


ORIGINAL RESEARCH

Beyond bladder dysfunction: assessing the full impact of radical hysterectomy on cervical cancer patients

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Abstract

Although bladder dysfunction is the most commonly reported complication after radical hysterectomy, there are other significant complications associated with cervical cancer surgery that have received less attention in the literature. This study aims to investigate the frequency of non-functional complications related to radical hysterectomy and identify significantly related risk factors associated with their occurrence. A retrospective study was conducted on consecutive patients diagnosed with early-stage cervical cancer who underwent radical hysterectomy at La Paz University Hospital between 2005 and 2019. The study collected data on intraoperative, short-term and long-term complications, and a multivariate analysis was performed to identify potential predictors of surgical complications. Of the 111 patients included in the study, 11.7% experienced intraoperative complications. Multivariate analysis indicated that the presence of microscopic parametrial involvement was significantly associated with an increased risk of intraoperative complications (Odds ratio (OR) = 16.7; 95% Confident interval (CI): 1.4–195). Urological complications were the most common short-term complications, affecting 14.4% of the patients. On the other hand, lymphedema was the most frequent long-term complication, with a prevalence of 18%. In univariate analysis, the International Federation of Gynecology and Obstetrics (FIGO) stage tended to be associated ($p = 0.05$) with postoperative complications. Furthermore, the performance of selective sentinel lymph node biopsy instead of lymphadenectomy was associated with a reduced incidence of lymphedema, from 18% to 3.8%. While urological complications are the most common after radical hysterectomy, other complications, such as genitourinary fistula or lymphedema, while less frequent, are also significant due to their negative impact on patients' quality of life. Thus, an accurate preoperative diagnosis is essential to prevent surgical complications.

Keywords

Hysterectomy; Intraoperative complications; Postoperative complications; Uterine cervical neoplasms

1. Introduction

Cervical cancer is the fourth most commonly diagnosed cancer and the fourth leading cause of cancer-related death among women worldwide [1, 2]. Despite the availability of screening programs and the increasing use of human papillomavirus vaccines, cervical cancer remains a significant global health issue [3].

Treatment for cervical cancer varies based on the tumor stage at diagnosis, the presence of histological risk factors and the patient's reproductive preferences. The standard treatment for early-stage cervical cancer without lymph node involvement is primary surgery, involving radical hysterectomy with pelvic lymphadenectomy, as it has demonstrated exceptional survival rates. Although radiotherapy has exhibited com-

parable survival outcomes in these stages, it is associated with higher risks of adverse events [2, 4].

The primary goal of radical hysterectomy is to completely remove the tumor by surgically resecting the uterus, including the cervix, parametria and upper vaginal margin. This approach allows for preserving ovarian function in young women and avoids the need for radiotherapy. In addition, radical hysterectomy enables the examination of the entire surgical specimen, providing valuable information on anatomopathological prognostic factors. It also helps in assessing the extent and characteristics of the tumor for determining further treatment options and prognostic outcomes [5].

However, performing this type of surgery requires a meticulous dissection that involves the removal of parametrial tis-

sues in close proximity to surrounding structures such as the bladder, ureters, rectum and neurovascular pelvic bundles. Consequently, the main complications associated with radical hysterectomy are often related to injury to these structures [5], especially functional alterations of the bladder and bowel caused by nerve injuries. Querleu-Morrow's classification categorizes radical hysterectomy into four types based on the extent of parametrial resection [6]. In addition, the degree of potential denervation following radical hysterectomy is directly linked to the extent of the surgery and its radicality [7].

The most commonly reported long-term complication associated with radical hysterectomy in the literature is lymphedema, which often occurs secondary to pelvic lymphadenectomy [8]. Other complications, such as pulmonary embolism, pneumonia, acute myocardial infarction and fluid or electrolyte imbalances, are relatively rare [5].

The objective of this study was to examine the non-functional complications of radical hysterectomy, defined as complications other than bladder and bowel dysfunction. While these complications may be less frequent, they are also highly significant and underreported in the literature. Furthermore, we aimed to analyze potential risk factors associated with their occurrence.

2. Material and methods

2.1 Patients and data selection

This was a retrospective study comprising consecutive patients diagnosed with early-stage cervical cancer at the Gynecologic Oncology Unit of La Paz University Hospital between January 2005 and December 2019. All patients underwent primary surgical treatment *via* radical hysterectomy or radical trachelectomy and received follow-up care at the same center. The 2008 International Federation of Gynecology and Obstetrics (FIGO) classification was used to stage cervical cancer [2], and all stages from IA1 with lymphovascular space invasion (LVSI) to IIA1 were included in the study. The Querleu-Morrow classification was used to describe the degree of radicality of the surgery [6]. All surgical procedures were performed by gynecologic oncologists with at least 10 years of experience.

