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## Laparoscopic hysterectomy after concurrent radiochemotherapy in locally advanced cervical cancer compared to laparotomy: a multi institutional prospective pilot study of cost, surgical outcome and quality of life

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35 The authors report no conflict of interest.

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16    All authors made substantial contributions to the concept and design or analysis and  
17    interpretation of the data. All authors participated in drafting and reviewing the manuscript.

18

1 • **Abstract**

2 **Objective:** Laparoscopy allows hysterectomies after chemoradiation to be performed  
3 without opening the abdominal wall. We measured the costs and quality of life for locally  
4 advanced cervical cancer patients operated on via laparoscopy compared to laparotomy.

5 **Study design:** We conducted an observational prospective multicenter study on locally  
6 advanced cervical cancer patients undergoing an extrafascial hysterectomy after concurrent  
7 chemoradiotherapy (CRT). We assessed the costs from the medical visit before surgery up  
8 to the first month after surgery from the providers' perspective and measured the quality of  
9 life using the EORTC QLQ-C30 and QLQ-CX24 up to six months.

10 **Results:** 62 patients (39 laparoscopy and 23 laparotomy) from December 2008 to November  
11 2011 were included. There was no difference in operative time, or intraoperative and  
12 postoperative complication rates between the two groups. Intraoperative transfusion and  
13 abdominal drain were significantly lower in the laparoscopy group (respectively,  $p=0.04$  and  
14  $p<0.01$ ), as well as the duration of hospital stay (7.3 d vs 5.7 d,  $p<0.001$ ). All patients who  
15 underwent laparoscopic hysterectomy were discharged to home, whereas 4 laparotomy  
16 patients used convalescence homes ( $p=0.01$ ). Mean costs at one month were €10,991 for  
17 laparotomy and €11,267 for laparoscopy ( $p=0.76$ ). Sexual activity is better for the  
18 laparoscopy group at six months ( $p=0.01$ ).

19 **Conclusion:** Laparoscopy for an extrafascial hysterectomy after CRT in locally advanced  
20 cervical cancer patients brought better quality of life with similar costs compared to  
21 laparotomy, and should therefore be the first choice for surgeons.

22

23 • **Key words:** Advanced cervical cancer, cost comparison, laparotomy, laparoscopy,  
24 quality of life, laparoscopic hysterectomy

## 1 Introduction

2 Cervical cancer is the second most frequent cancer in women, with approximately 500,000  
3 new cases diagnosed, and 270,000 deaths annually worldwide<sup>1-2</sup>. Although the incidence of  
4 cervical cancer has decreased in industrialized countries because of screening programs and  
5 progress in management of intraepithelial lesions, 60% of cases are at advanced stages at  
6 diagnosis. In France, the estimation of new cases in 2015 is 3,060, with the highest incidence  
7 among women in their 40s, leading to nearly 1,070 deaths and a 5-year survival rate of 17.2%  
8 in advanced stages<sup>3-4</sup>.

9 The gold standard for treating patients with locally advanced cervical cancer (LACC) is  
10 concurrent chemoradiotherapy with or without brachytherapy (CRT)<sup>5-6</sup>. Significant survival  
11 advantages of chemoradiation in cases of LACC, have been demonstrated in a meta-analysis<sup>7</sup>.

12 The value of completion surgery after CRT in LACC however, still remains debatable<sup>8-11</sup>, and  
13 few studies are available<sup>12-13</sup>. Furthermore, hysterectomy after CRT remains a questionable  
14 treatment option, in particular in cases of partial response. Results from multicenter studies  
15 have demonstrated that residual disease after concurrent chemoradiation therapy and  
16 brachytherapy impact on disease free survival<sup>14-16</sup>. Because the accuracy of imaging  
17 techniques are not sufficient to measure residual disease<sup>17-18</sup>, surgery remains the current  
18 practice in many countries. Furthermore, completion surgery reduces residual pathological  
19 disease, which represents an important prognostic factor<sup>19-23</sup>.

20 We previously assessed the consequences of hysterectomy by laparotomy after CRT and  
21 brachytherapy, and showed a high rate of grade 2/3 morbidity (26%), particularly due to  
22 urinary complications<sup>14</sup>. The feasibility and consequences of laparoscopic hysterectomy after  
23 RCT for LACC have not been sufficiently assessed. In a retrospective series of 102 patients,  
24 Colombo et al<sup>24</sup>. studied 56 laparoscopic hysterectomies over a period of 8 years. The

1 question arises as to whether this intervention improves the quality of life of these patients,  
2 and the efficiency cost and surgical outcome. A comparison of laparoscopy to laparotomy in  
3 terms of surgical outcome, cost and quality of life has not been prospectively assessed in the  
4 context of surgery after CRT in LACC. The treatment of cervical cancer is expensive and is  
5 estimated to total 44 million Euros annually in France, corresponding to a mean patient cost  
6 of €22,697 for stage III to €6,886 for stage V disease<sup>25</sup>.

7 Our study was aimed at assessing the benefit of laparoscopy, in terms of cost, surgical  
8 outcome and quality of life.

9

## 10 **Materials and methods**

### 11 *Study design and patient details*

12 Between December 2008 and November 2011, 62 consecutive patients (39 laparoscopy and  
13 23 laparotomy) from 13 French institutions were included in a prospective multicenter  
14 comparative observational non-randomized study.

