Annals of Surgical Oncology **14**(9):2654–2661
DOI: 10.1245/s10434-007-9493-6

Sentinel lymph node procedure followed by laparoscopic pelvic and paraaortic lymphadenectomy in women with IB2-II cervical cancer

Vincent Lavoué, MD,[1] Anne-Sophie Bats, MD,[1] Roman Rouzier, MD, PhD,[1] Charles Coutant, MD,[1] Emmanuel Barranger, MD,[1] and Emile Daraï, MD, PhD[1,2]

[1]Service de Gynécologie-Obstétrique, Hôpital Tenon, Assistance Publique des Hôpitaux de Paris, CancerEst, Université Pierre et Marie Curie, Paris VI, France
[2]Service de Gynécologie-Obstétrique, Hôpital Tenon, 4 rue de la Chine, 75020, Paris, France

Objective: To evaluate the contribution of the sentinel node (SN) procedure followed by pelvic and paraaortic lymphadenectomy to determine lymph node status in women with locally advanced cervical cancer.
Patients and methods: A total of 21 women with locally advanced cervical cancer underwent a first laparoscopic SN procedure and pelvic and paraaortic lymphadenectomy followed by concurrent chemoradiotherapy (CCR). Laparoscopic radical hysterectomy was performed after CCR when the pelvic and paraaortic nodes were not involved.
Results: SNs were detected by means of lymphoscintigraphy in 10 women (47.6%) and intra-operatively in 14 women (66.6%). Of the latter 14 patients, 9 (64%) had an involved SN and 1 of the remaining 5 had pelvic non-SN metastases. The SN false-negative rate was 10%. At final histology, 13 of the 21 women (62%) had lymph node metastases. The total number of recovered pelvic non-SNs was 262, and 10 nodes in 8 women were involved. The total number of paraaortic non-SNs was 255, and 2 nodes in 2 women were involved.
Conclusion: This study shows the poor correlation between pre-operative lymphoscintigraphy and surgical SN mapping in women with locally advanced cervical cancer. A high proportion of women had SN metastases, underlining the importance of multiple sectioning and immunohistochemical staining of SNs.

Cervical cancer is the most common cancer in women, with 471,000 new cases and 233,000 deaths annually[1]. Despite widespread cervical screening, cervical cancer is often locally advanced at diagnosis, especially in developing countries[2,3]. Lymph node status is the main prognostic factor in cervical cancer[4]. Despite improvements in imaging techniques, including computed tomography, MRI and (18)F-fluorodeoxyglucose positron emission tomography (PET), pelvic and paraaortic lymph node status remains difficult to determine, and some authors advocate systematic lymphadenectomy[5–8].

In women with locally advanced cervical cancer, the pelvic and paraaortic lymph nodes are involved in 16–31% of cases[9,10]. Concurrent chemoradiotherapy (CCR) is the reference treatment for locally advanced cervical cancer, but this ignores lymph node status[4,11–14]. Morice et al.[15] reported on the persistence of disease-positive pelvic and paraaortic lymph nodes after radiotherapy in 22% and 12% of cases,

Received April 18, 2007; accepted May 17, 2007; published online: July 3, 2007.

Address correspondence and reprint requests to: Emile Daraï, MD, PhD; E-mail: emile.darai@tnn.aphp.fr

Published by Springer Science+Business Media, LLC © 2007 The Society of Surgical Oncology, Inc.

respectively. Recently, Houvenaeghel et al.[16] found such results in pelvic and paraaortic lymph nodes in 15.9% and 11.7% of cases, respectively, after CCR. Several other reports have suggested that the removal of lymph node metastases may have a positive impact on survival[15,17,18].

Recently, the concept of the sentinel node (SN) procedure has emerged as an alternative to systematic lymphadenectomy in women with cervical cancer[19]. SN screening can contribute to upstaging by detecting micrometastases[20]. However, there are few data on the SN procedure combined with systematic pelvic and paraaortic lymphadenectomy before CCR in women with locally advanced cervical cancer. The aims of this study were to determine the laparoscopic SN detection rate in women with locally advanced cervical cancer who subsequently underwent pelvic and paraaortic lymphadenectomy. We also correlated the results of SN screening with clinical and histological prognostic factors.

