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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Title page(s)

- **Article type**: Original article
- **Full title**: 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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- **Conflict of interest statement**

The authors report no conflict of interest.

- **Funding**

This study was supported by a grant from the French National Cancer Institute dedicated to economic studies of innovative techniques.

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- **Abstract**

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

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

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

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

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

Introduction

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

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

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

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

question arises as to whether this intervention improves the quality of life of these patients, and the efficiency cost and surgical outcome. A comparison of laparoscopy to laparotomy in terms of surgical outcome, cost and quality of life has not been prospectively assessed in the context of surgery after CRT in LACC. The treatment of cervical cancer is expensive and is estimated to total 44 million Euros annually in France, corresponding to a mean patient cost of €22,697 for stage III to €26,886 for stage V disease[25].

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

Materials and methods

Study design and patient details

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

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

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

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

Treatment:

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

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

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

Studied parameters

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

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

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

Economic assessment

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

and follow-up care in the rehabilitation unit. In France, hospital care settings include conventional hospital in charge of an MSO, post-acute care and convalescence homing. Hospital provider perspectives include the hospital care setting in a global care pathway.

Cost calculations were made with the micro-costing method obtained from detailed observations, for all patients included in the study and quantities of consumable resources. The following consumable resources, linked to surgery, are counted and quantified for each patient, from economic items integrated into the case report form, and per center through the center survey as specific devices and annual activities. Direct costs include different surgery techniques, pathology requirements, supplies, depreciation for equipment, hospital stay, medical visits and surgical costs. Depreciation of the laparoscopic video System is included in the direct costs, and is proportional to the time of use in surgery. Depreciation costs were calculated based on a five-year straight-line depreciation. Costs are presented in Euros in 2010. A sensitivity analysis was performed to assess the potential effects of uncertainty inherent in the study.

Statistical analysis

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

Results

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

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

Preoperative treatment

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

Surgery

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

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

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

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

Cost at one-month

Resources used for each phase of the procedures are presented in Table 5, and detailed costs in Table 6. The direct cost of each procedure was not statistically different at one month: €10,991 (σ=3616) for laparotomy versus €11,267 (σ=4237) for laparoscopy, p=0.76.
Hospital stays for patients were significantly lower in the laparoscopy group (8.3 d vs 6.7 d, p<0.001). Post-hospital stay in a convalescence home was required for 17.4% (4/23) of the patients after laparotomy (21, 23, 24 and 30 days respectively), but was not required for any patients in the laparoscopy group who return home after surgery. The one-month follow-up step includes the additional cost convalescence for the laparotomy group, while all patients in laparoscopy group have hospital discharge at home. The one-month follow-up step results in significantly lower costs for the laparoscopic group compared to the laparotomy group (€929 vs. €1,739, p=0.05).

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

Quality of life up to 6 months

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

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

Discussion

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

Medical outcome and quality of life

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

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

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

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

Cost evaluation

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

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

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

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

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

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

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

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

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

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

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Table 1: Characteristics of patients

	Laparotomy group (n=23)	Laparoscopic group (n=39)	P value
Age at diagnosis (yr)			
Mean ± SD	52.2 ± 11.0	46.6 ± 11.4	0.1151
Performance Status Score (PSS)			
1	8 (34.8%)	20 (51%)	
2	12 (52.2%)	16 (43.5%)	0.4707
3	3 (13%)	3 (7.6%)	
Body Mass Index (BMI) (kg/m²)	24.1 ± 4.4	23.9 ± 5.8	0.3740
Mean ± SD			
FIGO stage			**0.0462**
IB2	1 (4.3%)	10 (25.6%)	
IIA	9 (39.1%)	7 (17.9%)	
IIB proximal	13 (56.5%)	22 (56.4%)	
Tumor size, clinic (mm)			0.5785
N	19	20	
Mean ± SD	44.7 ± 17.2	44.2 ± 7.2	
Tumor size, MRI (mm)			
N	20	37	0.4462
Mean ± SD	45.1 ± 12.8	48.1 ± 12.5	
At least one previous history of abdominal surgery	15 (65.2%)	10 (25.64%)	**0.032**
Lymph node staging	14 (60.9%)	31 (79.5%)	0.0667
Clinical response	15 (65%)	24 (60%)	0.2494
MRI response (%)	16 (69%)	32 (82%)	0.6451
Complete response	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
Lymphovascular invasion	2 (8.7%)	5 (12.8%)	1.0000
Free margins	21 (91.3%)	38 (97.4%)	1.0000
Missing	1	0	
No. of patients > 1 Positive pelvic lymph node involvement	17	25	0.3160
No. of patients > 1 Positive aortic lymph node involvement	3	3	1.0000
Preoperative complications N (%)	7 (30)	12 (30)	1,0000
Type of complications N (%)			0.84
chemotherapy	3 (43)	3 (25)	
radiotherapy	1 (14)	2 (17)	
surgery		3 (25)	
others	2 (29)	1 (8)	
chemotherapy and radiotherapy	1 (14)	2 (17)	
chemotherapy and surgery		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
Total hysterectomy	5 (21.7%)	8 (20%)	1.0000
Extrafascial hysterectomy	18 (78.3%)	33 (82.5%)	0.7448
Lymph node dissection	17 (73.9%)	28 (70%)	0.7811
Laparotomy incision –			
Pfannenstiel transversal	16 (69.48%)		
Midline	7 (30.43%)		
Laparoscopy **Open Laparoscopy**		31 (77.50%)	
Parietal peritoneum		9 (22.50%)	
Conversion to laparotomy*		3 (7.5%)	
Intraoperative transfusion	3 (13%)	0	**0.0446**
Abdominal drain	18 (78.3%)	3 (7.5%)	**<.0001**
Duration of abdominal drain (d) Mean ± SD	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
Intraoperative complications	2 (8.7%)	2 (5.1%)	0.6232
Urinary		2	
Vascular	1		
Heart shock	1		
Complications during hospitalization	3 (13%)	3 (7.7%)	0.6615
Digestive (Grade 1)	1		
Pain (Grade 1)		1	
Pain (Grade 2)	1	1	
Hemorrhage (Grade 2)	1		
Hemorrhage (Grade 3)		1	
Complications within 30 days	6 (26.1%)	6 (15.3%)	0.5160
Infectious (Grade 3)		1	
Digestive (Grade 2)	**1**		
Digestive (Grade 3)		1	
Urinary (Grade 1)		1	
Urinary (Grade 3)	1	1	
Pain (Grade 1)	1	2	
Pain (Grade 2)	2		

Hemorrhage (Grade1)	1

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

At home	19 (82.6%)	39 (100%)	
Convalescent home	4* (17.4%)	0	
Complications leading to rehospitalization	2** (8.7%)	3*** (7.7%)	1.0000
Duration of rehospitalization			
4 days	1	1	
10 days		1	
16 days	1		
26 days		1	
Complications leading to another intervention	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 abcess; 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**
Preoperative phase (1)	133.0 ± 49.0	122.1 ± 44.5	0.3486
Operative phase (2)	2 835.8 ± 585.4	5 201.4 ± 787.5	**<.0001**
Hospitalizations stay* (3)	6 654.3 ± 1 079.1	5 298.2 ± 1 967.2	**<.0001**
One-month follow-up (4)	1 739.7 ± 3 082.5	929.7 ± 3 613.9	**0.0570**
Total Cost (1+2+3+4)	**10 991 ± 36 16.9**	**11 262 ± 4 293.1**	0.8156

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

Figure 1: Chart flow