15 Inclusion criteria were invasive cervical cancer proven by a core biopsy before treatment,  
16 stage IB2, and IIA, IIB (proximal), M0, preoperative external platinum based  
17 radiochemotherapy, +/- utero-vaginal brachytherapy, and extrafascial hysterectomy (+/-  
18 lymphadenectomy, pelvic and latero aortic), via laparoscopy or laparotomy, with the  
19 feasibility of a one year follow-up. The choice of the surgical approach was at the discretion  
20 of the surgeon. Each surgeon used one of the two techniques. Surgeons trained in laparoscopy  
21 performed laparoscopic extrafascial hysterectomy, plus lymphadenectomy, whilst surgeons  
22 less trained in laparoscopy performed these procedure by laparotomy. Observational study is  
23 more suitable to capture current practice in a real-world situation.

1 Hysterectomy was proposed in cases when tumor residual at the end of the treatment was  
2 suspected.

3 Initial staging was defined according to the International Federation of Gynecology and  
4 Obstetrics (FIGO) staging system. Staging was performed using a clinical pelvic examination,  
5 Magnetic Resonance Imaging (MRI), and Computed Tomography (CT).

6 *Treatment:*

7 All patients received radiochemotherapy. Concomitant Cisplatin (CDDP) was given on the  
8 first day of each week of radiotherapy. Laparoscopic surgical staging of lymph node  
9 involvement, pelvic and/or aortic, was initially undertaken to set the field of external  
10 radiotherapy in some teams, in others it was a radiological stadification. Radiation therapy  
11 was administered at 1.8 Gy in 22 to 25 fractions according to international  
12 recommendations<sup>26</sup>.

13 Surgery consisted of an extrafascial hysterectomy. Patients undergoing a laparoscopy were  
14 positioned in the Trendelenburg position, and a 0°-laparoscope (10-mm umbilicus trocar) and  
15 three 5-mm trocars (left and right iliac fossa and upper pubic region) were inserted. The  
16 abdominal pressure was maintained at 12 mm Hg. Laparotomies were performed using a  
17 Pfannenstiel transverse incision or a midline incision.

18 Post-operative follow-up occurred from surgery to one month later, and included the hospital  
19 stay, and a first post-operative visit.

20 *Studied parameters*

21 Studied parameters were baseline demographic information (age, Performance Status Score,  
22 Body Mass Index), tumor characteristic (histology, initial tumor size determined clinically  
23 and by MRI before initiation of treatment, FIGO staging, nodal disease status), preoperative  
24 treatments (surgery for node staging, CRT, radiotherapy, brachytherapy), treatment response

1 (pathological results, tumor size) and complications according to the Chassagne glossary<sup>27</sup>.  
2 Economic data included the treatment modality, resources consumed, including mean  
3 personnel time, conversion to laparotomy and its causes, hospitalization, complications, and  
4 annual follow-up. We used the cancer QLQ-C30 version 3.0 from EORTC which is a quality  
5 of life instrument for use in international clinical trial in oncology and the EORTC QLQ-  
6 CX24 module which is dedicated to patients with cervical cancer and validated by the  
7 European Organization for research and Treatment of cancer. Quality of life was evaluated  
8 using a patient self-completed survey sent by post at four time periods, before surgery (T0),  
9 one week after surgery at the first visit (T1), and one (T2) and six months post-surgery  
10 (T3))<sup>28-29</sup>. Questionnaires were sent by prepaid envelopes to the Institut Curie (within 8 days  
11 with respect to T1, T2, or T3).

12 This study contained no modifications of standard practice in each institution, and informed  
13 consent was not required. It was approved by the regional ethical committee (Authorization n°  
14 908075).

### 15 *Economic assessment*

16 We conducted our analysis from the hospital provider's perspective. The direct costs  
17 associated with surgical strategies (laparoscopy or laparotomy) were taken into account in a  
18 prospective manner, from the medical visit prior to surgery up to the first month after surgery  
19 using unit costs. Costs of complications during hospitalization, costs of re-intervention for  
20 complications, and costs associated with longer hospitalization were also considered. The  
21 time period covered, 30 +/-5 days from surgery, allowed all important and relevant  
22 consequences and costs between two strategies to be measured and compared. Cost  
23 computation focused on inpatient follow-up care and the rehabilitation unit. The hospital  
24 provider perspectives included hospital stay in the Medicine, Surgery, Obstetrics (MSO) unit



1 and follow-up care in the rehabilitation unit. In France, hospital care settings include  
2 conventional hospital in charge of an MSO, post-acute care and convalescence homing.  
3 Hospital provider perspectives include the hospital care setting in a global care pathway.  
4 Cost calculations were made with the micro-costing method obtained from detailed  
5 observations, for all patients included in the study and quantities of consumable resources.  
6 The following consumable resources, linked to surgery, are counted and quantified for each  
7 patient, from economic items integrated into the case report form, and per center through the  
8 center survey as specific devices and annual activities. Direct costs include different surgery  
9 techniques, pathology requirements, supplies, depreciation for equipment, hospital stay,  
10 medical visits and surgical costs. Depreciation of the laparoscopic video System is included in  
11 the direct costs, and is proportional to the time of use in surgery. Depreciation costs were  
12 calculated based on a five-year straight-line depreciation. Costs are presented in Euros in  
13 2010. A sensitivity analysis was performed to assess the potential effects of uncertainty  
14 inherent in the study.

