Original Paper

Which is the Best Imaging Method in Pancreatic Adenocarcinoma Diagnosis and Staging - CT, MRI or EUS?

M.I. Costache[1,2], Cornelia Alexandra Costache[3], Cristiana Iulia Dumitrescu[4], A.A. Tica[4], M. Popescu[2,5], Elena Angela Baluta[5], Alina Carmen Anghel[5], A. Saftoiu[1,6], Daniela Dumitrescu[2,5]

[1]Department of Gastroenterology, Research Center of Gastroenterology and Hepatology, University of Medicine and Pharmacy Craiova, Romania

[2]Department of Radiology and Medical Imaging, University of Medicine and Pharmacy Craiova, Romania

[3]Department of Neurology, University of Medicine and Pharmacy Craiova, Romania

[4]Department of Pharmacology, University of Medicine and Pharmacy of Craiova, Romania

[5]Department of Radiology and Medical Imaging, Clinical Emergency County Hospital, Craiova, Romania

[6]Department of Endoscopy, Gastro-Unit, Copenhagen University Hospital Herlev, Denmark

ABSTRACT: Introduction. Imaging has a decisive role in the diagnosis and staging of pancreatic cancer, the most used imaging methods being computed tomography, magnetic resonance imaging and endoscopic ultrasonography. Material and method. They were studied retrospectively over a 3 years period, 140 patients with pancreatic cancer. Aim of the study: This study aims to determine the effectiveness of CT, MRI and EUS in diagnosis and staging of panceatic cancer. Results. CT showed a diagnostic accuracy of 83.3%, with sensitivity and specificity of 81.4% and 43% respectively. MRI showed superior diagnostic accuracy compared to CT (89,1%). However, EUS demonstrated the best diagnostic value in PC (accuracy of 92,7%). Concerning the locoregional staging, the 3 diagnostic methods showed similar result. There were no significant differences concerning the diagnosis of intra-abdominal metastases. Differences have appeared in the case of extra-abdominal. Thus, there were 4 cases of lung metastases which have been identified only on CT and MRI. Conclusion. EUS is the most effective technique used in the diagnosis of pancreatic cancer, the present study demonstrating an accuracy of 92.7%. Moreover, EUS offers the possibility to collect samples for cytological examination by EUS guided fine needle aspiration. However, there are some limitations of EUS in identifying extra-abdominal metastases. Thus, the assessment of tumor extension must be completing by performing CT or MRI.

KEYWORDS: pancreatic cancer, endoscopic ultrasound, EUS-FNA

Introduction

Pancreatic cancer is still one of the deadliest types of cancer, being the fourth leading cause of cancer death in the United States, after lung, breast or prostate, and colorectal cancer [1], approximately 200.000 of people dying each year of pancreatic adenocarcinoma [2].

Thus, the need for early diagnosis is extremely important. Imaging has proven to have a central and pivotal role in the staging and evaluation of pancreatic cancer, being involved in all the stages of clinical management of pancreatic diseases (detection and characterization of the pancreatic tumor mass, determination of local and vascular involvement, perineural and lymphatic invasion, invasion front assessment, detection of metastases and overall risk assessment of the disease for complete surgical removal) [3].

The most important types of imaging for the detection of pancreatic cancer are abdominal ultrasound, endoscopic ultrasound, endoscopic retrograde cholangiopancreatography, computed tomography, magnetic resonance, and positron emission tomography.

In clinical practice, the most used methods for the detection and characterization of pancreatic masses are CT, MRI and EUS.

Material and method

140 patients (with clinical suspicion of pancreatic neoplasm) were studied restrospectively, in the Research Center of Gastroenterology and Hepatology, University of Medicine and Pharmacy Craiova, Romania, between January 2014 and December 2016. The patients were structured into two groups of study: 100 patients with pancreatic cancer (the main group of study) and 40 patients with other

pancreatic masses - chornic pancreatitis and neuroendocrine tumors (the control group).

We assessed by CT, MRI and EUS the patients with clinical suspicion of pancreatic neoplasms. For Eus examination we used the conventional and Doppler mode, the contrast enhanced EUS, the qualitative strain elastography and the EUS guided FNA). All results were stored into a structured database.

The final diagnosis:

-for resected tumors, we performed the morfo pathological examination;

-for non-resectable tumors (the majority of the cases), the final diagnosis was made mainly based on cytological examination of the samples obtained through EUS guided FNA and analysing the imaging features of the tumor;

Using Microsoft Excel (Microsoft Corp., Redmond, WA, USA), we calculated the accuracy, the sensitivity, the specificity, the negative predictive value and the positive predictive value for each diagnostic technique.

