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Predictive factors of severe perioperative morbidity of Radical Hysterectomy with lymphadenectomy in Early-stage cervical Cancer: A French prospective multicentric cohort of 248 patients

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Short running title: Morbidity of radical hysterectomy: A French prospective multicentric cohort of 248 patients

Predictive factors of severe perioperative morbidity of Radical Hysterectomy with lymphadenectomy in Early-stage cervical Cancer: A French prospective multicentric cohort of 248 patients

Abstract

Objective: The purpose of this study was to assess the postoperative morbidity after radical hysterectomy (RH) for early-stage cervical cancer and to determine risk factors of severe perioperative morbidity.

Methods: Data of two prospective trials on sentinel node biopsy for cervical cancer (SENTICOL I & II) were analysed. Patients having a radical hysterectomy were included between 2005 and 2012 from 25 French oncologic centers. Postoperative complications were prospectively recorded in a pre-specified analysis.

Results: 248 patients met the inclusion criteria. The median age was 44.5 years [25 – 85]. 88.7% of patients had a stage IB1 disease. There were 71.4% epidermoid carcinomas and 25% adenocarcinomas. 125 patients (50.4%) had a laparoscopic-assisted vaginal RH, 88 patients (35.5%) had a total laparoscopic RH, 26 patients (10.5%) had an open RH and 9 patients (3.6%) had a robotic-assisted RH. Sixteen patients (6.4%) had intraoperative complications. On a multivariate analysis, intraoperative complications were significantly associated with BMI > 30 kg/m². The urinary, lymphovascular and neurologic complications rates were respectively 34.3%, 20.6% and 19.8%. 31 patients (12.5%) had severe postoperative complications (Clavien-Dindo ≥ 3 or CTCAE ≥ 3). On multivariate analysis, severe postoperative complications were associated with parametrial involvement, preoperative brachytherapy and inclusion in low surgical skills center.

Conclusions: This study based on prospective data showed that RH has low severe postoperative complications. The main complications were urinary infections and lower limb lymphedema. Patients with early-stage cervical cancer should be referred to expert center to ensure best surgical outcomes.

Keywords: “Cervical cancer”, “Surgery”, “Morbidity”, “Complications”, “Radical Hysterectomy”

Introduction

Cervical cancer is the second most common cancer among women and the third cause of cancer-related deaths in females with approximately 527 600 new cases and 265 700 deaths each year (1). According to main guidelines (2,3), surgery is the preferred option for early-stage cervical cancer (IB1 to IIA1 FIGO stage), especially in young patients.

Radical hysterectomy (RH) consists in the resection of the uterus, the cervix and the upper vagina associated with resection of the parametrial tissues. The extent of the parametrectomy should be tailored according to the tumor characteristics. Today the majority of operations proposed to the patients are B1 to C1 RH according to the Querleu-Morrow classification (4). Pelvic lymphadenectomy (PLN) is associated to RH, and sentinel lymph node biopsy (SLN) has been introduced more recently. This procedure is mostly performed by minimally invasive surgery for 20 years.

Although 5-year survival rates of 88–97% have been reported, RH-PLN is associated with several significant complications such as urinary, lymphovascular, neurologic and digestive morbidity which noticeably affects the quality of life of the patients (5–7). The actual rate of complications could be underestimated because only 5% of patients with this problem seek medical care for this reason (8) and because most data come from old or retrospective studies.

The aim of our study was to assess the morbidity of radical hysterectomy and nodal staging for early-stage cervical cancer, in the modern era, with multicentric prospective data.

Materials and Methods

The main objective was to describe pre and postoperative complications of RH-PLN. The secondary objective was to determine risk-factors of complication.

Population study

We performed an ancillary study on the database of two prospective multicentric studies on sentinel lymph node (SLN) biopsy (SENTICOL I and II). Design of the both studies have already been described elsewhere (9,10). In both studies, postoperative complications were prospectively recorded in a pre-specified analysis.

We performed a retrospective analysis of the two databases. We included cases with a radical hysterectomy. Patients who didn't undergo surgery, had trachelectomy or simple hysterectomy, were excluded. This study was approved by the Paris Descartes CPP (Ethical Committee). Patients included in the two studies signed an informed consent stating the use of data for secondary analyses.

Data analysis

For each patient, we extracted demographic characteristics, surgical history, and clinical data including FIGO stage. Operative records were reviewed, and data about the type of surgical approach, the type of hysterectomy performed according to the Querleu-Morrow classification, the type of lymph node staging (SLN biopsy only or additional pelvic lymphadenectomy), were collected. Pathological data was reviewed (tumor histology, lymphovascular space invasion, nodal status, number or removed nodes, parametrial status, vaginal margin status, surgical margin status and tumor size).

We used the Clavien-Dindo classification to assess the severity of early postoperative complications (≤ 30 days after surgery) and the CTCAE classification V 4.03 for late postoperative complications (> 30 days after surgery) (11). A severe complication was defined as grade ≥ 3 in the Clavien-Dindo classification or as grade ≥ 3 in the CTCAE classification.

We categorized 3 types of inclusion center according to the number of patients included and level of experience: type 1 (< 10 patients, 18 centers), type 2 (10 to 20 patients, 3 centers) and type 3 (> 20 patients, 4 centers).

Statistical analysis

Qualitative variables were expressed as n (%) and quantitative data as mean [range]. Patients were categorized into two groups according to the presence or the absence of complications. An univariate analysis was performed to identify risk factors of intraoperative and severe postoperative complications. We applied the chi-square test (or Fisher's test if the sample size was too small) to compare qualitative variables and the Student's t test to compare quantitative variables.

