

## LETTER

---

# Accuracy of CA 19-9 and Radiologic Imaging in Detecting Recurrence After Resection for Pancreatic Cancer

Cosimo Sperti<sup>1</sup>, Valentina Beltrame<sup>1</sup>, Sergio Bissoli<sup>2</sup>, Sergio Pedrazzoli<sup>1</sup>

<sup>1</sup>Third Surgical Clinic, Department of Surgery, Oncology and Gastroenterology, University of Padua. Padua, Italy.

<sup>2</sup>Department of Nuclear Medicine, Castelfranco General Hospital. Castelfranco Veneto, TV, Italy

Dear Sir,

among all gastrointestinal neoplasms, pancreatic cancer still remains difficult to treat. Resection, with or without adjuvant or neoadjuvant therapy, offers the only chance of long-term survival, although the percentage of patients cured of this disease is very small. Most patients' tumor recur within two years of surgery, and the pattern of recurrence is well known. Treatment of recurrent pancreatic cancer is a clinical challenge since effective therapeutic options (surgery and/or chemo-radiotherapy) have yet to be clearly demonstrated. Surveillance after resection of pancreatic carcinoma is commonly performed with serum CA 19-9 determination and imaging studies, i.e. abdominal ultrasonography and/or computed tomography (CT); magnetic resonance imaging or <sup>18</sup>fluorodeoxyglucose positron emission tomography (FDG PET) with CT acquisition (PET/CT) are used in selected cases. However, the value of follow-up in the early detection of recurrence, and its impact on the survival of patients with pancreatic cancer, is not clearly shown.

In the article recently published in JOP, Jahromi *et al.* [1] emphasized the value of CA 19-9 serum levels as reliable aid in detecting recurrent pancreatic adenocarcinoma in patients with CA 19-9 positive primary tumors. Combination of CA 19-9 with multi-detector CT (MDCT) or PET/CT is potentially

the most accurate method in detecting recurrent pancreatic carcinoma. Considering the lower cost of CT compared to PET/CT, the combination of CA 19-9 with CT is highly accurate and cost-effective.

We agree with Jahromi's [1] conclusions that CA 19-9 assay is a well-known simple and reproducible method to follow patients after resection for pancreatic cancer: elevation of the marker is generally, but not always, due to tumor's relapse. However, increased levels of CA 19-9 require radiologic imaging to confirm and localize the recurrence sites. It is well-known that local recurrence is difficult to distinguish at CT examination from abnormality caused by surgical procedures, and inflammatory alterations after radiotherapy [2]. Moreover, mesenteric lymphadenopathy persists even years after surgery (also in the case of benign disease) and it is impossible to differentiate reactive adenopathy from lymph node metastases. Node metastases can only be suggested by a progressive increase in lymph node diameter and/or the presence of recurrent tumor [3]. In such patients, PET can be extremely useful in differentiating postoperative changes and reactive adenopathy from local tumor relapse or lymph node metastasis.

However, the study of Jahromi *et al.* [1] includes only 20 patients resected for adenocarcinoma of the pancreas with high preoperative levels of CA 19-9 that dropped to a normal value postoperatively, and were followed-up with tumor marker determination, MDCT, and PET/CT. On the other hand, in a small but significant proportion of population this carbohydrate antigen is not expressed, and tumor recurrence may occur without serum marker elevation: so, which is the best imaging for detecting recurrences in patients with normal CA 19-9 levels?

Received June 26<sup>th</sup>, 2013 – Accepted September 4<sup>th</sup>, 2013

**Keywords** CA-19-9 Antigen; Pancreatectomy; Pancreatic Neoplasms; Positron-Emission Tomography and Computed Tomography; Recurrence

**Correspondence** Cosimo Sperti

3<sup>rd</sup> Surgical Clinic; Department of Surgery, Oncology and Gastroenterology; University of Padua; Via Giustiniani 2; 35128 Padua; Italy

Phone: +39-049.821.8845; Fax: +39-049.821.8821

E-mail: csperti@libero.it

In 2010, we reported our experience of 72 patients with resected pancreatic carcinoma from 1998 to 2007, and followed-up postoperatively with CA 19-9 assay, MDCT and FDG PET or PET/CT: pancreatic tumor relapsed in 63 patients (87.5%) [4]. Recurrent patients were divided in two groups: Group 1, CT-positive (n=35) and Group 2, CT non-diagnostic, FDG PET positive (n=28) recurrences. Tumor relapse was detected by CT in 35 patients and by FDG PET in 61. Five out of 35 Group 1 patients underwent surgery (2 R0, 2 bypass, 1 exploratory) vs. 10 out of 28 Group 2 patients (4 R0, 2 R2, 2 bypass, 2 exploratory): 2 patients had a second cancer resected thanks to FDG PET. Overall, FDG PET influenced treatment strategy in 32 of 72 patients (44%). Group 2 patients survived longer, but the difference was not statistically significant (P=0.09). Disease-free survival was similar in Groups 1 and 2. The association of CA 19-9 plus FDG PET showed a similar specificity and PPV (both 100%) compared to CA 19-9 plus CT group, but sensitivity was higher in the former group (77% vs. 50%).

