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A hybrid approach: a safe option for surgical treatment of early-stage cervical cancer

J. AMENGUAL VILA[1,2,3], A. TORRENT COLOMER[1,2,3], C. SAMPOL BAS[4], A. QUINTERO DUARTE[5], M. RUIZ COLL[1], J. RIOJA MERLO[1], O. CORDOBA[1,2,3]

[1]Obstetrics and Gynecology Department, Gynecologic Oncology Unit, Hospital Universitari Son Espases, Palma, Spain
[2]School of Medicine, Universitat de les Illes Balears (UIB), Palma, Spain
[3]Health Research Institute of the Balearic Islands, IdISBa, Palma, Spain
[4]Department of Nuclear Medicine, Hospital Universitari Son Espases, Palma, Spain
[5]Department of Pathology, Hospital Universitari Son Espases, Palma, Spain

Abstract. – OBJECTIVE: The aim of the study was to describe the surgical treatment of early-stage cervical cancer (CC) *via* minimally invasive surgery (MIS) and a sequential hybrid approach combining MIS and mini-Pfannenstiel. Evaluate sentinel lymph node (SLN) detection using a hybrid tracer (ICG-^{99m} Tc nanocolloid).

PATIENTS AND METHODS: Prospective, observational, descriptive, single-center study conducted at Son Espases University Hospital between January 2019 and September 2021. Patients with early-stage CC (FIGO 2018 IA1 with ILV-IIA1) who underwent surgical treatment with a follow-up of at least one year were included.

RESULTS: Thirty early-stage CC patients were included, of whom four (13.3%) were upstaged due to positive SLNs. In these cases, laparotomy was avoided, and paraaortic lymphadenectomy was performed *via* MIS approach. Twenty-six patients had a radical hysterectomy: 15 underwent a hybrid approach, 10 laparoscopy, and one laparotomy.

Patients undergoing laparoscopic surgery had a smaller estimated tumor size than those undergoing the hybrid approach.

The overall SLN detection rate was 96.1%, with 88.5% of cases occurring bilaterally. Five out of 26 patients (19.2%) presented SLN macrometastases, and five (19.2%) had atypical drainage. Surgery refined staging in 33.3% (10/30) of cases. No recurrences were reported after an average follow-up of 32 months.

CONCLUSIONS: MIS for SLN avoids laparotomy leading to rapid recovery and early adjuvant treatment initiation in nodal metastasis. In our study, tumor size is an important clinical implication in the surgical approach to be used. The hybrid tracer provided a high detection rate and combined the advantages of the two tracers. The hybrid approach has a quick recovery and optimal results.

Key Words:
Early-stage cervical cancer, Sentinel lymph node, Indocyanine green, Radiotracer, Radical hysterectomy, Surgical techniques, Minimally invasive surgery.

Introduction

Radical hysterectomy (RH) with bilateral pelvic lymphadenectomy is the standard surgical treatment for early-stage cervical cancer (CC)[1-3]. Over the last few decades, minimally invasive surgery (MIS) has been the main approach to treat these patients. The surgical method changed after the publication of the LACC trial[4] in favor of open surgery. In 2018, Ramirez et al[4], published the first prospective randomized phase III trial reporting much reduced disease-free survival (DFS) and overall survival (OS) in women operated *via* MIS *vs.* open surgery (86.0% *vs.* 96.5% DFS at 4.5 years, respectively).

Accordingly, the guidelines of the leading scientific societies recommend an open approach as the standard of care. On the contrary, for the study of nodal status, the MIS approach is preferred (level B)[3].

Lymph node staging is performed to assess the prognosis and guide the treatment; the standard lymph node staging procedure is a bilateral pelvic lymphadenectomy (with or without sentinel lymph node (SLN) mapping)[2].

The LACC trial was not designed to address the cause of these worse MIS results. The mechanisms underlying this increase in recurrence and mortality with MIS continue to be unclear. Some theories speculate that uterine manipulation could fragment the tumor and, perform

Corresponding Author: Amengual Vila Joana, MD; e-mail: amengual.joana@gmail.com

colpotomy in the presence of CO_2, and favor the spread into the abdominal cavity.