### 15 *Statistical analysis*

16 Cost comparisons were measured using a student's t-test, a Mann-Whitney test or an analysis  
17 of variance (ANOVA), and are reported as the mean  $\pm$  standard deviation. Tests for  
18 normality were carried out using a Kolmogorov-Smirnov test. Socio-demographic  
19 characteristics, clinical information and all categorical variables were compared using a Chi-  
20 square test or a Fisher's exact test. All tests were two-sided with a significant level of 5%.  
21 Data was analyzed using the SAS system software (version 9.2, SAS Institute Inc.).

### 22 **Results**

23 A flow chart of the study population is shown in Figure 1. Patient characteristics are presented  
24 in Table 1. The two groups were not statistically different except for cancer staging (FIGO)

1 and previous surgical histories. Patients in the laparotomy group had a more locally advanced  
2 disease and more previous abdominal surgery. Pathological results are presented in Table 2.

### 3 *Preoperative treatment*

4 Twenty-two patients in the laparotomy group (95.6%) and 38 patients in the laparoscopy  
5 group (95%) underwent brachytherapy. Completion radiotherapy after surgery was carried out  
6 for only one patient in each group and was related to residual lymph node disease.  
7 Complications related to pretreatment were the same in the two groups (7/23 (30.4%) in  
8 laparotomy vs 12/39 (30.7%) in laparoscopy,  $p=1.00$ ).

### 9 *Surgery*

10 Surgical characteristics are summarized in Table 3. Intraoperative transfusion was significantly  
11 lower in the laparoscopy group ( $p=0.04$ ). Similarly, abdominal drain was significantly lower  
12 in the laparoscopy group compared to the laparotomy group (78.3% vs. 7.5%,  $p<0.001$ ).  
13 Urinary catheterization did not differ between the two groups (23/23 vs 38/39,  $p=1.00$ ) like  
14 duration of urinary catheterization ( $4.5 \pm 1.4$  d vs  $3.9 \pm 1.9$  d,  $p=0.07$ ). The time between the  
15 end of prior therapy and the surgery is on average within 6 to 8 weeks.

16 Although the length of induction of anesthesia as well as the length of incision was  
17 significantly higher in the laparoscopy group (respectively, 37.6 min vs 29.4 min,  $p=0.03$  and  
18 168 min vs 210 min,  $p=0.04$ ), the overall mean operative time did not differ significantly  
19 between the two groups (258 min vs. 294 min,  $p=0.06$ ) (Table 3). In the laparoscopy group,  
20 three patients (3/39, 7.5%) had to be switched to the laparotomy group due to technical  
21 requirements, and all three had a previous history of abdominal surgery and brachytherapy  
22 before hysterectomy.

23 Intraoperative and postoperative complications are detailed in Table 4. Complications leading  
24 to re-hospitalization and/or re-intervention are presented in Table 5. Two patients in the

1 laparoscopic group required re-operation for post-operative intraperitoneal abscesses and  
2 post-operative bowel obstruction secondary to adhesion. There were no post-operative deaths  
3 within 30 days after surgery in either group.

#### 4 *Cost at one-month*

5 Resources used for each phase of the procedures are presented in Table 5, and detailed costs  
6 in Table 6. The direct cost of each procedure was not statistically different at one month:  
7 €10,991 ( $\sigma=3616$ ) for laparotomy versus €11,267 ( $\sigma=4237$ ) for laparoscopy,  $p=0.76$ .

8 Hospital stays for patients were significantly lower in the laparoscopy group (8.3 d vs 6.7 d,  
9  $p<0.001$ ). Post-hospital stay in a convalescence home was required for 17.4% (4/23) of the  
10 patients after laparotomy (21, 23, 24 and 30 days respectively), but was not required for any  
11 patients in the laparoscopy group who return home after surgery. The one-month follow-up  
12 step includes the additional cost convalescence for the laparotomy group, while all patients in  
13 laparoscopy group have hospital discharge at home. The one-month follow-up step results in  
14 significantly lower costs for the laparoscopic group compared to the laparotomy group (€29  
15 vs. €1,739,  $p=0.05$ ).

16 The extra costs of three conversions reached €18,157 ( $\sigma=€11,944$ ) per converted patient  
17 (min=11,131, max=31,949). The difference in cost between the two procedures was not  
18 significant, even if the 3 cases of conversion were not included in the analysis ( $p=0.96$ ).

19

#### 20 *Quality of life up to 6 months*

21 Assessment of quality of life using EORTC QLQ-C30 at one week after surgery was better  
22 for patients having undergone laparoscopy compared to laparotomy. At one month, global  
23 health and quality of life, physical functioning and role functioning were better in the  
24 laparoscopy group (respectively  $p=0.01$ ,  $p=0.01$ ,  $p=0.05$ ). At six months, the measurable

1 benefits remained for patients who underwent laparoscopy, in particular they experienced less  
2 fatigue than patients who underwent laparotomy ( $p=0.04$ ). Using the specific cervical cancer  
3 questionnaire, CX24, only sexual activity was significantly better at six months for the  
4 laparoscopy group ( $p=0.01$ ).

