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Comparison of intra-operative gamma probe detection with postoperative SPECT/CT of sentinel nodes related to the ovary.

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Abstract

Purpose

Tracer injection into ovarian ligaments has been shown to detect sentinel nodes (SNs) in patients with ovarian cancer. To determine the possibility that SNs are missed, this feasibility study compared their detection during surgery with postoperative SPECT/CT.

Methods

In eight patients (either ovarian or endometrial cancer), after a staging lymphadenectomy including resection of SNs related to the ovary, SPECT/CT scans were performed within 24 hours.

Results

SPECT/CT identified hotspots in four patients at sites where SNs were resected. In six patients additional localizations were found, mainly in the pelvic region.

Conclusions

Discrepancies between the γ-probe and SPECT/CT may be due to missed SNs during surgery, but with respect to pelvic hotspots, in the majority of cases they are more probably related to remnants of tracer at injection sites. With respect to sites where SNs were resected, remaining hot spots may have been caused by residual lymphatic flow after resection.

Introduction

In clinical early stage epithelial ovarian cancer (EOC) the International Federation of Obstetrics and Gynaecology (FIGO) recommends a staging procedure which includes a complete pelvic and para-aortic lymphadenectomy (1). However, a complete lymphadenectomy is associated with morbidity, including nerve and vessel injury, increased blood loss, increased operating time and the formation of lymph cysts and lymphedema (2-4). A sentinel node (SN) procedure may play an important role in the management of EOC. Few studies in patients with ovarian cancer have evaluated SN, partly because of the risk of tumor dissemination associated with the injection of tracers into the ovarian cortex (5-9). In a previous pilot study, we avoided possible tumor cell spillage by injection of tracers into the ovarian ligaments rather than into the ovarian cortex (10). We identified at least one SN in all patients with suspicion of ovarian cancer (n=21) (11). However, by the nature of this approach without pre-operative imaging of the sentinel node localizations, we were conscious that the single use of a γ probe and/or blue colorization to detect hotspots during surgery could lead to SNs being missed. With this in mind, in the present feasibility study we describe patients in whom, after resection of SNs identified by γ probe and blue dye examination, postoperative single photon emission computed tomography/computed tomography (SPECT/CT) was performed.

Material and methods

Patients

As described previously, patients diagnosed with a pelvic mass suggestive of a malignant ovarian tumor, and patients with high-grade endometrial cancer planned for staging laparotomy were eligible to participate in the study (10, 11). In this study we included both patients with suspicion of an ovarian malignancy as well as patients with a high-grade uterine carcinoma. The latter group of patients could also be included because these patients undergo the same surgical procedure: TAH with BSO and a pelvic
and para-aortic lymphadenectomy or lymph node sampling. All patients provided fully informed consent before enrollment in the study, and the protocol was approved by the Local Ethics Committee (approval number NL40323.068.12) (clinical trial registration number

NCT01734746).

Surgical procedure

The surgical procedure has been described in detail in previous reports (10, 11). Briefly, in patients with an adnexal tumor, tracer was injected on the dorsal and ventral sides of both the proper ovarian ligament and the suspensory ligament. Each of the four injections consisted of a standard dose of 0.2–0.5 mL of undiluted blue dye (Patent Blue V, 25 mg/mL, Guerbet Nederland B.V., Gorinchem, the Netherlands) and 20 MBq (total dose of 80 MBq) of technetium-99-m-labeled albumin nanocolloid, of particle size < 80 nm (99m Tc-nanocolloid or Nanocoll, GE Healthcare, Eindhoven, The Netherlands). Fifteen minutes later, the adnexal mass was removed and sent for frozen section analysis. If the ovarian mass was found to be malignant, the retroperitoneal space was opened, SNs were localized with the γ probe or visually (blue dye) and resected. After removal of the SNs, a complete standard staging procedure was performed including a comprehensive sampling of other lymph nodes in the different anatomic locations.

