

## Original article

Initial experience in sentinel lymph node detection in pancreatic cancer<sup>☆</sup>M. Beisani<sup>a,\*</sup>, I. Roca<sup>b,\*</sup>, R. Cardenas<sup>b</sup>, L. Blanco<sup>a</sup>, M. Abu-Suboh<sup>c</sup>, J. Dot<sup>c</sup>, J.R. Armengol<sup>c</sup>, J.J. Olsina<sup>d</sup>, J. Balsells<sup>a</sup>, R. Charco<sup>a</sup>, J. Castell<sup>b</sup><sup>a</sup> Department of HPB Surgery, Hospital Vall d'Hebron, Autonomous University of Barcelona, Barcelona, Spain<sup>b</sup> Department of Nuclear Medicine, Hospital Vall d'Hebron, Autonomous University of Barcelona, Barcelona, Spain<sup>c</sup> Department of Digestive Endoscopy, Hospital Vall d'Hebron, Autonomous University of Barcelona, Barcelona, Spain<sup>d</sup> Department of Surgery, Hospital Arnau de Vilanova, University of Lleida, Lleida, Spain

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## ABSTRACT

**Background:** The local recurrence of pancreatic cancer is around 30% when complete resection can be achieved. Extended lymphatic resections may improve survival, but increases severe morbidity. As accurate patient selection should be mandatory, a new method is presented for pancreatic sentinel lymph node (SLN) detection with lymphoscintigraphy and gamma probe.

**Materials and methods:** Seven patients with cT2N0M0 pancreatic head cancer were enrolled between 2009 and 2012 in this prospective study. One day prior to surgery, preoperative lymphoscintigraphy with echoendoscopic intratumoural administration of Tc<sup>99m</sup>-labelled nanocolloid was performed, with planar and SPECT-CT images obtained 2 h later. Gamma probe detection of SLN was also carried out during surgery.

**Results:** Radiotracer administration was feasible in all patients. Scintigraphy images showed inter-aortocaval lymph nodes in 2 patients, hepatoduodenal ligament lymph nodes in 1, intravascular injection in 3, intestinal transit in 5, and main pancreatic duct visualisation in 1. Surgical resection could only be achieved in 4 patients owing to locally advanced disease. Intraoperative SLN detection was accomplished in 2 patients, both with negative results. Only in one patient could SLN be confirmed as truly negative by final histopathological analysis.

**Conclusions:** This new method of pancreatic SLN detection is technically feasible, but challenging. Our preliminary results with 7 patients are not sufficient for clinical validation.

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## Experiencia inicial en la detección del ganglio centinela en cáncer de páncreas

## RESUMEN

## Palabras clave:

Cáncer de páncreas

Ganglio Centinela

Linfogammagrafía

**Objetivo:** Tras una resección quirúrgica completa, la recidiva local del cáncer de páncreas es de aproximadamente el 30%. La linfadenectomía extendida podría mejorar la supervivencia pero implica una morbilidad grave, por lo que una adecuada selección de los pacientes sería fundamental. Presentamos una nueva técnica de determinación del ganglio centinela (GC) en el cáncer de páncreas mediante el uso de SPECT/TC y sonda gamma.

**Materiales y Métodos:** Siete pacientes con cáncer de páncreas estadio cT2N0M0 fueron incluidos entre 2009 y 2012 en este estudio prospectivo. El día antes de la cirugía se realizó una ecoendoscopia con inyección intratumoral de un nanocoloide marcado con Tc<sup>99m</sup> y dos horas más tarde se obtuvieron imágenes planares y de SPECT-TC. Intraoperatoriamente se realizó asimismo un rastreo con sonda gamma para detectar el GC.

**Resultados:** La administración del radiotrazador fue posible en todos los pacientes. La linfogammagrafía detectó ganglios interaortocavos en 2 pacientes, ganglios en el ligamento hepatoduodenal en 1 paciente, inyección intravascular en 3 pacientes, tránsito intestinal en 5 pacientes y visualizó el conducto pancreático principal en 1 paciente. Debido a la progresión local, la resección quirúrgica pudo ser completada únicamente en 4 pacientes. La detección intraoperatoria del GC se completo en 2 pacientes, ambos con resultado negativo. Sólo en uno de estos pacientes el resultado pudo confirmarse con el estudio anatomopatológico definitivo.

<sup>☆</sup> Preliminary results of this study were briefly presented as an oral communication at the 47th Annual Meeting of the European Pancreatic Club held in Toledo (Spain) during June 2015.

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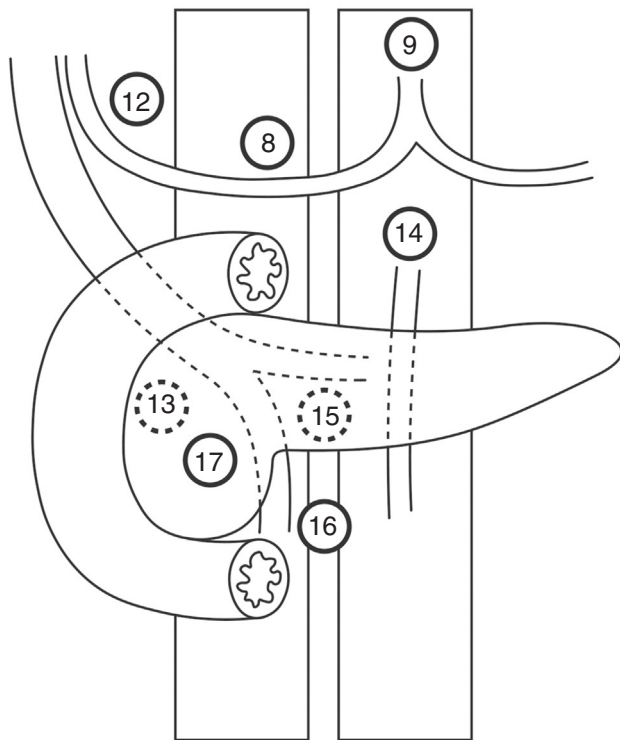
**Conclusiones:** Este nuevo método de detección del GC en cáncer de páncreas es viable pero complejo. Nuestros resultados preliminares con 7 pacientes no permiten una validación clínica.