PATIENTS AND METHODS

Patients

Between July 2003 and July 2006, 43 women with locally advanced cervical cancer corresponding to FIGO (International Federation of Gynecology and Obstetrics) stage IB2 or II were referred to the gynecology unit of Tenon Hospital, France[21]. All 43 women had biopsy-proven cervical cancer and underwent pelvic MRI; 21 of them underwent a first laparoscopic SN procedure followed by pelvic and para-aortic lymphadenectomy. The other 22 women were excluded from the study—among them, 15 had first-line concomitant chemoradiotherapy after refusing laparoscopic lymphadenectomy; 4 had pelvic and paraaortic lymphadenectomy without the SN procedure; 2 had laparotomic surgery because of previous major abdominal surgery; and the last patient, an 80-year-old woman, had laparoscopic radical hysterectomy and pelvic lymphadenectomy without radiotherapy or chemotherapy. All gave their informed consent to the study before treatment. The protocol was approved by the local ethics committee.

The medical records were reviewed to determine age, body mass index (BMI), history of prior abdominal surgery, tumor stage, histology, surgical procedure, intra- and postoperative complications, and the length of hospital stay. Outcome was obtained from the outpatient records.

Technique

Sentinel node procedure

On the day before surgery, at 1500, 1800, 2100, and 2400 hours, four peritumoral injections of 0.2 ml (20 MBq each) unfiltered technetium sulfur colloid (Nanocis; CIS Bio International, Saclay, France), one in each quadrant of the cervix, were administered via a 25-gauge spinal needle. Scintigraphic images were obtained 2 h after the injections and every 30 min thereafter until the SN was visualized with a triple-head gamma camera (Irix; Marconi Corporation, Cleveland, OH)—5-min static, anterior, and lateral projections were acquired with a matrix size of 512 × 512 pixels. If the SN was not visualized on the day of the injection, imaging was repeated the next day, 2 h before surgery.

Under general anesthesia, the patients were placed in a low lithotomy position. A speculum was placed in the vagina, and patent blue (Bleu Patenté; V; Guerbet Laboratory, Issy les Moulineaux, France) was injected pericervically through a 25-gauge spinal needle at 1500 and 2100 hours (1 ml per injection). Antimicrobial chemoprophylaxis (cefazoline 2 g intravenously) was administered at the beginning of the operation. Prophylactic subcutaneous heparin was administered the day before surgery and continued for 10 days. For the laparoscopic procedure, after pneumoperitoneal insufflation using a Veress needle, a 10-mm laparoscope was inserted through an umbilical incision and connected to a video monitor. Four stab incisions were made in the suprapubic area: two of 12 mm in the suprapubic area (Versaport; Auto Suture Company, Elancourt, France) and one of 5.5 mm in each iliac fossa. Six instruments were used: unipolar and bipolar electrocautery forceps, scissors, grasping forceps, and a lavage system. Since 2006, ultracision scissors (Ethicon endo-surgery) have been used.

After patent blue injection, the pelvic and lower paraaortic regions were inspected carefully for lymph ducts and dye uptake by lymph nodes. Hot pelvic and paraaortic lymph nodes were located using an endoscopic gamma probe (Eurorad, Strasbourg, France) inserted through a 12-mm suprapubic trocar. Hot lymph nodes were sought before opening the peritoneum. The gamma probe was angled laterally to avoid detecting radioactivity at the injection site.

After locating the SN, the peritoneum was opened and each blue and/or hot lymph node was removed separately in endoscopic bags (Endocatch; Auto Suture Company, Elancourt, France). The position of each SN was recorded, relative to the major pelvic vessels, vena cava, or aorta.

After the SN procedure, systematic transperitoneal lymph node dissection extending from the external iliac (and obturator nerve) to the level of the left renal vein was performed. All lymphatic tissue was removed and extracted in an endoscopic bag. The absence of residual pelvic or paraaortic radioactivity was verified before and after pelvic and paraaortic lymphadenectomy. Iliac common lymph nodes were counted with paraaortic lymph nodes.

The duration of the laparoscopic procedure was calculated from the insertion of the Veress needle to the last skin suture.

Histology

SNs and non-SNs were inspected by a pathologist. Lymph nodes with macroscopic metastases were sectioned and normal-appearing SNs were cut perpendicular to the long axis. All SNs were submitted to intra-operative imprint cytology. Air-dried cytological smears were prepared by scraping the cut surfaces and staining with a rapid May-Grünwald-Giemsa method. Each half-SN was sectioned at 3-mm intervals, which were analyzed at four additional levels of 150 μm and four parallel sections; one was used for hematoxylin and eosin (H&E) staining, and H&E-negative sections were examined by means of immunohistochemistry (IHC) with an anticytokeratin antibody cocktail (cytokeratins AE1-AE3; Dako Corporation, Glostrup, Denmark). Non-SNs were submitted totally and blocked individually after 3-mm sectioning and H&E staining.

