreatic cancer, MRI is a reliable imaging tool. For T staging, there is a significant correlation between preoperative MRI and the pathological results, and for N staging, there is a moderate correlation.	Moderate	Diagnostice protocol	
Kurita et al., 2021 [18]	Retrospective study	Japan	20	14 (70)	68.5	Even without pathologic evidence, high signal intensity in diffusion-weighted MRI may be an indication that surgery should be performed to remove early-stage pancreatic ductal adenocarcinoma.	High	Diagnostice protocol	Yes
Yang et al., 2017 [19]	Retrospective study	China	33	19 (57.6)	41–76	In the early diagnosis of pancreatic cancer, high-field MR perfusion imaging is clinically significant.	High	Diagnostice protocol	Yes
Costache et al., 2017 [20]	Retrospective study	Romania	130	NA	64	MRI is a significant tool for identifying extra-abdominal metastases in cases of pancreatic cancer.	Moderate	Diagnostice protocol	
Yang et al., 2015 [21]	Retrospective study	USA	10	5 (50)	59.5	They measured pancreas tumour mobility using a unique SG-KS-4D-MRI acquisition approach that can reconstruct high-resolution, artifact-free 4D-MRI images. The resulting pancreatic tumour motion trajectories matched 2D cine-MRI and 4D-CT results quite well.	High	Diagnostice protocol	Yes
Park et al., 2014 [22]	Retrospective study	Korea	83	56 (67.5)	62.2	Combining DW imaging with traditional MRI during the preoperative examination of small pancreatic adenocarcinomas increases the sensitivity of cancer detection.	High	Diagnostice protocol	yes
Bley et al., 2005 [23]	Retrospective study	Germany	19	11 (57.9)	62.8	MRI for preoperative pancreatic cancer staging tended to under-stage tumour size. MRI may not pick up micro-infiltration of peripancreatic tissue or the common bile duct, particularly in cases of small tumour size.	Moderate	Diagnostice protocol	

4.8 Standard Protocol For Pancreatic Cancer Evaluation

Ultra Sound: After a minimum 6-hour fast, the pancreas is examined using an ultrasound. The goals of the fast are to assure an empty stomach, reduce intestinal gas, and improve pancreatic visibility. Plans for US scans along the pancreatic duct include transversal, longitudinal, and oblique scans. By shifting the transducer and exerting compression when appropriate, bowel gas can be expelled. It is conceivable, and occasionally convenient, to use several scanning techniques, such as filling the stomach with water, inspecting the patient while they are suspended in inspiration or expiration, and shifting the patient's position to one of erect, supine, left and right decubitus. The water technique, which involves squeezing 100 to 300 mL of water via a straw, may be useful if the pancreas is difficult to see.[24]

4.9 CT

Pre-contrast images and early arterial phase (CT angiography phase) images of the aorta and superior mesenteric artery (17–25 s after the start of contrast injection), pancreatic phase (35–50 s after the start of contrast injection), and portal venous phase images (55–70 s after the start of contrast injection) are typically used in a pancreas-specific pancreatic cancer protocol. The best lesion to pancreas contrast can be found in pancreatic phase images because they display peak pancreatic parenchymal enhancement. Assessing the degree of venous involvement and looking for potential liver metastases can both be done with the aid of portal phase pictures.[25-,28]

Currently, it is common practise to account for fluctuations in the heart circulation time using the bolus tracking technique. For pancreatic imaging, a number of post-processing methods have been described. The most popular methods are minimum intensity projections (MIP), curved multiplanar reformations (CMPR), and multiplanar reformations (MPR) (MinIP).[27,29] The link between tumours and the pancreatic duct or nearby important tissues can be clearly shown by oblique coronal or sagittal MPR and CMPR along the pancreatic duct. Low-density structures like bile ducts and pancreatic ducts are clearly visible in MinIP pictures because they employ the lowest density values along each ray. For the pancreatic duct, a 3 mm MinIP slab thickness is advised. Also frequently employed to assess the link between tumours and nearby, increased vasculature are maximum intensity projections.[27,28,30]

4.10 MRI

In many medical facilities, individuals are required to fast for four to six hours prior to an MRI exam to allow the gallbladder to swell and reduce the signal from the stomach and duodenum beneath. Obtaining the following MR sequences is advised for a thorough assessment of the pancreatic parenchyma and pancreaticobiliary ductal system[31]: T1-weighted gradient-echo; T2-weighted axial and coronal sequences, typically turbo spin-echo; two-dimensional (2D) and three-dimensional (3D) MRCP; and T1-weighted 3D gradient-echo (GRE) before and after intravenous gadolin An increasingly popular, optional sequence for the detection and characterization of pancreatic lesions is diffusion-weighted imaging (DWI).[32]

