Role of abdominal ultrasonography in clinical staging of pancreatic carcinoma: a tertiary center experience

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KEY WORDS
abdominal ultrasound, diagnostic accuracy, pancreatic cancer, sensitivity, specificity

ABSTRACT

INTRODUCTION Various imaging modalities are used for the diagnosis and staging of pancreatic cancer. Abdominal ultrasonography is the most widely available method and usually the first-line diagnostic tool used in patients with suspicion of pancreatic carcinoma.

OBJECTIVES The aim of the study was to assess the clinical value of abdominal ultrasonography used in a tertiary center for staging of pancreatic carcinoma.

PATIENTS AND METHODS This prospective clinical trial included 454 consecutive patients with pancreatic cancer, who underwent a surgery between 2000 and 2012. The diagnostic accuracy of ultrasonography was established for each T category and lymph node involvement. Computed tomography and intraoperative staging of the pancreatic cancer were used as reference methods.

RESULTS The diagnostic accuracy of ultrasonography in cancer staging according to T categories was 94.1% for T1, 95.7% for T2, 85.4% for T3, and 81.7% for T4 tumors. The diagnostic accuracy of abdominal ultrasonography in the diagnosis of lymph node metastasis and assessment of tumor resectability was 66.1% and 74.8%, respectively.

CONCLUSIONS The results of our study summarize 12 years of our experience with abdominal ultrasonography in patients with pancreatic cancer and confirm that ultrasonography remains a valuable diagnostic modality in this patient group.

INTRODUCTION Pancreatic carcinoma remains one of the leading causes of cancer-related deaths in the world. In the years from 2000 to 2009, the incidence rate in the United States increased by 0.9% per year and the death rate increased by 0.5% per year.1 The overall 5-year survival rate reported worldwide does not exceed 5%. Even for patients with a tumor that has been surgically removed, the 5-year survival is only about 20% to 25%. In 2009 in Poland, pancreatic cancer was the second cause of death due to malignant gastrointestinal neoplasms in women and the third one in men.2

Over the years, various radiological imaging modalities have been used for the diagnosis and staging of pancreatic cancer, including abdominal ultrasonography, computed tomography (CT), magnetic resonance imaging (MRI), laparoscopy, and endoscopic ultrasonography.

Currently, thin-section, contrast-enhanced multi-detector CT is regarded as the investigation of choice in patients with pancreatic cancer. The sensitivity of CT in detecting pancreatic cancer is between 75% and 100% with specificity of 70% to 100%.3,4 MRI has been proved to be effective in the diagnosis and staging of pancreatic cancers; therefore, it should be used in centers where these facilities are readily available. Positron emission tomography–CT is a useful complementary investigation to exclude metastases outside the abdomen. Staging laparoscopy and laparoscopic ultrasonography are important in the restaging of locally advanced lesions after neoadjuvant therapy.3 However, in view of wide availability, noninvasiveness, low cost, and relatively high diagnostic accuracy, abdominal ultrasonography is routinely used as the first-line diagnostic modality in pancreatic cancer, and its sensitivity...
reaches 90%. The limitations associated with abdominal ultrasound examination, such as insufficient experience of the operator, low quality of the ultrasound equipment, or incorrect patient preparation, result in divergent opinions on its efficacy in pancreatic cancer staging. A significant advantage of this modality is its ability to detect liver metastases, which makes further imaging unnecessary. Morrin et al. demonstrated that grey-scale ultrasound combined with Doppler imaging has similar results to helical CT and CT angiography in detecting venous involvement.

The aim of our study was to assess the diagnostic accuracy of abdominal ultrasonography in staging of pancreatic carcinoma in all patients who underwent surgery between 2000 and 2012 in a tertiary care center. All examinations were performed by surgeons experienced in abdominal ultrasonography and the results were compared with intraoperative findings. We attempted to establish the role of abdominal ultrasonography performed by experienced diagnosticians in patients with pancreatic cancer.

