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Role of multidetector computed tomography in evaluation of resectability of pancreatic cancer

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Abstract

Background: Pancreatic cancer is one of the most significant causes and one of the most lethal malignant neoplasms in the world of cancer death in the developed nations. It was named the “silent killer” for its quiet course, late clinical presentation, and the trend of rapid growth. The aim of this study is to detect the reliability of multidetector CT (MDCT) as diagnostic tool in assessing the possibility of eradicating pancreatic cancer.

Results: Twenty-four patients (57%) were not suitable for surgery with non-resectable mass; the remaining eighteen patients (43%) were considered suitable according to MDCT criteria for surgical resection of the tumor. Fourteen out of the sixteen patients (87.5%) had a successful removal of the lump, while the remaining two cases (12.5%) during surgery, the mass was unresectable. The results of the pathology specimens showed that fourteen out of the fourteen patients (100%) had successful operation with no cancer cells in the margin, and a positive predictive value of 87.5% and accuracy of 89.47%.

Conclusions: The advancement of MDCT expertise improves the outcome of pancreatic cancer resectability.

Background

Pancreatic cancer is one of the most significant causes and one of the most lethal malignant neoplasms in the world of cancer death in the developed nations. Based on the GLOBOCAN 2018 estimates, pancreatic cancer causes about 459,000 new cases and 432,000 deaths per year, ranking as the seventh leading cause of cancer death in both sexes together [1]. Most patients are diagnosed later in life with a median age of 71 years at diagnosis and only 20% of diagnoses occurring before the age of 60 years [1]. Pancreatic cancer incidence and mortality worldwide correlate with rising age and are relatively more common in men than in women [2].

The prognosis is generally very bad, with a 5-year survival rate of 10% in the USA at the time of diagnosis. Complete surgical removal of the tumor is the only effective therapeutic option. Only 15–20% of people with

pancreatic cancer have a disease that is surgically able to be resected at the initial diagnosis. Even then, in the patients with resectable tumors, the prognosis remains low with a 5-year survival rate after surgery of about 20% [1].

However, its toll in more developed nations is higher. Reasons for large variations in death caused by pancreatic cancer rates are not yet entirely clear but may be attributable to a shortage of proper diagnosis, care, and categorization of cancer cases [2]. It was named the silent killer for its quiet course, late clinical presentation, and the trend of rapid growth [3].

There is still insufficient knowledge of the causes of pancreatic carcinoma, although some risk factors have been reported, such as cigarette smoking, diabetes mellitus, obesity, dietary factors, alcohol consumption, age, race, family history, genetic variables, infection with *Helicobacter pylori*, blood group non-O, and chronic pancreatitis [2].

Pancreatic cancer is primarily divided into two categories: the most common pancreatic adenocarcinoma

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(85% of cases) that occurs in the exocrine glands of the pancreas, and the less common pancreatic neuroendocrine tumor (PanNET) that arises in the endocrine tissue of the pancreas (less than 5%). Pancreatic adenocarcinoma has a very bad prognosis; typically after diagnosis, only 24% of people survive 1 year, and 9% live for 5 years [2].

The best way to diagnose a pancreatic tumor and to assess surgical resectability is usually high-quality computed tomography with intravenous contrast using a dual-phase pancreatic protocol. Endoscopic ultrasound (EUS) is a complementary staging procedure that is increasingly used and enables diagnostic confirmation when combined with fine needle aspiration [1].

While there is no strong agreement on the ideal therapy for borderline resectable pancreatic cancer [4, 5], neoadjuvant treatment has been recommended to increase the margin-negative (i.e., R0) resection rate for this illness and to enable proper patient selection for surgical procedures [6]. Regarding this, the “resect or palliate” decision relies on clinical staging system, which is focused on pre-surgical imaging findings. In order to prevent non-therapeutic laparotomy, accurate evaluation of tumor resectability based on computed tomography (CT) parameters is required. It is necessary to ensure that no patient with resectable tumor is refusing surgery due to a false-positive assessment of arterial invasion [7, 8].