This study aims to describe the clinical outcomes and follow-up of the sequential double hybrid approach to early-stage CC performed at Son Espases University Hospital between 2019 and 2021.

Patients And Methods

This was an observational, prospective, descriptive, single-center study that took place at Son Espases University Hospital. The selection criteria were: (1) women over 18 years old, (2) histological diagnosis of adenocarcinoma, squamous carcinoma, and adenosquamous CC by biopsy or conization, (3) women with clinically early-stage CC (FIGO 2018 IA1 with ILV, IA2, IB1, IB2, and IIA1), (4) women who have undergone a radical hysterectomy such as B or C according to the Querleu-Morrow classification, (5) women having ECOG performance status 0-2, and (6) no contraindications for the surgical procedure. The recruitment period started in January 2019, and we carried out an initial analysis considering all patients with at least 12 months of follow-up.

All subjects gave their informed consent for inclusion before participating in the study. This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Balearic Islands (IB 4954/22 PI; IB 4955/22 PI).

Exclusion criteria were: (1) locally advanced stages (FIGO IB3, II-IV; Except IIA1), (2) metastatic disease, (3) medical co-morbidities contraindicated for surgical treatment, (4) history of pelvic radiotherapy, and (5) pregnant women.

Physical gynecological exam by an expert oncologic gynecologist, pelvic MRI, and thorax-abdomen-pelvic CT or PET/CT scan was performed in all patients before surgery.

Injection Tracer: ICG-^{99m}Tc-Nanocolloid

The hybrid tracer was composed of 0.75 mL ICG added to a vial of ^{99m}Tc-nanocolloid. The final activity was 4.5 mCi in a global volume of 2 ml (NanoHSA, ROTOP, Curium Pharma, Belin, Germany). It was administered before surgery with the injection of 0.5 mL in four cervical cardinal points, peritumoral, through a 22 G needle. In patients receiving the tracer injection 24 hours before surgery, pre-operative SPECT/CT imaging was performed 60 and 120 minutes after tracer injection. When these images were available before surgery, they were assessed by a multidisciplinary team composed of nuclear medicine specialists and oncologic-gynecologic surgeons to improve SLN localization.

Surgery

All women underwent laparoscopic (Karl-Storz Endoscope, Tuttlingen, Germany) or robotic (da Vinci® Surgical System Version Xi, Intuitive Surgical Inc., Sunnyvale, CA, USA) surgery for SLN procedures based on the SLN algorithm described in the National Comprehensive Cancer Network guidelines (NCCN)[5,6].

A laparoscopic gamma probe compatible with a 10-12 mm diameter laparoscopic trocar was used to locate the radioactive intensity of ^{99m}TC. Fluorescence imaging near-infrared optical imaging by laparoscopic or fire-fly mode from the robotic da Vinci® Surgical System was employed. During surgery, a lymph node was regarded as an SLN when it was fluorescent and showed increased activity detected *via* the gamma probe.

In all cases, even when presenting negative SLNs, a complete bilateral pelvic lymphadenectomy was performed to validate the technique's performance in our center. To achieve quality and safety, current published studies[7-9] have evaluated the learning curve for SLN dissection in gynecologic cancer. It has been shown that the learning curve for successful SLN mapping stabilizes after 30 cases.

The hybrid approach consists, firstly, of performing the SLN biopsy by MIS. If the SLNs are disease-free, we continue with MIS to prepare the anatomical spaces to perform the radical hysterectomy up until the colpotomy. We then complete the surgery by mini-Pfannenstiel (8 cm) to perform the colpotomy without the presence of CO_2, followed by immediate removal of the uterus, protecting the tumor, and minimizing the time in the abdominal cavity.

In our cohort, tumor size and SLN status were considered a two-step flowchart algorithm. The surgical approach was divided into two groups, which are described in Figure 1.

Histological Assessment

SLNs underwent intra-operative frozen-section evaluation by an ultrastaging protocol. Subsequently, all SLNs were formalin-fixed and paraffin-embedded for pathological assessment, including Hematoxylin-Eosin (H&E) plus immunohistochemistry (IHQ) staining (mixed cytokeratin).