Results

Patients with pancreatic cancer are mainly men (61%-61/100), from urban areas (67%-67/100) and had a mean age of 64 years at the time of diagnosis.

Concerning the dimension and the location of the tumor, our study showed that pancreatic malignant tumors have an average size of 30 mm in diameter and they are located in 61% (61/100) of the cases at the head of the pancreas, in 19% (19/100) of the cases at the body of the gland, in 10% (10/100) at the tail of the pancreas and in 10% (10/100) the tumor is located in two regions of the pancreas (for example, the tumor may involve the head and the body or the body and the tail of the gland. (Fig. 1)

Computed tomography examination demonstrated an accuracy of 83.3%, with sensitivity and specificity of 81.4% and 43% respectively in the diagnosis of pancreatic adenocarcinoma, for the entire group of patients with pancreatic cancer (Table 1).

Magnetic resonance imaging showed diagnostic accuracy, sensitivity and specificity in pancreatic cancer of 89,1%, 89,5% and 63,4% respectively (Table 1).

It was observed that conventional endoscopic ultrasound examination had an accuracy of 82% for the diagnosis of pancreatic cancer, with sensitivity and specificity of 96.2% and 64% respectively.

Doppler mode EUS did not improve the diagnostic yield of EUS in pancreatic

adenoracinoma. However, using a combination of contrast-enhancement and elastography, the diagnostic accuracy reaches 93,7%, with a specificity of 90,3% and sensitivity of 97,5%, (Table 1). (Fig. 2)

To check if there are different results for the small tumors (less than 20mm in diameter), divided the group of patients with pancreatic cancer into two groups: those with tumors less than 20mm and those with tumors exceeding 20 mm.

For the group of patients having tumor less than 20 mm, the diagnostic accuracy for CT, MRI and EUS was 69%, 82% and 91% respectively.

The sensitivity was 73%, 84% and 94% respectively. For tumors greater than 20 mm, the results were comparable with the results for the entire group of patients with pancreatic cancer.

Table 1. Comparative diagnostic value of CT vs. MRI vs. EUS in pancreatic adenocarcinoma

	CT	MRI	EUS
Sensitivity	81,4%	89,5%	97,5%
Specificity	43%	63,4%	90,3%
Accuracy	83,3%	89,1%	93,7%
PPV	61,5%	71,4%	82,2%
NPV	56,7%	68,5%	71,3%

Concerning the locoregional staging of pancreatic cancer, computed tomography, magnetic resonance and endoscopic ultrasound showed similar results.

Unfortunately, only 14% (14/100) of the patients were in the first stage of the evolution at the time of diagnosis, 27% (27/100) and 35% (35/100) of the patients being in stages III and IV, respectively.

Thus, 35% (35/100) of the patients had metastases.

There were no significant differences between the three imaging methods in identifying the intra-abdominal metastases (liver metastases and the peritoneal metastases).

Differences have appeared in the case of extra-abdominal metastases (lung metastases). Thus, there were 4 cases of lung metastases which have been identified only on CT and MRI.

Discussion

Pancreatic adenocarcinoma represents one of the most aggressive type of cancer and the need of early diagnosis is extremely important. Imaging is very important in the management of

pancreatic cancer. In clinical practice, the most used methods for the detection and characterization of pancreatic masses are CT, MRI and EUS.

Computed tomography is the most used imaging method in pancreatic cancer, being available in most medical units compared to MRI or EUS [4]. The pancreas is ideally imaged by dual-phase (arterial and portal) contrast material–enhanced MDCT. Because they appear less perfused compared to the surrounding tissue, pancreatic adenocarcinomas are typically hypodense in all CT phases (fig. 1 a,b). The sensitivity of CT in the detection of pancreatic cancers has improved over the years (75–100%) with a specificity of 70–100%. [5, 6]. Our study confirms the published data and demonstrated an accuracy of 83.3%, with sensitivity and specificity of 81.4% and 43% respectively in the diagnosis of pancreatic adenocarcinoma. The exact size of the tumor is essential for diagnosis and staging. Computer tomography has a very good accuracy and sensivity for diagnosis pancreatic tumors greater than 2 cm [6], but the sensitivity of CT scan for lesions smaller than 2 cm is 69% with an accuracy of 73%. However,

computed tomography remains the most accesible imaging method in diagnosis the pancreatic cancer being an important tool to identify liver metastases and peritoneal metastases [6].

