# The Role of Completion Surgery After Concurrent Radiochemotherapy in Locally Advanced Stages IB2-IIB Cervical Cancer

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**Abstract.** *Background: The gold standard for treating patients with locally advanced stages of cervical cancer is concurrent radiochemotherapy (CRT), but recent studies have failed to demonstrate the effect of completion surgery on survival. The aim of this study was to evaluate the role of completion surgery in stage IB2-IIB cervical cancer. Patients and Methods: From 2002 to 2012, 80 women (stage IB2-IIB disease) underwent a pre-therapeutic pelvic and para-aortic lymphadenectomy associated with CRT. Results: Forty-six patients (57.5%) underwent completion surgery. Multivariate analysis identified pelvic lymph node status as a predictive factor for completion surgery (p<0.001) and histological type for tumor residue (p=0.04). In multivariate analysis, positivity of para-aortic nodes (p=0.01 for DFS and p=0.01 for OS) and emboli on completion hysterectomy (p=0.03 for DFS and p=0.006 for OS) were significant. Conclusion: Only patients without para-aortic metastases or limited pelvic involvement and with residual disease and emboli seem to be good candidates for completion surgery.*

The gold standard for treating patients with locally advanced stages of cervical cancer is concurrent radiochemotherapy (CRT). In a multicentre study including 1243 patients with locally advanced stages of cervical cancer, taking age, stage, pelvic node involvement and treatment delay into account, Vale *et al*. (1) showed by Cox regression that survival was significantly better for patients receiving CRT (hazard ratio, HR=0.77, 95% confidence interval, CI=0.60-0.98; $p$=0.037) compared with those receiving radiotherapy alone. Moreover, a recent meta-analysis including 13 trials confirmed that CRT improves 5-year survival by 6% (HR=0.81, $p$<0.001) compared with the same radiotherapy regimen (2). However, this meta-analysis failed to demonstrate the impact of completion surgery.

In a multivariate analysis, Ferrandina *et al*. showed that residual tumor and disease stage were the two most relevant prognostic factors for disease-free (DFS) and overall (OS) survival (3). However, despite advances in imaging techniques including computed tomography (CT), magnetic resonance imaging (RMI) and positron emission tomography (PET), it remains difficult to detect residual cervical disease in order to identify good candidates for completion surgery. Moreover, Touboul *et al*. suggested that the morbidity of completion surgery based on hysterectomy with or without lymphadenectomy is high in patients treated with initial CRT for locally advanced cervical cancer whereas the therapeutic value of such surgery remains unproven (4). In contrast, Houvenaeghel *et al*. found that combining CRT with curative surgery increased survival by reducing the risk of local relapse (5). This apparent discrepancy between series could be explained by the inclusion of a large spectrum of locally advanced stages of cervical cancer from stage IB2 to stage IV and modalities of radiotherapy.

Therefore, the aim of the present retrospective study was to evaluate the role of completion surgery in patients with locally advanced stages of cervical cancer (IB2-IIB) treated by pre-therapeutic pelvic and para-aortic lymphadenectomy followed by CRT.

## Patients and Methods

*Patients*. From 2002 to 2012, 80 women with locally advanced cervical cancer corresponding to 1988 International Federation of Gynecology and Obstetrics (FIGO) stage IB2 or II underwent a pre-therapeutic pelvic and para-aortic lymphadenectomy by laparoscopy in the gynecology unit of Tenon Hospital, France (6-8). All the

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women had biopsy-proven cervical cancer and had undergone pelvic MRI prior to surgery.

All the women gave informed written consent to the therapeutic procedures and to the analysis of data related to their malignancy in accordance with institutional guidelines and the Declaration of Helsinki. The protocol was approved by the local Ethics Committee.

The medical records were reviewed to determine age, the body mass index (BMI), tumor stage, histology, tumor size on MRI, surgical procedure, intra- and postoperative complications, and the final pelvic and para-aortic node status. Moreover, we recorded the type of completion hysterectomy, morbidity and presence of residual disease in the uterine cervix. We compared patient characteristics according to completion surgery and residual disease. Outcome was obtained from the outpatient records.

The predictive factors for DFS and OS were analyzed by univariate and multivariate analysis to provide survival data. Survival between groups according to completion surgery, residual disease and histological type was evaluated.

*Surgical procedure*. Systematic transperitoneal laparoscopic lymph node dissection extending from the external iliac (and obturator nerve) to the level of the left renal vein was performed.

