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Efficacy of Endoscopic Ultrasound in Preoperative Assessment of Pancreatic Head Tumors from A Surgical Perspective: A Prospective Study

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ABSTRACT

Background: Cancer of the pancreatic ducts, often known as pancreatic ductal carcinoma, is the most common type of pancreatic cancer.

Objectives: This study aimed to assess the accuracy, specificity, and sensitivity of endoscopic ultrasound in diagnosis of pancreatic head tumors and detection of lymph node metastasis, tumor size, vascular invasion and local infiltration of surrounding organs based on surgical assessment.

Patients and methods: This prospective study of forty consecutive patient who presented to the Gastrointestinal Surgical Center during the period from 2020 to 2023.

Results: There was statistical significance difference between the Endoscopic Ultrasound (EUS) results and CT vascular results only in the studied patients. There was high statistically significant difference between the EUS results and operational LNs results in the studied patients. There was high statistical significance difference between the EUS results and operational vascular results in the studied patients.

Conclusion: The use of EUS to confirm a pancreatic cancer diagnosis is highly encouraging. Lymph node metastases as well as vascular invasion can be effectively detected using this method. Removing the tumor entirely also improves the chances of a successful recovery after operation.

Keywords: Endoscopic ultrasound, Preoperative assessment, Pancreatic head tumors.

INTRODUCTION

Cancer of the pancreatic ducts, often known as pancreatic ductal carcinoma, is the most common type of pancreatic cancer. It ranks as the eighth most common cancer killer globally. The only treatment option available at the moment is surgical removal of the affected pancreatic cancer cells. However, only 20% of cases are amenable to this approach when diagnosed [(1,2)]. Forecasts indicate that the number of pancreatic cancer cases in Egypt would rise from 2,226 in 2013 to 2,836 in 2020 as well as 6,883 in 2050 [(3)].

Although cystadenocarcinoma & acinar cell carcinoma are also present, duct cell adenocarcinomas account for about 90% of pancreatic adenocarcinomas. While one-third originates in the pancreatic tail & body, two-thirds occur in the pancreatic head. A comprehensive genetic profile of pancreatic cancer has been compiled from a number of studies that have assessed the heritability of the disease's subtypes. Potentially increasing survival rates for pancreatic cancer patients, these genetic features may one day inform the development of targeted treatments [(4)].

Pain is a commonly reported symptom, especially in cases of tiny pancreatic tumors (under 2 cm). Pancreatic cancer pain typically develops slowly and has been going on for at least a month or two before the patient presents with symptoms. Epigastric, spreading to the sides and/or straight through to the back, it typically has a gnawing visceral aspect [(5)].

Although pancreatic enlargement is occasionally observed, the most common CT result of pancreatic cancer is a mass inside the pancreas [(2)]. The sensitivity of computed tomography (CT) in detecting pancreatic cancer ranges from 89 to 97% when using a helical multidetector row computed tomography scan that is augmented with contrast in multiple phases [(6)].

Based on surgical evaluation, the present research targeted to determine if endoscopic ultrasonography was more specific, accurate & sensitive than surgical examination in diagnosing pancreatic head cancers as well as detecting tumor size, vascular invasion, lymph node metastasis, & local infiltration of adjacent organs.

PATIENTS AND METHODS

This was a prospective study of forty consecutive patient who presented to the Gastrointestinal Surgical Center during the period from 2020 to 2023.

Inclusion criteria: Patients with pancreatic head cancer eligible for palliative or radical surgical intervention.

Exclusion criteria: Patients with tumors arise from the distal common bile duct, proximal-mid-duodenum & the ampulla of Vater. Patients who were unfit for surgery and refusing surgery or their ASA score IV.

$$\text{Unlimited population: } n = \frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2}$$

$$\text{Finite population: } n' = \frac{n}{1+\frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2 N}}$$

Sample size: Andrew Fisher's Formula, a sample

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calculation formula, was employed to determine the sample size. Find the population size (if available), confidence level, confidence interval, standard deviation (0.5 is a safe bet when the exact value is unavailable) and finally transform the confidence level into a Z-Score. The equation for calculating sample size:

Where:
ε is the margin of error. z is the z score. $\hat{p}$ is the population proportion. N is the population size.