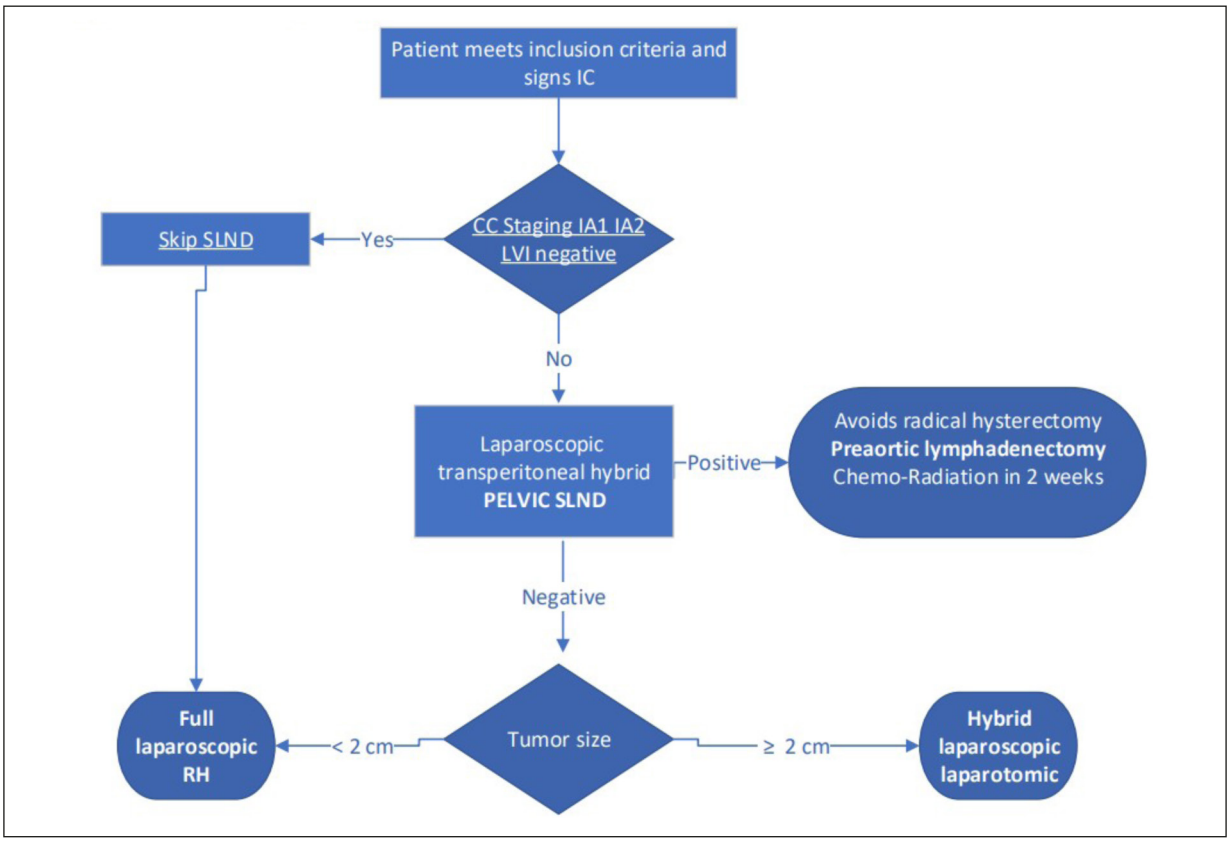

Figure 1. Flowchart surgical approach.

Lymph nodes obtained from pelvic lymphadenectomies were histologically evaluated by H&E.

A modification of the American Joint Committee on Cancer (AJCC; version 9) staging definitions for axillary nodes in breast cancer was adapted to classify SLN burden (macrometastasis: cells > 2.0 mm in diameter, micrometastasis: cells between 0.2-2.0 mm in diameter and isolated tumor cells < 0.2 mm in diameter and less than 200 cells)[10].

Data Collection

Data collection was carried out *via* the review of clinical records through the clinical-healthcare computer system (Millennium, Cerner Corporation, Kansas City, MO, USA) of the Son Espases University Hospital. Sociodemographic, intraoperative, and postoperative data were collected from the women who met the inclusion criteria. All information was encrypted and integrated into a data matrix, in a spreadsheet-like computer program with password access, designed specifically for this study and its subsequent analysis. The principal investigator was the person responsible for uploading the information into the database.