The size of lymph node metastases was estimated using an eyepiece micrometer. A micrometastasis was defined as a single focus of metastatic disease per lymph node, measuring no more than 2 mm. The presence of single non-cohesive tumor cells was recorded. SNs were considered positive when they contained macrometastases, micrometastases, or isolated tumor cells.

Analysis of SNs

SNs were recorded as blue-stained and/or hot (if the *in vivo* count exceeded three times the background). The false-negative rate was defined as the number of procedures with a negative SN and one or more positive non-SNs divided by the number of procedures with any positive paraaortic or pelvic lymph node.

Concurrent chemoradiotherapy

External pelvic radiation therapy was given through four orthogonal fields: antero-posterior (AT) and postero-anterior (PA), and two lateral fields. The superior limit of the AP/PA field was L4-L5 interspace. The inferior limit extended distally to the midportion of the obturator foramen or the lowest level of disease with a 3-cm margin and laterally 2 cm beyond the lateral margins of the bony pelvic wall. Superior and inferior limits of lateral fields were the same as those for the AP/PA field. The anterior limit of the lateral field was a horizontal line drawn at the anterior border of the pubic symphysis. The posterior limit of lateral field was placed at the S2-S3 interspace. Customized blocks were used to spare the anterior half of the rectum posteriorly and a proportion of the small bowel anteriorly.

Pelvic radiation therapy consisted of 40 Grays using 2.25 Gy per fraction, 4 days per week. All fields were treated daily with 15 MV. A vaginal booster dose of 20 Gy was given at 5–6 weeks by means of brachytherapy, which was performed after radical hysterectomy when uterine catheterization was no longer possible.

Concurrent chemotherapy was given during the first and fourth weeks of radiation therapy and consisted of a continuous 5-fluorouracil infusion (750 mg/m^2 per day) and a cisplatin bolus (20–25 mg/m^2 per day) 1 h before radiotherapy for days 1, 2, 4 and 5.

Laparoscopic radical hysterectomy was performed 6 weeks after the end of CCR, when the pelvic and paraaortic nodes were not involved.

For women with positive lymph nodes, an exclusive chemoradiotherapy was performed. The total dose of external radiotherapy delivered was 45 Gy with an iliac boost of 10 Gy followed by the same brachytherapy regimen. The chemotherapy protocol was the same as that previously described but was delivered on the first and the fifth weeks of irradiation.

Patients with positive aortic nodes received extended-field radiation up to the level of T12-L1. Lateral limits were set 4 cm from the midline.

Statistical analysis

Statistical analysis was based on Student's t-tests and the Mann-Whitney test for parametric and nonparametric continuous variables, respectively, and the Chi square test or Fisher's exact test, as appropriate, for categorical variables. *P* values less than 0.05 were considered to denote significant differences.

RESULTS

Epidemiological and clinical characteristics of the study population

During the study period, 21 women referred with cervical cancer underwent a SN procedure and a first laparoscopic pelvic and paraaortic lymphadenectomy before CCR. The FIGO stage was Ib2, IIa, and IIb in 6, 4, and 11 cases, respectively. The histology of the cervical tumors was determined by biopsy in 17 cases and after conization in 4 cases. The histological types were squamous cell carcinoma and adenocarcinoma in 20 cases and 1 case, respectively. The tumors were well-, moderately, and poorly differentiated in 15, 3, and 2 cases, respectively. The tumor grade was not determined on the diagnostic biopsy in 1 case.

Mean age was 48 years (range 32–75 years), and the mean BMI was 24.6 kg/m^2 (range 18.7–34.9 kg/m^2).

MR imaging showed a median tumor size of 46 mm (range 35–70 mm).

Lymphoscintigraphy

Lymphoscintigraphy showed one or several uptake foci corresponding to SNs in 10 women (47.6%), who had a mean of 1.6 SNs (range 1–2). SNs were detected bilaterally in 3 of these. All SNs were located in the pelvic region. Of the 11 women with negative lymphoscintigraphy, 3, 2 and 6 had FIGO stage Ib2, IIa, and IIb disease, respectively. No difference in the lymphoscintigraphic SN detection rate was found according to the FIGO stage. Only one woman with negative lymphoscintigraphy had diagnostic conization.