Methods

Perioperative assessment:

Patients were evaluated by clinical data through history taking from patient & duration of symptoms. Ultrasound of the abdomen as well as a three-phase computed tomography scan of the abdomen and pelvis were the imaging pillars upon which pancreatic head cancers were initially diagnosed and staged prior to surgery. Other medical facilities sent their patients to us for magnetic resonance cholangiopancreatography (MRCP). EUS was performed to examine the pancreas, CBD, duodenal papilla and ampulla of Vater. EUS examination was divided into two processes: direct observation to look for any obvious lesions around the ampulla by upper endoscopy and indirect observation to confirm the diagnoses by US. Preoperative diagnosis, determination of tumor size and nature and detection of enlarged lymph nodes or local infiltration were recorded, biopsies were taken from suspicious lesions.

Anesthetic evaluation: Patients with ASA Score I and II were included in the study.

Neoadjuvant therapy:

Few patients were referred to oncology medicine for neoadjuvant chemotherapy if the mass was of a large size (size > 3 cm) or if there was vascular encasement.

Surgical procedures:

Patients were treated by pancreaticoduodenectomy (i.e., Whipple procedure), which is a very complex surgical procedure and it consist of 2 phases: 1st phase (resection phase), which involved removal of the duodenum, pancreatic head, common bile duct, 1st 15 cm of the jejunum & gallbladder, and a partial gastrectomy in case of resectable tumors. Second phase (reconstruction phase), which involved pancreatic reconstruction either pancreatico-gastrostomy or jejunostomy depending on size of pancreatic duct, texture of pancreas also depend on the surgeon, biliary reconstruction (hepaticojejunostomy) between end CHD and side jejunum and gastrojejunostomy between side of stomach and side of jejunum.

Adjuvant therapy: Patients were referred to adjuvant treatment within 6 weeks following operation after the result of pathology.

Ethical considerations: The trial was approved by the Institutional Review Board of Mansoura gastroenterology surgical center and IRB code was MS.20.12.1323. All patients in this study were informed about complications, morbidity and mortality of the procedure and we had informed consents before procedure. They were also informed about their participation in this prospective study on their free will.

RESULTS

The majority of patients were males (65%) with mean age of 54.9 ± 14.16 years. 97.5 of them had chest diseases & cardiac diseases, 70% DM, 87.51% HTN and 57.5% Surgical history (Table 1).

Table (1): Distribution of the studied group in relation to demographic data and co-morbidities

Demographic data				
Gender	**Number n=40**		**Percent**	
Male	26		65	
Female	14		35	
Age (years)				
Mean ± S.D.	54.9 ± 14.16			
Co-morbidities	Yes		No	
	N	**%**	**N**	**%**
DM	12	30	28	70
HTN	5	12.5	35	87.51
Cardiac disease	1	2.5	39	97.5
Chest disease	1	2.5	39	97.5
Surgical history	17	42.5	23	57.5

All patients were evaluated by Triphasic CT abdomen & pelvis with pancreatic evaluation protocol. CT revealed that liver was healthy in (n = 40, 100%), the mean value for mass size was 3.17 ± 1.24, no loco regional lymphadenopathy in (n=24, 60%), while there was loco regional lymphadenopathy in (n=16, 40%). Regarding vascular relations, free SMV and PV (n=24, 60%), abutting SMV and PV (n=14, 35%), encasing SMV and PV (n=2, 5%) and free SMA in (n=40, 100%). The mean CBD was 12.95 ± 5.3, The mean PD was 4.86 ± 2.21 (Table 2).