*CRT*. External pelvic radiation therapy was given through four orthogonal fields: antero-posterior (AT) and postero-anterior (PA), and two lateral fields. Pelvic radiation therapy consisted of 40 Gy using 2.25 Gy per fraction, four days a week. All fields were treated daily with 15 megavoltage units. A vaginal booster dose of 20 Gy was given at 5-6 weeks by means of brachytherapy. Brachytherapy was performed after radical hysterectomy when uterine catherization was impossible.

CRT was given during the first and fourth weeks of radiotherapy and consisted of a continuous 5-fluorouracil infusion (750 mg/m$^2$/day), and a cisplatin bolus (20-25 mg/m$^2$/day) one hour before radiotherapy, on days 1, 2, 4 and 5.

When the pelvic and para-aortic nodes were not involved, completion surgery was performed six weeks after the end of CRT. Postoperative complications of completion surgery were classified according to Memorial Sloan-Kettering Cancer Center (MSKCC) (9).

Women with disease positive lymph node involvement underwent exclusive CRT regimen. For these women, 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 but delivered the first and the fifth week of irradiation.

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

*Statistical analysis*. Data were analyzed using the Chi-square test or the Fisher's exact test and the Student's *t*-test. Differences were considered significant when $p<0.05$. We used the Kaplan–Meier product limit method to describe OS and DFS, and the log-rank test to assess differences between patient groups. Survival was studied according to the completion surgery, residual disease and histological type. The multivariate survival analysis was performed using a Cox proportional hazard model. A value of $p<0.05$ was considered to denote a significant difference. All analyses were performed using the R package with the Design, Hmisc, and Survival libraries (http://lib.stat.cmu.edu/R/CRAN).

Table I. *Epidemiological and surgical characteristics of patients with stage IB2-IIB cervical cancer.*

| Characteristic | Patients (n=80) |
|---|---|
| Mean age, years (range) | 46 (28-78) |
| Post-menopausal patients | 33 (41.2%) |
| Mean body mass index, Kg/m$^2$ (range) | 23.6 (16.8-35.0) |
| Mean tumor size on MRI, mm (range) | 45.3 (12-80) |
| Tumor histology, n(%) | |
| Squamous cell carcinoma | 68 (85%) |
| Adenocarcinoma | 12 (15%) |
| FIGO classification, n (%) | |
| IB2 | 19 (23.8%) |
| IIA | 9 (11.2%) |
| IIB | 52 (65%) |
| Pre-therapeutic pelvic and para-aortic lymphadenectomy, n (%) | 100% |
| Positive pelvic nodes | 36 (45%) |
| Positive paraaortic nodes | 7 (8.7%) |
| Hysterectomy after CRT, n (%) | 46 (57.5%) |
| Simple hysterectomy | 32 (40%) |
| Radical hysterectomy | 14 (17.5%) |
| Residual disease on hysterectomy, n (%) | 19 (41.3%) |
| Mean size of residue, mm (range) | 12.15 (1-35) |

CRT: Concurrent radiochemotherapy, FIGO: International Federation of Gynecology and Obstetrics.

## Results

*Epidemiological and surgical characteristics*. The mean tumor size was 45.3 (range: 12-80) mm. Eighty-five percent of the patients had a squamous cell carcinoma. More than half of the patients had a moderately or poorly differentiated carcinoma and 65% had FIGO stage IIB disease (Table I).

All 80 patients underwent both laparoscopic pelvic and para-aortic lymphadenectomy and went on to have CRT and brachytherapy. Two out of the 80 patients required a conversion to laparotomy due to anesthetic disorders related to hypoventilation in one case and for ureteral injury requiring a ureter reimplantation in the other. Forty-six out of the 80 patients underwent a simple or radical hysterectomy after CRT in 32 and 14 cases, respectively. Among them, two patients had primary laparotomy and all the others were managed by laparoscopy, with two conversions in laparotomy.

*Final lymph node status*. Among the 39 patients (48.7%) with disease positive nodes, 10.3% of them had both pelvic and para-aortic positive nodes, 82% only pelvic positive nodes and 7.7% isolated para-aortic positive nodes.