Variables yielding p values lower than 0.2 by univariate analysis were entered into a multivariate logistic regression model to determine variables independently associated with intraoperative and severe postoperative complications of radical hysterectomy. Values of p lower than 0.05 were considered as significant.

Overall survival and free-recurrence survival were analysed by using Kaplan-Meier analysis and compared by applying log-rank test.

Data were recorded in an Excel files and statistical analyses were performed using XLStat software (AddInsoft V19.4).

Results

Between January 2005 and July 2012, 412 patients have been enrolled in SENTICOL I and SENTICOL II studies. 248 patients from 25 patients were finally included in the present study (Figure 1).

Patient and surgery characteristics

The median age was 44.5 years [25 – 85] and the median Body Mass Index (BMI) was 22.9 kg/m² [14.6 – 45]. 63 patients (25.4%) were included in type 1, 35 patients (14.1%) in type 2 and 150 patients (60.5%) in type 3 center. Most of the patients had FIGO stage IB1 disease (88.7%). 150 patients (60.5%) had a previous conisation. The majority of patients had squamous cell carcinoma (71.4%), 62 patients had adenocarcinoma (25%), 4 patients had adenosquamous carcinoma (1.6%) and one patient had adenoid kystic carcinoma (0.4%). At preoperative imaging, the median size of the tumor was 15 mm [0-50] and the tumor was larger than 20 mm in 35.1% of cases. 75 patients had a preoperative brachytherapy (30.2%). The sociodemographic and clinical characteristics are shown in Table 1.

Most patients (84.7%) had a type B procedure. Minimal invasive surgery was the main surgical approach (222 patients, 89.5%) whereas 26 patients have been operated on by laparotomy (10.5%). 30 patients (12.1%) were operated in two-steps by laparoscopy (First intervention for lymph node staging then a second intervention for radical hysterectomy).

75 patients (30.2%) had a SLN biopsy alone, 157 patients (63.3%) had an additional pelvic

lymphadenectomy and 16 patients also had a paraaortic lymphadenectomy (6.5%). The median number of removed SLN per patient was 3 [1-11]. In case of additional pelvic or paraaortic lymphadenectomy, the mean number of removed non-SLN per patient was 13 [3-72] (Table 1). Thirty patients had at least one positive lymph node (12.1%).

At final pathologic examination, 17.7% of patients had a tumor size larger than 20 mm. There were a parametrial spread in 4% of cases, a vaginal spread in 4.8% and positive surgical margin in 4.8%. Forty-six patients received adjuvant radiotherapy (18.1%).

Intraoperative complications

Sixteen patients (6.4%) had an intraoperative complication. Bladder was injured in 5 cases (2%) and ureter was injured in 2 cases (0.8%). Iliac artery injury during the pelvic lymphadenectomy occurred in 4 cases (1.6%) and in one case laparoconversion was necessary. No bowel injury was reported. In one case, uterus has been perforated after intrauterine cannulation due to postbrachytherapy cervical stenosis. A non-optimal patient positioning was responsible of intraoperative complications in 4 cases (1.6%) (one case of brachial plexus compression, one case of external popliteal sciatic nerve compression, one case of rhabdomyolysis and one case of compressive slough). Three of these complications occurred with a laparoscopic approach (Table 2).

In univariate analysis, intraoperative complications were more common in patients who have been operated on by laparotomy rather than by minimal invasive techniques (37.5% vs 8.6%, $p = 0.007$). Compared to patients who were operated by MIS approach, patients who were operated by laparotomy were significantly older (mean age: 53.9 ± 17.1 years vs 46.4 ± 11.5 years, $p = 0.003$) and had an higher BMI (27.2 ± 4.8 kg/m² vs 23.9 ± 5.5 kg/m² $p = 0.003$).

Intraoperative complications were associated with a tumor size ≥ 20 mm (46.7 % vs 17.3%, $p = 0.005$), parametrial spread (21.4% vs 3.1%, $p = 0.001$) and vaginal invasion (28.6% vs 3.6%, $p < 0.0001$). In the group of patients with no intraoperative complications, patients had a significant lower BMI (Mean of 23.9 kg/m² vs 28.4 kg/m², $p = 0.001$) (Table 3).

In multivariate analysis, only BMI > 30 kg/m² was identified as an independent risk factor of intraoperative complications (ORa = 4.9, 95%CI = [1.72 – 20.44], $p = 0.02$). Open approach seemed to be associated with more intraoperative complications than minimal invasive approach but didn't reach statistical significance (ORa = 3.64, 95%CI = [0.76 – 17.55], $p=0.11$).

Postoperative complications

Overall, severe postoperative complications (defined as Clavien-Dindo ≥ 3 and/or CTCAE ≥ 3) were reported in 31 patients (12.5%), 120 patients (48.4%) had non-severe complications and 97 patients (39.1%) were free of complications. Overall complications are summarized in Table 2.

The urinary complications were the most frequent postoperative complications with 106 events in 85 patients (34.3%). Most of them were minor urinary infection which occurred in 37 patients (14.9%). Dysuria was observed in 17 patients (6.9%) and urinary retention in 12 patients (4.8%). Severe complications consisted in uretero-vesical fistula in 4 patients (1.6%), vesico-vaginal fistula in 3 patients (1.2%) and hydronephrosis due to a unilateral ureteral stenosis in 3 patients (1.2%).

51 patients (20.6%) had 56 lymphovascular complications. The main complication was lower limbs lymphedema, which was bilateral in 20 cases (8.1%) and unilateral in 16 cases (6.5%). In 17 cases (6.8%), lower limbs lymphedema were assessed as grade II in the CTCAE classification. Fourteen patients had a pelvic lymphocele (5.6%). Three patients (1.2%) had a pelvic lymphocele which necessitated a radiologic drainage (Clavien-Dindo class III).