**PATIENTS AND METHODS**

**Patient selection** The study involved 454 consecutive patients with pancreatic cancer admitted to a tertiary referral hospital, who underwent surgery between the years 2000 and 2012. The inclusion criteria were as follows: pancreatic cancer confirmed preoperatively by fine-needle aspiration biopsy or core-needle biopsy performed intraoperatively or by histological examination of the specimen; preoperative abdominal ultrasonography and CT; signed informed consent for diagnostic procedures and surgery. The exclusion criteria were as follows: distant metastases confirmed by imaging studies before surgery; lack of informed consent; contraindications for general anesthesia.

All relevant data were collected prospectively using a standard electronic database (Magic2, Magic Software Enterprises). The authors analyzed the following variables: clinical and pathological features, staging of pancreatic cancer based on preoperative abdominal ultrasonography, type of surgical procedures, pathomorphological staging and staging of pancreatic carcinoma based on intraoperative findings and CT.

The study was performed in accordance with the ethical standards of the Declaration of Helsinki and Good Clinical Practice. The approval of an ethics committee was not required to conduct the present study, according to the legal system in Poland.

**Diagnostic procedures** Abdominal ultrasound examinations were performed in an outpatient clinic after patients with suspicion of pancreatic cancer had been consulted by a surgeon. After the ultrasound examination, patients were scheduled for CT, following which a decision on surgical treatment was made. The mean time between ultrasonography and surgery was 14 ±3.5 days. Ultrasound examinations were conducted using the GE Logiq 7 (Logiq 7, General Electric, Connecticut, United States), Hitachi EUB 6000, or Hitachi EUB 550 (Hitachi, Chiyoda, Tokyo, Japan) apparatus. All examinations were performed in the morning, and all patients were fasting on the day of the examination. Each examination was performed according to the established study protocol, including staging of pancreatic cancer. The T and N categories were established and analyzed according to the TNM Classification of Malignant Tumors. The infiltration of the major abdominal vessels (the aorta, celiac artery, superior or mesenteric artery, common hepatic artery, hepatic portal vein, superior mesenteric vein) was assessed with color Doppler and power Doppler ultrasonography. The ultrasound criteria of vascular invasion applied in this study were as follows: loss of normal hyperechogenic tissue between the tumor and the vessel, obstruction, or encasement by tumor tissue over more than half of the circumference of any vessel. The intraoperative finding of major artery infiltration, and, in most cases, also of major abdominal vein infiltration, precluded resection. Local lymph nodes were assessed as metastatic if they were hypoechochogenic and the size of their short axis exceeded 10 mm. All examinations were conducted by surgeons who verified their findings intraoperatively and performed more than 1000 abdominal ultrasonographies per year.

The final staging of pancreatic carcinoma was based on a histopathological examination of surgical specimen in resectable cases and on the results of intraoperative surgical assessment.

The assessment of retrieved lymph nodes was performed in patients in whom resections had been performed and in some patients with unresectable tumors in whom lymph nodes had been collected intraoperatively for a histopathological study. CT was used to determine the nodal status when the tumor was not resected and lymph nodes were not retrieved.

In all patients, abdominal CT and chest X-ray were required to exclude distant metastases for clinical staging before surgery.

**Surgery** None of the patients received neoadjuvant therapy prior to surgery. A Whipple or Traverso–Longmire procedure was used for tumors located in the head of the pancreas, a distal pancreatectomy for those located in the body or tail, and a total pancreatectomy for multifocal tumors. Regional lymph nodes were routinely resected en bloc with the tumor. We did not perform vascular resection with reconstruction. In patients who had a nonresectable tumor, exploratory laparotomy or gastroenteroanastomosis (or biliodigestive anastomosis in those with a tumor within the head of the pancreas) was performed (Table 2). A biliodigestive anastomosis was not performed if endoscopic biliary prosthesis was implemented before the surgery or planned after the surgery.
and 245 men (54.0%). The final results of the staging process are summarized in Table 1. Ultrasound scans and surgical specimens of cancer at different stages are presented in Figure 1A–C. Radical resection (R0) was performed in 32.6% of the patients, while the R1 or R2 procedure in 19.6%. In the majority of the patients (47.8%), an unresectable tumor was found intraoperatively and the procedure was limited to palliative patency restoration or exploratory laparotomy (Table 2).