Magnetic resonance imaging has been increasingly used in the evaluation of pancreatic tumors. The typical appearance of pancreatic carcinoma on MRI is hypointense on T1-weighted images and hyperintense or isointense on T2-weighted images (fig 1 c,d). The tumor shows diminished enhancement in the early phase of dynamic MR imaging and gradual enhancement in the late phase [7]. MRI has better contrast resolution than MDCT and is superior in detecting small tumors and metastases [8]. Moreover, MRI offer the possibility to examine the pancreatobiliary system noninvasively by magnetic resonance cholangiopancreatography (MRCP) with a very good accuracy. Our study fits into the published data, which shows that MRI has sensitivity between 81% and 99% and specificity between 70% and 93%. Limitations of MRI are related to cost, availability, and clinicians' familiarity with and predilection for CT imaging [4].
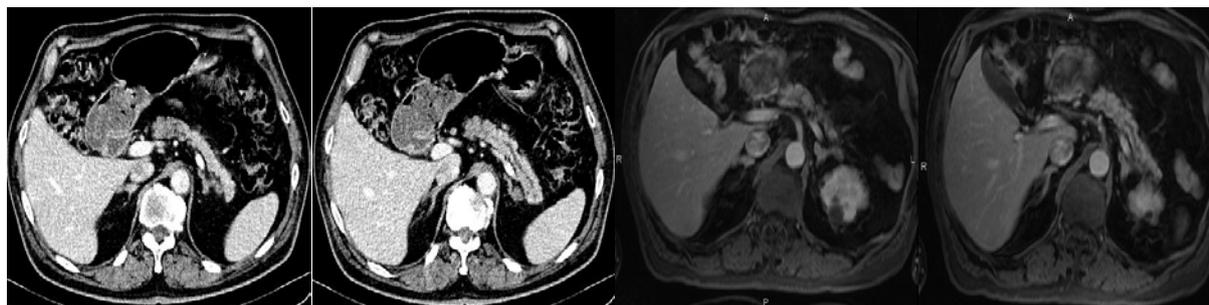

Fig.1. Pancreatic cancer-CT and MRI: hypodense (on CT) (a,b), hypointense (on MRI) (c,d) mass at the body of the pancreas accompanied by the dilatation of the Wirsung duct; diminished enhancement in the early phase of dynamic CT and MRI imaging

Ensoscopic ultrasound represents the most important imaging method for evaluating pancreatic diseases, having better diagnostic yield than computed tomography and magnetic resonance imaging for recognising early pancreatic tumors [9, 10].

On conventional EUS examination, pancreatic cancer appears as heterogeneous, hypoechoic mass, with irregular borders while on Doppler mode is hypovascular. On qualitative elastography pancreatic malignant tumor has generaly hard consistency and on CE-EUS, pancreatic adenocarcinoma is typically hypovascular during arterial and venous phase eventually with "wash-out" in the late venous phase (fig 2). These two

additional EUS techniques improve the diagnostic accuracy in pancreatic cancer. Thus, using a combination of contrast-enhancement and elastography, the diagnostic accuracy reaches 93,7%, with a specificity of 90,3% and sensitivity of 97,5%, comparing with conventional EUS examination where the accuracy, sensitivity and specificity were 82%, 96.2% and 64% respectively.

Moreover, EUS is able to detect focal lesions as small as 2-5 mm [11]. Our study demonstrated that EUS has a very good accuracy (91%) compared to CT (69%) and MRI (82%), in the diagnosis of pancreatic tumors less than 2 cm. EUS represents the only imaging method which allows to collect

samples from pancreatic masses for cytological examination. The accuracy of EUS-FNA for the diagnosis of pancreatic adenocarcinoma is reported to be 80–95% [12], with sensitivity and specificity of 85% and 98%, respectively, in a recently published meta-analysis [10, 13].

EUS represents also the best method for loco-regional staging in pancreatic cancer, but it has a limitation because it is not able to detect the extraabdominal metastases. Thus, CT or MRI examination must be used complementary.
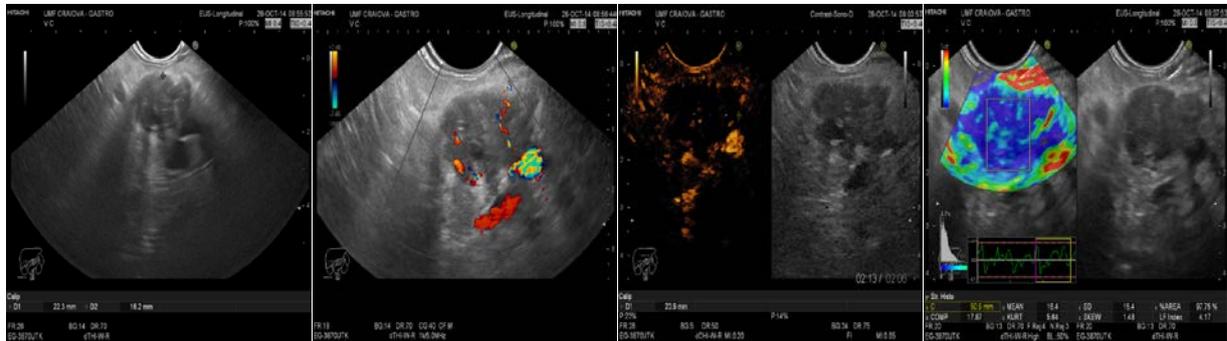