49 patients (19.8%) had 52 non-severe neurologic complications. We recorded 25 cases of genitofemoral nerve injury (bilateral in 9 cases and affected only sensitivity in 11 cases). We recorded 23 cases of obturator nerve injury (bilateral in 7 cases and was exclusively sensitive in 10 cases). No patients had severe postoperative neurologic complication.

Two patients (0.8%) had a peritonitis and two patients (0.8%) had a pelvic deep abscess. Two patients (0.8%) had a herniation through the umbilical scar (one was complicated of hernial stricture). One patient, with a known hepatic cirrhosis due to HCV infection and HIV co-infection, had liver decompensation 3 weeks after surgery. 11 patients (4%) had complete vaginal cuff dehiscence, whose 5 after a sexual intercourse and 5 patients had a vaginal scar necrosis (2%). One patient had a pulmonary embolism and one a lower limb vein thrombosis.

In the subgroup of 76 patients (30.2%) who had preoperative brachytherapy, 14 patients had severe postoperative complications (18.4%) and this rate seemed to be higher than in patients with no preoperative brachytherapy (18.4% vs 11.5%, $p = 0.08$). There were no differences between patients with and without preoperative brachytherapy in terms of urinary complications (38.2% vs 33.9%, $p = 0.52$) and neurologic complications (19.7% vs 20%, $p = 0.96$) but lymphovascular complications were more frequent in patients with preoperative brachytherapy than in patients without preoperative brachytherapy (28.9% vs 17%, $p = 0.03$).

In univariate analysis, no variable was significantly associated with severe postoperative complications. However, patients with severe postoperative complications seemed to have more parametrial invasion (9.7% vs 3.3%, $p = 0.1$) (Table 4). Patients who have been operated in type 3 inclusion center seemed to have less severe postoperative complications (13/150 patients, 8.7%) than patients from type 2 and 1 inclusion center (respectively 5/35 patients, 14.3% and 13/63 patients, 20.6%, $p = 0.052$).

Multivariate analysis identified two risk-factors of severe postoperative complications: parametrial invasion (ORa = 7.39, 95%IC = [1.37 – 39.72], $p=0.02$) and preoperative brachytherapy (ORa = 3.98, 95%IC = [1.29 – 12.34], $p=0.016$). Patients who have been operated in in type 3 center had lower risk of severe postoperative complications (ORa = 0.2, 95%IC = [0.06 – 0.66], $p=0.008$).

Follow-up and oncologic outcomes

The median follow-up was 49 months [0-130]. During follow-up, 13 patients (5.2%) were lost to follow-up, 23 patients (9.8%) had recurrent disease and 14 patients (6%) died from cervical cancer. Among patients who had recurrence, 7 patients had a local recurrence, 5 patients had a metastatic lymph node, 1 patient had a locoregional metastasis and 10 patients had distant metastasis. The median-time of recurrence was 21 months [2- 72].

Overall survival and recurrence-free survival rates didn't significantly differ at 5-year of follow-up between group of patients without and group of patients with severe complications (94.6% vs 90.9%, $p= 0.72$ and 92.2% vs 86.1%, $p = 0.67$ respectively) (Figure 2).

DISCUSSION

Few prospective data about the morbidity of radical hysterectomy with nodal staging are available. To our best knowledge, the present study is the first study that precisely assesses risk-factor of intraoperative and postoperative severe morbidity after this procedure. Through this prospective cohort of 248 patients, we have shown that postoperative complications were significant and were mainly urinary (34.3%), lymphovascular (20.6%) and neurologic (19.8%). However, the absolute rate of intraoperative complications (6.4%) and severe postoperative morbidity (12.1%) are

finally low.

In this study, obesity, defined as BMI > 30 kg/m², was significantly associated with a higher risk of intraoperative complications (ORa = 4.9, 95%CI = [1.72 – 20.44], p = 0.02). In a retrospective cohort of 497 patients who underwent laparoscopic surgery for gynecologic malignancies, Peng et al. didn't find any differences in intraoperative complication rates between non-obese, obese and morbid obese patients but the rates of major intraoperative complications were higher in obese and morbid obese patients group than in non obese patient (4.32% and 8.51% respectively versus 2.78%) (12). Similarly, for Frumovitz et al., there were no statistical differences in terms of intraoperative complications between normal-BMI, overweight, obese and morbid obese patients (6%, 4%, 6% and 6% respectively) but higher BMI was significantly correlated with higher estimated operative blood loss (p= 0.001) (13).

The type of surgical approach may have an impact on intraoperative complications. According to our results, open approach tends to be more at risk of intraoperative complication than minimal invasive approach. Safety and surgical benefits of MIS in treatment of early-stage cervical cancer have been described in the literature. Although intraoperative complications rate were not statistically significant between open and MIS approach, median blood loss are significantly lower and median hospital stay shorter (14–16). Less postoperative complications are reported in case of MIS approach (17). However, results of the LACC trial which compared open, laparoscopic and robotic surgery for RH will provide prospective data (18).

Urinary complications are the most frequent complications. Most were urinary infection. Bladder dysfunction is a major concern after RH-PLN. Rates coming from literature (up to 85%) are much higher than our (19,20). Classically, two steps of vesical dysfunctions are described in the early postoperative period (5,7). The first phase corresponds to a hypertonic one due to a spastic bladder with a low vesical compliance. This phase is usually transient during 8 to 12 weeks. In our study, this phase concerned 22 patients (8.9%). The second phase is characterized by a hypotonic and overdistended bladder. This phase results from an inappropriate management during the postoperative period and affected 14 patients (5.6%). An incomplete vesical voiding may result in lower urinary tract infection (33 patients, 13.3%) and upper urinary tract infection (7 patients, 2.8%). Long-term clinically significant bladder dysfunctions is the most common long-term complication of RH and occur in about 8 to 80% of patients (7,19–24). These dysfunctions are linked to detrusor overactivity,

increased bladder capacity and decreased bladder compliance (23) and concerned 6 patients (2.4%), 6 months after surgery. Voiding effort may result in pelvic static trouble but only one patient (0.4%) had a prolapse 6 months after surgery. Better selection of patients, use of less radical procedures, development of nerve-sparing RH may explain our results (25). Ureteral complications, fistula or stenosis, and bladder fistula are rare and estimated less than 2% (26–28). This rate was 2.8% (7 patients) in our study.