Table II. *Comparison of epidemiological and surgical characteristics of patients with and without completion surgery after concurrent radiochemotherapy.*

| | No completion surgery (n=34) | Completion surgery (n=46) | *p*-value |
|---|---|---|---|
| Mean age, years | 51.06 | 48.8 | 0.41 |
| Mean body mass index, Kg/m$^2$ | 23.43 | 22.82 | 0.18 |
| Mean tumor size on MRI, mm | 45.48 | 45.46 | 0.99 |
| Tumor histology, n (%) | | | |
| Squamous cell carcinoma | 29 (85.3%) | 39 (84.8%) | >0.99 |
| Adenocarcinoma | 5 (14.7%) | 7 (15.2%) | |
| FIGO classification, n (%) | | | |
| IB2 | 4 (11.8%) | 15 (32.6%) | 0.14 |
| IIA | 5 (14.7%) | 4 (8.7%) | |
| IIB | 25 (73.5%) | 27 (58.7%) | |
| Pre-therapeutic pelvic and para-aortic lymphadenectomy, n (%) | | | |
| Positive pelvic nodes | 27 (79.4%) | 9 (19.6%) | <0.001 |
| Positive paraaortic nodes | 5 (14.7%) | 2 (4.3%) | 0.11 |

Table III. *Comparison of epidemiological and surgical characteristics of patients with and without residual disease on completion surgery after concurrent chemoradiotherapy.*

| | No residual disease (n=27) | Residual disease (n=19) | p-value |
|---|---|---|---|
| Mean age, years | 49.24 | 47.84 | 0.66 |
| Mean body mass index, Kg/m$^2$ | 23.16 | 22.65 | 0.83 |
| Mean tumor size on MRI, mm | 45.08 | 46.26 | 0.78 |
| Tumor Histology, n (%) | | | |
| Squamous cell carcinoma | 27 (100%) | 12 (63.2%) | |
| 0.0004 | | | |
| Adenocarcinoma | 0 (0%) | 7 (36.8%) | |
| Emboli, n (%) | 1 (3.7%) | 6 (31.6%) | 0.03 |
| FIGO classification, n (%) | | | |
| IB2 | 7 (25.9%) | 8 (42.1%) | 0.20 |
| IIA | 4 (14.8%) | 0 (0%) | |
| IIB | 16 (59.3%) | 11 (57.9%) | |
| Pre-therapeutic pelvic and para-aortic lymphadenectomy, n (%) | | | |
| Positive pelvic nodes | 6 (22.2%) | 3 (15.8%) | 0.70 |
| Positive paraaortic nodes | 1 (3.7%) | 1 (5.3%) | >0.99 |

*Comparison of epidemiological and surgical characteristics of patients with or without completion surgery*. Patients who underwent completion hysterectomy were often negative for pelvic lymph nodes ($p<0.001$). Multivariate analysis found the only predictive factor for completion of surgery to be pelvic lymph node status ($p<0.001$) (Table II).

Three out of the 14 women undergoing a radical hysterectomy after CRT experienced a grade 4 complication by MSKCC including one pelvic abscess requiring a Hartman operation, one ureteral fistula requiring a ureteral reimplantation and one bilateral ureteral stenosis requiring an ileal conduit with ureteroileostomy. None of the 32 patients undergoing simple hysterectomy experienced grade 4 MSKCC complication ($p=0.03$).

*Comparison of epidemiological and surgical characteristics of patients with and without residual disease*. Histological residues were found in 19 cases (41.3%) among the 46 patients who underwent completion surgery. The mean size of residual disease was 12.1 mm (1-35 mm). Patients with histological tumor residue on completion hysterectomy did not differ from those without residue for age, mean tumor size on MRI, FIGO stage and pelvic or para-aortic node status. Significant differences in univariate analysis were the histological type: patients with adenocarcinoma of the cervix experienced more residues on completion surgery ($p<0.001$) and the presence of emboli on completion hysterectomy ($p=0.03$). In multivariate analysis, histological type remained significant ($p=0.04$) (Table III).

*DFS and OS*. The median follow up was 30.7 months (4.2-100.3) months. Twelve out of the 80 patients (15%) experienced disease relapse including three centropelvic recurrences (two of which occurred in patients without hysterectomy), three peritoneal carcinomatosis, one common iliac and one para aortic node recurrence, one parietal recurrence and three cases of visceral metastasis (lung and liver). The five-year DFS was 77% and the five-year OS was 75%. Univariable analysis for DFS and OS found that significant factors were the positivity of para-aortic nodes ($p<0.001$ and $p<0.0001$), the presence of emboli on completion hysterectomy ($p=0.0002$ and $p<0.0001$) and the size of the tumoral residue ($p=0.005$ and $p=0.02$) for DFS and OS respectively. In multivariate analysis, positivity of para-aortic nodes ($p=0.01$ for DFS and $p=0.01$ for OS), emboli on completion hysterectomy ($p=0.03$ for DFS and $p=0.006$ for OS) and the size of tumoral residue ($p=0.09$ for OS) remained significant (Figure 1).