Fig.2. Pancreatic cancer-EUS: heterogeneous, hypoechoic mass (EUS-conventional mode) (a), hypovascular (Doppler mode (b) and CE-EUS (c)), of hard consistency (elastography) (d) at the body of the pancreas

Conclusion

EUS is the most effective technique in the diagnosis and staging of pancreatic cancer, our study demonstrating an accuracy of 93.7%, utilising a combination of contrast-enhancement and elastography.

Moreover EUS is the only imaging method which offers the possibility to collect samples for cytological examination.

However, there are some limitations of EUS in identifying extra-abdominal metastases.

Thus, the assessment of tumor extension must be completing by performing CT or MRI.

Acknowledgements

All authors had equal contribution.

Conflict of interests

The authors declare that they have no conflict of interests.

Authors' contributions

Costache MI developed the study design. Costache MI, Baluta EA, Anghel AC performed all diagnostic methods (CT, MRI), supervised by the experience in imaging diagnosis of Dr. Dumitrescu D and Dr Popescu M and the great experience of professor Saftoiu A in EUS examination. Costache CA and Costache MI were involved in all data collection. We collaborated with Dr. Tica AA and Dr Dumitrescu CI regarding the choice of the anesthetic drugs for EUS procedures. Costache MI and Costache CA prepared all drafts and

redrafts of the paper. All authors provided editorial comment on draft versions of the paper. All authors have read and approved the final manuscript.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015, CA Cancer J Clin; 2015; 65(1):5-29
2. Lowenfels AB, Maisonneuve P. Epidemiology and prevention of pancreatic cancer, Jpn J Clin Oncol; 2004; 34(5):238-244
3. Costache MI, Costache CA. Angiogenesis, diagnosis and treatment in pancreatic cancer: up to date. In: Costache MI, Costache CA (Eds), 2016, Lambert Academic Publishing, Germany
4. Jimenez RE, Fernandez-Del Castillo C. Tumors of the Pancreas. Sleisenger and Fordtran's gastrointestinal and liver disease. In Jimenez RE, Fernandez-Del Castillo C (Eds), Ninth edition, Elsevier, 2010, Philadelphia, USA
5. Brennan DD, Zamboni GA, Raptopoulos VD, Kruskal JB. Comprehensive preoperative assessment of pancreatic adenocarcinoma with 64-section volumetric CT, Radiographics; 2007; 27(6):1653-1666.
6. Shrikhande SV, Barreto SG, Goel M, Arya S. Multimodality imaging of pancreatic ductal adenocarcinoma: a review of the literature, HPB (Oxford); 2012; 14(10):658-668
7. Brentnall TA. Pancreatic cancer surveillance: learning as we go, Am J Gastroenterol; 2011; 106(5):955-956.
8. Hanbidge AE. Cancer of the pancreas: the best image for early detection-CT, MRI, PET or US?, Can J Gastroenterol; 2002; 16(2):101-105
9. Gonzalo-Marin J, Vila JJ, Perez-Miranda M. Role of endoscopic ultrasound in the diagnosis of pancreatic cancer, World J Gastrointest Oncol; 2014; 15;6(9):360-368

10. Hewitt MJ, McPhail MJ, Possamai L, Dhar A, Vlavianos P, Monahan KJ. EUS-guided FNA for diagnosis of solid pancreatic neoplasms: a meta-analysis, Gastrointest Endosc; 2012; 75(2):319-331.

11. Lami G, Biagini MR, Galli A. Endoscopic ultrasonography for surveillance of individuals at high risk for pancreatic cancer, World J Gastrointest Endosc; 2014; 6(7):272-285

12. Harewood GC, Wiersema MJ. Endosonography-guided fine needle aspiration biopsy in the evaluation of pancreatic masses, Am J Gastroenterol; 2002; 97(6):1386-1391.

13. Costache MI, Iordache S, Karstensen JG, Săftoiu A, Vilmann P. Endoscopic ultrasound-guided fine needle aspiration: from the past to the future, Endosc Ultrasound; 2013; 2(2):77-85.

Corresponding Author: Cristiana Iulia Dumitrescu, Department of Pharmacology,
University of Medicine and Pharmacy of Craiova, Romania, 2 Petru Rareş Street, 200349 Craiova, Romania,
e-mail: dumitrescu.cristiana@gmail.com