Medical Sciences 2020 Vol. 8 (14), p. 29-34

e-ISSN: 2345-0592
Online issue
Indexed in *Index Copernicus*

Medical Sciences

Official website:
www.medicsciences.com

Endoscopic Ultrasound in the Diagnosis of Pancreatic Cancer

Matas Kalinauskas[1], Vaida Ruseckaitė[1], Vytautas Dūdėnas[1]

[1]*Lithuanian University of Health Sciences, Medical Academy, Faculty of Medicine*

Abstract

Introduction

Pancreatic cancer is a neoplasm with a mortality rate, which is almost equal to its occurrence. Pancreatic adenocarcinoma is the most common malignancy with an incidence of over 90% of all pancreatic cancers. It is especially lethal, as its 5 year overall survival rate is less than 5%. However, the rate of survival is gradually increasing due to the new treatment methods and the improvement of diagnostic techniques. Endoscopic ultrasound is a diagnostic method with the highest sensitivity, when detecting malignant pancreatic lesions.Aim

To review scientific literature and determine the benefits and drawbacks of endoscopic ultrasound in diagnosing and treating pancreatic cancer.

Materials and methods

Literature analysis. A research articles in English language on the "PubMed" 2010 to 2019 database. Keywords used in the search: “Endoscopic ultrasound”, “Pancreatic cancer”.

Results

Endoscopic ultrasound becomes the first choice method, when it comes to diagnosing small pancreatic tumors (<3cm), overlapping computer tomography and multi-detector-row computer tomography with EUS presenting a higher sensitivity (87%) and accuracy (92%) in detecting pancreatic tumors than MDCT. Furthermore, EUS plays a crucial role in diagnosis of small focal lesions and tumors with the help of EUS guided fine needle aspiration biopsy. Also, EUS guided FNA should be used in the preoperative examination of patients with pancreatic neoplasms. Moreover, EUS can be used as a palliative pain treatment for patients with PC with celiac plexus/ ganglion neurolysis.

Conclusions: many studies agree that EUS is a valuable tool in the diagnosis and treatment of pancreatic cancer and should be used in practice more often than not. The main drawbacks are its availability due to the price and personnel required.

Keywords: Endoscopic ultrasound, pancreatic cancer.

List of abbreviations

PC -pancreatic cancer

PDAC - pancreatic ductal adenocarcinoma

EUS - endoscopic ultrasound

FNA - fine needle aspiration

US - ultrasonography

CT - computer tomography

MRI- magnetic resonance tomography

MRCP - magnetic resonance cholangiopancreatography

MDCT - multi-detector-row computer tomography

CE-EUS - contrast – enhanced endoscopic ultrasound

CPN - celiac plexus neurolysis

CGN - celiac ganglion neurolysis

Introduction

Pancreatic cancer is a neoplasm with a mortality rate, which is almost equal to its occurrence. Pancreatic adenocarcinoma is the most common malignancy with an incidence of over 90% of all pancreatic cancers. It is especially lethal, as its 5 year overall survival rate is less than 5%. However, the rate of survival is gradually increasing due to the new treatment methods and the improvement of diagnostic techniques. [1, 2] For the previously mentioned characteristics of PC, early diagnosis is essential. Endoscopic ultrasound is a diagnostic method with the highest sensitivity, when detecting malignant pancreatic lesions. [3] EUS guided fine needle aspiration is especially useful for the differential diagnosis of PC or when a histopathological evaluation is needed. [1] What is more, EUS is also a helpful tool for preoperative staging of PC. [4] In this study we seek to evaluate the advantages of each available diagnostic tool in detection of PC. We also aim to compare EUS with traditional radiological screening methods – ultrasonography, computed tomography and magnetic resonance tomography.