For the detection of possible SNs related to the ovary, tracer injection in patients with endometrial cancer was identical to that in patients with an ovarian tumor, with injection on the right or left side. Fifteen minutes after injection, a complete hysterectomy with bilateral salpingo-oophorectomy was performed, followed by retroperitoneal exploration to identify and resect the SNs. In addition, standard pelvic and para-aortal lymph node sampling was performed according to protocol.

Postoperative SPECT/CT

Depending on the condition and mobility of the patient, a scintigram was performed within 24 hours after surgery. SPECT/CT images were acquired using a standard SPECT/CT camera (Precedence SPECT/6-slice CT scanner, Philips, Best, the Netherlands), equipped with dual 1.6 cm γ-detectors and low-energy general-purpose collimators. SPECT/CT data of the abdomen and pelvis were obtained by a noncircular orbit, a 64×64×16 matrix, and 64 angles over 180° and 30 seconds per stop, after which CT scanning was performed (120 kV, 30 mAs, slice thickness 2 mm).

Results

Patients

In eight patients (five patients with ovarian cancer, patient 1-5, and three patients with endometrial cancer, patient 6-8) in whom a surgical staging lymphadenectomy was performed including resection of SNs, a SPECT/CT was made within 24 hours postoperatively. The five patients with ovarian cancer were incorporated in a previous report, describing the feasibility of the intra-operative SN detection. [11] In none of the patients, a pre-operative CT scan as part of the diagnostic work-up showed signs of tumor spread (either intra-abdominal of pathological lymph nodes). The three patients with endometrial cancer had normal ovaries on CT scan as well as during surgery.

SN detection

Figure 1 shows the hotspot locations identified with the γ probe transperitoneally (A), with the γ probe during retroperitoneal exploration (B), and with SPECT/CT postoperatively (C). At least one hotspot was detected in each of these eight patients using the γ probe transperitoneally. During retroperitoneal exploration, 20 hotspots were detected with the γ probe. In seven patients (88%) SNs corresponded to a transperitoneally identified hotspot, with five patients (nr. 1, 2, 5, 6, and 7; 71%) having more than one SN in this region. In addition, two patients (nr. 1 and 3; 25%) had SNs in regions not initially identified transperitoneally. In one patient the transperitoneally detected hotspot in the low aortocaval region could not be recognized at retroperitoneal exploration. In contrast, in this patient a SN was detected in the high aortocaval region. In two patients (nr 1 and 6; 25%), the SNs were also visible by blue staining.

Postoperative SPECT/CT showed at least one hotspot in all eight patients, for a total of 11 hotspots. In four patients, in total five hotspots (one in nr. 1, 6, and 7, two in nr. 5; 45%) were identified at sites where SNs were resected (three aortocaval and two pelvic). The remaining six hotspots all were located in the pelvic region. Figure 2 shows the lymphatic drainage from a right ovarian tumor after resection of a SN at the aortocaval region, illustrated by SPECT/CT.

Histopathology

All 20 tissue specimens related to transperitoneally identified hotspots, contained at least one lymph node. In one patient one tissue specimen contained two lymph nodes (figure 1). In one patient with endometrial cancer lymph node metastases were found in both SNs at histopathology (figure 1).

Discussion

In the present feasibility study, SN detection during surgery by γ probe in patients with an ovarian or high-grade endometrial cancer by injecting tracers in the ovarian ligaments, was compared with detection by postoperative SPECT/CT imaging. In four patients one or more hotspots could still be identified at locations where the sentinel nodes were resected. Furthermore, in six patients hotspots were detected in the pelvic regions that were not identified during surgery.

As already previously reported, retroperitoneal exploration was more successful than transperitoneal examination in detecting a higher number of SNs (11). This could be explained by a better and more precise accessibility of the lymph node locations but possibly also because of a longer time interval after injection of the tracer. The inability of SPECT/CT to detect these hotspots was obviously due to the resection of these SNs during surgery. However, in four patients, SPECT/CT detected residual activity at these sites. This may have been caused by residual lymphatic flow containing tracer after resection, with tracer fluid accumulating at the site of the SN resection.