The National Comprehensive Cancer Network Guidelines (version 2.2017 [9]); suggest a pancreatic protocol using MDCT, consist of pancreatic and portal venous phases, particularly CT angiography with thin-section axial images, MPR, and MIP or 3D volumetric images, for preliminary assessment of patients with clinical suspicions of having pancreatic cancers. CT shows good predictive sensitivity of the resectability of pancreatic cancer [10]. At present, in an effort to standardize the imaging criteria of the local resectability of pancreatic cancers, many guidelines describe the vessels to be evaluated and the imaging standards for determining the tumor

vascular relationship: abutment (< 180°), encasement (> 180°), and reconstruction potential. Even so, tumor differentiation from inflammatory conditions and accurate evaluation of circumferential and longitudinal tumor-vascular relationship are still challenging, especially in tortuous vessels. Furthermore, imaging evaluation of the vascular reconstruction possibilities may be subjective [10].

The main goal of our study was to determine the role of the preoperative MDCT categorization of the local resectability of pancreatic cancer and to identify its sensitivity, specificity, and accuracy levels.

Methods

The patients were referred to diagnostic radiology department for preoperative MDCT evaluation and staging of pancreatic tumor.

Patients

The study was conducted during the period of June 2018 to February 2019. This study included 42 patients, their age group from 36 to 80 years old (the mean age 58.8 years). They were 18 females their age group from 36 to 71 years old (the mean age 56.4 years) and 24 males their age group from 39 to 80 years old (the mean age 60.6 years).

Inclusion criteria

Patients with signs and symptoms related to gastrointestinal diseases and/or reported by ultrasound or previous abdominal CT scan to have pancreatic lesions

Exclusion criteria

- Proven pancreatitis or pseudo pancreatic cyst
- History of allergy to contrast media
- Renal impairment
- Pregnant females

Table 1 NCCN Criteria for CT Resectability of Pancreatic Cancer

Resectable	Artery: no contact with the celiac axis, SMA, or CHA Vein: no contact or abutment with the SMV or PV
Borderline resectable	Artery: A. Head or uncinate process Abutment or encasement of the common hepatic artery without extension to the celiac axis or hepatic artery bifurcation or abutment to the SMA or variant artery B. Body or tail Abutment to the celiac axis or encasement of the celiac axis without involvement of the aorta, GDA, and SMA Vein: encasement of the SMV or PV or abutment to the IVC
Unresectable (locally advanced)	Artery: encasement of the SMA or celiac axis, abutment or encasement of the first jejunal SMA branch, or abutment of the celiac axis and aortic involvement Vein: occlusion or tumor thrombosis of SMV or PV or abutment or encasement of the first jejuna SMV branch
Unresectable (metastatic)	Distant metastasis including non regional lymph node metastasis.