In this initial analysis, we included patients with at least one year of follow-up after the surgical procedure.

Statistical Analysis

A descriptive analysis of all variables was performed to define the characteristics of the study group with frequencies and percentages for qualitative variables and with measures of central position and dispersion for quantitative variables; those with normal distribution were expressed as mean and standard deviation and, those with non-normal distribution, as median and interquartile range.

For characteristics comparable from the basal point of view between the surgery types, techniques such as the U-Mann Whitney or Student's *t*-test (according to normal) and the Chi-square test or exact Fisher's test were applied, for quantitative and qualitative variables, respectively, to contrast possible differences of interest. A value of $p < 0.05$ was considered to indicate a significant difference. Data analysis was performed using IBM-SPSS v. 26 statistical software (IBM Corp., Armonk, NY, USA).

Results

Over the study period, 79 cases of CC were diagnosed: 5 (6.3%) *in situ* carcinomas, 26 (32.9%) early-stage CC, and 48 (60.7%) locally advanced or metastatic CC.

Preoperative Results

Thirty patients with clinically early-stage CC were included in the study, according to the inclusion criteria. All patients have at least one year of follow-up.

Four of the 30 patients had a positive SLN in the ultrastaging analysis. These four cases presented a negative computed tomography (CT) for pelvic and paraaortic lymph node involvement. Two had atypical drainage: one drained directly into the inframesenteric paraaortic area and one into the deep presacral zone.

In these patients, paraaortic staging lymphadenectomy was performed and could be correctly sorted into chemoradiotherapy, avoiding RH. They were upgraded to a FIGO stage IIIC1 or IIIC2. Laparotomy was avoided in 13.3% (4/30) of patients, and they initiated chemoradiation therapy two weeks after the intervention. Currently, they are disease-free after more than two years.

The study was conducted on 30 patients, 4 underwent paraaortic lymphadenectomy, 15 hybrid surgery, 10 laparoscopic surgery, and one patient had a laparotomy as they presented a 20 cm diameter myoma and were diagnosed with colon cancer at the same time (synchronous cancer).

Patient and disease characteristics are presented in Table I. Median age, body mass index (BMI), antecedent conization, and histological features were not significantly different between the two groups.

Conization was carried out before surgery in 17 patients (56.6%). Conized patients had smaller tumors (mean: 1.4 cm) than non-conized patients (mean: 2.6 cm). Primarily, in tumors less than 2 cm, the purpose of conization was to reach the diagnosis, assess the tumor size, detect the presence of LVSI, and reduce tumor volume. After surgical treatment, previously conized patients were less likely to require adjuvant treatment (56% of non-conized patients required adjuvant treatment *vs.* 8% of conized patients; p=0.023).

In terms of staging, 64% of patients presented stages ≤ IB1 (tumors ≤ 2 cm) and 36% stages ≥ IB2 (tumors ≥ 2 cm). Patients with laparoscopic surgery had a smaller estimated tumor size than those with hybrid surgery (0.4 [0.1-1.5] *vs.* 2.3 [0.8-3.0]; p = 0.019). Most patients undergoing laparoscopic surgery had a tumor diameter ≤ 2 cm (90%). In contrast,

Table I. Clinical patient and disease characteristics.

	Patients (N = 25)		
Characteristics	**Hybrid (N = 15)**	**Laparoscopic (N = 10)**	***p*-value**
Median age, yr. (range)	46 (38-49)	47 (44 -56)	p=0.973
Body-mass index - Kg/m^2	26 (23-27)	23 (22-24)	p=0.267
Conization	9/15 (60%)	6/10 (60%)	p=1.00
Histology			
Squamous	10 (66.6%)	7 (70%)	NA
Adenocarcinoma	2 (13.3%)	2 (20%)	
Adenosquamous	3 (20%)	1 (10%)	
Preoperative tumor size	2.3 (0.8-3.0)	0.4 (0.1-1.5)	p=0.019
≤ 2 cm	8 (53.3%)	8 (80%)	p=0.380
> 2 cm	7 (46.6%)	2 (20%)	
FIGO Stage 2018			
IA1/IA2	3 (20%)	5 (50%)	NA
IB1	5 (33.3%)	3 (30%)	
IB2	3 (20%)	0	
IB3	1 (6.6%)	1 (10%)	
IIA1	3 (20%)	1 (10%)	
Grading			
G1/G2	9 (60%)	9 (90%)	NA
G3	6 (40%)	1 (10%)	
LVSI			
Absent	10 (66.6%)	9 (90%)	p=0.360
Present	5 (33.3%)	1 (10%)	