Results

Ultrasonography

Ultrasonography (US) is usually performed as a first – line imaging modality on patients with PC. It is also performed on asymptomatic patients as painless, cost – effective screening method. The frequency of US has also increased and it has a significant role in the detection of PC. US is a great imaging method in terms of its low – cost and non – invasiveness. Recent studies have also shown that early diagnosed PC had mostly UG findings, such pancreatic cysts or dilated pancreatic ducts. However, US is highly dependent on the skills of the examiner and requires a lot of experience in order to diagnose accurately. The sensitivity of US is 75 – 89% and specificity 90 – 99%. [20] As mentioned before, it is dependent on the experience of the examiner, the patient´s body mass, gas in the bowels and the topography of the pancreas. In order to obtain better visualization of the pancreas, US should be performed on multiple planes – longitudinal, transverse and oblique. It is also suggested that the patient should only eat a light meal on the evening before the procedure and refrain himself from eating on the morning of the procedure. This reduces the amount of gas in the bowels. It is also important to use multiple methods to improve the visualization of the pancreas during US. For example, ask the patient to hold his breath during inspiration or expiration, change the position into Fowler´s, where the hands of the patient are placed behind his back and apply more pressure on the abdominal wall with the transducer. In some cases, the liquid – filled stomach method can also be used. When using this method, the patient is required to drink up to 300 ml of still water. This helps to create a gastric sonic window by pushing the gas to the fundus of the stomach. This method should not be used on patients, who have undergone gastric surgery, as the fluid does not remain in the correct anatomical location. When detecting a small pancreatic cyst or a lesion, a high – frequency transducer can be used. In this case, it is important to change the patient´s position and to suspend breathing during inspiration or expiration. [9]

Computer Tomography

Abdominal computer tomography is one of the methods used for initial screening once clinical signs of pancreatic cancer manifest. The goal of screening is to determine the presence of a malignancy in the pancreas and evaluate if it is resectable. Typically an ill-defined, hypoattenuated mass in the pancreas is seen. Smaller lesions tend to be isoattenuating, which makes diagnosis difficult. Secondary signs are pancreatic duct cut off or dilatation, dilatation of common bile duct, contour abnormalities and parenchymal atrophy. If both the pancreatic and the common bile duct are dilated, it is called a double duct sign, which is present in 62% to 77% cases of pancreatic cancer, but is not a diagnostic sign, as benign adenomas and autoimmune pancreatitis may display it as well [16]. If the tumor is sizeable enough, an enlargement of the whole pancreas can be observed. Sensitivity of computed tomography depends on the chosen technique and size of tumor (lesions that are <2cm in diameter have a low sensitivity). The highest sensitivity technique is triple-phase contrast-enhanced thin-slice helical computed tomography, known as MDCT [17]. This technique allows the imaging of larger volumes of tissue and acquiring venous and arterial phases in a shorter time period. This allows evaluating vascular involvement in the tumor, which is an important factor when determining operability [5].

A so-called pancreas protocol is used when pancreatic cancer is suspected, which consists of scanning a patient in 3 dynamic phases of contrast injection. 1) The first 30 seconds after injection, called the arterial phase. Peripancreatic arteries and superior mesenteric artery are evaluated during this phase. 2) A period between peak enhancement of the aorta and peak enhancement of the liver is called the pancreatic phase. During this phase, the difference between healthy pancreas tissue and tumor tissue is most conspicuous. 3) 60-70 seconds after injection, the portal venous phase occurs. During this time splenic, portal and superior mesenteric veins can be evaluated. Due to peak liver enhancement, it is also an optimal time to evaluate the liver for metastases. [15]

Screening Methods of Pancreatic Cancer

For people with high risk of pancreatic cancer (this includes mutation carriers of PDAC-prone gene mutations, for example: CDKN2A, BRCA1, BRCA 2, STK11/LKB1 and relatives of patients with familial pancreatic ductal adenocarcinoma (PDAC)) there are no clear screening guidelines yet, or when surgical treatment may come in to play.[9] MRI and MRCP both are able to detect small pancreatic and pancreatic duct abnormalities, mostly of cystic origin and they also have a better visualization of the soft tissue of pancreas than CT.[8] When it comes to the question whether we should use EUS or MRI for early diagnosis of PC, there aren't a lot of studies made that compare these methods directly. Several studies have been done comparing the sensitivity using CT, MRI and EUS for pancreatic lesions in patients with high risk of PC. All the individuals chosen for this study underwent CT, MRI and EUS screening and of 216 patients 96 were identified with a minimum of one pancreatic mass/lesion (84 were found cystic and 3 solid) by at least one imaging method. CT detected 11%, MRI 33,3% and EUS 42,6% of pancreatic lesion for these patients.[9,14] For detecting malignancies in the pancreas smaller than 30mm in diameter the results of sensitivities of all three methods were given: CT - 53%, MRI - 67%, EUS - 93%. However, for local liver metastasis EUS imaging was found not accurate enough mostly because of the limited anatomical view of the liver and both CT and MRI were found better in this case.[19] Another recent study was done comparing EUS and MRI for high-risk individual screening of pancreatic lesions. It concluded that both modalities are important in detecting early pancreatic abnormalities. MRI has 89% sensitivity in visualizing cystic lesions of any size compared to EUS 38%. However, EUS had a 100% sensitivity for imaging solid lesions, whereas MRI 0% was found redundant. The concluding results of the study stated that both methods EUS and MRI were integral in screening of high-risk individuals, rather than one being superior to another.[18]