In a retrospective cohort of 264 patients who underwent pelvic lymphadenectomy with or without paraaortic lymphadenectomy for gynecologic cancer, the rate of lower limb lymphedema was 23.1% one year after surgery (29) and higher than ours of 14.5%. The authors found that this complication was associated with BMI > 25 kg/m², adjuvant radiotherapy, the presence of a lymphocele and a full lymphadenectomy performed. In a cohort of 591 patients who underwent total hysterectomy and pelvic lymphadenectomy for endometrial cancer, Yost et al. found the same risk factors with an overall prevalence of lower limb lymphedema of 47% at 6.2 years of follow-up (30). In a prospective cohort of 292 patients with cervical cancer, Zikan et al. observed a lymphocele postoperative rate of 16.1%, whose 5.8% were symptomatic (31). In our study, we found lower rate of 5.6% of postoperative lymphocele. This difference may be due to higher rate of paraaortic lymphadenectomy of 41.4% and a main surgical approach by laparotomy in 82.5% of cases whereas in our study, the paraaortic dissection rate was 6.5% and surgical approach by laparotomy rate was 10.5%.

Neurologic complications are not directly linked to the RH itself but to pelvic lymphadenectomy. Irritation of the genitofemoral or obturator nerves may be induced by manipulation and direct thermal or electrical injury by monopolar diathermy. In a cohort of 1000 pelvic lymphadenectomy for gynecologic cancer, Querleu et al. observed 3 intraoperative obturator nerve injury, a genitofemoral nerve dysesthesia and a partial palsy of the psoas muscle (32). In a cohort of 80 patients who underwent radical hysterectomy by robot-assisted approach, Persson et al. described 8 genitofemoral nerve injuries (10%) and one partial obturator nerve palsy (1.2%) (33). In a review of the literature, Kruijdenberg et al. found a neurologic complication rate of 3.4% after robotic-assisted RH and 2% after laparoscopic RH (34). Our results highlighted higher neurologic complications rates, and this may be explained by the prospective record of complications.

Our results showed better surgical outcomes if patients were referred to expert centers with high surgical skills. As recommended in the last ESGO guidelines, surgery should be performed by

gynecologic oncologist and trained surgeon in a specialized team dedicated to management of gynecologic cancers (3). Treatment in expert center with a high-volume of surgical procedures has been highlighted in ovarian cancer (35) and was defined as quality indicators (36).

We found that preoperative brachytherapy was an independent risk-factor of severe postoperative morbidity. For intermediate and high-risk of early-stage cervical cancer, preoperative brachytherapy followed by surgery may be an acceptable option to primary surgery in order to decrease tumoral size and eradicate LVSI (3). In a cohort of 162 patients who underwent laparoscopic radical hysterectomy after receiving brachytherapy, Uzan et al. suggested that preoperative brachytherapy didn't increase peri- and postoperative morbidity (37). However, they reported a severe morbidity rate of 20.4% (33/162 patients with grade IIIA or IIIB of the Clavien-Dindo classification) which was higher than our.

One of the limitations of this study is the retrospective analysis of two databases which were not designed to our specific objectives and therefore some details lacked, such as the mean blood loss or the need of urinary self-catheterisation. In our cohort, 84,7% of the radical hysterectomy were type B and complications rates may be more important in case of more aggressive radical hysterectomy. This may be associated with the important number of small cervical cancer in this series: 65% of patients had preoperative tumor size smaller than 2 cm and only 17% were bigger than 2 cm at the definitive histological examination. These rates may be explained by the inclusion criteria of SENTICOL I and SENTICOL II studies due to the exclusion of patients who had neoadjuvant radiotherapy or chemotherapy. The strengths of this study are that all data related to postoperative morbidity were prospectively recorded in a quality-checked database and population study was homogeneous with a long follow-up. Moreover, patients came from multiple institutions taking in account different levels of surgical expertise and different levels of learning curve.

Conclusion

This study using prospective data, confirms that radical hysterectomy has significant postoperative morbidity but low severe postoperative complications. The main complications were

urinary infections and lower limb lymphedema. Incidence of complications is lower in experienced and patients with early-stage cervical cancer should be referred to expert center to ensure best surgical outcomes.

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Figure 1. Flow-chart of the population study

