The Role of Imaging Techniques in Diagnosing Pancreatic Cancer

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Imaging techniques play an essential role in the diagnosis, staging and establishing the treatment protocols in pancreatic cancer. Our proposed study explores and improves recent discoveries in the field of pancreatic cancer, especially relying on complex imaging techniques such as Computer Tomography (CT), Nuclear Magnetic Resonance (MR 3T), Ultrasonography (US) and Endoscopic Ultrasonography (EUS). In the case of pancreatic tumors, regardless of their origin, imaging exams also allow the evaluation of local and distant extension, with important prognostic and treatment ramifications. CT exams alongside RM and EUS offer a highly sensible and specific diagnosis of pancreatic tumors, with the added advantage of concomitant evaluation of adjacent parenchymatosus abdominal organs.

Keywords: Pancreatic cancer; Ultrasonography; Computer Tomography; Magnetic Resonance; Endoscopic Ultrasonography

Experimental part

Materials and method

The study was carried out as a prospectiv study at the Department of Radiology and Medical Imaging, Craiova Emergency County Hospital, the Imaging Department, Research Center in Gastroenterology and Hepatology and the Pathology and Histopathology and Immunohistochemistry Laboratories of the Morphopathology Department at the University of Medicine and Pharmacy of Craiova.

The study was performed on a group of 201 patients with the following pancreatic tumors: 170 adenocarcinomas, 24 cystadenocarcinomas, 5 pancreatic metastasis and 2 neuroendocrine tumors (insulinomas).

CT examination was carried out using a SIEMENS SOMATOM unit with 20 sipes. Imaging exploration was performed sequentially, with our without non-iodine based contrast agents administered orally or intravenously. Patient body scan was performed continuously, with a low examination period, with concomitant data acquisition, during a single apnoea period without any respiratory movement-generated artifacts. The orally administered contrast agent used was Gastrografin (200 mL with 20 min before the examination and another 400 mL immediately before the examination, in order to observe the distension and opacification of the duodenum.

CT examination was initiated with a topogram on which the areas of interest were highlighted, followed by cross sections using 5 mm slices gapped by 5 mm, and 3 mm slices gapped by 3 mm for small lesions, respectively.

For the postcontrast study, non-iodine based intravenous contrast agents were used-Ultravist 370 and Iopamiro 370, with overall low toxicity and good local and tissular tolerance. A 1mL/ kg bodyweight bolus dose was administered, followed by the same type of sections and subsequent comparison between the resulting images.

Image acquisition was performed in the arterial, parenchymal and venous portal phases in order to differentiate benign and malignant pancreatic tumors. The venous portal and the parenchymal phases proved to be superior to the arterial phase in detecting malignant tumors, especially pancreatic adenocarcinomas. The arterial phase was useful for visualizing pancreatic blood vessels, while the portal phase proved to be more useful in detecting vascular invasion and liver metastasis. The images obtained using 3D, multipianar in coronal and sagittal planes and volumetric reconstructions were stored on DVDs and printed on radiology film in certain cases.

MR was performed using a Philips Ingenia 3 Tesla system. The MR-based imaging techniques are: T1 FLASH weighted sequences (fast low angle shot) or 2DFSPGR
limiting duodenal motility. Such as butylscopolamine (Bucospan) were used for requiring i.v. propofol for sedation. Anti-spasticity agents most of the cases, with a small percentage of patients 383 OUT). The examination was performed a jeun, using an ultrasound unit and a HITACHI EUB 8500 ultrasound unit, linked to a ALOKA PROSOUND 5000 endoscopy system with a 5 and 10 Mhz frequence of the head and body of the pancreas. The epigastric window of approach, with transveral and sagittal sections of the long axis of the lineal vein and sagittal sections were used, for the corporeal region exploration for visualizing the pancreas, the patient was asked to take a deep breath and remain locked in inspiration (Valsalva maneuver) as much as possible. In order to obtain a better window of exploration for visualization of the digestive tract walls as well as adjacent structures. The quality of the images was superior to those obtained using transabdominal US due to avoiding interposed structures such as fat or air.

**Results and discussions**

The patients’ US examination recorded the location and the size of the tumor; the presence of elements characteristic for chronic pancreatitis (reduced volume; non homogenous, with an occasional nodular structure and with calcifications); the size of the Wirsung duct; the aspect of the gull bladder and the intrahepatic bile ducts; the presence of hepatic metastasis as well as lymph node metastasis; the absence or the presence of ascites.