The diagnostic accuracy of abdominal ultrasonography in all patients was established as 85.6% for all T categories. The diagnostic accuracy for specific T categories is presented in Table 3. The highest accuracy was observed for T1 and T2 tumors (91.1% and 95.7% respectively), while for more advanced lesions, the accuracy was lower: 85.4% for T3 and 81.7% for T4. Sensitivity, specificity, and negative and positive predictive values for specific T categories are presented in Table 4. The number of patients with different T categories assessed by ultrasonography and the number of patients with different final categories are presented in Table 5. We did not analyze statistical analysis
The diagnostic accuracy exceeding 94% was observed in patients with T1 and T2 lesions although those patients constituted the minority of those surgically treated at our department during the 12 years of study. For more advanced tumors (T3 and T4), the accuracy was lower but still above 80%. A relatively high accuracy for T1 and T2 lesions may result from the experience of sonographers. All examinations were conducted by surgeons who verified their findings intraoperatively and performed more than 1000 abdominal ultrasound examinations per year. Lower accuracy for T4 lesions probably resulted from difficulties in the assessment of vascular invasion on ultrasound examination. In our previous study summarizing the value of ultrasonography in 409 patients with pancreatic cancer,\textsuperscript{19} higher accuracy was observed for T3 and T4 tumors (89.4% and 92.1%, respectively) but after analyzing the whole group of 454 patients, the results were less favorable. This confirms that even with a better quality of ultrasound equipment, it is still difficult to precisely determine the advanced stages of pancreatic carcinoma and its resectability.

DISCUSSION

Diagnostic accuracy for establishing T categories The results of our study indicate that abdominal ultrasonography remains a relatively accurate diagnostic tool in patients with pancreatic carcinoma. The present study evaluated the diagnostic accuracy of ultrasound examination in establishing a T category of pancreatic cancer according to the TNM classification.\textsuperscript{8} The diagnostic accuracy exceeding 94% was observed in patients with T1 and T2 lesions although those patients constituted the minority of those surgically treated at our department during the 12 years of study. For more advanced tumors (T3 and T4), the accuracy was lower but still above 80%. A relatively high accuracy for T1 and T2 lesions may result from the experience of sonographers. All examinations were conducted by surgeons who verified their findings intraoperatively and performed more than 1000 abdominal ultrasound examinations per year. Lower accuracy for T4 lesions probably resulted from difficulties in the assessment of vascular invasion on ultrasound examination. In our previous study summarizing the value of ultrasonography in 409 patients with pancreatic cancer,\textsuperscript{19} higher accuracy was observed for T3 and T4 tumors (89.4% and 92.1%, respectively) but after analyzing the whole group of 454 patients, the results were less favorable. This confirms that even with a better quality of ultrasound equipment, it is still difficult to precisely determine the advanced stages of pancreatic carcinoma and its resectability.
The greatest difficulty in assessing the stage of pancreatic tumor by ultrasound imaging is associated with the identification of extrapancreatic tumor extension (cT3) and vascular invasion (cT4). Thus, the diagnostic accuracy decreases with a higher T category. This phenomenon was observed in other studies on abdominal ultrasonography. Dabizzi et al.,9 showed that the sensitivity of ultrasonography in detecting pancreatic tumors can reach 95%, which is consistent with the results of our study. In addition, Michl et al.,10 demonstrated that ultrasonography may have similar sensitivity to that of CT for detecting small lesions (<2 cm, cT1), especially when advanced imaging techniques are used. Karlson et al.,11 in a study on 919 consecutive patients undergoing pancreatic ultrasonography, reported a specificity of ultrasonography for the detection of pancreatic carcinoma to be 90%. A high accuracy of ultrasonography for pancreatic cancer (95.9%) was reported by Tanaka et al.,11 in a study on 51 patients with confirmed pancreatic malignancy. In 8% of the patients, a tumor diameter of less than 1 cm was observed on ultrasonography. A lower accuracy of abdominal ultrasonography (89%) for diagnosing malignant tumors in the head of the pancreas was reported by Grossjohann et al.11 This study included only 49 patients and was conducted by radiologists who did not verify their findings intraoperatively. The diagnostic accuracy of ultrasonography in assessing arterial invasion (cT4) was lower in previous articles—it was up to 90% when power Doppler imaging was used.13 In another study, Trede et al.14 reported a diagnostic accuracy of 83.0% for vascular invasion and 85.1% for extrapancreatic tumor invasion. A study by Kaneko et al.13 included only 40 consecutive patients and the one by Trede et al.14 included 58 consecutive patients. Our prospective study, which involved 454 patients, probably resulted in more reliable and accurate outcomes.