Patients with advanced tumor stage, according to the FIGO staging system, were excluded from the study. Additionally, those with incomplete clinical history or who underwent non-radical hysterectomy were also excluded.

Postoperative complications were categorized into two groups: short-term complications, which included complications occurring within the first 30 days after surgery, and long-term complications, which encompassed complications that occurred beyond that 30-day period.

Based on the existing literature, the following potential predictors of complications were selected for analysis: patient's age at diagnosis, body mass index, clinical tumor stage according to FIGO classification, tumor size, previous conization prior to radical hysterectomy, tumor size in the conization specimen, type of parametrial resection, duration of surgery, specific surgical procedures performed, number of lymph nodes removed, histological tumor, node and metastasis (TNM) stage, histological subtype and presence

of microscopic parametrial invasion. These factors were examined to determine their association with the occurrence of complications.

2.2 Statistical analysis

Mean and standard deviation (SD) are used for normally distributed variables and the descriptive analysis of quantitative variables, while median and interquartile range (IQR) are used for variables that did not follow a normal distribution. Student's *t*-test was employed to compare normally distributed variables and the Mann-Whitney test for non-normally distributed variables. Qualitative variables are described using frequency distributions and percentages. In addition, qualitative variables were compared using either the Pearson χ^2 test or Fisher's exact test, depending on the specific circumstances.

The effect of the variables on the occurrence of complications was evaluated using odds ratios (OR) and their corresponding 95% confidence intervals (CI). A backward stepwise logistic regression model was employed to adjust for different covariates. Covariates with *p*-values less than 0.2 in the univariate analysis were included in the multivariate analysis. All statistical analyses were conducted using the SPSS v.26 software (IBM Corp., Armonk, NY, USA), and the alpha error was set at 5%.

3. Results

3.1 Descriptive analysis

A total of 111 patients, with a mean age of 44.8 ± 10.3 years and a mean body mass index of 25.8 ± 4.6 kg/m², were included in this study. Most patients (*n* = 95; 85.6%) were classified as FIGO stage Ib1. Two patients (1.8%) underwent radical hysterectomy despite having a pre-surgical stage IA1. Although it would not be indicated according to current recommendations, in the past it was an option for cases with lymphovascular invasion [4]. Minimally invasive surgery was performed in 97 cases (87.3%), and most of the open surgeries were performed before 2008, which was the most commonly preferred surgical approach before that year. There were no cases of conversion from minimally invasive to open surgery. Radical hysterectomy was performed in 103 (92.8%) patients, while the remaining 8 (7.2%) patients underwent radical trachelectomy. In this study, 80 patients (72%) underwent parametrial resection of type C1 according to the Querleu-Morrow classification [6], which involves transection of the paracervix at its junction with the internal iliac vascular system while preserving the nerves. Comparatively, the resection of the paracervix was performed at the level of the ureter (type B) in 28 patients (25.2%). We also observed that limited radical hysterectomy (Type A) was performed in only 3 patients (2.7%). Table 1 summarizes the baseline features of the investigated patients and their tumor and treatment characteristics.

3.2 Intraoperative complications

Surgical intraoperative complications were observed in 13 (11.7%) patients. The mean duration of hospitalization fol-

TABLE 1. Patient, tumor and treatment characteristics.

	Mean	SD
Age (yr)	44.8	10.3
Body mass index (kg/m ²)	25.8	4.6
Tumor size in cone	16.2	8.7
Duration of surgery (min)	244.4	61.6
Intraoperative bleeding (mL)	150.0	201.3
Number of pelvic nodes removed	12.7	7.2
Final pathological tumor size (mm)	20.8	15.5
	N	%
Previous conization		
Yes	50	45.0
No	61	55.0
Surgical approach		
Laparoscopic	96	86.4
Robotic	1	0.9
Open	14	12.6
Type of parametrial resection		
A	3	2.7
B	28	25.2
C1	80	72.0
Bilateral salpingo-oophorectomy or salpingectomy		
Yes	85	76.6
No	26	23.4
Selective sentinel node biopsy		
Yes	64	57.7
No	46	41.4
Unknown	1	0.9
Pelvic lymphadenectomy		
Yes	86	77.5
No	25	22.5
Clinical tumor size		
Microscopic	33	29.7
≤2 cm	13	11.7
>2 cm	56	50.5
Unknown	19	17.1
FIGO stage at diagnosis		
IA2	2	1.8
IA1	5	4.5
IB1	96	85.6
IB2	4	3.6
IIA1	4	3.6
Definitive TNM stage		
pT1a1	5	4.5
pT1a2	6	5.4
pT1b1	71	64.0
pT1b2	8	7.2
pT2a	2	1.8
pT2b	5	4.5
Higher	14	12.6
Histological type		
Squamous cell carcinoma	73	65.8
Adenocarcinoma	31	27.9
Other	6	5.4
Unknown	1	0.9
Microscopic parametrial invasion		
Yes	8	7.2
No	103	92.8