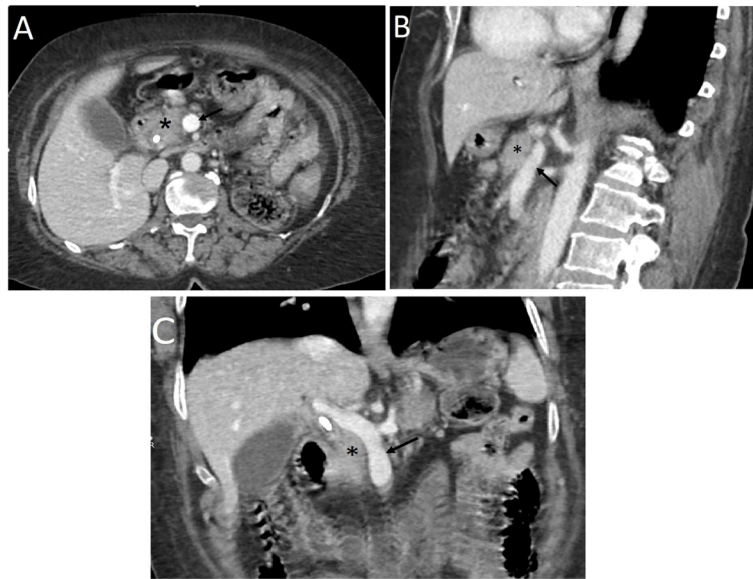


Fig. 1 (A) Axial MDCT with (B) sagittal and (C) curved coronal reformation (venous phase) in a 63 years old female shows a pancreatic head mass (star) abutting the portal and SM veins by $<180^\circ$ with no distortion or thrombosis (black arrows) which are CT signs of resectability while during surgery the mass was adherent to portal vein with failed surgical resection (false positive case)

All the patients were subjected to the following:

(I) Informed written consent

All participants in our study were fully explained the risks and benefits of the protocol. Privacy and confidentiality of all patient information has been ensured. All data provision were supervised and used for scientific purpose only.

(II) Full history and clinical examination

- Complaint
- Past history of any medical problem

(III) General and abdominal examinations by the referral clinician

(IV) Laboratory investigations

- Complete blood count (CBC)
- Liver and renal function tests
- Serum amylase and lipase
- Tumor markers: serum CA 19-9 level

(V) Abdominal ultrasound

Imaging techniques

The cases were examined by multidetector computed tomography (MDCT), in the radiology department by Toshiba Aquilion Prime Machine-64 detectors.

1. Patient preparation

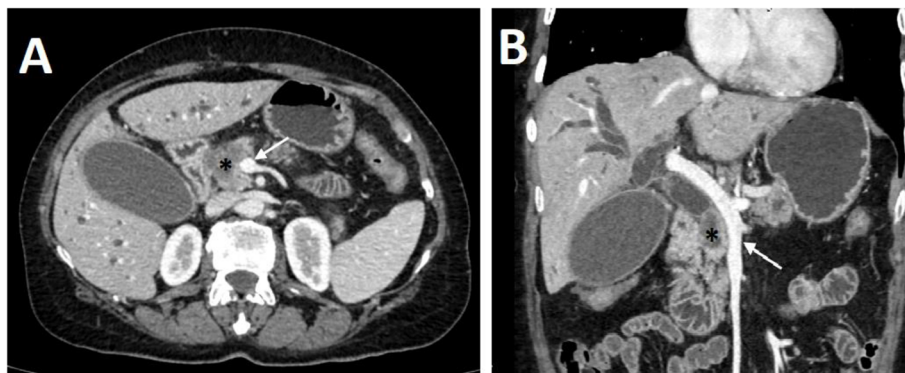


Fig. 2 (A) Axial MDCT with (B) coronal reformation (venous phase) in a 57 years old female shows a pancreatic head mass (star) encasing the SMV (white arrows) by $>180^\circ$ with no distortion or thrombosis which are CT signs of borderline respectability (true positive case)

Table 2 Classifications of patients according to preoperative MDCT criteria

Resectable group		Unresectable Group		Total
Resectable	Borderline	Locally advanced	Metastatic	
13	5	6	18	42

The patient was advised to fast for at least 6 h before the examination and given spasmolytic drug (Buscopan 20–40 mg, immediately IV or 10–15 min before examination IM) that should be administered to dilate the duodenum and to decrease peristaltic movement of the stomach and duodenum.

2. Oral contrast material

Oral contrast by using negative contrast media as water (1000 ml) before the examination to determine the duodenum and define the pancreatic head region

3. Intravenous contrast

All cases were injected with Omnipaque 350 (Amersham, GE Healthcare, Canada) at flow rate 4–5 ml/s. The dose was 1 ml/kg.

4. Three phase protocol and scan timing

After triggering the bolus tracking threshold of 50 H.U. of the aorta at the corresponding celiac axis level, scanning delay was 5 s for early arterial phase, 15 s for pancreatic phase, and 50 s for delayed venous phase.