Phoa et al.,15 and Bronstein et al.,16 reported the accuracy of CT in assessing a T category of pancreatic cancer to be 100% if the lesion was larger than 2 cm and 70% if it did not exceed 2 cm. Borbath et al.17 and Sheridan et al.18 reported the accuracy of MRI in assessing the T category of pancreatic cancer to be from 88% to 91%. The above results indicate that abdominal ultrasonography performed by an experienced sonographer allows to assess the stage of pancreatic cancer, although the results are not as reliable and accurate as those obtained by CT or MRI.

The overall diagnostic accuracy of abdominal ultrasonography in 454 patients analyzed in our study was established at 85.6%. Based on the previously published reports, the accuracy of abdominal ultrasonography in detecting pancreatic tumors ranges between 75% and 95%.5,13,15,25 Our results show that the efficacy of ultrasound examination in detecting pancreatic cancer is only slightly lower than that of other imaging methods such as MRI or 64-slice multidetector row CT with angiography, which are currently being considered as having the highest diagnostic accuracy (94% to 100%).3,5,25 High diagnostic accuracy of CT in solid tumors results from isotropic resolution (the same resolution in all dimensions), collimation allowing to obtain the layers of less than 1 mm in width, and multidetector imaging.27 A few previous studies reported high sensitivity of abdominal ultrasonography (up to 94%).23,26 As a consequence, this modality was recommended as the primary examination in cases with suspicion of pancreatic cancer.13 The results of other studies suggested lower sensitivity of ultrasonography (below 70%) and recommended CT as the primary diagnostic modality.26 These confounding findings probably result from restrictions in patient selection, small study groups, and different levels of experience in ultrasonography. The number of false-negative results on ultrasonography decreases if investigators may confirm their diagnosis intraoperatively. Therefore, the diagnostic accuracy of abdominal ultrasonography performed by surgeons should be higher, as observed in our study.

**Lymph node involvement** In our study, the lowest diagnostic accuracy of ultrasonography was observed for lymph node metastases (66.1%). Gorelick et al.19 evaluated the accuracy of abdominal ultrasonography in assessing lymph node involvement to be 77%, while Sofuni et al.20 and Bunk et al.,21 who used the color Doppler mode, reported a higher accuracy, namely, of 80% to 82.5%. Trede et al.14 reported an accuracy of 76.6%. In contrast, Chen et al.22 questioned the accuracy of a routine ultrasound examination for diagnosing lymph node metastases in patients with pancreatic cancer, reporting an accuracy of only 33%. Our results confirm that ultrasonography should not be regarded as the optimal approach to lymph node assessment in patients with pancreatic cancer. On the other hand, lymph node metastases do not preclude pancreatic resection, so their presence is not as important for the surgeon as vessel infiltration.

**Assessment of resectability** Abdominal ultrasonography allows not only surgeons but also general practitioners to establish a correct diagnosis. When performed by experienced sonographers, abdominal ultrasonography may predict the type of surgical treatment with an accuracy of 74.8%. The accuracy for detection of major artery involvement (the superior mesenteric artery or celiac axis) was even higher—81.7%. The most crucial factor affecting resectability of pancreatic cancer is infiltration of the superior mesenteric artery or celiac axis or both (described as category T4 in the TNM classification). Currently, the gold standard for evaluating resectability of pancreatic tumors remains the intraoperative assessment of tumor advancement by the surgeon, particularly with regard to major vessel infiltration. However, in
the majority of our patients, pancreaticoduodenectomy had not been performed in the case of major vessel infiltration.