The marked discrepancy between the γ probe and SPECT/CT, in that some hotspots in the pelvic region were only detected by SPECT/CT, can most probably be explained by the injection sites of the tracer. These hotspots were mainly located at the level of the external iliac vessels and/or the psoas muscle, where the suspensory ligament reaches the pelvis and passes close to the iliac vessels. Although hysterectomy and bilateral salpingo-oophorectomy also included resection of the sites of tracer injection in the suspensory ligament near the psoas muscle, the latter could not always be performed completely. Two hotspots were found near the pouch of Douglas, being

possibly remnants of leakage of tracer fluid during injection. Postoperative lymphatic mapping with SPECT/CT, as in our study, was intended only to validate the SN procedure. One technique that may be of great interest is the intra-operative use of a portable gamma camera, which may result in real time imaging (12). This method may provide an overview of all radioactive hotspots throughout the entire surgical field.

Conclusion

SNs may be safely detected in patients with EOC by injecting the tracers into the ovarian ligaments. However, intra-operative γ probe detection and postoperative SPECT/CT imaging showed discrepancies in SN detection. Whether the hotspots visualized on SPECT/CT were actually missed SNs cannot be determined from these data. Large, multicenter trials are needed to compare the histology of SNs and non-SNs, and to evaluate whether intra-operative imaging with a mobile gamma camera improves the accuracy of SN identification. This should also be related to the significant developments in the use of fluorophores and fluorescent signatures, such as in prostatic cancer, and hybrid tracers.

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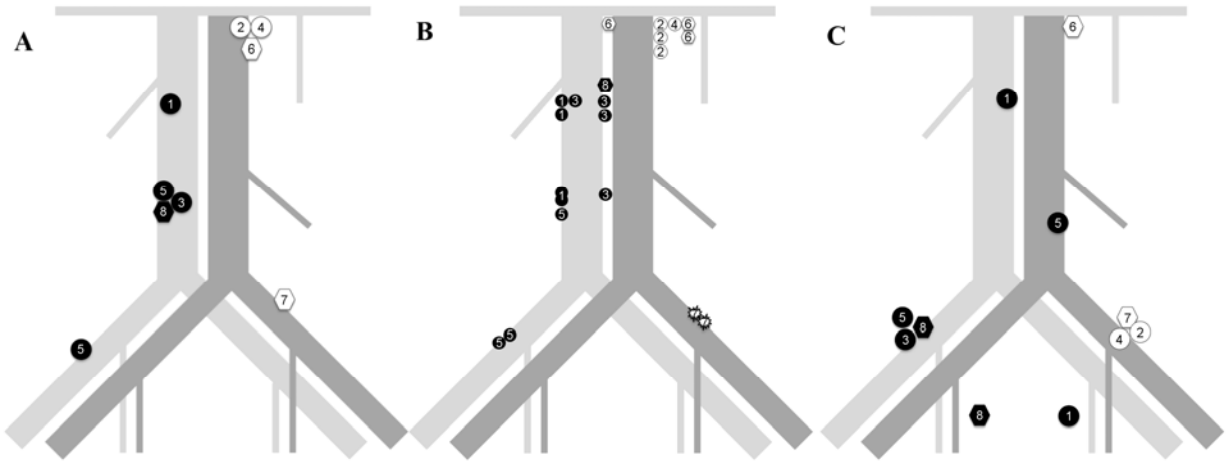

Figure 1. Detection of SNs in patients with a malignant tumor.
A) Transperitoneal detection of hotspots. B) Hotspot localizations during retroperitoneal exploration. C) Localizations of hotspots seen on SPECT-CT postoperative.

Numbers represents the study numbers given to the patients with a malignant tumor.
Black figures = patients with injection at right side; white figures = patients with injection at left side; circles = patients with ovarian cancer; hexagons = patients with endometrial cancer; stars = SNs containing metastasis.