Patient DFS and OS were compared for three groups: those with residual disease or not on hysterectomy, those who underwent completion surgery or not, and histological type (epidermoïd carcinoma or adenocarcinoma). Regarding the presence or the absence of a residual disease on completion hysterectomy, no significant difference was found for DFS ($p=0.27$) nor for OS ($p=0.09$). Nevertheless, OS seems to be worse in cases of residue. Regarding whether completion surgery had been performed or not, no difference was found for DFS ($p=0.75$) nor for OS ($p=0.92$). The same findings were true for histological type ($p=0.70$ for DFS and $p=0.94$ for OS).

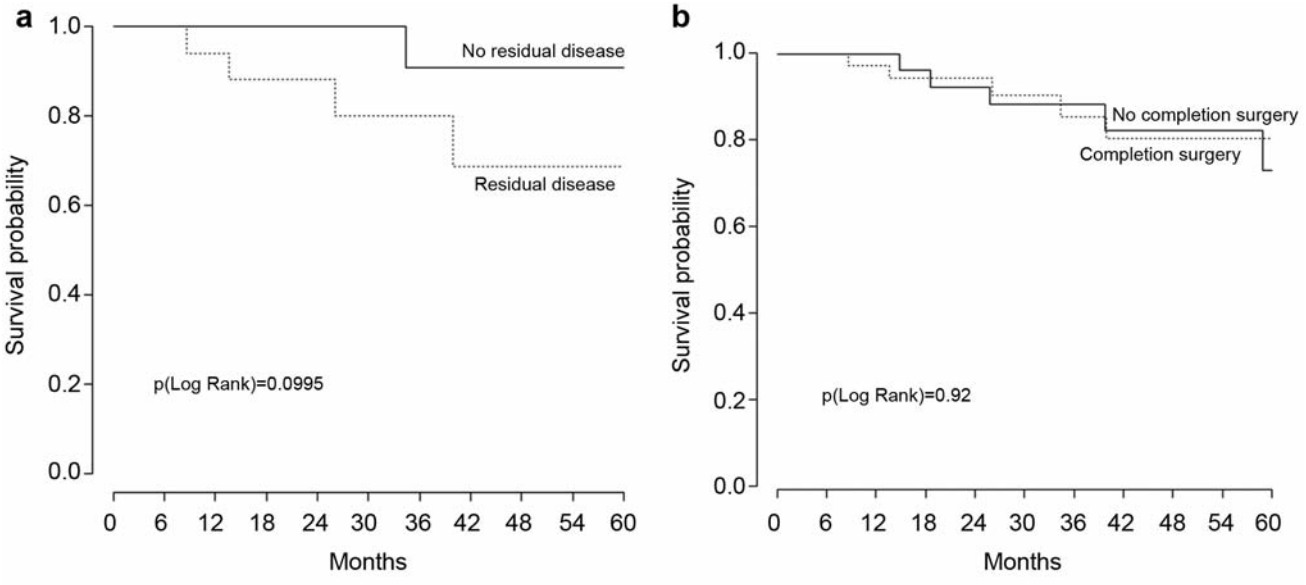


Figure 1. *Overall Survival according to residual disease on hysterectomy after CRC (a) or performance of completion surgery (b).*