The adenocarcinomas which could be visualized during the US exam presented as hypoechoic, poorly differentiated, irregularly shaped masses presenting a peripheral hypoechoic halo as a result of peritumoral sclerosis.

Regarding the location of the tumors, the results of the US exploration coincided with the CT scans, with the majority of cancers being located in the head of the pancreas. Additionally, the distension of the gull bladder was highlighted in 79.15% of the cases and the distension of the intrahepatic bile ducts in 76.78% of the cases, seen as transsonic images with a double duct aspect as well as a heavily enlarged main bile duct (fig. 1 and 2).

Small sized tumors localized in the head of the pancreas were difficult to detect using US, requiring EUS and/or MRCP examination for visualization. In the patient group, US did not visualize the pancreatic tumor in 29.36% of the cases, with a 67.66% overall sensitivity for detecting pancreatic tumors being.

A high-frequency US transducer placed at the end of an endoscope was used for the examination, which allowed the ultrasonographic transmural visualization of the digestive tract walls as well as adjacent structures. The quality of the images was superior to those obtained using transabdominal US due to avoiding interposed structures such as fat or air.

**Trans-abdominal US exam.** The trans-abdominal US exams were done using ALOKA SSD 5000 and HITACHI 8500 EUB US equipment. The examination was performed a jeun, with the patient in dorsal decubitus and/or left lateral decubitus using the convex transducer with a 3.5-5 Mhz or a 2.5 Mhz frequence, respectively, for overweight patients, for obtaining axial, sagittal and oblique sections. Weighted T2 sequences were used in which fluids showed a hyperintense signal. The acquisition was made in a coronal plane for a better enhancement of the pancreatic and biliar ducts. The processing of the 3D images was done using a high-performing algorithm.

**Magnetic resonance cholangiopancreatography (MRCP)** as a newly developed imaging technique was used to enhance RM. The method highlights the pancreatic and biliar ducts due to their liquid-rich content. Weighted T2 sequences were used in which fluids showed a hyperintense signal. The acquisition was made in a coronal plane for a better enhancement of the pancreatic and biliar ducts. The processing of the 3D images was done using a high-performing algorithm.

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The objectives of CT scanning were detecting: the size and interactions between the pancreatic tumor and adjacent structures; the presence and localization of metastasis; the presence of locoregional and distant adenopathies.

CT examination highlighted the following aspects of the malignant tumors: the tumoral mass with a non homogenous structure and iodine uptake; tumoral necrosis with a hypodense aspect and fluid densities; cystic and tessular density structures indicative of malignant transformation; tumors of the pancreatic head were identified based on either complete blockage of the main bile duct determined by direct contact with the tumor or the double duct aspect presented as the distention of both the main bile duct and the pancreatic duct; the distention of the main bile duct and the intrahepatic bile ducts; the distention of the Wirsung duct corresponding to the body or the tail of the pancreas; the distention of the main bile duct; multiple images with low, iso/hypodense, low uptake densities suggestive of hepatic metastasis.

The optimum sequences were obtained during the arterial and portal phases. During the portal phase, the portal, superior mesenteric and peripancreatic veins present the maximum contrast, thus facilitating the discovery of the tumors and, in the same, the visualization of the hypovascular hepatic metastasis which are more visible during this phase because of the high contrast of the hepatic parenchyma.

Using volumetric acquisitions, arterial and superior abdominal 3D reconstructions were obtained which were useful in evaluating the direct contact between the neoplastic lesion and the peripancreatic vessels.

During the CT examination, TNM staging was also performed, identifying the criteria for unresectability as well as the disappearance of the pancreatic fat plane around the celiac trunk and the superior mesenteric artery.

Unlike abdominal US, the primary pancreatic tumor could not be visualized in only 10.5% of the cases with the accuracy of CT examination being 89.5% (figs. 3-5).

MRCP examination was useful in evaluating and characterizing the pancreatic adenocarcinomas as well as their staging.

MR 3T examination has pointed out the presence of a tissular mass in the uncinate process, with a minimal extension towards the pancreatic head, well delimited, with the disappearance of the anatomical space with the superior mesenteric vein; Wirsung duct with normal caliber and signal; the overall aspect suggests an insulinoma.

For 32 patients included in our study CT and MR examinations were not able to highlight the required characteristics for a complete diagnosis so additional information was obtained using EUS.

EUS was proved to be useful in staging pancreatic tumors and simultaneously enabled us to differentiate solid tumors from cystic, neuroendocrine or papillary tumors.
The main advantage of the technique was the possibility to perform a ultrasound guided fine needle aspiration. For 4.9% of the patients EUS was not able to detect the main pancreatic tumor, these results being similar to those published in other studies which describe EUS sensibility as being roughly 92%.