## 5 **Discussion**

6 Our prospective multicenter study compared the feasibility of laparoscopic versus laparotomic  
7 hysterectomy after CRT in LACC. Whilst these procedures had equal hospital costs at one  
8 month, the quality of life was considerably better for the laparoscopy patients.

### 9 *Medical outcome and quality of life*

10 Few studies have assessed the clinical outcomes and complications of hysterectomy after  
11 CRT in LACC. Colombo PE *et al.*<sup>24</sup>, included 56 laparoscopy patients after RCC over a 8  
12 year period, and Chereau E *et al.*<sup>8</sup>, studied 42 laparoscopy patients over a 10 year period.

13 Regarding complications, our study revealed no major intraoperative, early postoperative, or  
14 late postoperative complications within 30 days in the two groups. In the retrospective cohort,  
15 of Colombo PE *et al.*<sup>24</sup>, morbidity rates and urinary complications were significantly reduced  
16 in the laparoscopy group compared to the laparotomy group for radical hysterectomy and not  
17 simple extrafascial hysterectomy. Other recent published studies showed total laparoscopic  
18 radical surgery is feasible in patients with LACC receiving preoperative CT/RT.<sup>30-31</sup>

19 As expected, from a patient perspective, hysterectomy by laparoscopy after concurrent  
20 radiochemotherapy with or without brachytherapy seems to result in better quality of life  
21 compared to open surgery. We measured the quality of life for a cohort of 62 patients over a  
22 six-month follow-up period. Radical pelvic surgery via laparotomy and chemoradiation are  
23 associated with a significant impairment of sexual function in cervical cancer patients<sup>32-33</sup>. We

1 observed a clinically relevant improvement in the overall quality of life and sexual function  
2 scores which was significantly better at six months for the laparoscopy group. This  
3 information can be used to guide medical decision making, and highlights that surgical  
4 approaches should always be tailored to minimize the negative impact of surgery.

#### 5 *Cost evaluation*

6 Using the *microcosting* method, our prospective series demonstrated that laparoscopy hospital  
7 costs were not significantly different at one month compared to the open procedure. The  
8 longer length of operating time, the costly single-use consumables, equipment and materials  
9 used for laparoscopy and the extra cost of conversion (failure of laparoscopy) are offset by a  
10 shorter length of stay and a reduction in the use of a convalescence home following  
11 hospitalization.

12 Existing publications report heterogeneous data for the type of surgery, types of cost  
13 components and inclusion criteria. No costs studies using the *microcosting* method with a one  
14 month follow up after surgery have been previously reported. Dennis et al.<sup>34</sup> found that the  
15 cost for radical hysterectomy was highest for robotic, followed by standard laparoscopy, and  
16 lowest for laparotomy. In our study, only surgical and anesthetic instrumentations have been  
17 included in the cost calculation; the cost calculation did not include staff costs, hospital stay,  
18 follow-up, or resources pertaining to medical data acquisition.

19 Wright et al.<sup>35</sup> found that both laparoscopic and robotic radical hysterectomies were  
20 associated with lower transfusion requirements and shorter hospital stays than abdominal  
21 hysterectomy ( $p < 0.05$ ). However, they did not use a prospective and observational design,  
22 and did not report direct per-patient costs. In their study, costs were estimated using a national  
23 database, which is less powerful for comparing population sub-groups or for matching  
24 economic data to clinical outcomes at the individual patient level. Observational studies

1 provide accurate and detailed information on health care consumption at an individual patient  
2 level. Significantly, such data allow modeling studies of healthcare costs to be refined, and  
3 are critical in guiding decision-making with regard to healthcare resource allocation.

4 The length of stay for patients undergoing laparoscopy in our cohort was longer than the  
5 average length reported in the literature for other countries, such as in USA for example. Bell  
6 et al.<sup>36</sup> in 2008 reported an average length of stay of 2 +/- 1.2 days for laparoscopy in the  
7 USA, while Lachance et al.<sup>37</sup> reported a 4 day stay for patients undergoing hysterectomy in  
8 the USA. Wright et al.<sup>35</sup> reported a median length of stay of 3 days for abdominal radical  
9 hysterectomy, and 2 days for laparoscopic surgery in the USA. This could be explained by the  
10 differences in national health care and reimbursement systems. In the past few years, trends in  
11 France are to reduce the length of stay. In France, Colombo PE et al.<sup>24</sup>, reported a 5 day  
12 hospital stay after laparoscopy versus 8 days for laparotomy.

13 Once the relevant range of costs has been identified, the individual items must be measured  
14 and valued. The level of accuracy of cost studies is determined by the identification of cost  
15 components, (gross costing and/or microcosting) and valuation of cost components (top-down  
16 and/or bottom-up costing). In the *microcosting* approach, all relevant cost components are  
17 defined at the most detailed level and in the bottom-up approach. Cost components are valued  
18 by identifying resources used directly for a patient, resulting in patient specific unit costs.<sup>36</sup>  
19 Our study used the combination of *microcosting* and the bottom-up costing approach, which  
20 is generally believed to be the gold standard methodology for the costing of healthcare  
21 services.

22 This reporting care pathway with a one-month follow-up including transitional care such as  
23 rehabilitation makes our study original and relevant. Rehabilitation care represents an  
24 important potential benefit for minimally invasive surgery as it represents a large and relevant

1 cost component. Our analysis was conducted from the hospital provider perspective,  
2 including inpatient hospitalization in MSO and stays in follow-up and rehabilitation care.