N: number of patients. *SD*: standard deviation; *FIGO*: International Federation of Gynecology and Obstetrics; *TNM*: Tumor, node and metastasis.

lowing surgery was 6.8 ± 5.2 days. Three patients required blood transfusions during or after surgery, and four patients needed admission to an Intensive Care Unit (ICU). There were no reports of deaths during surgery. Table 2 presents the types of intraoperative complications observed in this study.

TABLE 2. Intraoperative complications.

	N	%
Intraoperative complications	13	11.7
Vascular injury	3	2.7
Intestinal injury	3	2.7
Bladder injury	5	4.5
Ureteral injury	1	0.9
Nerve injury	1	0.9
Intraoperative transfusion	3	1.8
Admission in ICU	4	3.6

N: number of patients; *ICU*: Intensive Care Unit.

Univariate analysis identified several variables significantly associated with the occurrence of intraoperative complications, including the presence of cervical conization prior to radical hysterectomy, duration of surgery, type of parametrial resection, histological tumor type and microscopic parametrial invasion in the definitive surgical specimen.

Multivariate logistic regression was then conducted to evaluate the association of these significant variables with intraoperative complications, and the results revealed that parametrial involvement (OR = 16.7, 95% CI: 1.4–195.0; $p = 0.02$) was the only factor significantly associated with intraoperative complications (Table 3).

3.3 Postoperative complications

Of the 111 patients included in this study, 42 (37.8%) experienced some type of postoperative complication within the first 30 days following surgery. Among them, seven patients (6.3%) required reoperation, one patient experienced hemorrhagic shock due to splenic decapsulation and required splenectomy, two patients needed exploratory laparotomy for postsurgical peritonitis resulting from a vaginal abscess and rectal perforation, two patients required surgical drainage of lymphocysts, one patient needed repair of a vesicovaginal fistula, and another patient required a urinary diversion due to ureteral obstruction.

Long-term surgical complications were observed in 33 (29.7%) cases. The most frequently reported long-term complication was lymphedema, affecting 20 (18%) women. However, it should be noted that the diagnosis of lymphedema was based on subjective signs reported by the patients and physical examinations, as standardized objective measures were not used. A summary of both short and long-term complications is shown in Table 4. When analyzing if there was a relationship between the rate of lymphedema and radiotherapy treatment after radical hysterectomy, no statistically significant differences in the rate of lymphedema were found between patients who received

adjuvant radiotherapy and those who did not ($p = 0.18$).

Moreover, it should be noted that in univariate analysis, there was a trend toward an association ($p = 0.07$) between the TNM histological tumor stage and short-term postoperative complications and between FIGO stage ($p = 0.05$) and long-term postoperative complications.

4. Discussion

In this retrospective study, the most frequent complications after radical hysterectomy were urological, consistent with the current literature. Functional disorders are the most commonly reported complications and are thought to be caused by the disruption of sympathetic and parasympathetic nerves during the resection of posterior, anterior and lateral parametria, which run towards the bladder and rectum in the inferior portion of uterosacral ligaments, cardinal ligaments and bladder pillars [8–10]. Therefore, the most common symptoms in the first year after surgery are bladder atony and urinary retention [11]. Bladder dysfunction has been reported to occur in up to 47% of cases [12–14]. In this present study, 15% of women experienced bladder dysfunction in the first month after surgery, which decreased to 3.6% after 30 days. Zapardiel *et al.* [9] reported that the type of parametrectomy is significantly related to voiding recovery, with type C2 being associated with the longest interval to voiding recovery ($p < 0.001$) and the highest risk for delayed voiding recovery over one week (OR = 5.843, $p = 0.011$).