Laparoscopic SN procedure

A SN was identified in 14 women (66.6%), with a mean of 2.2 SNs per woman (range 1–4). A total of 31 SNs were removed, being blue and hot, hot alone, and blue alone in 8, 13 and 10 cases, respectively. SNs were detected bilaterally in 5 (36%) of the 14 women. The SNs were located in the obturator fossa, the external iliac area (lateral group), the interiliac area, and near the aortic bifurcation in 23 (74%), 2 (6%), 5 (17%), and 1 case (3%), respectively (Table 1). No SN was detected in the parametrium. One woman had a SN in the area of the aortic bifurcation and another 2 SNs in the right obturator fossa. None of the woman had an isolated paraaortic SN.

TABLE 1. *Location of the 31 sentinel lymph nodes.*

Site	No. of sentinel lymph nodes (%)
Obturator fossa	23 (74%)
External iliac (lateral group)	2 (6%)
Interiliac area	5 (17%)
Aortic bifurcation	1 (3%)
All	**31 (100%)**

In 7 women, no SN was detected intra-operatively. All these women had negative lymphoscintigraphy. The FIGO stage was Ib2 and IIb in 2 and 5 women, respectively.

SN detection by preoperative lymphoscintigraphy and intraoperative examination was discordant in 7 women: 2 women had no SN on lymphoscintigraphy, although at least 1 SN was detected intra-operatively; 2 women had bilateral SNs on lymphoscintigraphy, although only 1 SN was detected intra-operatively; and 3 women had a unilateral SN on lymphoscintigraphy, although bilateral SNs were detected intra-operatively.

Laparoscopic pelvic and paraaortic lymphadenectomy

Laparoscopic pelvic and paraaortic lymphadenectomy took an average of 198 min (range 150–300 min), including the SN procedure (mean 45 min). In 1 woman a bladder injury occurred, which was repaired by laparoscopic suturing. The mean number of pelvic non-SNs was 12.4 (range 5–21) and paraaortic non-SNs was 12 (range 4–25).

Histology of SNs and non-SNs

SN imprint cytology was performed intra-operatively in 14 women, in whom at least 1 SN had been previously detected, and was shown to be positive in 3. SN metastasis was diagnosed post-operatively by means of H&E staining in 9 (64%) of the all 14 women, with macrometastasis in 7 and micrometastasis in 2. All SNs that were negative by H&E staining were examined by IHC, and no additional SNs were found to be positive. In 3 patients, the SN was the only positive lymph node; 5 patients had positive pelvic SNs and non-SNs and negative paraaortic nodes; and in the remaining woman, the SN was the only positive pelvic node (macrometastasis), although this patient also had a positive paraaortic node (micrometastasis).

Of the 5 women with negative SNs, 1 had a positive non-SN. Her SN was located in the left pelvic region,

TABLE 2. *Lymph node status according to the FIGO stage.*

FIGO Stage	Total no. of patients	SN and non-SN pelvic node-positive patients	SN and non-SN paraaortic node-positive patients
Ib2	6	2	0
IIa	4	3	1 (micrometastasis)
IIb	11	8	1 (macrometastasis)
All	**21**	**13**	**2**

while the positive non-SN was located in the right pelvic region. The SN false-negative rate was 10%.

Among the 7 women with no detected SNs, 2 had positive non-SNs, one of which was in the pelvic region and the other in the pelvic and paraaortic regions.

Of the 21 women, 13 (62%) were shown to have node metastases at final histology. The total number of pelvic non-SNs was 262 (including 10 positive nodes in 8 women) and the total number of paraaortic non-SNs was 255 (including 2 positive nodes in 2 women) (Table 2).

Follow-up and determinants of recurrence

All the patients underwent concurrent chemotherapy and pelvic radiotherapy. The 2 women with positive paraaortic lymph nodes also received paraaortic irradiation.

Laparoscopic radical hysterectomy (Piver II hysterectomy) was performed in 8 women, 6 weeks after CCR. Histological examination showed residual cancer in 5 of these cases, measuring more than 1 cm in diameter in 4 cases and less than 1 cm (6 mm) in 1.

Mean follow-up was 17.3 months (range 2–36 months). At the end of the study, 17 women were alive with no signs of recurrence (Table 3). The projected overall survival rates among the 21 women are shown in Fig. 1. Four recurrences were observed a mean of 14 months after treatment (range 9–20 months). The first woman developed a common iliac node metastasis 9 months after initial laparoscopy and was treated with radiotherapy and chemotherapy. She was alive, with no evidence of disease, 6 months after diagnosis of the recurrence. The second woman had a central pelvic recurrence 20 months after initial laparoscopy. She was alive and receiving palliative chemotherapy 15 months after diagnosis of the recurrence. Neither of these women had undergone radical hysterectomy—because of pelvic node metastases in the first woman and pelvic and paraaortic node metastases in the second. The third woman had a paravertebral recurrence 12 months after initial laparoscopy and died 5 months later. The fourth developed liver metastases 14 months after initial laparoscopy and died 16 months later. These latter two women had undergone radical hysterectomy, because they were free of pelvic and paraaortic lymph node involvement.

