1130-0108/2011/103/1/1-4
Revista Española de Enfermedades Digestivas

Rev Esp Enferm Dig (Madrid)
Vol. 103, N.° 1, pp. 1-4, 2011

Editorial

Pancreatic cancer. A multidisciplinary approach

Pancreatic cancer (PC) still is a significant, unresolved health issue with highly similar incidence and mortality rates. It is the most lethal form of digestive cancer with a 5-year survival rate of 5%. The most common demographic risk factor is advanced age, particularly 70-80 years, as well as being a male and belonging to populations of Jewish origin or black ethnicity. Among environmental, non-hereditary factors tobacco smoking and a hyperproteic diet with extreme fat contents stand out. Obesity with a body mass index (BMI) ≥ 30 increases the risk of PC by 72 %(1). The multivariate analysis of this study shows that moderate physical activity significantly reduces the risk of PC. Diabetes mellitus (DM) and chronic pancreatitis (CP) are both interrelated, and risk is independent from DM duration and higher in insulin-dependent individuals. Various factors are interrelated: tobacco with hereditary CP, where PC develops 20 years earlier. The incidence of PC is clearly higher in patients with CP and amounts to 1.4%-2.7%; cumulative risk at 10 and 20 years is 1.8 and 4%, respectively. The problem here is the challenging diagnosis of PC in these patients. Hereditary factors include hereditary CP, familial atypical multiple mole melanoma syndrome, Peutz-Jeghers syndrome, hereditary breast cancer, and germ-line mutation of p16.

The following considerations may be derived from studies intended to assess the various disorders associated with PC development: an increased prevalence of PC may be seen in patients with pancreas divisum with an odds ratio of 2.4 (2); there is a potential association of infection with some *Helicobacter* species (H-specific 6S rDNA) (3); a possible association with hepatitis B virus infection during the replicative phase has been reported (4); active alcoholism and smoking speed up the process and cancer develops at an earlier age (5); PC in young patients is associated to a higher frequency of prior acute pancreatitis episodes (6).

PC symptoms relate to anatomic site; thus, tumors in the head of the pancreas usually result in bile obstruction signs including jaundice. Those in the body and tail, and usually tumors in the uncinate process may induce pain in the upper half of the abdomen, back pain, early satiety, weight loss, asthenia, anorexia, and symptoms associated with gastric voiding difficulties. Similarly, diabetes onset may be the first clinical feature developing in around 10% of patients. Many of these non-specific symptoms may mimic other primary tumors (such as ampullomas, bladder cancer, and cholangiocarcinomas), metastatic tumors (mainly renal), or benign conditions (chronic pancreatitis, peptic ulcer disease, etc.).

Regarding the diagnostic strategy, in patients with suspected PC abdominal ultrasounds provides valuable information as a first approach. Then, when findings are inconclusive, helical computerized tomography (CT) with multiplanar recon-

Editorial

struction is essential for the diagnosis and staging of these tumors, as well as to inform on vascular invasion status. However, in patients with clear clinical clues and a negative CT echoendoscopy or endoscopic ultrasonography (EUS) is crucial because of its higher sensitivity, as compared to CT and magnetic resonance imaging (MRI), for the diagnosis of tumors smaller than 2.5 cm (7,8). Some authors claim that the negative predictive value of EUS in the identification of PC is 100% (9). However, in case of concurrent chronic pancreatitis, a recent acute pancreatitis event (< 4 weeks), or diffuse pancreatic involvement by the tumor, EUS may be inconclusive (10). There is more controversy regarding EUS accuracy for PC staging, which may be equal to or higher than that provided by other imaging techniques. In this regard the systematic review by DeWitt (8) highlights EUS superiority versus multi-slice helical CT in the assessment of a tumor's locoregional extent and vascular involvement at the splenoportal axis. As regards the use of EUS-FNAP for these tumors, the technique should be performed when results are expected to modify clinical management, as occurs when histology is suspected to be other than ductal adenocarcinoma (e.g., lymphoma, endocrine tumors, pancreatic mestastases), in non-resectable tumors with potential for palliative chemotherapy, and in lesions of doubtful resectability with potential for pre-surgical neoadjuvancy (11,12). On the other hand, a greater number of examinations using radial echoendoscopy in selected patients (higher-risk groups, persistent GI symptoms such as abdominal pain in the absence of findings by other imaging techniques, etc.) would possibly spare the need for prior gastroscopy and facilitate detection in earlier stages of disease.

It is widely accepted that a pancreatic tumor is unresectable when distant metastases are present or there is a local invasion or arterial (celiac trunk, hepatic artery, superior mesenteric artery) or venous (portal vein, superior mesenteric vein) vessels (13). But reality at the time of surgery may be more complex, and a tumor with no vascular invasion may be found to be non-resectable because of a severe peritumoral desmoplastic component; similarly, surgical team expertise in radical and revascularization techniques may significantly influence tumor resectability. As far as surgical techniques are concerned, it must be highlighted that pancreatic anastomosis is a critical step and represents the primary cause of morbidity and mortality. On the other hand, the use of octreotide to inhibit pancreatic secretion reduces post-operative complications (14). Surgical technique selection will depend on tumor site. For tumors in the head of the pancreas the classical Whipple technique or Watson's pylorus-preserving modality do not significantly differ concerning surgery duration or post-operative morbidity and mortality rates.(15). Watson's technique has wider acceptance because of its less resective nature, potential shorter duration, improved access to biliary anastomosis, greater post-operative weight gain, and better quality of life. Regarding lymphadenectomy extent (16), several Japanese papers reveal that extended or extensive lymphadenectomy —depending on tumor site— do not increase morbidity and mortality, and has no significant effect on survival rates. Despite the fact that even tumors < 3 cm have a better prognosis than those bigger in size, their recurrence and survival rates are clearly improbable or unlikely.