## Discussion

*Impact of completion surgery on survival*. A debate exists on the relevance of completion surgery after CRT in women with locally advanced stages of cervical cancer: on one hand the positive impact on survival and on the other, the risk of surgical complications. Hence, it is important to identify good candidates that could benefit from completion surgery. In our study, the rate of complete response was significantly lower in patients with cervical adenocarcinomas, while age, tumor size, stage of disease and clinical response did not correlate with complete pathological response. Our results could be explained by the small sample size but also by the characteristics of the population. Indeed, only patients with stage IB2 to IIB were included in our study, while most other authors include patients with stage IB2 to IVA under the term locally advanced cervical cancers (4, 5). Moreover, clinical response appeared to be of little relevance in selecting patients for completion surgery as most of our patients exhibited microscopic residual disease. In multivariate analysis, Ferrandina *et al*. demonstrated that clinical response, stage of disease, and histological type predicted response to CRT (3). Patients with no residual disease had a significantly longer DFS than patients with microscopic ($p$=0.01), and macroscopic ($p$=0.0001) residual tumor. These results are in agreement with those of other authors supporting the notion that complete pathological response to CRT is a surrogate endpoint of OS (4, 10, 11). In our study, 41.3% of patients exhibited residual disease after CRT. These results are in agreement with those of previous studies showing that complete pathological response is obtained in only 40% to 60% of patients with locally advanced stages of cervical cancer. This brings into question the efficacy of completion surgery on reducing the risk of local recurrence (4-5). One recent report confirmed a decrease in both the incidence of local recurrence and the relative risk of disease progression or death (HR=0.41, 95%CI=0.20-0.85) in favor of completion surgery, although no impact on OS was observed (12).

*Impact of complete pathological response*. Other parameters have been evaluated to determine complete pathological response with a view to selecting patients for completion surgery. In addition to clinical response, Kirova *et al*. found that normalization of squamous cell carcinoma antigen (SCCA) levels after CRT was an independent predictor of complete pathological response, suggesting that women with abnormal SCCA levels would be good candidates for completion surgery (13). These results are in agreement with those of Ferrandina *et al*. (14) showing that the SCCA level identified patients with locally advanced cervical cancer with a poor chance of pathological response to CRT and an unfavorable outcome, and that the lack of pathological complete response to persistence of microscopic foci on CRT retained an independent negative prognostic role for DFS. However, Hirakawa *et al*. demonstrated that positive serum SCCA immediately after CRT was a predictive factor for distant

recurrence (15), suggesting that these patients would benefit more from adjuvant therapy rather than completion surgery.

Another parameter important in deciding on completion surgery is the assessment of residual tumor after CRT. A study using MRI evaluation of residual disease three to eight weeks after CRT underlined the high risk of false-positive results (16,17). However, these authors suggested that better results could be obtained by adding diffusion-weighted MRI to conventional MRI sequences. The contribution of PET in cervical cancer has been also evaluated (18). A SUV max of primary cervical tumor greater than 5.3 has been identified as an inde¬pendent factor of poor prognostic (19) and post-treatment metabolic response was predictive of both cause-specific and progression-free survival after CRT. In a preliminary study, Yoshida *et al*. found that PET could be used to assess the response to treatment of cervical cancer (20). Therefore, there is a need for additional data to identify good candidates for completion surgery.

Another tool for selecting patients for completion surgery would be based on individual parameters. Using predictor variables including age, SCCA level, tumor size, parametrial invasion, hydronephrosis, bladder/rectal invasion, and lymph node metastasis in a Cox regression model, Tseng *et al*. built a nomogram for predicting the 5-year OS, with a concordance index of 0.69 (21). However, the discriminatory ability of the nomogram indicates that this population cannot be considered homogeneous with respect to risk of death and that it requires external validation. Finally, as in the study of Tseng *et al*. (21), prognostic factors for OS in the multivariate analysis were the presence and level of nodal spread (disease positive pelvic nodes alone: HR=2.03; positive para-aortic nodes: HR=5.46; $p<0.001$) (4). Therefore, completion surgery should be restricted to patients without para-aortic lymph node metastases or those limited to pelvic areas.

*Surgical morbidity of completion surgery*. Other issues on completion surgery include the type of surgery and the risk of complication. In our study, the overall rate of grade 4 postoperative complications by MSKCC was higher after radical than simple hysterectomy (0% for simple hysterectomy *vs*. 21% for radical hysterectomy). Ferrandina *et al*. (3) reported an overall rate of surgical complications of 33% after radical hysterectomy, with 10% of patients experiencing severe toxicities. Our complication rate is similar to that reported by Touboul *et al*. (4), affecting up to 25% of patients, and was significantly higher after radical than simple hysterectomy. Moreover, Motton *et al*. found that OS and DFS were not better after radical than after simple hysterectomy (22). Therefore, when completion surgery is indicated, the best option would appear to be a simple hysterectomy.