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## Introduction

At diagnosis, around 80% of pancreatic neoplasms are unresectable.<sup>1</sup> When curative treatment can be pursued with a combination of surgical and adjuvant therapies, high recurrence rates lead to 5-year survival of less than 25%.<sup>1–3</sup> Histopathological study of surgical specimens shows around 70% lymphatic invasion<sup>4,5</sup> and local recurrence as high as 30%.<sup>6–9</sup>

Conventional resection comprises pancreatoduodenectomy and standard lymphadenectomy (SL) of peripancreatic and periduodenal lymph nodes, stations 8, 12, 13, 14 and 17 according to the Japanese Pancreatic Society<sup>10–12</sup> (Fig. 1). As complete surgical resection (R0) is the only chance of long-term survival,<sup>13,14</sup> Fortner<sup>15</sup> in 1973 proposed an aggressive approach that included total pancreatectomy, subtotal gastrectomy, vascular resection and accurate para-aortic lymphadenectomy. Since then, four randomised studies<sup>16–19</sup> and a meta-analysis<sup>20</sup> have been conducted to compare this extended resection with the conventional approach. Although no clear benefit for survival has been reported, Pedrazzoli et al.<sup>16</sup> suggested that an extended lymphadenectomy (EL) including coeliac, superior mesenteric artery and interaortocaval lymphatic groups (stations 8, 9, 12, 13, 14, 15, 16 and 17 according to the Japanese Pancreatic Society) could actually improve survival in the subgroup of patients with positive lymph nodes on the final histopathological study after resection. Nonetheless, morbidity was greater in the EL group compared to the SL group.



**Fig. 1.** Schematic surgical field of an open pancreatoduodenectomy and main lymphatic stations according to the Japanese Pancreatic Society.

The implementation of an effective sentinel lymph node (SLN) technique for pancreatic cancer would permit the preoperative identification of patients with lymphatic dissemination and thus avoid unnecessary morbidity in patients who would not benefit from EL. Two unsuccessful attempts to map pancreatic lymphatic drainage using methylene blue injection of the tumour have already been reported.<sup>21,22</sup> Lymphoscintigraphy with SLN analysis is a standard technique in malignant melanoma, breast cancer, head and neck cancer and others.<sup>23,24</sup> It consists of intratumoral injection of a radiotracer ( $Tc^{99m}$ -nanocolloid injected by echoendoscopy), mapping of the individual lymphatic spread of each patient with planar and tomographic images (SPECT-CT) and, 24 h later, surgical resection of the identified SLN using intraoperative gamma probe detection. We decided to test an approach using radiotracer by means of lymphoscintigraphy and intraoperative gamma probe for SLN detection in pancreatic cancer.

## Material and methods

A single centre exploratory study was designed and approved by the local Ethics Committee to assess the technical viability and clinical role of the SLN technique in pancreatic cancer.

Patients ( $n = 7$ ) with clinically diagnosed T2N0M0 (stage II) pancreatic head cancer were included after giving their informed consent. Exclusion criteria were previous abdominal surgery or abdominal radiotherapy. The enrolment period was from December 2009 to May 2012.

Preoperative assessment of all seven patients consisted of endoscopic ultrasound, MRI and angio-CT. During endoscopic ultrasound examination one day prior to planned surgery, the intratumoural injection of  $Tc^{99m}$ -labelled nanocolloid (0.1–0.2 ml, 4 mCi) was performed. Efforts were made to prevent intestinal leakage. In the first two patients, the endoscopic needle was completely filled with a dilution of the radiotracer (20 mCi in 1 ml volume) but only 0.1–0.2 ml (4 mCi) was injected. In the following cases, the needle was filled with only 0.2 ml of dilution. The radiotracer was then injected into the tumour until gas was observed and, at that point, the needle was withdrawn. This modification reduced the presence of intestinal activity although it was not completely eliminated.

After 2 h in the endoscopy unit recovery room, the patient was transferred to the nuclear medicine department to obtain anterior, posterior and lateral planar lymphoscintigraphic images and SPECT-CT fused frames (Gammacamera General Electric Hawkeye 4, 20 s/frame, 1 image/6 degrees, CT for AC).

Using the location information obtained by SPECT-CT images, intraoperative gamma probe detection (Europrobe 2, Technetium probe) was used to identify activity of the SLN, which was harvested and sent for intraoperative histopathological study prior to specimen resection. Open pylorus-preserving pancreatoduodenectomy with SL was then performed if no arterial or extrapancreatic invasion was detected (Fig. 2). Reconstruction consisted of a duct-to-mucosa termino-lateral pancreatojejunostomy, a termino-lateral hepaticojejunostomy and an antecolic duodenojejunostomy. If the malignancy proved unresectable, a biliary and/or digestive diversion without lymphatic harvesting was performed according to the patient's clinical status. Patients received standard post-operative care. Postoperatively,

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