3 One limitation of our study is the small sample size, which is common to many similar studies  
4 in this specific field. Ferrandina et al.<sup>20</sup> included 174 patients over a ten year period, Colombo  
5 et al.<sup>24</sup>, 102 patients over 8 years (including 56 laparoscopies), and Chereau et al.<sup>8</sup> 80 patients  
6 over 10 years (including 42 laparoscopies). Another limitation is that our study was non-  
7 randomized. However, even if randomized studies represent the standard practice in clinical  
8 research, our observational study describes current treatment in representative centers. These  
9 issues had to be raised in our conclusion. Compared to previously published studies using  
10 retrospective data in single institutions or databases, our study is prospective, consecutive and  
11 multi institutional. We provide more comprehensive and accurate individual and primary data  
12 per patient, in a setting that is relevant to current treatment protocols.

13  
14 Laparoscopic radical hysterectomy after radiochemotherapy for the treatment of LACC is  
15 feasible, results in lower intraoperative transfusion and abdominal drain interventions, a  
16 shorter hospital stay, less convalescent time, and results in a better quality of life with similar  
17 costs at one-month compared to laparotomy. For these reasons, when hysterectomy is  
18 indicated for the treatment of LACC after chemoradiation and brachytherapy, the  
19 laparoscopic approach must be the first choice.

20

21

22

## 1   **References**

- 2   **1.** Parkin DM and Bray F (2006) Chapter 2: The burden of HPV-related cancers. *Vaccine 24 S3 S11-*  
3    25.
- 4   **2.** Munoz N, Castellsague X, de Gonzalez AB et al. (2006) Chapter 1: HPV in the etiology of human  
5    cancer. *Vaccine 24 S3 S1-S10*.
- 6   **3.** Institut National de Veille Sanitaire. Les cancers en France en 2013. Collection état des lieux et  
7    des connaissances, ouvrage collectif édité par l'INCa, Boulogne-Billancourt, janvier 2014.  
8    [[www.e-cancer.fr/component/.../11505-les-cancers-en-france-edition-2013](http://www.e-cancer.fr/component/.../11505-les-cancers-en-france-edition-2013)]
- 9   **4.** Institut National de Veille Sanitaire. Données épidémiologiques sur le cancer du col de l'utérus –  
10    Etat des connaissances – Actualisation 2008 – InVS.  
11    [[http://invs.sante.fr/publications/2008/cancer\\_col\\_uterus\\_2008/cancer\\_col\\_uterus\\_2008.pdf](http://invs.sante.fr/publications/2008/cancer_col_uterus_2008/cancer_col_uterus_2008.pdf)]
- 12   **5.** McNeil C. New standard of care for cervical cancer sets stage for next questions. *J Natl Cancer*  
13    Inst. 1999;91:500-1.
- 14   **6.** Whitney CW, Sause W, Bundy BN, et al. Randomized comparison of fluorouracil plus cisplatin  
15    versus hydroxyurea as an adjunct to radiation therapy in stage IIB-IVA carcinoma of the cervix  
16    with negative para-aortic lymph nodes: a Gynecologic Oncology Group and Southwest Oncology  
17    Group study. *J Clin Oncol.* 1999 May;17(5):1339-48.
- 18   **7.** Green J, Kirwan J, Tierney J, et al. Concomitant chemotherapy and radiation therapy for cancer of  
19    the uterine cervix. *Cochrane Database Syst Rev.* 2005
- 20   **8.** Chereau E, De La Hossery C, Ballester M, et al. The role of completion surgery after  
21    concurrent radiochemotherapy in locally advanced stages IB2-IIB cervical cancer. *Anticancer Res.*  
22    2013 ;33:1661-6.
- 23   **9.** Ferrandina G, Ercoli A, Fagotti A, et al. Completion surgery after concomitant chemoradiation in  
24    locally advanced cervical cancer: a comprehensive analysis of pattern of postoperative  
25    complications. *Ann Surg Oncol.* 2014 May;21(5):1692-9.