DISCUSSION

This study shows that the SN procedure is not very helpful in a population of women with locally advanced cervical cancer and a high rate of lymph node involvement. SN detection by preoperative lymphoscintigraphy and surgical mapping correlated poorly.

The SN identification rate was only 66%, and the false-negative rate was relatively high. In previous studies of women with cervical cancer, the SN procedure with both radiocolloid and patent blue labeling identified a SN in 75–100% of patients[22–24]. However, there are few data on the SN procedure in women with locally advanced cervical cancer. A previous study also showed that the SN procedure was less accurate in advanced than in early-stage cervical cancer[22]. This could be related to the fact that advanced stages can be responsible for local lymphovascular space involvement, which can alter the diffusion of radiocolloid and/or patent blue and, hence, can be a source of underestimation of lymph node involvement. To improve SN detection rate, the use of high volumes of radiocolloid and dilution of patent blue could be used[25]. SN identification by lymphoscintigraphy correlated poorly with the number and location of SNs detected during surgery. These results are in keeping with those of a previous study of women with early-stage cervical cancer, in which pre-operative lymphoscintigraphy correlated poorly with surgical SN mapping[26]. Frumovitz et al. included women who had a second radiocolloid injection without further lymphoscintigraphy. The discordance between lymphoscintigraphic and surgical SN mapping raises questions as to the cost-effectiveness of systematic pre-operative lymphoscintigraphy.

Node status is a major prognostic factor in women with cervical cancer and influences the use of adjuvant therapy. In our study, 62% of the women had lymph node metastases, compared with only 31% of women with FIGO stage Ib2 and II disease in previous studies[9,10]. This difference could partly be due to the small size of our study population. However, despite the relatively low SN detection rate, our results underline the contribution of this technique to

TABLE 3. *Epidemiological and histological characteristics of women with and without recurrent cervical cancer. NS not significant*

Characteristics	Women without recurrence (n = 17)	Women with recurrence (n = 4)	P value
Mean age, years (range)	48.9 (32–75)	47.7 (34–46)	NS
FIGO stage			NS
Ib2	5	1	
IIa and IIb	12	3	
Histology			NS
Squamous cell carcinoma	16	4	
Adenocarcinoma	1	0	
Histological grade			NS
Well differentiated	12	3	
Moderately differentiated	4	0	
Poorly differentiated	1	1	
Tumor size (mm)			NS
< 20 mm	0	0	
20–40 mm	7	1	
> 40 mm	10	3	
Sentinel lymph node			NS
Women with positive sentinel lymph node	7	2	
Pelvic lymph node			NS
Women with positive pelvic lymph node	11	2	
Women with positive paraaortic lymph node	1	1	NS
Women undergoing radical hysterectomy	6	2	
Women with residue on radical hysterectomy	3	2	
Women with paraaortic radiotherapy	1	1	

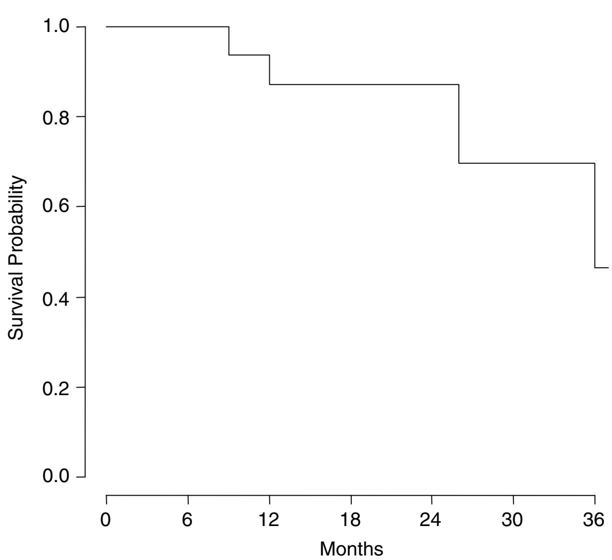

FIG. 1. Projected overall survival of the 21 women

lymph node upstaging when combined with systematic multiple node sectioning and immunohistochemistry.