Both MRI and EUS are superior to CT in early screening of high-risk individuals, but when to choose one over the other is still unclear. MRI may be a non-invasive method, that can accurately detect other extrapancreatic masses and has a high sensitivity for visualizing cystic lesions, but for some patients it may be difficult to do this test due to claustrophobia. Also, if a lesion is spotted on MRI imaging it could require further investigation and even a biopsy with EUS-FNA for confirmation of a malignant process. On the other hand, with EUS the biopsy can be done with a single procedure. Furthermore, EUS has a superior ability to detect small <30mm tumors and solid masses in the pancreas. However, EUS can be discomforting for patients because it is an invasive procedure. It requires anesthesia so there is a higher risk of anesthesia related complications. Also, the sensitivity of the method relies a lot on the experience of the operator. Having taken this into account, as mentioned before no clear guidelines are available for physicians, therefore, studies suggest that both EUS and MRI together must be considered for screening for high risk individuals.[14]

Capabilities of Endoscopic Ultrasound

EUS examination is done under general anesthesia. Most times the patient is lied down on his left side in the decubitus position. The ultrasound probe can be placed either by the patient's head or feet. [1]

EUS is considered as a far better method than a conventional CT, when diagnosing PC. Although CT can be used to visualize a large mass or lesion around the pancreas, EUS has a higher sensitivity and specificity when indentifying small tumors that cannot be seen by other imaging modalities and is more sensitive for early cancer detection [3, 5]. Studies have been made comparing multi-detector-row CT (MDCT)and EUS for PC diagnosis. Research concluded that EUS presented a higher sensitivity (87%) and accuracy (92%) in detecting pancreatic tumors than MDCT. Furthermore, the accuracy of diagnosing PC can be increased by using contrast – enhanced harmonic EUS. The basic principle of this method is that CE-EUS helps visualize the vascularity and blood flow of the lesion which is located in the pancreatic parenchyma. Intravenous injection of contrast material during a conventional EUS session can help differentiate inflammatory process from a malignant tumor. It is extremely helpful in visualizing pancreatic adenocarcinomas which usually remain hypoechogenic, while other neoplasms or inflammatory lesions are isoechogenic or hyperechogenic. Studies confirmed, that using contrast material during EUS when detecting pancreatic adenocarcinomas the sensitivity was 94% and specificity was 89%. However, CE-EUS is limited by its high contrasting agent cost and shortage of professionals, who expertise in this area. [1, 3, 6, 7]

Furthermore, the role of EUS is crucial, when a patient is confirmed with atypical parenchymal changes in the pancreas. For example: enlargement of the pancreatic gland, dilatation of pancreatic ducts with no obstruction to be seen. For these cases, if needed, a biopsy by FNA can be taken. EUS - guided FNA is extremely accurate for diagnosing focal lesions and small tumors, which are less than 3 cm. Some of the indications for EUS – guided FNA are: planning palliative, adjuvant or neoadjuvant chemotherapy for unresectable pancreatic lesions; to confirm the diagnosis of pancreatic adenocarcinomas or other tumor before a radical treatment; differential diagnosis from inflammatory pseudotumor or a fibrous nodule. [1,3,5] Also, EUS-FNA has a sensitivity of 96,7% and specificity of 100% for diagnosing para-aortic lymph node metastasis, which is considered as one of the contraindications for surgical treatment, concluding that EUS-guided FNA should be included in the preoperative examination of patients with pancreatic neoplasms. [8] The accuracy of EUS – guided FNA for pancreatic lesions varies between 87%-95.8%. [5] EUS is also superior compared to CT for tumor staging. Studies show, that T staging sensitivity and specificity is between 72%-90% and 87% for vascular invasion, whereas CT staging is 30% and 55% respectively. The staging for N by EUS shows accuracy of 50%-86%. [4, 8, 9]