In addition to functional disorders, the most common complications of radical gynecological procedures, intraoperative injuries to the ureter and bladder are also significant complications of radical hysterectomies [15]. The incidence of intraoperative urological complications during radical hysterectomy is considered to be highest compared to other gynecological surgeries, possibly due to the extensive dissection required to remove the ureteral adventitial tissue and bladder tissue during these radical procedures. The presence of a cervical mass further contributes to the complexity of the procedure and the potential for complications [16]. Ureteral injuries typically occur during the unroofing of the ureteral tunnel and dissection of the distal portion of the ureter near its entry into the bladder, which is the most challenging part of the dissection in radical hysterectomies. Bladder injuries can occur during the dissection to achieve an adequate vaginal resection margin. While bladder injuries are readily identifiable and can be repaired easily, ureteral injuries often go unnoticed during surgery, and clinical signs may manifest in the days following the operation.

It is reported that the incidence of perioperative urological complications during radical hysterectomy ranges from 1.3% to 7.8% [16–20]. In a meta-analysis of 38 studies performed by Hwang *et al.* [15], who compared perioperative urological complications of radical hysterectomies with lymph node dissection in open versus laparoscopic surgery, intraoperative urological complications were reported in 3.7% of patients who underwent laparoscopic radical hysterectomy. The incidence of bladder injury (2.5%) was significantly higher than ureter injury (1.3%) ($p = 0.001$). Moreover, intraoperative urological complications in the laparoscopic group showed a significant association with obese patients but not in patients

TABLE 3. Univariable and multivariable logistic regression analyses of the risk factors for the occurrence of intraoperative surgical complications.

Intraoperative complications			
Univariate analysis			
Risk Factors	Intraoperative Complications		<i>p</i> value
	Yes N (%)	No N (%)	
Conization	2 (95.9)	47 (4.1)	0.059
Type of parametrial resection	11 (90.0)	11 (10.0)	0.191
Histological type	98 (89.9)	11 (10.1)	0.101
Parametrial involvement	4 (36.4)	4 (4.0)	0.003
	Mean (SD)	Mean (SD)	<i>p</i> value
Duration of surgery (min)	256.5 (49.2)	233.9 (53.1)	0.202
Multivariate analysis			
Risk factors	OR	95% CI	<i>p</i> value
Parametrial involvement	16.7	(1.4–195.0)	0.024

N: number of patients; *SD*: standard deviation; *OR*: odds ratios; *CI*: confidence intervals.

TABLE 4. Percentage of short-term (≤ 30 days) and long-term (> 30 days) complications.

	N	%
Short-term (≤ 30 days) complications	41	36.9
Bladder disfunction	16	14.4
Fistula	3	2.7
Infection	4	3.6
Fever	6	6.3
Other	12	10.8
Reintervention	7	6.3
Long-term (> 30 days) complications	33	29.7
Lymphedema	20	18.0
Bladder disfunction	4	3.6
Vaginal vault dehiscence	3	1.8
Other	7	6.3

N: number of patients.

with a standard body mass index ($OR = 1.08$). Further, the authors also reported that laparoscopic radical hysterectomy was associated with a significantly higher risk of intraoperative and postoperative urologic complications than abdominal radical hysterectomy ($OR = 1.35$). In another recent study involving over 12,000 patients who underwent radical hysterectomy, a 7.4% rate of urological injuries requiring urologic procedures was reported. The most common urologic interventions included double J stent placement, bladder repair, percutaneous nephrostomy and ureteroneocystostomy [12]. These findings highlight the importance of prompt recognition and appropriate management of urological injuries during radical hysterectomy to minimize their impact on patient outcomes. In our current study, bladder injury was observed in 5 patients (4.5%) and ureteral injury in one patient (0.9%), representing an overall intraoperative urological injury incidence of 5.4%, which aligns with existing literature.

In the multivariate analysis of intraoperative complications in our study cohort, we identified a significantly higher risk of intraoperative complications in patients with parametrial involvement detected in the microscopic pathological study after

surgery ($p = 0.02$). This result could be attributed to the greater surgical complexity associated with parametrial involvement, leading to a higher likelihood of complications in these cases. However, it is important to note that patients with parametrial involvement should not typically undergo primary surgery by radical hysterectomy, as they are more suitable candidates for chemoradiation therapy. A more accurate preoperative diagnosis of the tumor stage could potentially help prevent complications in these patients. Our initial literature inspection revealed no other studies that specifically associate parametrial involvement with complications in this type of surgery.