5. Slice thickness

Contrast-enhanced phases are carried out craniocaudally with thin collimation (0.5 or 0.625 mm), 120 kVp, and the milliamperes automatically modulated. Five millimeters axial images are sent to the image archiving and communication system, as well as 5 mm coronal and sagittal reconstructed images, and 0.5 mm thick sections are sent to the workstations for custom processing and analysis [11].

Image analysis

All images were interpreted on Toshiba Vitrea Workstation, and the standard plane is axial plane. Multiplanar

Table 4 Resectability of MDCT correlated with pathological results

Free margin	Involved margin	Total
14	0	14

reconstruction (MPR), curved multiplanar reconstruction (cMPR), maximum intensity projection (MIP), minimum intensity projections (MinIP), and volume rendering technique.

The images were analyzed by two expert radiologists with 15 and 20 years experience respectively. Inter-observer agreement was taken. In cases of conflict, the decision was taken by the senior radiologist.

Then, our patients were classified according to the National Comprehensive Cancer Network (NCCN) criteria for CT Resectability of Pancreatic Cancer (version 1.2017) into four clinical stages (resectable, borderline resectable, locally advanced, and metastatic) (Table 1) [9].

No touch, abutment, encasement, occlusion, or tumor thrombosis are characterized as the degree of tumor—vascular contact. Abutment was characterized as tumor contact with a circumference of the vessel not exceeding 180° (Fig. 1). Encasement was characterized as involvement of tumors with a vessel radius of more than 180° or that caused vascular disfigurement (Fig. 2). Hazy fat planes between tumor and vessels were not considered as vascular invasion. Lymph nodes greater than 1 cm in the diameter of the short-axis and necrotic lymph nodes have been known as metastatic lymph nodes. Regional lymph nodes included (a) lymph nodes along the common bile duct, common hepatic artery, portomesenteric vein, and pancreaticoduodenal branches for pancreatic head masses, and (b) lymph nodes along the common hepatic artery, celiac axis, splenic artery, and splenic hilum for masses in pancreatic body or tail. Variant anatomy of the arteries, including accessory or replacement right hepatic artery and common hepatic artery, and degree of tumor interaction with variant arteries have also been assessed [9].

Correlation with postoperative surgical and pathological results

The intraoperative finding whether the tumor was surgically resectable or not and pathological data as cell type of the tumor and free resection margin were all collected and compared to radiological data obtained from

Table 3 Resectability of MDCT correlated with surgical outcome

Resectable tumors by surgery	Unresectable tumors by surgery	Total
14	2	16 (two cases refused surgery)

preoperative CT, and validity of CT in accurately assessing the tumor resectability is studied.

Results

Our study showed that most cases were unresectable, 24 cases (57%), that include cases with tumor metastasis (18 case) and cases with locally advanced tumor (6 cases) while resectable cases were 18 cases (43%) that include cases with resectable tumor (13 cases) and borderline resectable tumor (5 cases).

The cases that underwent tumor resection surgery were 16 cases (two cases refused surgery). Among these cases, 14 cases had a successful resection surgery (87.5%), and only two cases (12.5%) were unresectable during surgery. All resectable cases showed free tumor margin on postoperative pathology report, 14 cases of 14 (100%) (Tables 2, 3, and 4).

Regarding factors affecting resectability of pancreatic cancers, we found that tumor size, location, patient gender, or age group had no significant effect on resectability of pancreatic cancers according to NCCN (Table 5). Degree of arterial and venous involvement and degree of

lymphatic spread have significant effect on resectability of pancreatic cancers according to NCCN and the type of surgical interference respectively (Table 6).

Discussion

Our study enfases on widening the range of pancreatic tumor resectability, as resectable tumors with free tumor margins in pathology improve the prognosis for patients and increases life span. Early detection of local spread and vascular involvement also help in avoiding unnecessary operative interference with its hazardous effect on patients. The question we were seeking for was detecting the sensitivity of MDCT especially vascular encasement and lymph node involvement to help in patient management plane.