Moreover, EUS can be used as a palliative pain treatment for patients with PC. An acceptable method is EUS – guided celiac plexus neurolysis/block using alcohol or phenol. The substance is injected into or around the celiac plexus or ganglion. EUS provides a better pathway and allows to avoid vessels, which you could damage using a percutaneous approach. Most PC patients require morphine or other narcotic analgesia, which may cause dependency and other systemic malfunctions overtime. Studies show, that patients with CPN procedures tend to consume less narcotic analgesia than people without the procedure. Furthermore, celiac ganglion neurolysis showed better pain management results than celiac plexus neurolysis: CGN 73.5% *vs* CPN 45.5%. [10, 11]. Also, for patients with unresectable PC radiotherapy, more particularly brachytherapy, guided with EUS can be used. A study has been made using Iodine-125 radioactive seed, which was placed inside the malignant lesion for local cell destruction. The results of the trial showed that from a total of 15 patients 27% responded partially to treatment, 20% had only minimal response, and in 33% of patients the treatment didn't work at all. Although, 30% of patients expressed a mild diminishment in symptoms, more particularly pain, but the effect was not long lasting. There were, however, three patients who experienced adverse (pancreatitis, pseudocyst formations) local effects and three patients who experienced systematic adverse effects (hematologic toxicity). The results concluded that a study of EUS guided brachytherapy alongside systemic chemotherapy in patients with unresectable PC could give better results than radiotherapy alone. These studies were made, but a significant improvement on survival rates was not achieved, only moderate correction of pain was prominent. [10]

Discussion

The use of EUS in the diagnosis and treatment of pancreatic cancer has been growing more wide-spread in the recent years. Many studies agree that its use is important in both the initial diagnosis and preoperative staging, mainly in the evaluation of vascular invasion of the portal vein and vessels of the spleen, as well as in the treatment of pain via CPN [11, 12]. This is especially true for the diagnosis of small (<5mm) solid tumors, unresectable pancreatic lesions and metastases, which are not available to transcutaneous biopsy. EUS is also valuable in the differential diagnosis between fibrous and inflammatory nodules, when the histology result of the lesion is doubtful. EUS and MRI are the most valuable imaging modalities in the diagnosis of PC. What is more, EUS has a major advantage, compared to MRI - it is valuable in aiding FNA procedures, which allow doctors to evaluate both the local tumor (T) and lymph nodes (N). The advantages of EUS over CT are lack of ionizing radiation and higher sensitivity and specificity. It does, however, have drawbacks, as it is an invasive procedure that often requires anesthesia, highly trained physicians with specialized knowledge. The advancement of cross – sectional imaging techniques, such as helical CT, has greatly reduced the use of EUS in the staging and diagnostics of PC. [13] Due to these reasons and the fact that PC has a low incidence in the general population (<1%), it is not advised to use EUS as a screening method. The exception would be patients with confirmed familial pancreatic cancer. [14]

Conclusion

US is the optimal tool for initial screening of PC due to its safety and availability. It is however too highly dependent on the operators skill. CT is highly sensitive if proper screening modalities are used. This makes it a good tool for following up of known patients, but ineffective for initial screening. MRI is the most sensitive of traditional radiological methods. It is however incapable of detecting solid lesions in the pancreas. Using EUS in combination with MRI is the best available option for detecting pancreatic cancer. Many studies agree that EUS is a valuable tool in the diagnosis and treatment of pancreatic cancer. The main drawbacks are its availability due to the price and personnel required. However, due to its higher

sensitivity and specificity than CT, it should be used whenever available in the initial diagnosis and staging of PC.