Most metastatic nodes detected in our study were located in the pelvic region, and only 2 of the 21 women showed paraaortic node involvement. As a result, only 2 women required irradiation of the paraaortic region. Combining a first laparoscopic pelvic and paraaortic lymphadenectomy with the SN procedure has the advantage of allowing radiotherapy to be adapted to lymph node status; this avoids the need for systematic paraaortic radiotherapy, which would have been unnecessary in 90% of our patients. Hacker et al. found that debulking lymph node metastasis before radiotherapy improved disease control[17]. Dargent et al.[27] detected pelvic node involvement in 40% of women when lymphadenectomy was performed before radiotherapy, and 17.6% after radiotherapy, showing the limited efficacy of radiotherapy for sterilizing nodal metastases. Likewise, Morice et al.[15] detected disease-positive pelvic and paraaortic lymph nodes in 22% and 12% of cases, respectively, after radiotherapy. Finally, after CCR followed by laparoscopic lymphadenectomy, Houvenaeghel et al.[16] detected positive pelvic and paraaortic lymph nodes in 15.9% and 11.7% of cases, respectively.

The therapeutic and prognostic relevance of systematic pelvic and paraaortic lymphadenectomy is controversial in women with advanced-stage cervical cancer. Using a mathematical model, Kupets et al.[28] found that the benefit of lymph node debulking in women with FIGO stage Ib, IIb, and IIIb disease was only 1, 2, and 4%, respectively. However, Hacker et al.[17] reported a 3-year survival rate of 66% after removal of positive paraaortic lymph nodes. In a series of 266 women, Cosin et al.[18] found that survival after removal of macrometastases was similar to that after removal of micrometastases. Morice et al.[15] reported that pelvic control, disease-free survival, and overall survival increased after debulking of pelvic and paraaortic lymph node metastasis. Recently, Houvenaeghel et al.[29] reported that laparoscopic removal of positive paraaortic lymph nodes was associated with an improvement in survival. Finally, in a large series, Marnitz et al.[30] stated that debulking of involved lymph nodes significantly improved overall survival and should be performed prior to primary chemoradiation. In contrast, Lai et al.[31] found that survival was worse after laparoscopic staging than after clinical staging. However, these unexpected results could be due to intergroup differences in the proportion of women with advanced-stage disease and/or in the interval before adjuvant therapy.

The approach to lymphadenectomy is controversial. One experimental study[32] showed that the extraperitoneal route to paraaortic lymphadenectomy was associated with a reduction in adhesions and post-radiotherapy morbidity. However, this approach does not permit the evaluation of pelvic lymph nodes and carries a risk of lymphocele, necessitating routine preventive peritoneal fenestration[33]. We chose to use transperitoneal lymphadenectomy, which provides access to both the pelvic and para-aortic regions. This choice was endorsed by the high rate of pelvic lymph node positivity. Transperitoneal laparoscopic pelvic and paraaortic lymphadenectomy were used by Marnitz et al.[30], but complete pelvic lymphadenectomy was not always performed, and they reported that women with positive paraaortic nodes and fewer than 5 nodes removed had poorer 5-year survival than those who had more than 5 nodes removed. These results raise the question of how many nodes must be removed for a lymphadenectomy procedure to be considered representative. The mean number of paraaortic lymph nodes removed by the transperitoneal route in our study was 14, a number similar to that obtained using the retroperitoneal approach in previous studies[33].

Further surgery after CCR carries a risk of complications and is therefore controversial[34]. MRI and PET scan have a limited capacity to detect small tumor residues. In our study, 5 of the 8 women who underwent radical hysterectomy after CCR had a cervical tumor residue. Our results are in keeping with those of Houvenaeghel et al. who found that 7 of 20 women with FIGO stage Ib or II cervical cancer had a residual tumor after CCR. Moreover, Keys et al.[35] demonstrated that hysterectomy increased significantly free-recurrence survival. Finally, using multivariate analysis, Rouzier et al.[36] found that the recurrence rate was directly related to the FIGO stage, lymph node status, and the presence of residual tumor tissue. In women with early-stage cervical cancer treated by initial surgery, a previous study showed that Piver type-II radical hysterectomy was associated with less morbidity than Piver type-III surgery, without compromising survival[37]. Regarding locally advanced cervical cancer treated by first CCR, further trials are required to identify women who require additional surgery, and also to choose between radical and simple hysterectomy.

In conclusion, despite the small size and retrospective nature of this study, our results suggest that the SN procedure is not well suited for assessing lymph node status in women with locally advanced cervical cancer. However, when determined, SN status improved the assessment of lymph node status, probably because of the use of multiple sectioning and systematic immunohistochemical analysis. Moreover, initial laparoscopic pelvic and paraaortic lymphadenectomy allows adjuvant radiotherapy to be tailored to lymph node status. Finally, the high rate of residual tumors raises questions as to the indications and modalities of hysterectomy after CCR.