From January 2008 to December 2011, other 68 patients who had undergone resection for pancreatic cancer, have been followed with CA 19-9 determination, CT and PET/CT in our Department. Fifty-eight tumors recurred after resection: PET/CT showed the site of recurrent disease in 12 patients with CT inconclusive findings (5 patients had normal CA 19-9 serum levels), and confirmed CT features in 46. There were only two false positive PET/CT in two patients with suspected CT imaging of liver and lung metastasis, respectively. The liver lesion was excised: pathologic examination showed only signs of cholangitis. The pulmonary lesion disappeared at subsequent 1-month CT examination. Moreover, PET/CT revealed a second tumor, successfully resected, in 3 patients (2 colonic adenoma with high grade dysplasia and 1 adenocarcinoma of the lung); in two patients the second tumor appeared before the occurrence of pancreatic cancer relapse. Among the 12 patients with PET positive/CT negative recurrences, 2 patients underwent surgery (1 R0 resection), 7 chemotherapy, 1 radio-chemotherapy, 1 chemotherapy and stereotactic radiotherapy, 1 only supportive therapy. Four patients are still alive from 14

to 25 months; median survival time was 19 months (range 10-66 months).

Multimodality imaging is critical in the management of pancreatic cancer. PET/CT is increasingly viewed as a useful, accurate, and cost-effective modality in diagnosing and managing pancreatic cancer [5]. It is reasonable to believe that contrast-enhanced PET/CT performed with modern PET/CT scanners, may offer high-resolution anatomic information for surgical and radiotherapeutic planning, and functional information for whole-body staging and re-staging of patients with this neoplasm [5, 6].

In conclusion, tumor recurrence is detected earlier by FDG PET than by CT, and treatment strategy is influenced in a significant percentage of patients. However, the real benefit of an earlier diagnosis of recurrent pancreatic cancer is still to be defined since we are waiting for more effective therapies.

---

**Conflict of interest** The authors have no potential conflict of interest

---

#### References

1. Jahromi AH, Sangster G, Zibari G, Martin B, Chu Q, Takalkar A, Shi R, Amiri HS. Accuracy of multi-detector computed tomography, fluorodeoxyglucose positron emission tomography, and CA 19-9 levels in detecting recurrent pancreatic adenocarcinoma. *JOP* 2013; 24: 466-68.
2. Kim JK, Ha HK, Han DJ, Auh YH. CT analysis of postoperative tumor recurrence patterns in periampullary cancer *Abdom Imaging* 2003; 28: 384-91.
3. Ishigami K, Yoshimitsu K, Irie H, Tajima T, Asuyama Y, Hirakawa M, Kakihara D, Shioyama Y, Nishihara Y, Yamaguchi K, Honda H. significance of mesenteric lymphadenopathy after pancreaticoduodenectomy for periampullary carcinomas: evaluation with serial MDCT studies. *Eur J radiol* 2007; 61:491-98.
4. Sperti C, Pasquali C, Bissoli S, Chierichetti F, Liessi G, Pedrazzoli S. Tumor relapse after pancreatic cancer resection is detected earlier by 18-FDG PET than by CT. *J Gastrointest Surg* 2010; 14: 131-140.
5. Dibble EH, Karantanis D, Mercier G, Peller PJ, Kachnic LA, Subramaniam RM. PET/CT of cancer patients: part 1, pancreatic neoplasms. *AJR Am J Roentgenol.* 2012 Nov;199(5):952-67.
6. Asagi A, Ohta K, Nasu J, Tanada M, Nadano S, Nishimura R, Teramoto N, Yamamoto K, Inoue T, Iguchi H. Utility of contrast-enhanced FDG-PET/CT in the clinical management of pancreatic cancer. Impact on diagnosis, staging, evaluation of treatment response, and detection of recurrence. *Pancreas* 2013; 42: 11-19.