Table (2): Summarize the finding in EUS

EUS results	N	%
Uncinate process		
Free	37	92.5
Infiltrated	3	7.5
Vascular		
Free	24	60
Abutting SMV and PV	14	35
Encasing SMV and PV	2	5
Abutting SMA	0	100
Encasing SMA	0	100
Regional LNs		
No	24	60
Enlarged	16	40
Biopsy		
No	19	47.5
Benign	5	12.5
Adenocarcinoma	16	40
Liver metastasis		
No	40	100
Yes	0	0
Mass size		
Mean ± S.D.	3.17±1.24	
CBD		
Mean ± S.D.	12.95±5.3	
PD		
Mean ± S.D.	4.86±2.21	

Superior mesenteric vein (SMV), portal vein (PV), superior mesenteric artery (SMA) lymph nodes (LNs), common bile duct (CBD), PD: pancreatic duct.

Regarding operation type, 73.2% underwent Whipple procedure and 24.4% underwent palliative bypass (Table 3).

Table (3): Distribution of patients according to operation type.

Operation type		
Whipple	30	73.2
Palliative bypass	10	24.4

There was statistical significance difference between the EUS results and CT vascular results only in the studied patients (Fissure's Exact test=11.436 and P=0.008) (Table 4).

Table (4): Relation between the EUS results and CT results

EUS results	CT results			Test of significance	P value
Liver metastasis	**Yes**	**No**		**Not computed**	
Yes	**0(0%)**	**0(0%)**			
No	**0(0%)**	**40(100%)**			
Sensitivity	**0%**				
specificity	**100%**				
PPV	**0%**				
NPV	**100%**				
LNs	**No**	**Enlarged**			
No	**16(66.67%)**	**8(33.33%)**		**Chi-Square test 0.073**	**1.000**
Enlarged	**10(62.5%)**	**6(37.5%)**			
Sensitivity	**61.54%**				
specificity	**42.86%**				
PPV	**66.67%**				
NPV	**37.5%**				
Vascular	**Free**	**Abutting SMV, SMA & PV**	**Encasing SMV, SMA & PV**		
Free	**18(75%)**	**6(25%)**	**0(0%)**	**Fissure's Exact test 11.436**	**0.008***
Abutting SMV, SMA & PV	**9(64.3%)**	**4(28.6%)**	**1(7.1%)**		
Encasing SMV, SMA & PV	**0(0%)**	**0(0%)**	**2(100%)**		
Sensitivity	**53.85%**				
specificity	**66.67%**				
PPV	**43.75%**				
NPV	**75%**				

	EUS results	CT results
Mass size		
Range	0.7-6.5	0.8-7.5
Mean ± S.D.	3.17±1.24	3.38±1.42
Median	3	3.25
Mode	2.5	2
Independent Student t-test= 0.743	**P value=0.460**	

P value is considered significant if ≤0.05

There was high statistically significant difference between the EUS results and operational LNs results in the studied patients by Chi-Square test=20.417 (P ≤0.001). There was high statistically significant difference between the EUS results and operational vascular results in the studied patients by Fissure's Exact test=30.628 (P ≤0.001) (Table 5).

Table (5): Relation between the EUS results and operation results.

EUS results	Operation results			Test of significance	P value
Liver metastasis	**Yes**		**No**	**Not computed**	
Yes	**0**		**0**		
No	**6(15%)**		**34(85%)**		
Sensitivity	**0%**				
specificity	**100%**				
PPV	**0%**				
NPV	**85%**				
LNs	**Not**		**Enlarged**		
Not	**19(79.2%)**		**5(20.8%)**	**Chi-Square test 20.417**	**≤0.001****
Enlarged	**1(6.3%)**		**15(93.8%)**		
Sensitivity	**95%**				
specificity	**75%**				
PPV	**79.2%**				
NPV	**93.8%**				
Vascular	**Free**	**Abutting SMV, SMA & PV**	**Encasing SMV, SMA & PV**		
Free	**21(87.5%)**	**1(4.2%)**	**2(8.3%)**	**Fissure's Exact test 30.628**	**≤0.001****
Abutting SMV, SMA & PV	**1(7.1%)**	**9(64.3%)**	**4(28.6%)**		
Encasing SMV, SMA & PV	**0(0%)**	**0(0%)**	**2(100%)**		
Sensitivity	**83.33%**				
specificity	**95.45%**				
PPV	**93.75%**				
NPV	**84%**				