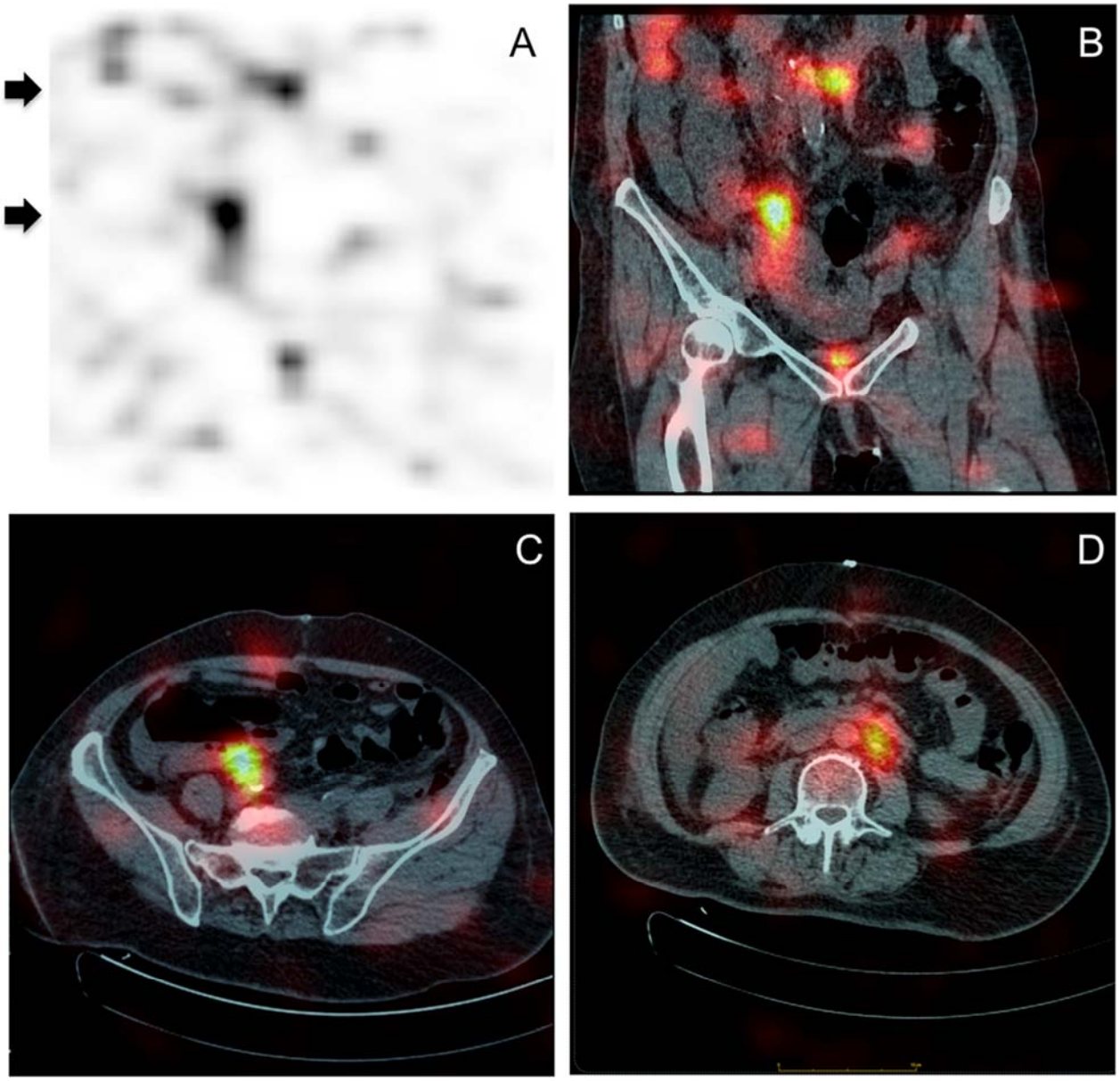

Figure 2. Example of lymphatic drainage from a right ovarian tumor (patient nr. 5) as illustrated by SPECT/CT.

Example of lymphatic drainage from a right ovarian tumor as illustrated by SPECT/CT. Upper and lower arrows on the MIP image (A) and coronal slice (B) corresponding to the respective transversal position, i.e. iliaca externa (C) and para-aortal low (D). The para-aortal lymph node in this patient was resected during operation.