Endoscopic ultrasonography can avoid unnecessary laparotomies in patients with pancreatic adenocarcinoma and undetected peritoneal carcinomatosis

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ABSTRACT

Background/Objective: To assess the relationship between the presence of ascites detected by endoscopic ultrasonography (EUS) and peritoneal carcinomatosis (PC) in patients with pancreatic adenocarcinoma.
Methods: Consecutive patients who underwent a EUS for preoperative staging of a pancreatic adenocarcinoma between 1998 and 2014 were retrospectively reviewed. The diagnosis of PC was confirmed by histopathology or peritoneal fluid cytology. The main outcome of the study was the relationship of ascites at EUS and PC in patients with pancreatic cancer. Secondarily, to evaluate the relationship between this finding and survival as well as the development of PC during follow-up.
Results: A total of 136 patients were included: 30 patients with local unresectable tumor or metastatic disease and 106 potentially-resectable candidates based on CT staging. EUS showed ascites in 27 (20%) patients, of whom 8 (29.6%) had PC. The sensitivity, specificity, PPV, NPV and accuracy of ascites by EUS in the detection of PC in this group of patients were 67%, 85%, 30%, 96% and 83%, respectively. Ascites detected by EUS was the only independent predictive factor of PC with an OR of 11 (CI 95%: 3–40). The detection of ascites by EUS was associated with a shorter survival (median survival time 7,3 months; range 0–60 vs 14.2 months; range 0–140) (p = 0.018) and earlier development of PC during follow-up (median 3.2 months, range 1.4–18.1 vs 12.7 months, range 5.4–54.8; p = 0.003).
Conclusion: The finding of ascites at EUS in patients with pancreatic adenocarcinoma is highly associated with PC and a poor outcome.

Introduction

Survival in pancreatic adenocarcinoma is very low, with an overall 5-year survival rate of less than 5% [1]. Radical resection is the only chance of cure, but only 15% of the tumors are resectable at presentation as the vast majority are locally advanced or present metastatic disease [2,3]. Although survival rates following radical surgery in specialised centers reach around 15% at 5 years, overall mortality and morbidity are very high (2–5% and 30–40%, respectively) [4,5]. Therefore, an accurate preoperative evaluation and staging is crucial in order to adequately select patients with resectable tumors for surgery, thus preventing unnecessary laparotomies.

Peritoneal carcinomatosis (PC) dramatically decreases the survival of patients with pancreatic cancer [6] and must be ruled out before deciding management. However, it is difficult to identify small peritoneal metastases by means of CT scan [7]. This was

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demonstrated in a study by Adachi et al. in which CT failed to detect 27% of peritoneal metastases and 45% of stage IV disease in a cohort of patients with gastric cancer [8]. In pancreatic cancer, staging laparoscopy may demonstrate previously unrecognized small peritoneal and liver metastases in 20–30% of patients, changing the therapeutic strategy in nearly 15% of them [9,10]. Thus, current guidelines recommend performing an exploratory laparoscopy before resection in left-sided large tumors and/or in case of high CA19.9 levels or when neoadjuvant treatment is considered [11].

The finding of ascites is associated with the presence of PC in patients with gastric cancer [7,12] and EUS has shown to be the most accurate method for the diagnosis of ascites due to the close proximity of the echoendoscope to the peritoneum [13,14]. Nguyen and Chang detected ascites in 79 out of 565 (14%) patients with a previous CT who underwent EUS examination for various indications. Only 14 out of these 79 patients (18%) had ascites at CT, although PC was not suspected [14]. Additionally, EUS offers the possibility of sampling the ascitic fluid by EUS FNA during the same procedure [15,16]. However, information regarding the role of EUS in the evaluation of PC in pancreatic adenocarcinoma is scarce [17,18].

The aims of this study were: first, to assess the value of ascites detected by EUS for the diagnosis of PC in patients with pancreatic adenocarcinoma and to compare it with other tumor-related factors used in clinical practice; and second, to evaluate the prognostic value of ascites at EUS in this set of patients.

Patients and methods

Study design

The clinical records of consecutive patients with pancreatic adenocarcinoma who underwent an EUS at the Hospital Clinic (Barcelona, Spain) between 1998 and 2014 were retrospectively reviewed. Patients with radiographically-resectable lesions were referred to EUS to confirm resectability whereas patients with unresectable disease at CT were referred for cytological confirmation by EUS-FNA. Exclusion criteria were: lack of cytological or histological confirmation of PC, other diseases causing ascites or incomplete EUS. All patients were explored with abdominal CT following standard protocols. Gold standard was the histopathology of a peritoneal nodule or peritoneal fluid cytology, both obtained at the time of surgery. The Hospital Clinic's Institutional Review Board approved the study protocol.