ACKNOWLEDGEMENTS

We thank Alain Toledano and Emmanuel Touboul (Department of radiotherapy) for their contribution to the manuscript.

REFERENCES

1. Parkin DM. Global cancer statistics in the year 2000. *Lancet Oncol* 2001; 2(9):533–543.
2. Abed Z, O'Leary M, Hand K, et al. Cervical screening history in patients with early stage carcinoma of the cervix. *Ir Med J* 2006; 100(1):140–142.
3. Miller AB. Quality assurance in screening strategies. *Virus Res* 2002; 89(2):295–299.
4. Green JA, Kirwan JM, Tierney JF, et al. Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and meta-analysis. *Lancet* 2001; 358(9284):781–786.
5. Lin WC, Hung YC, Yeh LS, Kao CH, Yen RF, Shen YY. Usefulness of (18)F-fluorodeoxyglucose positron emission tomography to detect para-aortic lymph nodal metastasis in advanced cervical cancer with negative computed tomography findings. *Gynecol Oncol* 2003; 89(1):73–76.
6. Yeh LS, Hung YC, Shen YY, Kao CH, Lin CC, Lee CC. Detecting para-aortic lymph nodal metastasis by positron emission tomography of 18F-fluorodeoxyglucose in advanced cervical cancer with negative magnetic resonance imaging findings. *Oncol Rep* 2002; 9(6):1289–1292.
7. Rose PG, Adler LP, Rodriguez M, Faulhaber PF, Abdul-Karim FW, Miraldi F. Positron emission tomography for evaluating para-aortic nodal metastasis in locally advanced