References

1. Wangermez, M. (2016). Endoscopic ultrasound of pancreatic tumors. *Diagnostic and Interventional Imaging*. https://doi.org/10.1007/s00464-015-4510-5
2. Okano, K., & Suzuki, Y. (2014). Strategies for early detection of resectable pancreatic cancer. *World Journal of Gastroenterology*. https://doi.org/10.3748/wjg.v20.i32.11230
3. Luz, L. P., Al-Haddad, M. A., Sey, M. S. L., & Dewitt, J. M. (2014). Applications of endoscopic ultrasound in pancreatic cancer. *World Journal of Gastroenterology*. https://doi.org/10.3748/wjg.v20.i24.7808
4. Bhutani, M. S., Koduru, P., Joshi, V., Saxena, P., Suzuki, R., Irisawa, A., & Yamao, K. (2016). The role of endoscopic ultrasound in pancreatic cancer screening. *Endoscopic Ultrasound*. https://doi.org/10.4103/2303-9027.175876
5. Lee, E. S., & Lee, J. M. (2014). Imaging diagnosis of pancreatic cancer: A state-of-the-art review. *World Journal of Gastroenterology*. https://doi.org/10.3748/wjg.v20.i24.7864
6. Sugimoto, M., Takagi, T., Suzuki, R., Konno, N., Asama, H., Watanabe, K., … Ohira, H. (2017). Contrast-enhanced harmonic endoscopic ultrasonography in gallbladder cancer and pancreatic cancer. *Fukushima Journal of Medical Science*. https://doi.org/10.5387/fms.2017-04
7. Cho, M. K., Moon, S. H., Song, T. J., Kim, R. E., Oh, D. W., Park, D. H., … Kim, M. H. (2018). Contrast-enhanced endoscopic ultrasound for differentially diagnosing autoimmune pancreatitis and pancreatic cancer. *Gut and Liver*. https://doi.org/10.5009/gnl17391
8. Suzuki, R., Takagi, T., Sugimoto, M., Konno, N., Sato, Y., Irie, H., … Ohira, H. (2018). Endoscopic ultrasound-guided fine needle aspiration for pancreatic cancer. *Fukushima Journal of Medical Science*. https://doi.org/10.5387/fms.2018-14
9. Zhang, L., Sanagapalli, S., & Stoita, A. (2018). Challenges in diagnosis of pancreatic cancer. *World Journal of Gastroenterology*. https://doi.org/10.3748/wjg.v24.i19.2047
10. Oh, S. Y., Irani, S., & Kozarek, R. A. (2016). What are the current and potential future roles for endoscopic ultrasound in the treatment of pancreatic cancer? *World Journal of Gastrointestinal Endoscopy*. https://doi.org/10.4253/wjge.v8.i7.319
11. Teshima, C. W., & Sandha, G. S. (2014). Endoscopic ultrasound in the diagnosis and treatment of pancreatic disease. *World Journal of Gastroenterology*. https://doi.org/10.3748/wjg.v20.i29.9976
12. Urayama, S. (2015). Pancreatic cancer early detection: Expanding higher-risk group with clinical and metabolomics parameters. *World Journal of Gastroenterology*. https://doi.org/10.3748/wjg.v21.i6.1707
13. Welinsky, S., & Lucas, A. L. (2017). Familial pancreatic cancer and the future of directed screening. *Gut and Liver*. https://doi.org/10.5009/gnl16414
14. McGuigan, A., Kelly, P., Turkington, R. C., Jones, C., Coleman, H. G., & McCain, R. S. (2018). Pancreatic cancer: A review of clinical diagnosis, epidemiology, treatment and outcomes. *World Journal of Gastroenterology*. https://doi.org/10.3748/wjg.v24.i43.4846
15. Wong, J. C., & Raman, S. (2010). Surgical resectability of pancreatic adenocarcinoma: CTA. *Abdominal Imaging*. https://doi.org/10.1007/s00261-009-9539-2
16. Sahani, D. V., Bonaffini, P. A., Catalano, O. A., Guimaraes, A. R., & Blake, M. A. (2012). State-of-the-art PET/CT of the pancreas: Current role and emerging indications. *Radiographics*. https://doi.org/10.1148/rg.324115143
17. Dibble, E. H., Karantanis, D., Mercier, G., Peller, P. J., Kachnic, L. A., & Subramaniam, R. M. (2012). PET/CT of cancer patients: Part 1, pancreatic neoplasms. *American Journal of Roentgenology*. https://doi.org/10.2214/AJR.11.8182
18. Nakai, Y., Takahara, N., Mizuno, S., Kogure, H., & Koike, K. (2019). Current status of endoscopic ultrasound techniques for pancreatic neoplasms. *Clinical Endoscopy*. https://doi.org/10.5946/ce.2019.025
19. Kitano, M., Yoshida, T., Itonaga, M., Tamura, T., Hatamaru, K., & Yamashita, Y. (2019). Impact of endoscopic ultrasonography on diagnosis of pancreatic cancer. *In Journal of Gastroenterology*. https://doi.org/10.1007/s00535-018-1519-2
20. Ashida, R., Tanaka, S., Yamanaka, H., Okagaki, S., Nakao, K., Fukuda, J., … Katayama, K. (2019). The role of transabdominal ultrasound in the diagnosis of early stage pancreatic cancer: Review and single-center experience. *Diagnostics*. https://doi.org/10.3390/diagnostics9010002