LVSI = lymphovascular invasion; NA = Not applicable.

with the hybrid technique, 42.8% of patients had tumors ≤ 2 cm and 57.1% greater than 2 cm.

Of the 30 patients initially included in the study, due to a clinically early stage, 26 (86.6%) presented criteria for nodal status analysis. The four patients in whom SLN analysis was not performed were FIGO stage IA1/IA2 stage without lymphovascular space invasion (LVSI).

Surgery

95 SLNs were identified. The mean nodes per hemipelvis were two (1.0-3.0) on the right and one (1.0-2.0) on the left. The overall SLN detection rate was 96.1%, with 88.5% of cases occurring bilaterally. SLN results are described in Table II.

Four of these presented SLN metastases, and one was a parametrial node metastasis diagnosed in the hysterectomy specimen (5 out of 26 patients [19.2%]). The atypical drainage rate was 19.2% (common iliac, parametrial, presacral, and aorto-iliac bifurcation) (Figure 2). Of the nodes in atypical locations, 50% were metastatic (Figure 3).

Of the five macrometastatic SLNs, four were both radioactive and fluorescent and were diagnosed intraoperatively. The fifth lymph node was detected in the final pathology analysis of the uterus at the lateral parametrium. The median size of the SLN metastases was 5.4 mm (range: 3-9 mm).

All patients with metastatic SLN presented tumors larger than 2 cm (median 2.86 cm) and 80% had positive LVSI than those with negative SLN (mean: 1.8 cm). Among the five patients with positive SLNs, none had non-sentinel node involvement.

Among the patients who did not present tracer drainage or unilateral drainage, (3/26 [11.5%]) all had tumors larger than 2 cm with some clinical characteristics that could interfere with the drainage of the tracer, such as the presence of myomas, endometriosis, or prior conization (Tables III-IV).

LVSI was present in 33.3% of patients, corresponding to histologic grade G2 and G3 tumors; 70% of these patients required adjuvant chemoradiation (ChRT) therapy for exhibiting risk factors.

Type B and C radical hysterectomy, according to the Querleu-Morrow classification1, were performed in 26 patients after the nodal status study (Figure 3).

Postoperative Results

The surgical resection margins were disease-free in 96% of patients. Only one patient presented with an affected focal vaginal margin. After hybrid surgery, she was diagnosed with a 2.5 cm diameter tumor, stage FIGO IIA1, due to the involvement of the upper vaginal. Adjuvant therapy with ChRT was prescribed, and after three years of follow-up, she remains disease-free.

There were no intra-operative complications in any patient. Three cases (11.5%) of Clavien-Dindo Class III postoperative complications were recorded:

- Iatrogenic distal ureteral damage. On day 3, a ureterocystostomy was performed by laparoscopy.

Table II. Sentinel Lymph nodes' detection rates.

	Double hybrid (Tc99 + ICG)	Senticol-1[15] (Tc +/- Blue)	Freitas/Baiocchi[16] (Tc + Blue)	P. Ramírez/G. Salvo[17] (Tc +/- Blue +/- ICG)
Total patient	26	139	57	188
Total included groins for SLN biopsy	89	454		
SLN/patient	3 (1.0-3.0)	3 (0-10)		
Overall pelvic detection	25/26 (96.1%)	98%	84%	90%
Bilateral pelvic detection	23/26 (88.5%)	77%	58%	62%
≤ 2 cm (≤IB1)	14/14 (100%)			
> 2 cm (≥IB2)	9/12 (75%)			
Unilateral pelvic detection	2/26 (7.6%)	94%		
Not pelvic drainage	1/26 (3.8%)	2%		
Node involvement	0/3			
SLN atypical drainage	5/26 (19.2%)			
Empty node packet	1/26 (4%)			
Positive SLNs	5/26 (19.2%)	17%		
False negative	0%	8%		
NPV	100%	98%		
Sensibility	100%	92%		

Tc99=99mTechnetium nanocolloid; ICG=indocyanine green; SLN = sentinel lymph node; NPV=negative predictive value.