Our study showed that most cases were unresectable, 24 cases (57 %), while resectable cases were 18 cases (43%); the result is approximately agreeing with Low et al. [12] who found that in his study the non-resectable disease is seen at 75% of patients while Frelove and Walling [13] found that about only 15 to 20% of patients with pancreatic adenocarcinoma have resectable disease

Table 5 Gender, age group, location, size, and effect on biliary tree in comparison to MDCT resectability criteria

	NCCN								P value
	Resectable		Borderline resectable		Locally advanced		Metastatic		
	Count	%	Count	%	Count	%	Count	%	
Gender									0.502
Male	7	29%	2	8%	5	21%	10	42%	
Female	6	33%	3	17%	1	6%	8	44%	
Age group									0.220
30–39	1	50%	0	0%	1	50%	0	0%	
40–49	2	40%	1	20%	2	40%	0	0%	
50–59	5	31%	1	6%	2	13%	8	50%	
60–69	4	29%	2	14%	1	7%	7	50%	
70–79	1	25%	0	0%	0	0%	3	75%	
80–89	0	0%	1	100%	0	0%	0	0%	
Location									0.127
Head/neck	13	36%	5	14%	4	11%	14	39%	
Body/tail	0	0%	0	0%	2	33%	4	67%	
Size									0.352
<2 cm	0	0%	0	0%	0	0%	0	0%	
2–4 cm	9	43%	3	14%	3	14%	6	29%	
4–6 cm	3	27%	0	0%	2	18%	6	55%	
>6 cm	1	10%	2	20%	1	10%	6	60%	
Biliary tree									0.386
Not dilated	2	18%	1	9%	0	0%	8	73%	
Dilated	7	33%	3	15%	4	19%	7	33%	
Stent	4	40%	1	10%	2	20%	3	30%	

Table 6 Degree of arterial, venous, and lymphatic involvement in comparison to MDCT resectability criteria

	NCCN								P value
	Resectable		Borderline resectable		Locally advanced		Metastatic		
	Count	%	Count	%	Count	%	Count	%	
Arteries^a									
No contact	12	48%	3	12%	2	8%	8	32%	0.010
Abutment	1	17%	2	33%	0	0%	3	50%	
Encasement	0	0%	0	0%	4	36%	7	64%	
Occlude	0	0%	0	0%	0	0%	0	0%	
Veins^b									
No contact	5	63%	0	0.0%	0	0%	3	37%	0.000
Abutment	8	62%	2	15%	0	0%	3	23%	
Encasement	0	0%	3	37%	1	13%	4	50%	
Occlude	0	0%	0	0%	5	38%	8	62%	
Lymphatics									
No enlarged lymph nodes	3	43%	3	43%	0	0%	1	14%	0.006
Regional lymph nodes	10	34%	2	7%	6	21%	11	38%	
Non-regional lymph nodes	0	0%	0	0%	0	0%	6	100%	
Surgery									
No surgery	1	5%	1	5%	3	16%	14	74%	0.000
P.D	11	79%	3	21%	0	0%	0	0%	
Exploration	0	0%	1	17%	1	17%	4	66%	
Bypass	1	33%	0	0.0%	2	67%	0	0.0%	

^aArteries include celiac axis, SMA, CHA, or variant artery, including accessory right hepatic artery, replaced right hepatic artery, replaced common hepatic artery, and origin of the replaced or accessory artery

^bVeins include SMV, PV, or IVC

at the time of diagnosis. Khattab et al. [3] found that only 15 to 20% of the patients have resectable disease at the time of presentation. The cause of relatively higher incidence of resectable tumors in our study as compared with both Low et al. [12] and Freelove and Walling’s [13] studies indicate that development in MDCT has a significant role in detection of pancreatic tumors in early

stage and therefore make greater use for coming surgical interference.