	EUS results	Operation results
Mass size		
Range	0.7-6.5	1-10
Mean ± S.D.	3.17±1.24	3.86±1.96
Median	3	3
Mode	2.5	3
Independent Student t-test= 1.896	**P value=0.062**	
CBD		
Range	4-25	4-20
Mean ± S.D.	12.95±5.3	11.32±4.55
Median	13	10
Mode	15	10
Independent Student t-test= 1.477	**P value=0.144**	
PD		
Range	2-10	1-8
Mean ± S.D.	4.86±2.21	3.86±1.85
Median	4	3
Mode	4	2
Independent Student t-test= 0.880	**P value=0.381**	

DISCUSSION

A total number of 40 patients underwent endoscopic ultrasound evaluation prior to surgical resection. The majority of them (65%) were males with mean age of 54.9 ± 14.16 years. 97.5 of them had chest diseases & cardiac diseases, 70% DM, 87.51% HTN and 57.5% surgical history. While, in the study of **Janssen *et al.*** [7], more than half (56%) of them were females and their age ranged from 51-66 with median age of 62 years, whereas in the study of **Okasha *et al.*** [8], the average age of the cases that were considered was 32.78 years. Females made up the majority of the examined cases (17 out of 18 instances, or 94.44%) [8].

About a third of instances may not exhibit any symptoms at all when it comes to the presentation. Nevertheless, the initial signs & symptoms were sometimes vague. In nearly forty percent of instances, people report experiencing abdominal pain. Increased abdominal girth, vomiting, anorexia, nausea, jaundice (from bile duct constriction), as well as weight loss are among symptoms that may be present. Acute abdominal pain may be a symptom of capsule rupture in certain patients. **Yu *et al.*** [9] regarding individuals' presentation, abdominal pain was the most common (n=29, 72.5% of patients), followed by jaundice (n=23, 57.5% of patients), and accidentally detected (n =2, 5% of patients). Our results are supported by study of **Okasha *et al.*** [8] as they reported that all cases presented with abdominal pain, while only three cases reported anorexia and weight loss. On examination, a palpable abdominal mass was detected in 4 cases (22.22%). Similarly, **Dong *et al.*** [10] noticed that 63 individuals (54.8%) came with abdominal pain as their primary complaint.

All patients were evaluated by Triphasic CT abdomen & pelvis with pancreatic evaluation protocol, CT revealed liver was healthy in the 40 (100%) patients, the mean value for mass size was 3.17 ± 1.24. There was no loco regional lymphadenopathy in 24 (60%), while there was loco regional lymphadenopathy in 16 (40%). Regarding vascular relations, there was free SMV and PV (n=24, 60%), abutting SMV and PV (n=14, 35%), encasing SMV and PV (n=2, 5%) and free SMA in (n=40, 100%). The mean CBD was 12.95 ± 5.3 and the mean PD was 4.86 ± 2.21. While, in the study of **Janssen *et al.*** [7] Out of the 160 individuals who underwent CT before surgery, 88% had MRI/MRCP, 40% had CT alone, and 29% had a combination of the two. In the trial of **Okasha *et al.*** [8], the identified lesions had sizes varying from 3.5 to thirteen centimeters. Lesions were seen in eight cases (44.44% of the total) on the body and seven cases (38.89%) on the head. On the other hand, tail lesions were present in two cases (11.11%), although only one case (5.56%) had an impact on the uncinate process. The preferred method of treatment was complete surgical resection. The tumor's lack of aggressiveness as well as minimal malignant potential gave it a fantastic prognosis in the long run [11].