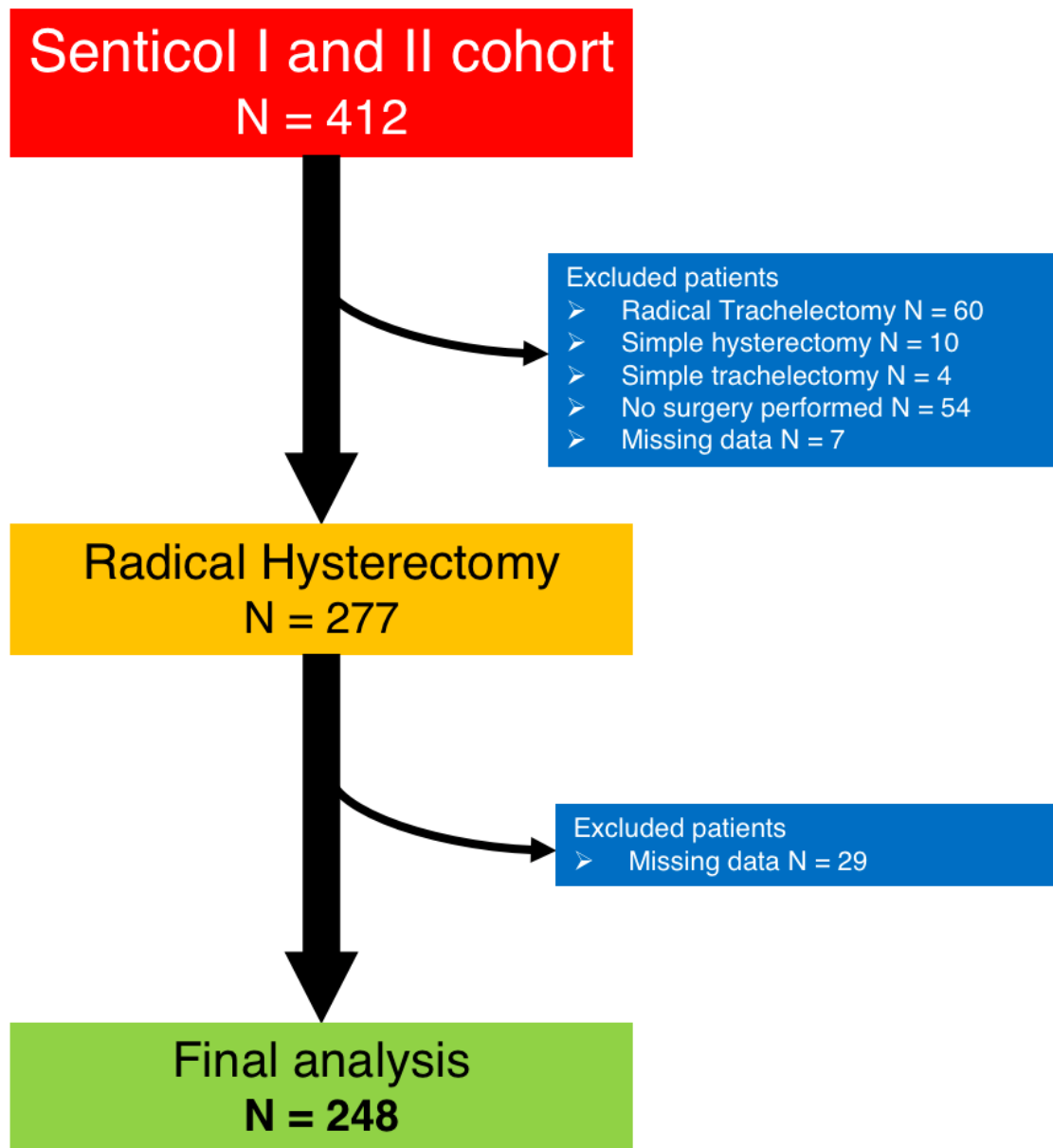
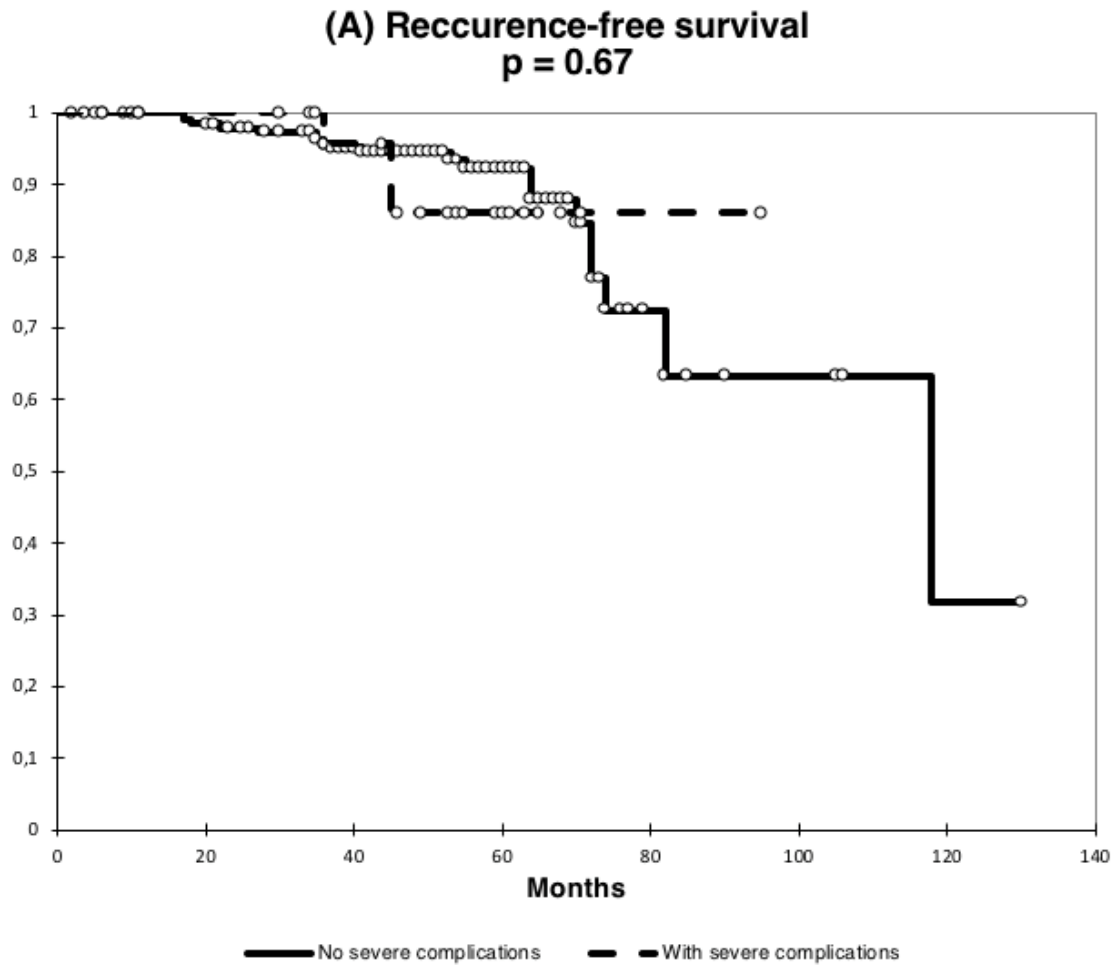


