

Pancreatic Cancer and New Onset Diabetes: An Early Indication of Disease?

Linda J. Szymanski, DO

Pancreatic carcinoma is the fourth leading cause of cancer death in the USA, and it continues to have a dismal five-year survival of about 5%.¹ The median age at diagnosis is 69 years in whites and 65 years in African Americans.² At the time of diagnosis most cases of pancreatic cancer have distant metastasis (50%) or local or regional spread (29%). Only 3% have tumors that are confined to the pancreas.³ Less than 15% have surgically resectable disease with the overall five-year survival rate being directly correlated with the size and the stage of the tumor (30 mm: 10-20%; <20mm: 30-60%; <10mm: >75%)⁴⁻⁹. The remaining 85 % of cases are unresectable with an average mean survival of four to six months.

Clinically, most cases of pancreatic cancer are detected with symptom onset such as painless jaundice, shoulder or abdominal pain, and a concurrent increase in serum CA19-9. Unfortunately, symptom onset corresponds to radiological features of unresectability (metastasis) and poor prognosis. Studies have shown, through examination by radiology, that as little as six months prior to symptom onset, most cases of pancreatic cancers are resectable.^{10,11} In order to detect pancreatic cancer earlier and to improve long-term survival, modalities that enable us to screen asymptomatic individuals will facilitate early detection and increase survival.

In recent literature, a temporal association of new-onset diabetes prior to diagnosis of pancreatic carcinoma has been established.¹² It has been proposed that new-onset diabetes is one of the manifestations of pancreatic carcinoma. The pathogenesis of pancreatic cancer has not yet been clarified; however, pancreatic cancer is associated with a diabetic state that may resolve with surgical resection.^{13,14} Evidence supporting this relationship shows that patients with new-onset diabetes have a higher probability than general population of subsequently being diagnosed with pancreatic cancer, and that 74% to 88% of pancreatic cancer patients have new-onset diabetes occurring 24 months prior to diagnosis.¹⁵ Thus new onset sporadic diabetes could be used as a surrogate marker for the screening of early, otherwise asymptomatic cancer.

There is a substantial window of opportunity for clinicians to suspect pancreatic cancer between the time that individuals meet the biochemical diabetes and the time of evaluation for potential cancer. Proposed strategies that rely on physician-diagnosed, new-onset diabetes might capture up to 25% of cancers in the >50-year age group.¹⁶ Clinicians with patients, particularly in the >60-year age group who have new onset diabetes and who are without a family history of diabetes, should pursue further clinical evaluation to exclude potential pancreatic cancer. Current clinical workup includes assessment of serum tumor markers (CEA, CA19.9, CA125), CT scan of the abdomen, or endoscopic ultrasonography. Early detection is dependent on future development of more sensitive and specific biomarkers for pancreatic carcinoma.

References

1. Greenlee RT, Murray T, Bolden S, et al. Cancer statistics, 2000. *CA Cancer J Clin*. 2000;50(1):7–33.
2. Erickson RA, Larson CR, Shabahang M. Pancreatic Cancer. eMedicine website. <http://emedicine.medscape.com/article/280605-overview>. Updated December 7, 2010. Accessed January 3, 2011.
3. Key C. Cancer of the pancreas. In: Ries LAG, Young JL, Keel GE, et al, eds. SEER survival monograph: cancer survival among adults: US SEER program, 1988-2001, patient and tumor characteristics. Bethesda, MD: National Cancer Institute, 2007.
4. Conlon KC, Klimstra DS, Brennan MF. Long-term survival after curative resection for pancreatic ductal adenocarcinoma. Clinicopathologic analysis of 5-year survivors. *Ann Surg*. 1996;223(3): 273–279.
5. Sohn TA, Yeo CJ, Cameron JL, et al. Resected adenocarcinoma of the pancreas-616 patients: results, outcomes, and prognostic indicators. *J Gastrointest Surg*. 2000;4(6): 567–579.
6. Furukawa H, Okada S, Saisho H, et al. Clinicopathologic features of small pancreatic adenocarcinoma. A collective study. *Cancer*. 1996;**78(5)**:986–990.
7. Shimizu Y, Yasui K, Matsueda K, et al. Small carcinoma of the pancreas is curable: new computed tomography finding, pathological study and postoperative results from a single institute. *J Gastroenterol Hepatol*. 2005; 20(**10**):1591–94.
8. Ishikawa O, Ohigashi H, Imaoka S, et al. Minute carcinoma of the pancreas measuring 1 cm or less in diameter—collective review of Japanese case reports. *Hepatogastroenterology*. 1999;46(25):8–15.
9. Tsuchiya R, Noda T, Harada N, et al. Collective review of small carcinomas of the pancreas. *Ann Surg*. 1986;203(1):77–81.
10. Gangi S, Fletcher JG, Nathan MA, et al. Time interval between abnormalities seen on CT and the clinical diagnosis of pancreatic cancer: retrospective review of CT scans obtained before diagnosis. *AJR Am J Roentgenol*. 2004;182(4): 897–903.
11. Pelaez-Luna M, Takahashi N, Fletcher JG, Chari ST. Resectability of presymptomatic pancreatic cancer and its relationship to onset of diabetes: a retrospective review of CT scans and fasting glucose values prior to diagnosis. *Am J Gastroenterol*. 2007;102(10):2157–2163.
12. Chari ST, Leibson CL, Rabe KG, et al. Pancreatic cancer-associated diabetes mellitus: prevalence and temporal association with diagnosis of cancer. *Gastroenterology*. 2008;134(1):95–101.
13. Permert J, Ihse I, Jorfeldt L, et al. Improved glucose metabolism after subtotal pancreatectomy for pancreatic cancer. *Br J Surg*. 1993;80(8):1047–1050.
14. Fogar P, Pasquali C, Basso D, et al. Diabetes mellitus in pancreatic cancer follow-up. *Anticancer Res*. 1994;14(6B):2827–2830.
15. Pannala R, Leirness JB, Bamlet WR, et al. Prevalence and clinical profile of pancreatic cancer-associated diabetes mellitus. *Gastroenterology*. 2008;134(4): 981–987.
16. Pannala R, Basu A, Petersen GM, Chari ST. New-onset diabetes: a potential clue to the early diagnosis of pancreatic cancer. *Lancet Oncol*. 2009;10(1):88–95.