The main goals of EUS explorations were: identifying the main tumor and accurately describing its size; the presence of a Doppler signal in the tumor; visible tumor presence in the vascular lumen; blood vessels with an abnormal outline; the loss of the hyperechoic interface between the blood vessel and the parenchyma; collateral veins developed inside the tumor mass because of the obstruction of the main anatomical vascular trajectories; the presence of small sized metastasis, localized within the left hepatic lobe, undetectable by abdominal US; EUS ductal and parenchymal criterias for chronic pancreatitis.

The most encountered EUS image was a hypoechoic, non homogenous tumor mass with a size between 15 and 50 mm, with Doppler signal in the majority of cases (90%) (figs. 7-9).

Finally, EUS proved to be highly valuable in diagnosing and staging tumors of the pancreatic head, being superior to CT and MR examinations in most cases, especially for detecting small sized lesions.

The correlation between US studies and CT scans. The first set of statistical correlations was between the exploration systems used for detecting tumors and tumor localization. For calculating the degree of correlation between the two systems used for tumor evaluation (US and CT), we included the 170 patients evaluated using both methods, encompassing the overall tumor area. We maintained the same CT classification areas and the US segment classification, according to the criterias described under Materials and Method (table 1).

Segment analysis presented differences between US and CT examinations for describing tumor localisation. For 10 of these patients, US examination indicated the presence of the tumor in a segment in the near vicinity of the of the area indicated by CT examination (fig. 10). Thus, 5 tumors which were initially described as being in the cephalic region of the pancreas, were placed in the adjacent area mentioned by the CT scan. Additionally, seven tumors which were initially placed inside the pancreatic body were described as being a part of the caudal region of the pancreas after CT examination (fig. 10).

Statistical analysis of the correlations between the two methods used for evaluating carcinomas was based on the \(\chi^2\) correlation test. Using this algorithm, the evaluation techniques in our study proved to be highly efficient in locating tumors, represented by the \(p\) value determined for each value obtained using the \(\chi^2\) test (table 2).

In all cases, the relative error for locating the tumor was due to the large size or shape of tumors which created the impression of the neoplastic lesion originating in one area while extending in another. For this reason, we considered that the US-based diagnosis had a high degree of relative correlation, in concordance with the diagnosis obtained from the CT scan. The correlations between the endoscopic and CT examinations. The global assessment of the size of the tumor has led to their induction into 3 sets of categories (I=<2 cm, II= 2-4 cm, III=>4 cm) following the measurements done using the two evaluation techniques (both EUS and CT scan).

The weight of the defining classes has justified the presence of a larger number of tumors diagnosed as having

| Table 1 | PATIENT DISTRIBUTION ACCORDING TO SEGMENT LOCALIZATION AND ANATOMIC AREAS OF THE PANCREAS |
|---------|-----------------------------------------------|
| Group   | Pancreatic Segment | US General Group | CT General group |
| Area I  | head              | 113              | 108              |
| Area II | body              | 35               | 47               |
| Area III| tail              | 22               | 15               |
| Total   |                   | 170              | 170              |
between 2 and 4 cm using a CT scan compared to the lot examined using EUS, where the majority of tumors diagnosed had under two centimeters (table 3) (fig. 11).

The statistical analysis of the correlations between the two methods used in measuring the size of carcinomas was based on the $\chi^2$ correlation test.

### Table 3
**CT/EUS TUMOR SIZE**

| Class | Endoscopic Size | EUS Group | CT Group |
|-------|-----------------|-----------|----------|
| I     | <2 cm           | 10        | 5        |
| II    | 2-4 cm          | 14        | 15       |
| III   | >4 cm           | 8         | 11       |

In this situation, the correlation in terms of tumor size between the two evaluation techniques was statistically significant, based on the $p$ values determined from each result of the chi-squared test (table 4).

The comparative analysis of the tumor size using the two techniques was shown to be similar for 23 of the patients, representing 73% of the cases studied.

For the remaining 9 patients in our study, we recorded differences between the two exploration techniques.

For 8 of these patients, the difference resulted from underestimation of tumor size following CT examination in comparison to EUS, the latter proving to be more reliable in approximating the tumor size (table 4). A single case was registered in which the tumor size was overestimated, mainly due to the tumor being an insulinoma which the CT scan could not detect while EUS managed to identify it.