Figure 2. Recurrence-free survival (A) and overall survival (B) curves of group with and no severe postoperative complications



(B) Overall survival
p = 0.72

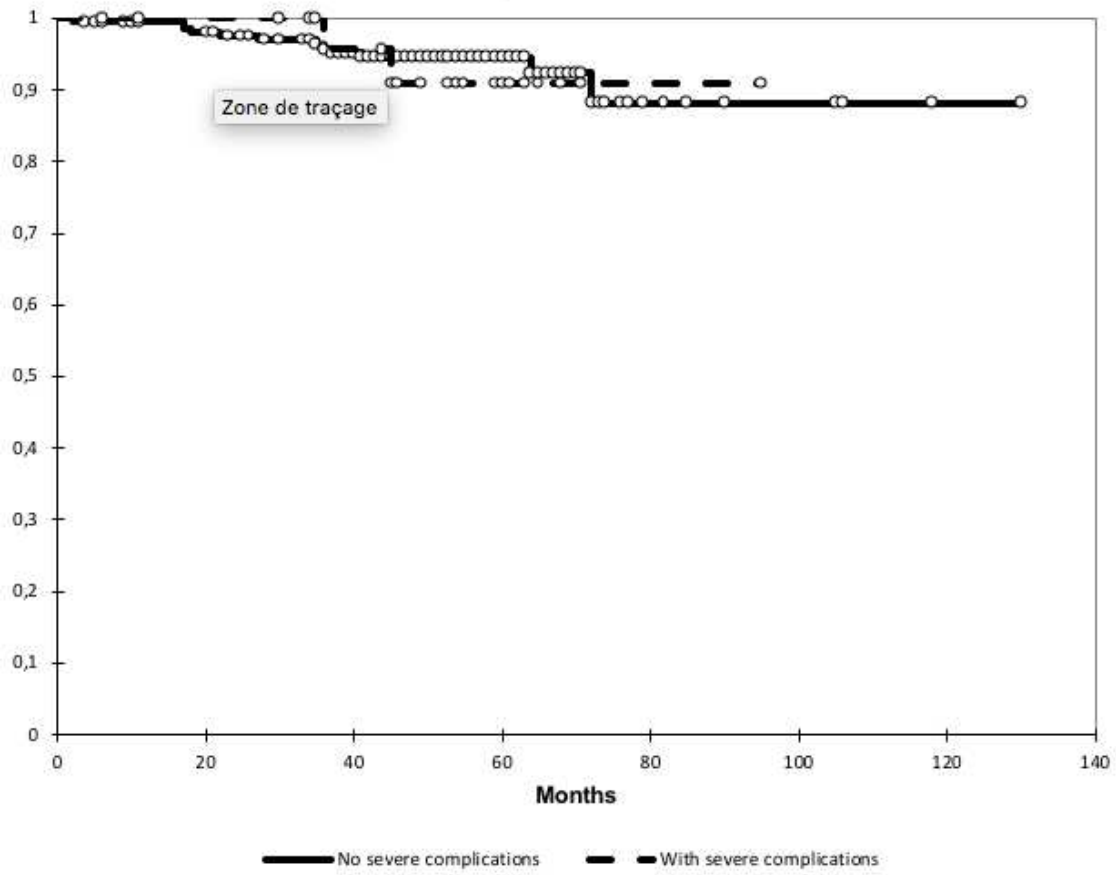


Table 1. Clinicopathologic and surgical characteristics of patients

	Total population N = 248	N Median	(%) [range]
Age (years)			
	Median	44.5	[25 – 85]
	< 30	8	3.2%
	30-60	195	78.6%
	> 60	45	18.1%
BMI (kg/m²)			
	Median	22.9	[14.6 – 45]
	< 18,5	15	6%
	18,5 – 25	155	62.5%
	< 25-30	44	17.7%
	> 30	34	13.7%
Parity			
	0	45	18.1%
	≥1	203	81.9%
Menopausal status			
	Yes	84	33.9%
	No	164	66.1%
History of previous pelvic surgery			
	0	128	51.6%
	1	85	34.3%
	≥ 2	35	14.1%
FIGO stage			
	IA1 with emboli	6	2.4%
	IA2	14	5.6%
	IB1	220	88.7%
	IB2	1	0.4%
	IIA	6	2.4%
	IIB	1	0.4%
Histology			
	Squamous cell carcinoma	177	71.4%
	Adenocarcinoma	62	25%
	Adenosquamous	4	1.6%
	Adenoid kystic carcinoma	1	0.4%
	Unknown	4	1.6%
Presence of LVSI in the biopsy			
	Yes	48	19.4%
	No	166	66.9%
	Unknown	34	13.7%
Tumoral size at preoperative imaging			
	Median	15	[0 – 50]
	Size < 20 mm	121	48.8%
	Size ≥ 20 mm	87	35.1%
	Unknown	40	16.1%
Preoperative LEEP			