- 1 **10.** Sun L, Sheng X, Jiang J, et al. Surgical morbidity and oncologic results after concurrent  
2 chemoradiation therapy for advanced cervical cancer. *Int J Gynecologic Obstet.* 2014  
3 May;125(2):111-5.
- 4 **11.** Favero G, Pierobon J, Genta ML, et al. Laparoscopic extrafascial hysterectomy (completion  
5 surgery) after primary chemoradiation in patients with locally advanced cervical cancer: technical  
6 aspects and operative outcomes. *Int J Gynecol Cancer.* 2014 Mar;24(3):608-
- 7 **12.** Houvenaeghel G, Lelievre L, Gonzague-Casabianca L, et al. Long-term survival after concomitant  
8 chemoradiotherapy prior to surgery in advanced cervical carcinoma. *Gynecol Oncol.* 2006  
9 Feb;100(2):338-43.
- 10 **13.** Delpech Y, Haie-Meder C, Rey A, et al. Para-aortic involvement and interest of para-aortic  
11 lymphadenectomy after chemoradiation therapy in patients with stage IB2 and II cervical  
12 carcinoma radiologically confined to the pelvic cavity. *Ann Surg Oncol.* 2007 Nov;14(11):3223-  
13 31
- 14 **14.** Classe JM, Rauch P, Rodier JF et al. Surgery after concurrent chemoradiotherapy and  
15 brachytherapy for the treatment of advanced cervical cancer: morbidity and outcome: results of a  
16 multicenter study of the GCCLCC (Groupe des Chirurgiens de Centre de Lutte Contre le  
17 Cancer). *Gynecol Oncol.* 2006;102(3):523-9.
- 18 **15.** Hequet D, Marchand E, Place V, Fourchette V, De La Rochefordière A, Dridi S, Coutant C,  
19 Lecuru F, Bats AS, Koskas M, Bretel JJ, Bricou A, Delpech Y, Barranger E. Evaluation and  
20 impact of residual disease in locally advanced cervical cancer after concurrent chemoradiation  
21 therapy: results of a multicenter study. *Eur J Surg Oncol.* 2013 Dec;39(12):1428-34.
- 22 **16.** Poujade O, Morice P, Rouzier R, et al. Pathologic response rate after concomitant neo-adjuvant  
23 radiotherapy and chemotherapy for adenocarcinoma of the uterine cervix: a retrospective  
24 multicentric study. *Int J Gynecol Cancer.* 2010 Jul;20(5):815-20
- 25 **17.** Ferrandina G, Petrillo M, Restaino G, et al. Can radicality of surgery be safely modulated on the  
26 basis of MRI and PET/CT imaging in locally advanced cervical cancer patients administered  
27 preoperative treatment? *Cancer.* 2012;118:392-403.

- 1 **18.** Vincens E, Balleyguier C, Rey A, et al. Accuracy of magnetic resonance imaging in predicting  
2 residual disease in patients treated for stage IB2/II cervical carcinoma with chemoradiation  
3 therapy : correlation of radiologic findings with surgicopathologic results. *Cancer*. 2008;113:2158  
4 -65.
- 5 **19.** Fanfani F, Fagotti A, Gagliardi ML, Ferrandina G, Monterossi G, Gallotta V, Zannoni GF,  
6 Scambia - Pre-hysterectomy cone biopsy is able to predict response in locally advanced cervical  
7 cancer patients submitted to neo-adjuvant chemoradiation. *G. Eur J Surg Oncol*. 2013  
8 Sep;39(9):1025-9
- 9 **20.** Ferrandina G, Margariti PA, Smaniotto D, et al. Long-term analysis of clinical outcome and  
10 complications in locally advanced cervical cancer patients administered concomitant  
11 chemoradiation followed by radical surgery. *Gynecol Oncol* 2010;119:404–40.
- 12 **21.** Jurado M, Martinez-Monge R, Garcia-Foncillas J, et al. Pilot study of concurrent cisplatin, 5-  
13 fluorouracil, and external beam radiotherapy prior to radical surgery p/\_ intraoperative electron  
14 beam radiotherapy in locally advanced cervical cancer. *Gynecol Oncol* 1999;74:30–7.
- 15 **22.** Ferrandina G, Legge F, Fagotti A, et al. Preoperative concomitant chemoradiotherapy in locally  
16 advanced cervical cancer: safety, outcome, and prognostic measures. *Gynecol Oncol*  
17 2007;107:127-32.
- 18 **23.** Distefano M, Fagotti A, Ferrandina G, et al. Preoperative chemoradiotherapy in locally advanced  
19 cervical cancer: long term outcome and complications. *Gynecol Oncol* 2005;99:S166–70.
- 20 **24.** Colombo PE, Bertrand MM, Gutowski M, et al. Total laparoscopic radical hysterectomy for  
21 locally advanced cervical carcinoma (stages IIB, IIA and bulky stages IB) after concurrent  
22 chemoradiation therapy: surgical morbidity and oncological results. *Gynecol Oncol*.  
23 2009;114:404-9.
- 24 **25.** Arveux P, Bénard S, Bouée S, et al. Invasive cervical cancer treatment costs in France. *Bull*  
25 *Cancer*. 2007;94(2):219-24.

- 1 **26.** Cellini N, Smaniotto D, Scambia G, et al. Chemoradiation with concomitant boost followed by  
2 radical surgery in locally advanced cervical cancer: a dose-escalation study. *Am J Clin Oncol.*  
3 2008;31(3):280-4.
- 4 **27.** Chassagne D, Sismondi P, Horiot JC, et al. A glossary for reporting complications of treatment in  
5 gynecological cancers. *Radiother Oncol.* 1993;26:195-202.
- 6 **28.** Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and  
7 Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials  
8 in oncology. *J Natl Cancer* 1993. 85: 365-76
- 9 **29.** Greimel ER, Vlastic K, Waldestrom A, et al. The European Organization for Research and  
10 Treatment of Cancer (EORTC) Quality-of-Life Questionnaire Cervical Cancer Module. EORTC  
11 QLQ-CX24. *Cancer* 2006;107:1812-22.
- 12 **30.** Gallotta V, Ferrandina G, Chiantera V, Fagotti A, et al. Laparoscopic Radical Hysterectomy After  
13 Concomitant Chemoradiation in Locally Advanced Cervical Cancer: A Prospective Phase II  
14 Study. *J Minim Invasive Gynecol.* 2015 Jul-Aug;22(5):877-83.
- 15 **31.** Gallotta V, Fanfani F, Scambia G. Minilaparoscopic nerve sparing radical hysterectomy in locally  
16 advanced cervical cancer after neoadjuvant radiochemotherapy. *Gynecol Oncol.* 2014  
17 Mar;132(3):758-9.
- 18 **32.** Park SY, Base DS, Nam JH, et al. Quality of Life and Sexual Problems in Disease-Free Survivors  
19 of Cervical Cancer Compared with the General Population. *Cancer* 2007; 110: 2716-25.
- 20 **33.** Mantegna G, Petrillo M, Fuoco G, et al. Long-term prospective longitudinal evaluation of  
21 emotional distress and quality of life in cervical cancer patients who remained disease-free 2-years  
22 from diagnosis. *BMC Cancer* 2013; 18:13:127.
- 23 **34.** Dennis T, Mendonc C de, Phalippou J, et al. Study of surplus cost of robotic assistance for radical  
24 hysterectomy, versus laparotomy and standard laparoscopy. *Gynecologie Obstetrique & Fertilité*  
25 2012; 40:77-83
- 26 **35.** Wright JD, Herzog TJ, Neugut AI, et al. Comparative effectiveness of minimally invasive and  
27 abdominal radical hysterectomy for cervical cancer. *Gynecol Oncol.* 2012 ;127(1):11-7.