In medicine, and PC is not an exception, diagnosis is considered an individualized process, however not to the extent that so is treatment too. Multidisciplinarity and current multimodal therapies allow us now to walk towards an increased capacity to make decisions as sound as possible for each individual patient. The dramatic, complex problem of pancreatic cancer requires that this option is made clear. Combining an earlier diagnosis based on risk profiles, prognosis stratification according to individual criteria, which to a great extent is linked to a better molecular classification of

Editorial

tumors, and most importantly a combined use of resources to establish the best possible combined treatment options is the real current challenge in managing this type of cancer. Thus, multimodal combined management programs are bearing fruit, as seen in the references included in the excellent manuscript by Morales Soriano et al. (17), which is published in this issue of *Revista Española de Enfermedades Digestivas* and gives cause to this editorial. In this scenario that is lacking optimism regarding the prognosis for this type of tumors, the paper by Morales Soriano et al. further considers the need for combined teams and an improved use of extant resources leading to improved results, with special emphasis on earlier, more accurate diagnosis, refined surgical techniques, greater attention to perioperative and postoperative care, and implementation of novel chemotherapy —and even radiation therapy— protocols. Their valuable contribution by sharing their prolonged experience in this kind of approach should encourage other teams to joint in an effort to develop powerful multicenter clinical trials aimed at shedding light on multimodal therapy options, as the authors themselves conclude in their contribution.

A. López-Martín[1], L. F. Carballo-Álvarez[2]

[1]Unidad de Aparato Digestivo. Hospital Universitario Morales Meseguer. Murcia. Spain.
[2]Servicio de Aparato Digestivo. Hospital Universitario Virgen de la Arrixaca. Murcia. Spain.

REFERENCES

1. Michaud DS, Giovannucci E, Willet WC et al. Physical activity, obesity, height and the risk of pancreatic cancer. JAMA 2001; 286 (8):921-9.
2. Nishino T, Toki F, Oi I, et al. Prevalence of pancreatic and biliary tract tumours in patients with pancreas divisum. Gastrointest Endos. 2005 61(5):AB195.
3. Ljhung A, Waldstrom T, Ishe I, et al. Helicobacter species in chronic pancreatitis, pancreatic adenoma and pancreas cancer. Gastroenterology. 2005;128(4) Suppl 2:A-474.
4. Yang H, Su J, Jen C, et al. Chronic hepatitis B infection in active replication is a risk factor for pancreatic cancer – a long term cohort study. Gastroenterology. 2005;128(4) Suppl 2:A-745.
5. Zisman A, Nickolov A, Gorchow A, et al. Smoking and alcoholic use associated with markedly earlier age of onset in pancreatic adenocarcinoma. Gastroenterology. 2005;128(4) Suppl 2:A-53.
6. Ludwig E, Dawood S, Olson S, et al. Young pancreatic cancer patients are more likely to report a history of pancreatitis than their older counterparts. Gastroenterology. 2005; 128(4) Suppl 2:A-472.
7. DeWitt J. EIS and pancreatic tumors. In: Hawes R, Fockens P, editors. Endosonography. London: Elsevier; 2006:177-203.
8. DeWitt J, Devereaux BM, Lehman GA, et al. Comparison of endoscopic ultrasound and computed tomography for the preoperative evaluation of pancreatic cancer: a systematic review. Clin Gastroenterol Hepatol 2006; 4:717-25.
9. Klapman JB, Chang KJ, Lee JG, et al. Negative predictive value of endoscopic ultrasound in a large series of patients with a clinical suspicion of pancreatic cancer. Am J Gastroenterol 2005; 100:2568-61.
10. Bhutani MS, Gress FG, Giovannini M, et al. No endosonographic Detection of Tumor (NEST) Study: a case series of pancreatic cancers missed on endoscopic ultrasonography. Endoscopy 2004; 36:385-9.
11. Horwhat JD, Paulson EK, McGrath K, et al. A randomized comparison of EUS-guided FNA versus CT or US-guided FNA for the evaluation of pancreatic mass lesions. Gastrointes Endos 2006;63:966-75.
12. De Witt J, Kahaled M. The role of endoscopic in the evaluation os susoected pancreatic malignancy. ASGE Clinical Update 2008;16:1-4.
13. Puli SR, Singh S, Hagedorn CH, Reddy J, Olyaee M. Diagnostic accuracy of EUS for vascular invasion in pancreatic and periampullary cancer: A meta-analysis and systematic review. Gastrointest Endosc 2007; 65(6):788-97.

Editorial

14. Yeo CJ, Cameron JL, Lillemoe KD et al. Does prophylactic octreotide decrease the rates of pancreatic fistula and other complications after pancreaticoduodenectomy? Results of a prospective randomized placebo-controlled trial. Ann Surg 2000; 232:419-429.
15. Seiler CA, Wagner M, Schaller B, Sadowski C, Kulli C, Büchler MW. Randomized prospective trial of pylorus-preserving vs. Clasical duodenopancreatectomy: initial clinical results. J Gastroenterol Surg 2000;4:443-452.
16. Yeo CJ, Cameron JL, Lillemoe KD et al. Pancreaticoduodenectomy with or without distal gastrectomy and extended retroperitoneal lymphadenectomy for periampullary adenocarcinoa, part 2: randomized controlled trial evaluating survival, morbidity and mortality. Ann Surg 2002; 236:355-365.
17. Morales Soriano R, Cuadrado A, Noguera JF, Dolz C, Vilella A, et al. Evaluación multidisciplinaria y tratamiento mutimodal del cáncer de páncreas resecado. Estudio Observacional. Revista Española de Enfermedades Digestivas. 2011; 103:5-12.