The present study showed that according to preoperative evaluation by EUS and CT, 38 patients were resectable and 2 patients were irresectable, these 2 patients underwent palliative bypass due to repeated plastic stent replacement more than 4 times due to high cost of metallic stent for these patients. Neoadjuvant chemotherapy was given to 2 patients due to large mass size and vascular encasing and there was a good response to chemotherapy and theses 2 patients underwent surgical resection with free safety margin. All of patient in studied group underwent exploration in our Gastroenterology Surgical Centre through Right subcostal incision. On exploration liver was healthy in 29 (72.5%), cholestatic in 3 (7.5%), cirrhotic in 2 (5%), liver metastasis in 6 (15%) more in RT liver lobe, which proved metastasis by frozen pathology intraoperative. There were no peritoneal nodules in all patients and this was a drawback of EUS. Pancreatic reconstruction was performed PG in 12 (30%), PJ in16 (40%) and there was no pancreatic reconstruction in 2 patients due to atrophic pancreas. In the study of **Janssen *et al.*** [7] in 148 individuals (82%), the decision to resect was warranted. Based on the kind of lesion, 105 patients had a justifiable resection, whereas 67% of patients with cystic lesions had one. Fifty individuals (86% accuracy) had the accurate diagnosis based on cross-sectional analysis among the 58 patients (32% of the total) who had resection with no preoperative EUS. Five individuals (9% of the total) had a resection that was not warranted, even though most of this subgroup had a valid reason for the procedure. In the study of **Dong *et al.*** [10], a majority of the lesions were seen in the pancreatic head. Hence, the Whipple technique was the gold standard, with additional procedures for example subtotal pancreatic resection as well as duodenum-preserving pancreatic head resection also being used.

The current study showed that total complications occurred in 7 (17.5%) of patients, no mortality, pancreatic leak occurred in 7 (17.5%) of patients, 5 of them were managed with conservative measures and the other 2 patients underwent surgical intervention. intestinal leak occurred in 1 (2.5%) of patients, biliary leak occurred in 2 (5 %) of patients. Post-operative bleeding was in 1 (2.5%) and it was secondary to pancreatic leak, post-operative wound infection occurred in 3 (7.5%) of patients. **Okasha *et al.*** [8] reported that all cases had a smooth postoperative course with the exception of one (5.56%) patient who died from abdominal sepsis due to anastomotic leaking after undergoing pancreatico-duodenectomy. Cases were followed up for at least 1.5 years, and subsequent imaging did not find either local or distant recurrences.

Our results showed that there was statistically significant difference between the EUS results and CT

vascular results only in the studied patients with sensitivity of 53.9% and specificity of 66.7%. In previous studies held by **Tanaka *et al*. [(12)], Vege *et al*. [(13)]** and **Jang *et al*. [(14)]** using EUS appears to be a very sensitive yet unspecific approach.

Our results showed that there was high statistically significant difference between the EUS results and operational vascular results in the studied patients with sensitivity of 83.3% and specificity of 95.5%. Examining the celiac artery, superior mesenteric artery, portal vein/superior mesenteric vein, as well as pancreatic cancer are the main arteries to look at. Pancreatic cancer resectability is dependent on invasion presence & degree. Neoadjuvant therapy improved survival compared to upfront surgery in cases where vascular invasion makes resectability dubious. Compared to CT, which has a sensitivity of fifty-eight percent & specificity of Ninety-five percent when it comes to vascular invasion, EUS has an impressive eighty-six percent as well as ninety-three percent respectively [(15)].

Our results showed there's high statistical significance difference between the EUS results and operational LNs results in the studied patients with sensitivity 95% and specificity 75%. There was also reporting on the evaluation of lymph node metastases using EUS. On ultrasound, tumors in the liver often appear as hypoechoic, spherical masses larger than 10 mm in diameter. Compared to CT, which had a sensitivity of 24% as well as a specificity of 88%. EUS had a much higher sensitivity of 58% & specificity of 85% in a systematic review. It is recommended to conduct EUS-guided tissue acquisition if the results alter the therapy selection, as EUS was superior to CT but still has low sensitivity [(16)].

CONCLUSION

The use of EUS to confirm a pancreatic cancer diagnosis was highly encouraging. Lymph node metastases as well as vascular invasion could be effectively detected using this method. Removing the tumor entirely also improved the chances of a successful recovery after surgery.

- **Consent for publication:** All authors agreed to submit the work.
- **Availability of data and material:** Available.
- **Competing interests:** None
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