- 1 **36.** Bell MC, Torgerson J, Seshadri-Kreaden U, et al. Comparison of outcomes and cost for  
2 endometrial cancer staging via traditional laparotomy, standard laparoscopy and robotic  
3 techniques. *Gynecol Oncol.* 2008 Dec;111(3):407-11.
- 4 **37.** Lachance J.A., Darus C.J., Stukenborg G.J., et al. A cost comparison of two strategies for treating  
5 stage IB2 cervical cancer. *Int J Gynecol Cancer* 2008; 18:274–278.
- 6 **38.** Drummond M. F. *Methods for the Economic Evaluation of Health Care Programmes.* Oxford:  
7 University Press; 2005.

**Table 1:** Characteristics of patients

	Laparotomy group (n=23)	Laparoscopic group (n=39)	P value
<b>Age at diagnosis (yr)</b>			
Mean ± SD	52.2 ± 11.0	46.6 ± 11.4	0.1151
<b>Performance Status Score (PSS)</b>			
1	8 (34.8%)	20 (51%)	
2	12 (52.2%)	16 (43.5%)	0.4707
3	3 (13%)	3 (7.6%)	
<b>Body Mass Index (BMI) (kg/m<sup>2</sup>)</b>	24.1 ± 4.4	23.9 ± 5.8	0.3740
Mean ± SD			
<b>FIGO stage</b>			<b>0.0462</b>
IB2	1 (4.3%)	10 (25.6%)	
IIA	9 (39.1%)	7 (17.9%)	
IIB proximal	13 (56.5%)	22 (56.4%)	
<b>Tumor size, clinic (mm)</b>			0.5785
N	19	20	
Mean ± SD	44.7 ± 17.2	44.2 ± 7.2	
<b>Tumor size, MRI (mm)</b>			0.4462
N	20	37	
Mean ± SD	45.1 ± 12.8	48.1 ± 12.5	
<b>At least one previous history of abdominal surgery</b>	15 (65.2%)	10 (25.64%)	<b>0.032</b>
<b>Lymph node staging</b>	14 (60.9%)	31 (79.5%)	0.0667
<b>Clinical response</b>	15 (65%)	24 (60%)	0.2494
<b>MRI response (%)</b>	16 (69%)	32 (82%)	0.6451
<b>Complete response</b>	10 (43.5%)	25 (64.1%)	0.1487

Categorical data N(%) statistical test is only on documented data. Non parametric tests: Wilcoxon or exact test

**Table 2:** Pathology results

	Laparotomy group (n=23)	Laparoscopic group (n=39)	P value
<b>Lymphovascular invasion</b>	2 (8.7%)	5 (12.8%)	1.0000
<b>Free margins</b>	21 (91.3%)	38 (97.4%)	1.0000
<b>Missing</b>	1	0	
<b>No. of patients &gt; 1 Positive pelvic lymph node involvement</b>	17	25	0.3160
<b>No. of patients &gt; 1 Positive aortic lymph node involvement</b>	3	3	1.0000
<b>Preoperative complications N (%)</b>	7 (30)	12 (30)	1,0000
<b>Type of complications N (%)</b>			0.84
<b>chemotherapy</b>	3 (43)	3 (25)	
<b>radiotherapy</b>	1 (14)	2 (17)	
<b>surgery</b>		3 (25)	
<b>others</b>	2 (29)	1 (8)	
<b>chemotherapy and radiotherapy</b>	1 (14)	2 (17)	
<b>chemotherapy and surgery</b>		1 (8)	

Categorical data N(%) statistical test is only on documented data. Non parametric tests: Wilcoxon or exact test