- Dehiscence of vaginal cuff with bowel evisceration after sexual intercourse four weeks after surgery, which was repaired vaginally.
- Persistent vaginal lymphorrhea one month after surgery, solved satisfactorily with nodal sclerosis *via* interventional radiology.

The two surgical techniques have similar operation times: 226 min (170.0-305.0) laparoscopically and 268 min (250.0-290.0) hybrid.

In 36.6% of cases, the pre-surgical study estimated a tumor size different from the real size (26.6% were larger and 10% were smaller). Surgery refined staging in 33.3% (10/30) of cases (Figure 4). Of the 30 patients, 9 (30%) were upstaged due to the detection of sentinel node metastases, to a larger post-operative tumor size or by the detection of vaginal mucosal involvement, and one was downstaged. This upstage is an important factor in selecting the appropriate treatment modality.

Eight of the 26 (30.7%) patients who underwent a radical hysterectomy received adjuvant therapy [five chemoradiotherapy, two External Beam Radiation Therapy (EBRT) plus brachytherapy, and one brachytherapy]; 87.5% (7/8) of these patients had a tumor larger than 2 cm (≥ IB2; p=0.011).

The average hospital stay for laparoscopic procedures was two days (2.0-4.0) and three days (2.0-3.0) for the hybrid technique (p=0.605).

The median follow-up was 32 months (range, 21-50 months), and no recurrence has been

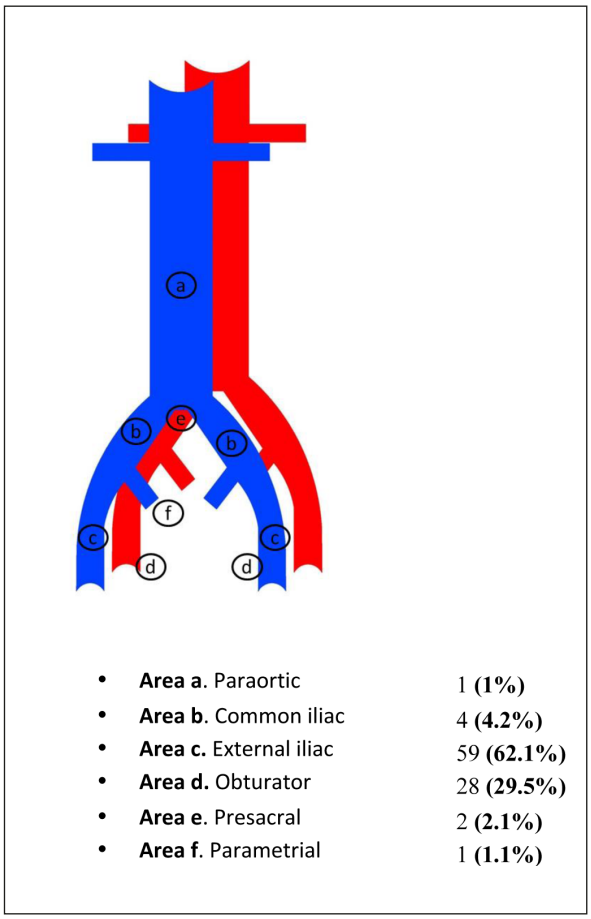

Figure 2. Sentinel lymph node distribution.

Table III. Description of patients with failed drainage.

Age	BMI	Patient characteristics	Clinical size (cm)	Intraoperative Tracer	Drainage	LND	Histopatologic
38	26	Mioma 9 cm	3	Hybrid (ICG+Tc99)	Unilateral (right)	Negative	Adenocarcinoma
74	27	–	4	Hybrid (ICG+Tc99)	Unilateral (left)	Negative	Squamous
55		Conization	1	Hybrid (ICG+Tc99)	Unilateral (right)	Negative	Adenocarcinoma
65	24	Conization Mioma 4 cm Endometriosis	2.4	Hybrid (ICG+Tc99)	No drainage	Negative	Squamous

BMI=Body mass index; ICG=indocyanine green; Tc99= 99 technetium nanocolloid; LND = Lymphadenectomy.