*Limitations of the study*. Some limitations of the current study have to be underlined. Firstly, the retrospective nature of the study cannot avoid bias. However, only one prospective study is available on completion surgery after CRT in locally advanced stages of cervical cancer but unfortunately this trial was closed because of poor accrual (23). The results of this phase III trial comparing hysterectomy with no hysterectomy in patients with a complete (clinical and radiological) response after chemoradiation therapy for stage IB2 or II cervical cancer failed to demonstrate any benefit of completion surgery. Secondly, although only patients with a low incidence of lymph node metastases underwent completion surgery, we failed to demonstrate a positive impact on survival, probably linked to sample size.

## Conclusion

Our results support the feasibility of completion surgery (simple hysterectomy should be preferred to radical hysterectomy) after CRT in patients with stage IB2-IIB cervical cancer by laparoscopy, with acceptable morbidity, although only patients without para-aortic metastases or limited pelvic involvement and patients with residual disease and emboli on completion surgery. Despite advances in imaging techniques, the impossibility of adequately evaluating residual disease after CRT makes it necessary to focus on individual identification of predictive factors of survival (nomogram) to select patients who might benefit from completion surgery to limit local recurrence. Moreover, studies on precise molecular characteristics of cervical cancer remain needed for a better understanding and characterization of cervical cancer prognosis and therapeutic management.

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## References

1 Vale CL, Tierney JF, Davidson SE, Drinkwater KJ and Symonds P: Substantial improvement in UK cervical cancer survival with chemoradiotherapy: results of a Royal College of Radiologists' audit. Clin Oncol (R Coll Radiol) *22(7)*: 590-601, 2010.

2 Chemoradiotherapy for Cervical Cancer Meta-analysis Collaboration (CCCMAC). Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: individual patient data meta-analysis. Cochrane Database Syst Rev *20;(1)*: CD008285, 2010.

3 Ferrandina G, Margariti PA, Smaniotto D, Petrillo M, Salerno MG, Fagotti A, Macchia G, Morganti AG, Cellini N and Scambia G: Long-term analysis of clinical outcome and complications in locally advanced cervical cancer patients administered concomitant chemoradiation followed by radical surgery. Gynecol Oncol *119(3)*: 404-410, 2010.

4 Touboul C, Uzan C, Mauguen A, Gouy S, Rey A, Pautier P, Lhommé C, Duvillard P, Haie-Meder C and Morice P: Prognostic factors and morbidities after completion surgery in patients undergoing initial chemoradiation therapy for locally advanced cervical cancer. Oncologist *15(4)*: 405-415, 2010.

5 Carcopino X, Houvenaeghel G, Buttarelli M, Esterni B, Tallet A, Goncalves A and Jacquemier J: Equivalent survival in patients with advanced stage IB-II and III-IVA cervical cancer treated by adjuvant surgery following chemoradiotherapy. Eur J Surg Oncol *34(5)*: 569-575, 2008.

6 Barranger E, Grahek D, Cortez A, Talbot JN, Uzan S and Darai E: Laparoscopic sentinel lymph node procedure using a combination of patent blue and radioisotope in women with cervical carcinoma. Cancer *15;97(12)*: 3003-3009, 2003.

7 Barranger E, Cortez A, Commo F, Marpeau O, Uzan S, Darai E and Callard P: Histopathological validation of the sentinel node concept in cervical cancer. Ann Oncol *15(6)*: 870-874, 2004.

8 Barranger E, Cortez A, Uzan S, Callard P and Darai E: Value of intraoperative imprint cytology of sentinel nodes in patients with cervical cancer. Gynecol Oncol *94(1)*: 175-180, 2004.

9 Chi DS, Franklin CC, Levine DA, Akselrod F, Sabbatini P, Jarnagin WR, DeMatteo R, Poynor EA, Abu-Rustum NR and Barakat RR: Improved optimal cytoreduction rates for stages IIIC and IV epithelial ovarian, fallopian tube, and primary peritoneal cancer: a change in surgical approach. Gynecol Oncol *94(3)*: 650-654, 2004.

10 Gadducci A, Teti G, Barsotti C, Tana R, Fanucchi A, Orlandini C, Fabrini MG and Genazzani AR: Clinicopathological variables predictive of clinical outcome in patients with FIGO stage Ib2-IIb cervical cancer treated with cisplatin-based neoadjuvant chemotherapy followed by radical hysterectomy. Anticancer Res *30(1)*: 201-v8, 2010.

11 Colombo PE, Bertrand MM, Gutowski M, Mourregot A, Fabbro M, Saint-Aubert B, Quenet F, Gourgou S, Kerr C and Rouanet P: Total laparoscopic radical hysterectomy for locally advanced cervical carcinoma (stages IIB, IIA and bulky stages IB) after concurrent chemoradiation therapy: surgical morbidity and oncological results. Gynecol Oncol *114(3)*: 404-409, 2009.