cervical cancer before surgical staging: a surgicopathologic study. *J Clin Oncol* 1999; 17(1):41–45.
8. Choi HJ, Roh JW, Seo SS, et al. Comparison of the accuracy of magnetic resonance imaging and positron emission tomography/computed tomography in the presurgical detection of lymph node metastases in patients with uterine cervical carcinoma: a prospective study. *Cancer* 2006; 106(4):914–922.
9. Landoni F, Maneo A, Colombo A, et al. Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. *Lancet* 1997; 350(9077):535–540.
10. Michel G, Morice P, Castaigne D, Leblanc M, Rey A, Duvillard P. Lymphatic spread in stage Ib and II cervical carcinoma: anatomy and surgical implications. *Obstet Gynecol* 1998; 91(3):360–363.
11. Rose PG, Bundy BN, Watkins EB, et al. Concurrent cisplatin-based radiotherapy and chemotherapy for locally advanced cervical cancer. *N Engl J Med* 1999; 340(15):1144–1153.
12. Tewfik HH, Buchsbaum HJ, Latourette HB, Lifshitz SG, Tewfik FA. Para-aortic lymph node irradiation in carcinoma of the cervix after exploratory laparotomy and biopsy-proven positive aortic nodes. *Int J Radiat Oncol Biol Phys* 1982; 8(1):13–18.
13. Greer BE, Koh WJ, Stelzer KJ, Goff BA, Comsia N, Tran A. Expanded pelvic radiotherapy fields for treatment of local-regionally advanced carcinoma of the cervix: outcome and complications. *Am J Obstet Gynecol* 1996; 174(4):1141–1150.
14. Malfetano JH, Keys H, Cunningham MJ, Gibbons S, Ambros R. Extended field radiation and cisplatin for stage IIB and IIIB cervical carcinoma. *Gynecol Oncol* 1997; 67(2):203–207.
15. Morice P, Castaigne D, Pautier P, et al. Interest of pelvic and paraaortic lymphadenectomy in patients with stage IB and II cervical carcinoma. *Gynecol Oncol* 1999; 73(1):106–110.
16. Houvenaeghel G, Lelievre L, Rigouard AL, et al. Residual pelvic lymph node involvement after concomitant chemoradiation for locally advanced cervical cancer. *Gynecol Oncol* 2006; 102(1):74–79.
17. Hacker NF, Wain GV, Nicklin JL. Resection of bulky positive lymph nodes in patients with cervical carcinoma. *Int J Gynecol Cancer* 1995; 5(4):250–256.
18. Cosin JA, Fowler JM, Chen MD, Paley PJ, Carson LF, Twiggs LB. Pretreatment surgical staging of patients with cervical carcinoma: the case for lymph node debulking. *Cancer* 1998; 82(11):2241–2248.
19. Barranger E, Grahek D, Cortez A, Talbot JN, Uzan S, Darai E. Laparoscopic sentinel lymph node procedure using a combination of patent blue and radioisotope in women with cervical carcinoma. *Cancer* 2003; 97(12):3003–3009.
20. Yabushita H, Shimazu M, Yamada H, et al. Occult lymph node metastases detected by cytokeratin immunohistochemistry predict recurrence in node-negative endometrial cancer. *Gynecol Oncol* 2001; 80(2):139–144.
21. Changes in definitions of clinical staging for carcinoma of the cervix and ovary: International Federation of Gynecology and Obstetrics. Am J Obstet Gynecol 1987; 156(1):263–264.
22. Barranger E, Coutant C, Cortez A, Uzan S, Darai E. Sentinel node biopsy is reliable in early-stage cervical cancer but not in locally advanced disease. *Ann Oncol* 2005; 16(8):1237–1242.
23. Lambaudie E, Collinet P, Narducci F, et al. Laparoscopic identification of sentinel lymph nodes in early stage cervical cancer: prospective study using a combination of patent blue dye injection and technetium radiocolloid injection. *Gynecol Oncol* 2003; 89(1):84–87.
24. Plante M, Renaud MC, Tetu B, Harel F, Roy M. Laparoscopic sentinel node mapping in early-stage cervical cancer. *Gynecol Oncol* 2003; 91(3):494–503.
25. Altgassen C, Paseka A, Urbanczyk H, et al. Dilution of dye improves parametrial SLN detection in patients with cervical cancer. *Gynecol Oncol* 2007; 105(2):329–334.
26. Frumovitz M, Coleman RL, Gayed IW, et al. Usefulness of preoperative lymphoscintigraphy in patients who undergo radical hysterectomy and pelvic lymphadenectomy for cervical cancer. *Am J Obstet Gynecol* 2006; 194(4):1186–1195.
27. Dargent D, Lamblin G, Romestaing P, Montbarbon X, Mathevet P, Benchaib M. a retrospective analysis of two comparative series. *Int J Gynecol Cancer* 2005; 15(3):468–474.
28. Kupets R, Thomas GM, Covens A. Is there a role for pelvic lymph node debulking in advanced cervical cancer?. *Gynecol Oncol* 2002; 87(2):163–170.
29. Houvenaeghel G, Lelievre L, Gonzague-Casabianca L, et al. Long-term survival after concomitant chemoradiotherapy prior to surgery in advanced cervical carcinoma. *Gynecol Oncol* 2006; 100(2):338–343.
30. Marnitz S, Kohler C, Roth C, Fuller J, Hinkelbein W, Schneider A. Is there a benefit of pretreatment laparoscopic transperitoneal surgical staging in patients with advanced cervical cancer?. *Gynecol Oncol* 2005; 99(3):536–544.
31. Lai CH, Huang KG, Hong JH, et al. Randomized trial of surgical staging (extraperitoneal or laparoscopic) versus clinical staging in locally advanced cervical cancer. *Gynecol Oncol* 2003; 89(1):160–167.
32. Occelli B, Narducci F, Lanvin D, et al. [Comparison of transperitoneal versus extraperitoneal laparoscopic para-aortic lymphadenectomy: randomized experimental study]. *Ann Chir* 2000; 125(1):9–17.
33. Sonoda Y, Leblanc E, Querleu D, et al. Prospective evaluation of surgical staging of advanced cervical cancer via a laparoscopic extraperitoneal approach. *Gynecol Oncol* 2003; 91(2):326–331.
34. Classe JM, Rauch P, Rodier JF, et al. Surgery after concurrent chemoradiotherapy and brachytherapy for the treatment of advanced cervical cancer: morbidity and outcome: results of a multicenter study of the GCCLCC (Groupe des Chirurgiens de Centre de Lutte Contre le Cancer). *Gynecol Oncol* 2006; 102(3):523–529.
35. Keys HM, Bundy BN, Stehman FB, et al. Radiation therapy with and without extrafascial hysterectomy for bulky stage IB cervical carcinoma: a randomized trial of the Gynecologic Oncology Group. *Gynecol Oncol* 2003; 89(3):343–353.
36. Rouzier R, Morice P, De Crevoisier R, et al. Survival in cervix cancer patients treated with radiotherapy followed by radical surgery. *Eur J Surg Oncol* 2005; 31(4):424–433.
37. Landoni F, Maneo A, Cormio G, et al. Class II versus class III radical hysterectomy in stage IB-IIA cervical cancer: a prospective randomized study. *Gynecol Oncol* 2001; 80(1):3–12.