A review of the electronic medical records was performed. Variables retrieved were: patient demographics, comorbidities, performance status, CA19.9 and standard blood tests, EUS findings (location and size of the tumor, presence of ascites, lymph nodes), CT staging, type of surgery, findings at surgery and follow-up.

EUS, CT scan and surgical procedures

EUS was performed using a radial echoendoscope (GF-UM20, GF-UM160, GF-UE160, Olympus America Inc., Melville, NY) followed by a sectorial echoendoscope (GF-UC140P, GF-UCT140, Olympus America Inc., Melville, NY) when EUS-FNA was indicated according to the standard technique described elsewhere [19]. Procedures were performed by 3 experienced endosonographers (OS, AG and GF-E, with more than 200 procedures/year). Patients were placed in the left lateral decubitus position and conscious sedation with intravenous midazolam or fentanyl plus propofol was used in all patients according to the judgment of the anesthesiologist. The presence of a small amount of ascites was identified as an hypoecogenic triangle-shaped area under the left hepatic lobe and/or around the duodenum (Fig. 1).
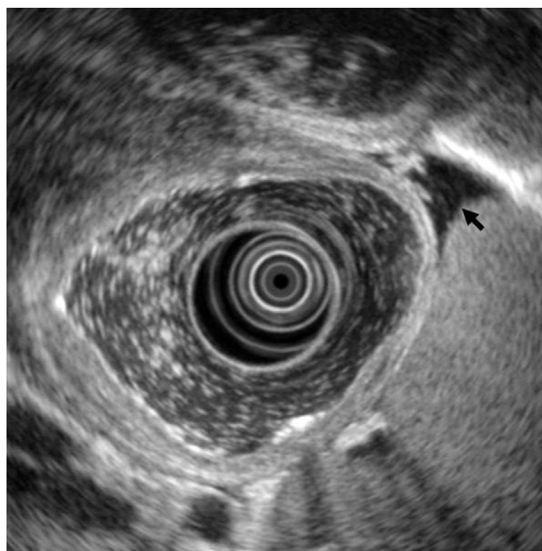
Fig. 1. Minimum amount of ascites detected by EUS seen as a hypoechogenic (black) triangle adjacent to the gastric wall (arrow).

For the abdominal CT, a four-phase pancreatic MDCT protocol acquisition was used after 2005 (Somatom Sensation 64, Siemens, Erlangen). Before this date, single and two-slice CT were used. In all cases, iodinated contrast medium was administered and portal venous and delayed phases were obtained. All series were routinely reconstructed with 3 mm thickness/increment in the axial and coronal planes for examination.

The gold standard was the cytological or histological confirmation of PC by means of surgery or diagnostic paracentesis. Sugical procedures varied from exploratory laparoscopy and/or derivative surgery to radical pancreatectomy. If ascites was present, 20 cc were directly aspirated. Peritoneal lavage was not routinely performed. When peritoneal nodules were visible, a biopsy was performed.

The main outcome of the study was the confirmation of PC and its relationship with the finding of ascites at EUS. Secondary outcomes were survival and development of PC during follow-up.

Statistical analysis

Quantitative variables are expressed as mean + SD and group comparisons were calculated by the non-paired Student's t-test. Categorical variables are expressed as frequency (%) and were compared with Chi-Square test. CA 19.9 was used as a categorical variable (<or >300 U/mL). In addition, a multivariate logistic regression analysis (with variables with statistical significance in the univariate analysis and other clinical variables usually associated with poor prognosis) was carried out to assess the existence of predictive factors of peritoneal carcinomatosis and the odds ratio (OR) was calculated to indicate the associated risk. Performance characteristics of ascites at EUS in diagnosing peritoneal carcinomatosis and their 95% confidence interval (CI) were calculated by using the standard formulas. Survival as well as development of PC during follow-up were estimated by log-rank test and the association between baseline variables and survival was analyzed by Cox's proportional-hazards regression model.

To evaluate the clinical impact of the presence of ascites at EUS in patients with pancreatic cancer, likelihood ratios (LR) and pre and post-test positive and negative probabilities of PC were calculated. The positive likelihood ratio (positive LR) assesses the