Yes	150	60.5%
No	92	37.1%
Unknown	6	2.4%
Preoperative brachytherapy		
Yes	76	30.6%
No	166	66.1%
Unknown	7	2.8%
Number of step-surgery		
1	218	87.9%
2	30	12.1%
Type of surgical approach		
LARVH	125	50.4%
Laparoscopy	88	35.5%
Laparotomy	26	10.5%
Robot-assisted laparoscopy	9	3.6%
Type of RH (Querleu-Morrow)		
B	210	84.7%
C	29	11.7%
Unknown	9	3.6%
Nodal staging		
SLN alone	75	30.2%
SLN + PL	157	63.3%
SLN + PL + PAL	16	6.5%
Number of SLN per patient	3	[1-11]
Number of Nodes per patient if PL done	13	[3-72]
Patients with positive SLN		
Yes	27	10.9%
No	215	86.7%
Unknown	6	2.4%
Patients with ≥ 1 positive node		
Yes	30	12.1%
No	218	87.9%
Final pathologic exam		
Tumor size		
Median		
< 20 mm	185	74.6%
≥ 20 mm	44	17.7%
Unknown	19	7.7%
LVSI		
Yes	76	30.6%
No	172	69.4%
Parametrial invasion		
Yes	10	4%
No	230	92.7%
Unknown	8	3.2%
Vaginal invasion		
Yes	12	4.8%
No	226	91.1%
Unknown	10	4%
Positive margin		
Yes	12	4.8%
No	226	91.1%

Unknown	10	4%
Adjuvant radiotherapy		
Yes	46	18.5%
No	198	79.8%
Unknown	4	1.6%

Table 2. Intraoperative and postoperative complications

Variable N = 248	n	%
Intraoperative complications		
Bladder	5	2%
Ureter	2	0.8%
Vascular	4	1.6%
Other	5	2%
Severe complications		
Vaginal cuff dehiscence	11	4%
Fistula	7	2.8%
Severe abdominal infection	4	1.6%
Hydronephrosis	3	1.2%
Lymphocele drainage	3	1.2%
Hemorrhagic complications	2	0.8%
Thromboembolic events	2	0.8%
Other	3	1.2%
Urinary tract complications		
Urinary infections (lower and upper tract)	48	19.4%
Dysuria	17	6.9%
Stress urinary incontinence	14	5.6%
Urinary retention	12	4.8%
Hypotonic bladder	3	1.2%
Prolapsus	1	0.4%
Other	11	4.4%
Lymphovascular complications		
Lower limb lymphedema	36	14.5%
Lymphocyst	14	9.3%
Pubic lymphedema	4	1.6%
Inguinal lymphedema	2	0.8%
Neurologic complications		
Genito-femoral nerve	25	10.1%
Obturator nerve	23	9.3%
Lateral femoral cutaneous nerve	3	1.2%
Pudendal nerve	1	0.4%

Table 3. Univariate analysis of risk factors of intraoperative complications

Predictive variable	Group with intraoperative complications N = 16		Group without intraoperative complications N = 232		P
	n median	[%] [range]	n median	[%] [range]	
Type of inclusion center					
Type 1	6	37.5%	57	24.6%	0.51
Type 2	2	12.5%	33	14.2%	
Type 3	8	50%	142	61.2%	
Age [years]					
Median	44	[25 – 77]	45	[25 – 85]	0.61
< 45	9	56.3%	115	49.6%	0.6
≥ 45	7	43.8%	117	50.4%	
BMI [kg/m²]					
Median	27.9	[19.5 – 39.8]	22.8	[14.6 – 45]	0.001
< 18,5	0	0%	15	6.5%	0.001
18,5 – 25	8	50%	147	63.4%	
< 25-30	0	0%	44	19%	
> 30	8	50%	26	11.2%	
Parity					
0	2	12.5%	43	18.5%	0.54
≥ 1	14	87.5%	189	81.5%	
Menopausal status					
Yes	6	37.5%	78	33.6%	0.75
No	10	62.5%	154	66.4%	
History of previous pelvic surgery					
0	8	50%	120	51.7%	0.89
≥ 1	8	50%	112	48.3%	
FIGO stage					
IA1 with emboli – IA2	1	6.3%	19	8.2%	0.99
IB1	15	93.8%	205	88.4%	
IB2-IIIB	0	0%	8	3.4%	
Histology					
Squamous cell carcinoma	11	68.8%	166/228	72.8%	0.73
Adenocarcinoma	5	31.2%	57/228	25%	
Other type	0	0%	5/228	2.2%	
Presence of LVSI in the biopsy					
Yes	3/14	21.4%	45/200	22.5%	0.93
No	11/14	78.6%	155/200	77.5%	
Tumoral size at preoperative imaging					
Size < 20 mm	6/14	42.9%	115	50.3%	0.23
Size ≥ 20 mm	8/14	57.1%	79	40.7%	
Preoperative LEEP					
Yes	9	56.2%	141/226	62.4%	0.74
No	7	43.8%	85/226	37.6%	
Preoperative brachytherapy					
Yes	4	25%	72/225	32%	0.56
No	12	75%	153/225	68%	