Table 2 : Minimum technical specifications for pancreas protocol magnetic resonance imaging:[33]

Feature	Specification	Comment
Scanner type	primary magnetic field of 1.5 T or more.	Low-field magnets are inappropriate.
Coil type	multichannel, phased-array torso coil.	Unless patient-specific conditions forbid its usage.
Gradient type	High-speed gradients of the most recent generation (covering the upper abdomen enough)	-----
Slice thickness	For dynamic series, 5 mm or less, and 8 mm or fewer for other imaging	-----
Breath holding and matrix	Approximately 20 seconds of breath holding time with a 128 by 256 minimum grid.	Instructions for holding your breath are very crucial.
Injector	An ideal power injector would be dual-chamber.	Bolus tracking and MR fluorescence are preferred.
Contrast injection rate	Gadolinium chelate at 1.5–2 mL/s.	ideally yielding the final dose as indicated by the seller.
Minimum sequences	T1-weighted, gradient echo (3D preferred), T2-weighted, turbo spin echo (axial, coronal), MRCP (preferable in 2D and 3D), Post-Gd, and T1-weighted gradient echo are all acceptable imaging modalities.	-----
Mandatory dynamic phases	Portal-venous phase, equilibrium phase, and arterial	-----
Dynamic timing	After contrast injection, arterial: 20–40 s, portal venous: 45–65 s, and equilibrium: 3–5 min.	-----

5. DISCUSSION

MRI is a chemical imaging technology with properties including no ionizing radiation, many imaging sequences, and high soft-tissue sensitivity. It can detect small lesions of pancreatic cancer and has a better effect on the detailed display, which can be beneficial in the diagnosis of pancreatic cancer [34]. We found that in most included studies, MRI is the most significant and sensitive diagnostic tool for the diagnosis of pancreatic cancer and extra-pancreatic metastases. Earlier investigations demonstrated that MRI is the best imaging technique for primary pancreatic cancer. The general benefits of MRI include its multifunction, multiplane imaging, high soft tissue resolution, radiation-free nature, and lack of trauma. Additionally, MR perfusion imaging offers simultaneous anatomical and functional display, and repeated exams can be carried out to track the effectiveness of the therapy [35]. High-field MR perfusion imaging offers helpful information on intra-tumor perfusion and hemodynamic changes in addition to the enhanced delineation of pancreatic lesions due to high soft tissue resolution and vivid contrast. Perfusion imaging is anticipated to boost the tumor detection rate and the quality of diagnostic accuracy from this angle [36]. However, Bley *et al.* [23] reported that MRI under-staged the tumor size and did not detect the micro-infiltration of peri-pancreatic tissues**;** however, this study has a small population sample and was conducted over ten years ago. This review (Table 1) also reported that MRI is clinically significant too in staging pancreatic cancer. The ongoing advancement of MR dynamic strengthening and related imaging technologies has significantly enhanced the detection of lesions by MRI, accurate staging, and the assessment of surgical resectability. By keeping an eye on changes in vascular morphology and the surrounding structure of the lesions, it may be possible to increase the diagnostic staging rate of cancers [37]. According to several researchers, the pancreatic cancer tissues in individuals had uniformly hyperintense diffusion-weighted imaging (DWI) with distinct borders. MRI successfully combined functions and morphology because it could also dynamically reflect the motion of water molecules within the insult, chemical alterations, and other factors. Since MRI can effectively combine functions and morphology, it is used in the preoperative staging of pancreatic cancer with excellent accuracy [38]. A study we reported has used the practicality of an SG-KS-4D-MRI method that combines self-gating-based k-space sorting with 3-dimensional (3D) radial sampling to produce respiratory phase-resolved 3D-MRI images to assess the motion of the pancreatic tumor [21]. With an isotropic high spatial resolution of 1.56 mm, a set scan period of 8 minutes, and little intra-phase motion artifacts, the SG-KS-4D-MRI technology provides a number of potential advantages over other 4D-MRI techniques [39]. **Yang *et al.*** reported that the average motion pattern produced by SG-KS-4D-MRI is significantly better than single-instance data and may be a better indicator of the anticipated breathing motion. It also produces significantly increased spatial resolution and voxel isotropy [21].

6. CONCLUSION

This review demonstrated that MRI has a significant role in the diagnosis and staging of pancreatic cancer. Utilizing multiple imaging modalities, there have lately been substantial advancements in pancreatic imaging, such as SG-KS-4D-MRI and DW imaging with traditional MR.

7. AUTHOR CONTRIBUTION STATEMENT

All authors contributed and collaborated in data collection, extraction, paper writing, revising and production.

8. CONFLICT OF INTEREST

Conflict of interest declared none.

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