12 Léguevaque P, Motton S, Delannes M, Querleu D, Soulé-Tholy M, Tap G and Houvenaeghel G: Completion surgery or not after concurrent chemoradiotherapy for locally advanced cervical cancer? Eur J Obstet Gynecol Reprod Biol *155(2)*: 188-192, 2011.

13 Kirova YM, Bourhaleb Z, Alran S, Campitelli M, Plancher C, Fourchotte V, Beuzeboc P, Petrow P, Cottu P, de Cremoux P, Sastre-Garau X and de la Rochefordière A: Preoperative concomitant radiochemotherapy in bulky carcinoma of the cervix: Institut Curie experience. Cancer Radiother *13(4)*: 291-297, 2009.

14 Ferrandina G, Macchia G, Legge F, Deodato F, Forni F, Digesé C, Carone V, Morganti AG and Scambia G: Squamous cell carcinoma antigen in patients with locally advanced cervical carcinoma undergoing preoperative radiochemotherapy association with pathological response to treatment and clinical outcome. Oncology *74(1-2)*: 42-49, 2008.

15 Hirakawa M, Nagai Y, Inamine M, Kamiyama K, Ogawa K, Toita T, Murayama S and Aoki Y: Predictive factor of distant recurrence in locally advanced squamous cell carcinoma of the cervix treated with concurrent chemoradiotherapy. Gynecol Oncol *108(1)*: 126-129, 2008.

16 Vincens E, Balleyguier C, Rey A, Uzan C, Zareski E, Gouy S, Pautier P, Duvillard P, Haie-Meder C and Morice P: Accuracy of magnetic resonance imaging in predicting residual disease in patients treated for stage IB2/II cervical carcinoma with chemoradiation therapy : correlation of radiologic findings with surgicopathologic results. Cancer *15;113(8)*: 2158-2165, 2008.

17 Thomassin-Naggara I, Fournier LS, Roussel A, Marsault C and Bazot M: Diffusion-weighted MR imaging of the female pelvis. J Radiol *91(3 Pt 2)*: 431-438; quiz 439-440, 2010.

18 Lai CH and Yen TC: When and how often should PET scans be performed in the management of cervical cancer? Expert Rev Anticancer Ther *10(7)*: 983-986, 2010.

19 Chou HH, Chang HP, Lai CH, Ng KK, Hsueh S, Wu TI, Chen MY, Yen TC, Hong JH and Chang TC: (18)F-FDG PET in stage IB/IIB cervical adenocarcinoma/adenosquamous carcinoma. Eur J Nucl Med Mol Imaging *37(4)*: 728-735, 2010.

20 Yoshida Y, Kurokawa T, Kawahara K, Yagihara A, Tsuchida T, Okazawa H, Fujibayashi Y, Yonekura Y and Kotsuji F: Metabolic monitoring of advanced uterine cervical cancer neoadjuvant chemotherapy by using [F-18]-Fluorodeoxyglucose positron emission tomography: preliminary results in three patients. Gynecol Oncol *95(3)*: 597-602, 2004.

21 Tseng JY, Yen MS, Twu NF, Lai CR, Horng HC, Tseng CC, Chao KC and Juang CM: Prognostic nomogram for overall survival in stage IIB-IVA cervical cancer patients treated with concurrent chemoradiotherapy. Am J Obstet Gynecol *202(2)*: 174.e1-7, 2010.

22 Motton S, Houvenaeghel G, Delannes M, Querleu D, Soulé-Tholy M, Hoff J and Léguevaque P: Results of surgery after concurrent chemoradiotherapy in advanced cervical cancer: comparison of extended hysterectomy and extrafascial hysterectomy. Int J Gynecol Cancer. 20(2):268-75, 2010.

23 Morice P, Rouanet P, Rey A, Romestaing P, Houvenaeghel G, Boulanger JC, Leveque J, Cowen D, Mathevet P, Malhaire JP, Magnin G, Fondrinier E, Berille J and Haie-Meder C: Results of the GYNECO 02 study, an FNCLCC phase III trial comparing hysterectomy with no hysterectomy in patients with a (clinical and radiological) complete response after chemoradiation therapy for stage IB2 or II cervical cancer. Oncologist *17(1)*: 64-71, 2012.

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