Overall, in an overwhelming percentage of cases CT examination underestimated the size-based staging of the tumor in comparison to EUS, the main reason being that CT examination only took the tumoral surface into account whilst ignoring the size of the tumor in its entirety, size which proved to be notably larger, as we have seen.

This conclusion is sustained, furthermore, through the study of the statistical parameters obtained from the measurements performed by either CT or EUS. The statistical analysis using the $t$-test did not indicate any difference the tumor size for the two groups in terms of mean value or distribution based on size (table 5) (fig. 12).

Thus, the interval bracket for the results obtained through CT examination was larger than the one obtained using
EUS. However, the interval in which the majority of results were situated, defined as the standard deviation for the mean value was larger for both groups and pushed towards the upper limit of the interval bracket due to the average size being, in both cases, larger than the mean value for the tumor size. It should be noted that tumors analyzed using CT scan presented an average tumor diameter larger than the ones examined with EUS.

Over 95% of solid malignant pancreatic tumors are represented by ductal adenocarcinomas [10]. In most of the cases, analyzing the tumors characteristics and distinguishing them from surrounding tissue has proven difficult despite the large number of imaging techniques being available [14-16], combinations of these techniques being necessary most of the time [11]. If a pancreatic mass is detected, a proper differential diagnosis is needed in order for the patient to receive proper treatment with the intention of improving the prognosis [12, 13].

At the moment, CT scan has proven to be the most reliable tool for diagnosing and staging pancreatic cancer [17]. MR is considered the mandatory imaging standard examination for the differential diagnosis of pancreatic masses [11, 19, 20]. The results of the microscopic examination are required for distinguishing between different types of pancreatic tumors [18, 24-26].

Studies by Prokop et al, Edlich et al and Haaga R.J et al with patients suspected as having pancreatic tumors have found changes in volume and density of the pancreas, the invasion of the peripancreatic fat, blood vessels and regional lymph nodes, as well as distant metastasis [1, 21, 22].

Bartalozzi and Catalano describe the RM characteristics of pancreatic tumors as hypointense masses during the T1 weighted sequence [5, 23, 27, 28]. Additionally, the authors suggest that the pancreas is hyperintense in comparison to the liver during the T1 sequence, with the contrast between the tumor and normal parenchyma being stronger than the one between the pancreas and the liver [23, 29, 30].

More so, the MR aspect of pancreatic adenocarcinomas in our study was represented by changes such as hypointense signal during the T1 sequence, iso/ hyperintense signal during the T2 due to the presence of necrosis and cystic degeneration and hypointense signal after the paramagnetic agent during the T1 sequence [24, 31, 32, 33]. In addition, the examination using the contrast agent allowed us to formulate a correct preoperative assessment by visualizing vascular invasion, adenopathies or distant metastasis [11].

In order to describe focal pancreatic lesions, we used \( b \) values of 0s/mm², 20 s/mm², 500 s/mm² and 100 s/mm², resulting in a mean ADC value for pancreatic adenocarcinoma [34-36] of 1.02±0.17x10⁻³ mm²/s, significantly higher than the one corresponding to acute pancreatitis which was 0.81±0.19x10⁻³ mm²/s.

The results we obtained suggest that it’s possible to differentiate between a pancreatic adenocarcinoma or an acute pancreatitis lesion and a chronic phase pancreatic mass [37, 38] by using large \( b \) values during MR DWI sequences. This has been confirmed by other authors, as well [24].

Conclusions
Pancreatic cancer is a devastating disease, with an abysmal prognosis and an important mortality and morbidity factor, which an increased incidence, according to the study. The analysis of the localization of the primary tumor seems to indicate that cancers of the pancreatic head are predominant, followed by body and tail in this particular order.

If the US represents the screening exam used for evaluating pancreatic pathology, useful for guiding towards a diagnostic, latest generation imaging techniques allow us to accurately describe the malignant lesion as well as the status of its progression. CT plays a major role in exploring the hepatic-biliary-pancreatic regions, with multislice spiral CT being a mainstay for describing pancreatic tumors. This technology allows the scanning of the whole abdomen within one cycle of voluntary apnea with concomitant analysis of the pancreas and secondary lesions, including pancreatic metastasis.

As for pancreatic tumors, regardless of origin, the imaging examination allows us to accurately assess the loco-regional and distant extension of the tumor with great prognostic implications and concordant therapeutic decisions.

CT examination correlated with MR and EUS represent a highly specific and sensible option for detecting pancreatic cancer, with the added advantage of being able to simultaneously explore other parenchymatous organs of the abdomen.

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Manuscript received: 14.12.2018