Number of step-surgery					
1	13	81.3%	205	88.4%	0.4
2	3	18.8%	27	11.6%	
Type of surgical approach					
LARVH	4	25%	125	52.2%	0.007
Laparoscopy	6	37.5%	82	35.3%	
Laparotomy	6	37.5%	20	8.6%	
Robot-assisted laparoscopy	0	0%	9	3.9%	
Type of RH (Querleu-Morrow)					
B	14/15	93.3%	196/224	87.5%	0.5
C	1/15	6.7%	28/224	12.5%	
Nodal staging					
SLN alone	4	25%	71	30.6%	0.91
SLN + PL	11	68.8%	146	62.9%	
SLN + PL + PAL	1	6.3%	15	6.5%	0.93
Number of SLN per patient	3.5	[1 – 8]	3	[1 – 11]	
Number of Nodes per patient if PL done	13.5	[7 – 36]	13	[3 – 72]	0.45
Patients with positive SLN					
Yes	3	18.8%	24	10.3%	0.3
No	13	81.3%	208	89.7%	
Patients with ≥1 positive node					
Yes	3	18.8%	27	11.6%	0.4
No	13	81.3%	205	88.4%	
Final pathologic exam					
Tumor size					
< 20 mm	8/15	53.3%	177/214	82.7%	0.005
≥ 20 mm	7/15	46.7%	37/214	17.3%	
LVSI					
Yes	5	31.3%	71	30.6%	0.82
No	11	68.8%	161	69.4%	
Parametrial invasion					
Yes	3/14	21.4%	7/226	3.1%	0.001
No	11/14	78.6%	219/226	96.9%	
Vaginal invasion					
Yes	4/14	28.6%	8/224	3.6%	<0.000 1
No	10/14	71.4%	216/224	96.4%	
Positive margin					
Yes	1/15	6.7%	11/223	4.9%	0.77
No	14/15	93.3%	212/223	95.1%	

Table 4. Univariate analysis of risk factors of severe postoperative complications

Predictive variable	Group with complications N = 31		Group without complications N = 217		P
	n median	[%] [range]	n median	[%] [range]	
Type of inclusion center					
Type 1	13	23.1%	50	41.9%	0.05
Type 2	5	13.8%	30	16.1%	
Type 3	13	63.1%	137	41.9%	
Age [years]					
Median	45	[25 - 67]	44	[25 - 85]	0.77
< 45	12	38.7%	112	51.6%	0.18
≥ 45	19	61.3%	105	48.4%	
BMI [kg/m²]					
Median	22.8	[16.8 – 36.8]	22.9	[14.6 – 45]	0.81
< 18,5	1	3.2%	14	6.4%	0.87
18,5 – 25	21	67.7%	134	61.8%	
< 25-30	5	16.1%	39	18%	
> 30	4	12.9%	30	13.8%	
Parity					
0	5	16.1%	40	18.4%	0.76
≥ 1	26	83.9%	177	81.6%	
Menopausal status					
Yes	11	35.5%	73	33.6%	0.84
No	20	64.5%	144	66.4%	
History of previous pelvic surgery					
0	17	54.8%	111	51.2%	0.7
≥ 1	14	45.2%	106	48.8%	
FIGO stage					
IA1 with emboli - IA2	3	9.7%	17	7.8%	0.53
IB1	28	90.3%	192	88.5%	
IB2-IIB	0	0%	8	3.7%	
Histology					
Squamous cell carcinoma	21	67.7%	156/213	73.2%	0.47
Adenocarcinoma	10	32.3%	52/213	24.4%	
Other type	0	0%	5/213	2.3%	
Presence of LVSI in the biopsy					
Yes	6/27	22.2%	42/187	22.5%	0.98
No	21/27	77.8%	145/187	77.5%	
Tumoral size at preoperative imaging					
Size < 20 mm	15/29	51.7%	106/179	59.2%	0.45
Size ≥ 20 mm	14/29	48.3%	73/179	40.8%	
Preoperative LEEP					
Yes	19	61.3%	131	62.1%	0.93
No	12	38.7%	80	37.9%	
Preoperative brachytherapy					
Yes	14	45.2%	62/208	29.5%	0.08
No	17	54.8%	148/208	70.5%	
Number of step-surgery					

1	25	80.6%	193	88.9%	<i>0.18</i>
2	6	19.4%	24	11.1%	
Type of surgical approach					
MIS	29	93.6%	193	88.9%	<i>0.43</i>
Laparotomy	2	6.4%	24	11.1%	
Type of RH (Querleu-Morrow)					
B	26/30	86.7%	184/209	88.1%	<i>0.83</i>
C	4/30	13.3%	25/209	11.9%	
Nodal staging					
SLN alone	15	48.4%	60	27.6%	<i>0.06</i>
SLN + PL	15	48.4%	142	65.4%	
SLN + PL + PAL	1	3.2%	15	6.9%	
Number of SLN per patient	3	[2 – 10]	3	[1 – 11]	<i>0.21</i>
Number of Nodes per patient if PL done	12	[7 – 29]	13	[3 – 72]	<i>0.25</i>
Patients with positive SLN					
Yes	3	9.7%	24	11%	<i>0.78</i>
No	28	90.3%	193	89%	
Patients with ≥1 positive node					
Yes	3	9.7%	27	12.4%	<i>0.66</i>
No	28	90.3%	190	87.6%	
Final pathologic exam					
Tumor size					
< 20 mm	24/30	80%	161/199	80.9%	<i>0.91</i>
≥ 20 mm	6/30	20%	38/199	19.1%	
LVSI					
Yes	6	19.3%	70	32%	<i>0.14</i>
No	25	80.7%	147	68%	
Parametrial invasion					
Yes	3	9.7%	7/209	3.3%	<i>0.1</i>
No	28	90.3%	202/209	96.7%	
Vaginal invasion					
Yes	2/30	6.7%	10/208	4.8%	<i>0.66</i>
No	28/30	93.3%	198/208	95.2%	
Positive margin					
Yes	3	9.7%	9/207	4.3%	<i>0.21</i>
No	28	90.3%	198/207	95.7%	
Adjuvant Radiotherapy					
Yes	7	22.6%	39/213	18.3%	<i>0.57</i>
No	24	77.4%	174/213	81.7%	