Our study showed that among the commonest causes of unresectability in non-resectable group (24 cases) were vascular invasion which was seen in 62.5% of cases (15 cases), and lymph node metastases also seen in 25% of cases (6 cases) followed by distant metastases in 75%

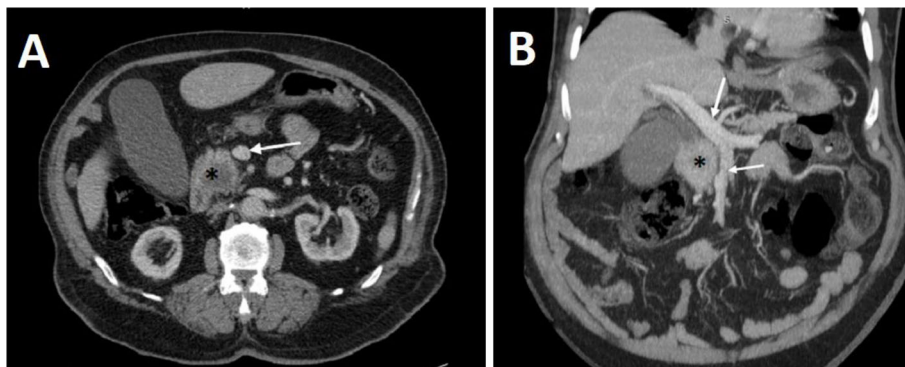


Fig. 3 (A) Axial MDCT with (B) coronal reformation (venous phase) in a 69 years old man shows a pancreatic head mass (star) with definite fat planes separating it from portal and SM veins (white arrows) which are CT signs of definite respectability (true positive case)

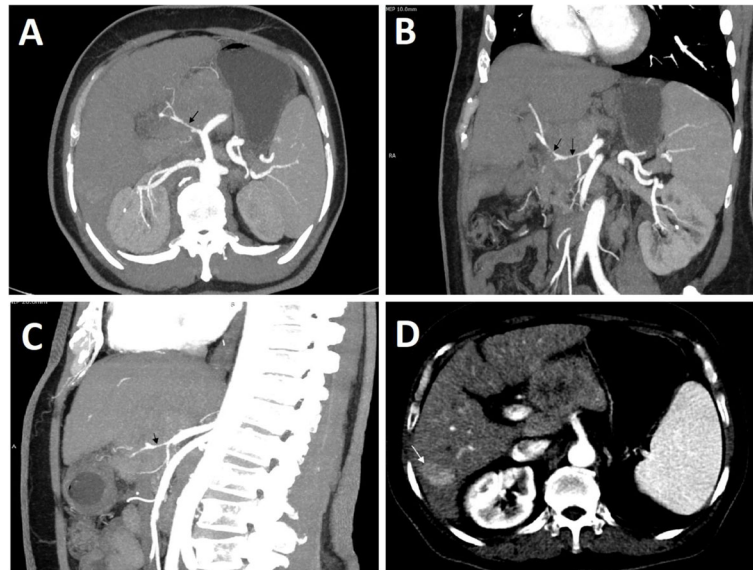


Fig. 4 (A) Axial MDCT with (B) coronal and (C) sagittal reformation (MIP arterial phase) in a 78 years old man shows a pancreatic body mass encasing the CHA (black arrows in A, B, C), with hepatic metastasis (white arrow in D) which are CT signs of definite unresectability (true negative case)

of cases (18 cases). This is in agreement with Zakharova et al. [14] who stated that most of pancreatic lesions are unresectable due to vascular involvement in the form of obliteration of the fat planes between the mass and the vessels, partial or total encasement. Our results are also in agreement with Freelove and Walling [13] who explained that the majority of tumors are not surgically resectable because of metastasis and invasion of the major vessels posterior to the pancreas. Khattab et al. [3] stated that tumors are considered unresectable when metastatic disease or local vascular invasion is present. They added that the vessels most often involved are the celiac trunk, the hepatic artery, the superior mesenteric artery, as well as, the superior mesenteric vein and the portal vein. Zakharova et al. [14] mentioned that in the absence of metastatic disease, which would exclude resection, determination of vascular invasion is an important parameter for estimating pancreatic cancer resectability.