**Table 3:** Surgical characteristics

	Laparotomy group	Laparoscopic group	P value
<b>Total hysterectomy</b>	5 (21.7%)	8 (20%)	1.0000
<b>Extrafascial hysterectomy</b>	18 (78.3%)	33 (82.5%)	0.7448
<b>Lymph node dissection</b>	17 (73.9%)	28 (70%)	0.7811
<b>Laparotomy incision –</b>			
<b>Pfannenstiel transversal</b>	16 (69.48%)		
<b>Midline</b>	7 (30.43%)		
<b>Laparoscopy</b>	<b>Open Laparoscopy</b>	31 (77.50%)	
	<b>Parietal peritoneum</b>	9 (22.50%)	
<b>Conversion to laparotomy*</b>		3 (7.5%)	
<b>Intraoperative transfusion</b>	3 (13%)	0	<b>0.0446</b>
<b>Abdominal drain</b>	18 (78.3%)	3 (7.5%)	<b>&lt;.0001</b>
<b>Duration of abdominal drain (d) Mean ± SD</b>	4.6 ± 1.7	6.0 ± 1.0	0.1460

*Categorical data n(%) statistical test is only on documented data. Non parametric tests: Wilcoxon or exact test*

*\*No echec pneumoperitoneum*

**Table 4:** Intraoperative and postoperative complications

	Laparotomy group	Laparoscopic group	P value
<b>Intraoperative complications</b>	2 (8.7%)	2 (5.1%)	0.6232
<b>Urinary</b>		2	
<b>Vascular</b>	1		
<b>Heart shock</b>	1		
<b>Complications during hospitalization</b>	3 (13%)	3 (7.7%)	0.6615
<b>Digestive (Grade 1)</b>	1		
<b>Pain (Grade 1)</b>		1	
<b>Pain (Grade 2)</b>	1	1	
<b>Hemorrhage (Grade 2)</b>	1		
<b>Hemorrhage (Grade 3)</b>		1	
<b>Complications within 30 days</b>	6 (26.1%)	6 (15.3%)	0.5160
<b>Infectious (Grade 3)</b>		1	
<b>Digestive (Grade 2)</b>	1		
<b>Digestive (Grade 3)</b>		1	
<b>Urinary (Grade 1)</b>		1	
<b>Urinary (Grade 3)</b>	1	1	
<b>Pain (Grade 1)</b>	1	2	
<b>Pain (Grade 2)</b>	2		



Hemorrhage (Grade1)	1
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Categorical data n(%) statistical test is only on documented data. Non parametric tests: Wilcoxon or exact test

**Table 5:** Resources used for each phase of the procedures

	Laparotomy group	Laparoscopic group	P value
<b>Pre-operative phase</b>			
No. of surgeon visits Mean $\pm$ SD	3.5 $\pm$ 1.6	2.9 $\pm$ 1.4	0.1346
No. of anesthesia visits Mean $\pm$ SD	2.3 $\pm$ 0.9	2.4 $\pm$ 1.0	0.7909
No. of other visits Mean $\pm$ SD	5.9 $\pm$ 5.1	4.3 $\pm$ 4.4	0.2279
<b>Operative phase</b>			
Mean operative time (min) Mean $\pm$ SD	258 $\pm$ 66	294 $\pm$ 90	0.0601
Length of induction (min) Mean $\pm$ SD	29.4 $\pm$ 14.8	37.6 $\pm$ 14.7	<b>0.0363</b>
Length of incision, skin to skin (min) Mean $\pm$ SD	168 $\pm$ 72	210 $\pm$ 84	<b>0.0461</b>
<b>Hospitalization stay</b>			
Hospital stay (days) Mean $\pm$ SD	7.3 $\pm$ 1.2	5.7 $\pm$ 2	<b>&lt;.0001</b>
Continuous care unit. N (%)	3 (13.04%)	1 (2.56%)	1.0000
Intensive care unit. N (%)	0	1 (2.5%)	
<b>One month follow-up</b>			
Hospital discharge. N (%)			<b>0.0159</b>

<b>At home</b>	19 (82.6%)	39 (100%)	
<b>Convalescent home</b>	4* (17.4%)	0	
<b>Complications leading to rehospitalization</b>	2** (8.7%)	3*** (7.7%)	1.0000
<b>Duration of rehospitalization</b>			
<b>4 days</b>	1	1	
<b>10 days</b>		1	
<b>16 days</b>	1		
<b>26 days</b>		1	
<b>Complications leading to another intervention</b>	0	2****	0.2934

\*four patients stayed 21, 23, 24 and 30 days at a convalescent home \*\* Bowel distension with interaperitoneal seroma \*\*\* Functional occlusive syndrome and urinary retention \*\*\*\* patient 1, post operative intraperitoneal abscess; patient 2 :post operative bowel obstruction secondary to adhesion

**Table 6:** Comparison of costs for each phase of the procedures (Euros)

	Laparotomy group (€)	Laparoscopic group (€)	P value
<b>Preoperative phase (1)</b>	133.0 ± 49.0	122.1 ± 44.5	0.3486
<b>Operative phase (2)</b>	2 835.8 ± 585.4	5 201.4 ± 787.5	<.0001
<b>Hospitalizations stay* (3)</b>	6 654.3 ± 1 079.1	5 298.2 ± 1 967.2	<.0001
<b>One-month follow-up (4)</b>	1 739.7 ± 3 082.5	929.7 ± 3 613.9	<b>0.0570</b>
<b>Total Cost (1+2+3+4)</b>	<b>10 991 ± 36 16.9</b>	<b>11 262 ± 4 293.1</b>	0.8156

\*including conventional hospitalization, continuous care unit, intensive care unit

Figure 1: Chart flow