Based on the obtained results, it might be concluded that the preoperative ultrasound examination is a relatively valuable method for predicting the type of surgery in patients with pancreatic cancer. Less favorable results were reported by American scientists who evaluated the accuracy of abdominal ultrasonography for assessing vascular infiltration by pancreatic cancer to be merely 60%. Other studies reported a higher accuracy of abdominal ultrasonography, reaching 80% to 96% when the color Doppler mode was used. Minniti et al. reported the accuracy of ultrasonography to be 81.4%, which was lower than that of CT (86%). The advancement in surgical techniques has enabled to use resection for more advanced pancreatic tumors. The diagnosis of such borderline resectable tumor requires the use of CT to obtain reliable information on vascular invasion. Therefore, CT should be performed in each patient with pancreatic cancer before any decisions on treatment.

Conclusions

Despite the use of new diagnostic imaging techniques, pancreatic cancer remains one of the leading causes of death from cancer, and the overall 5-year survival rate is 5% or lower. The results of our study summarize 12 years of our own experience with abdominal ultrasonography and suggest that ultrasound examination still remains a valuable diagnostic modality in patients with pancreatic cancer. This examination should be recommended not only by general practitioners suspecting pancreatic malignancy but also by surgeons as the first-line diagnostic procedure in patients with pancreatic cancer. Abdominal ultrasonography is useful in recognizing metastatic disease when resection is contraindicated, in clinical staging (T category), and in predicting resectability. Moreover, when both pancreatic tumor and distant metastases are found on ultrasonography, there is no need to assess resectability by CT as the treatment starts with chemotherapy. Ultrasonography also remains a useful tool to confirm pancreatic carcinoma by fine-needle aspiration biopsy, which is obligatory before starting chemotherapy. Further research on preoperative staging of pancreatic cancer is needed to evaluate the diagnostic value of other options available in ultrasound imaging such as contrast-enhanced examination, harmonic imaging, cross-beam, or sonoelastography.

REFERENCES


ARTYKUŁ ORYGINALNY

Rola ultrasonografii jamy brzusznej w określaniu klinicznego stopnia zaawansowania raka trzustki – doświadczenia ośrodka referencyjnego

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SŁOWA KLUCZOWE

czułość, dokładność diagnostyczna, rak trzustki, swoistość, ultrasonografia jamy brzusznej

STRESZCZENIE

Wstęp
W diagnostyce i określaniu stopnia zaawansowania raka trzustki stosuje się wiele metod obrazowania. Ultrasonografia jamy brzusznej jest metodą najbardziej powszechną i zazwyczaj wykorzystywaną jako pierwsze narzędzie diagnostyczne u chorych z podejrzeniem raka trzustki.

CELE

CELE
Celem badania była ocena wartości klinicznej ultrasonografii jamy brzusznej wykonywanej w ośrodku referencyjnym w ustalaniu stopnia zaawansowania raka trzustki.

PACJENTI I METODY


WYNIKI

Dokładność diagnostyczna ultrasonografii w rozpoznawaniu stopnia zaawansowania raka trzustki wynosiła odpowiednio dla poszczególnych kategorii: 94,1% dla T1, 95,7% dla T2, 85,4% dla T3 oraz 81,7% dla guzów w stopniu zaawansowania T4. Dokładność diagnostyczna ultrasonografii jamy brzusznej w rozpoznawaniu przerzutów do węzłów chłonnych i określaniu resekcyjności guza wynosiła odpowiednio 66,1% oraz 74,8%.

WNIOSKI

Wyniki niniejszego badania podsumowują 12 lat własnych doświadczeń w zakresie wykorzystania ultrasonografii u chorych z rakiem trzustki i pozwalają na uznanie ultrasonografii za wartościową metodę diagnostyczną w tej grupie chorych.