In our study, 18 cases showed more than one cause of unresectability. The total sites of involvement were 48; among these sites, the vascular invasion represented 50%, lymph node metastases 12.5%, and distant

metastases 37.5%. Zakharova et al. [14] found that most of pancreatic lesions are unresectable due to vascular involvement. Patent portal vein (PV), superior mesenteric vein (SMV), and a fat plane between the tumor and the superior mesenteric and celiac arteries without distant metastasis are potentially resectable (Fig. 3). They stated that these patients must be scheduled for immediate surgical resection (Table 7).

Distant metastases in our study as cause of unresectability was seen in (75%) 18 cases; the liver was the first organ to be affected, 15 cases (83%) in total agreement with Tamm et al. [15] who found that pancreatic cancer typically metastasized to the liver, peritoneum, and lungs, with metastases to osseous structures being less common. Low et al. [12] stated that distant metastasis as a cause of unresectability can be seen in 75% of patients (Fig. 4), with metastases to the liver and peritoneum representing 85% of these patients (Table 8).

In our study, MDCT was helpful in detection and localization of pancreatic mass lesions and degree of vascular invasion and lymphatic and distant metastasis, with positive predictive value of 87.5% and accuracy 89.47% as Pietryga and Morgan [16] stated that the reported sensitivity of MDCT for the detection of pancreatic adenocarcinoma is as high as 89–97% (Table 9).

Table 7 Cause of unresectability

Location	Art.	Vein	Lymph	Met.
Head and neck	36	7	9	4
Body and tail	3	2	2	2
Mixed	3	2	2	0
Total	42	11	13	6

Table 8 Site distribution of metastatic lesions in the 42 studied cases

	Liver	Lung	Peritoneum	Non-regional LN
No.	15	2	2	6

Table 9 Accuracy and positive and negative predictive values of resectability of MDCT in correlation with surgical outcomes

Positive predictive values	87.5%
Negative predictive values	100%
Sensitivity	100%
Specificity	60%
Accuracy	89.47%

Conclusion

In our study, we found that multidetector computed tomography (MDCT) is an accurate technique for diagnosing and staging pancreatic cancer, as it provides information on the location, size, and severity of the tumor while also being non-invasive. MDCT even has the ability to improve the selection of people who can benefit from surgical removal of the tumor so that major preoperative morbidity and mortality from unnecessary surgery can be prevented.

The small number of cases that underwent surgery in this study was one of our limitations. Cases with distant metastasis with no definite local vascular involvement and/or local lymph node involvement were another problem we faced as we could not confirm the diagnosis of vascular and lymph node involvement without surgery; also, the small sample size of borderline cases (5 cases, one of them refused surgery) was a limitation of this study. We hope that we can give more concern to those borderline cases in new studies and help to increase the chance for their surgical resectability.

Abbreviations

MDCT: Multidetector computed tomography; NCCN: National Comprehensive Cancer Network; GLOBOCAN: Global Burden of Cancer Study; MPR: Multiplanar reconstruction; cMPR: Curved multiplanar reconstruction; MIP: Maximum intensity projection; MinIP: Minimum intensity projections; PV: Portal vein; SMV: Superior mesenteric vein

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s43055-021-00496-z>.

Additional file 1.

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Authors' contributions

HA made substantial contributions to the conception and design of the work, and analysis and interpretation of data. MS drafted the work and revised it. RM designed the work, analysis, and interpretation of data, and drafted the work and revised it. All authors have equal sharing as regard writing of the manuscript, the collection and analysis of data, and revising the final manuscript; all authors have read and approved the submitted version. All authors have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author

was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Availability of data and materials

All data and material are available.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the research ethics committee, faculty of medicine, Menofia University. All study procedures were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments. No available ethics committee's reference number.

A written consent was taken from all patients prior to the study to be included in our study.

Consent for publication

A written consent was taken from all patients prior to the study for publication.

Competing interests

The authors declare that they have no competing interests.

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