In addition to the aforementioned complications, genitourinary fistulas are also significant due to their clinical consequences following radical hysterectomies. The reported rate of fistulas has been as high as 30% [21], possibly due to the more extensive parametrial resection that was commonly performed. However, more recent studies have shown a decrease in the fistula rate to under 3% [18, 19, 22], consistent with our cohort's findings (2.7%). Thus, a reduction in fistula rates can be attributed to improvements in surgical techniques and increased expertise in performing radical hysterectomies.

Lower-extremity lymphedema is the most common long-term effect following radical hysterectomy and has been associated with increased anxiety, depression and decreased self-confidence, all contributing to a diminished quality of life [7, 23]. The reported incidence of lymphedema secondary to cervical cancer surgeries varies widely, ranging from 7% to 55% [23, 24]. This wide variation can be attributed to the lack of standardized objective measurements and the reliance on subjective data from patient-reported symptoms [25]. In our cohort, lymphedema was also the most frequent long-term complication, affecting 18% of women. However, since January 2017, all patients undergoing radical hysterectomy were enrolled in the SENTIX trial [26] (26 patients of the total), where systematic lymphadenectomy was replaced by selective sentinel node biopsy followed by routine assessment of lymphedema during each follow-up visit. Currently, only one of these patients (3.8%) has developed lymphedema. The rates of lower extremity lymphedema were previously described by Niikura *et al.* [27], who utilized a sentinel lymph node mapping algorithm, resulting in a decrease in lymphedema rates from 42% to 8.7%. The ongoing prospective trials, including SENTIX [26], PHENIX [28] and SENTICOL III [29], would provide additional data on this subject in the near future, and it is anticipated that findings from these trials may contribute to significant reductions in the incidence of late complications, such as lower-extremity lymphedema, in this type of surgery.

Additionally, the rates of lymphedema reported in literature are higher in patients who receive adjuvant radiotherapy following radical surgery [23, 30, 31]. However, in our analysis this association wasn't found.

Sexual dysfunction is a commonly reported long-term complication following radical hysterectomy, primarily attributed to the shortened vagina and damage to the sympathetic nerves responsible for lubrication. However, this important issue is often not adequately recorded in the patient's clinical history, as in our cohort. The underreporting of sexual dysfunction in clinical records can lead to insufficient attention and support for patients experiencing these challenges. It is crucial to recognize the impact of sexual dysfunction and address it proactively in order to provide comprehensive care and improve the quality of life for patients who have undergone radical hysterectomy.

Our study has several limitations that should be considered. Firstly, its retrospective nature and the small number of patients may limit the generalizability of the findings. The retrospective design introduces the possibility of incomplete or inaccurate information, which could affect the validity and reliability of the collected data. As a result, the number and characteristics of complications and the relationships between the variables studied may have been underestimated. Additionally, the inclusion of a mix of surgical approaches, including both open and minimally invasive surgery and different types of radicality, further adding complexity to the interpretation of the results. Thus, the heterogeneity in surgical techniques and approaches might have introduced confounding factors and limited the ability to extrapolate our findings to broader populations.

5. Conclusions

While functional complications are commonly reported after radical gynecological procedures, there are few articles available in literature that address other less frequent but significant complications that can greatly impact a patient's quality of life, such as genitourinary fistulas and lymphedema. This original paper not only explains the complications beyond the functional ones, but also provides a comprehensive review of the evidence available in literature.

In our cohort, we found that microscopic parametrial invasion was associated with higher rates of intraoperative complications. Additionally, the use of selective sentinel lymph node biopsy instead of lymphadenectomy resulted in a notable decrease in the rate of lymphedema from 18% to 3.8% in our study. Accurate preoperative diagnosis of tumor stage and knowledge of risk factors associated with operative complications are vital in improving the comprehensive management of oncological patients.

AVAILABILITY OF DATA AND MATERIALS

The data presented in this study are available on reasonable request from the corresponding author.

AUTHOR CONTRIBUTIONS

MAE—conception, data collection, manuscript writing, manuscript review, editing and final approval; MAG—data analysis, manuscript review, editing and final approval; VGP—conception, data collection, manuscript review, editing and final approval; MG—conception, data collection, manuscript review, editing and final approval, JS—conception, data analysis, manuscript review, editing and final approval; MDD—conception, data collection, manuscript review, editing and final approval; AH—conception, data analysis, manuscript review, editing and final approval; IZ—conception, data collection, data analysis, manuscript review, editing and final approval.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The data for this study were obtained through a review of patients' medical records, following approval from the Ethics and Clinical Research Committee of La Paz University Hospital (Ref. PI-3668).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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