Table IV. Description of patients with failed drainage.

Grade	LVSI	Postsurg. tumor size (cm)	FIGO stage	RH margins	Adjuvant treatment
G3	Negative	2	IIA1	Negative	EBRT + BT
G2	Negative	5.5	IIA2	Negative	No
G1	Negative	1	IB1	Negative	No
G3	Positive	2.5	IIA1	Positive	QRT

LVSI = Lymphovascular space invasion; Postsurg. = postsurgical; RH = Radical Hysterectomy; EBRT = External Beam Radiation Therapy; BT = Brachytherapy.

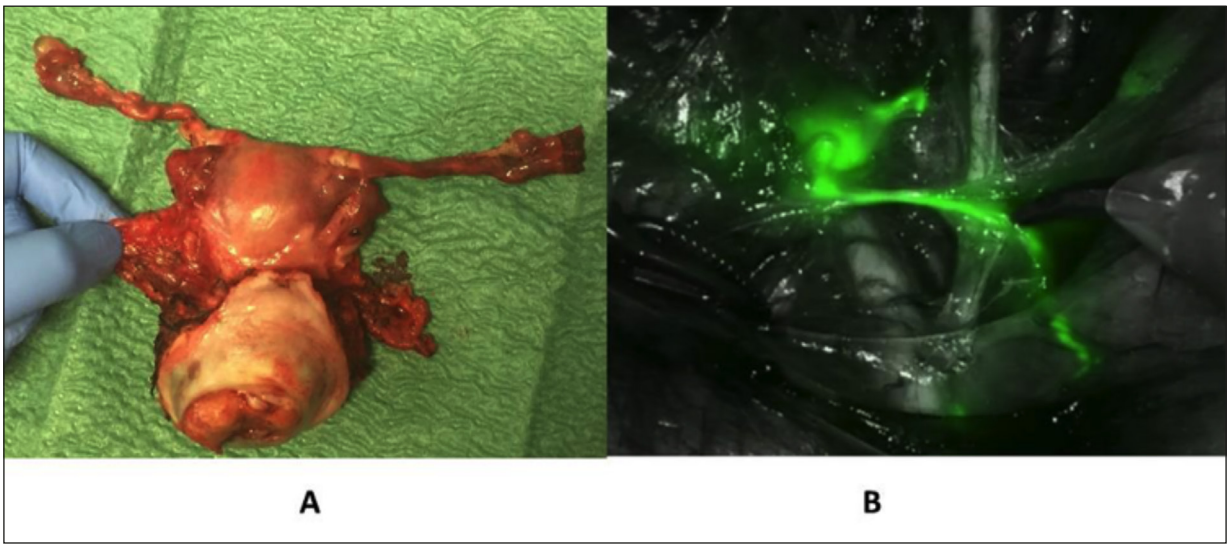

Figure 3. **A**, Radical hysterectomy type C (Querleu and Morrow). **B**, Parametrial right sentinel node.

detected in any patient (86.2% followed up over two years and 36.3% over three years). Only one patient had to undergo a partial laparoscopic colpectomy due to a de novo vaginal intraepithelial neoplasia 3 (VAIN3). Eighteen months after surgery, the patient was diagnosed with persistent HPV genotype 16 (she had FIGO IA2, G2, LVSI-negative, and free margins at upfront surgery).

Discussion

The results of the LACC trial[4] and database analysis[11] were unexpected and thus led to a change in the surgical approach for early-stage CC. Many institutions have abandoned the use of MIS for RH and others have developed different strategies to continue using a minimally invasive approach.

It remains to be seen why a minimally invasive approach may lead to lower survival. Possible explanations include the use of insufflation with CO_2 circulation, promoting dispersion of tumor cells, and the use of a uterine manipulator, which may disrupt larger tumors and cause spread during surgery.

A sub-analysis of the LACC trial showed that, in tumors less than 2 cm, the results were similar between laparoscopy and open surgery. The authors respond that the study has no statistical

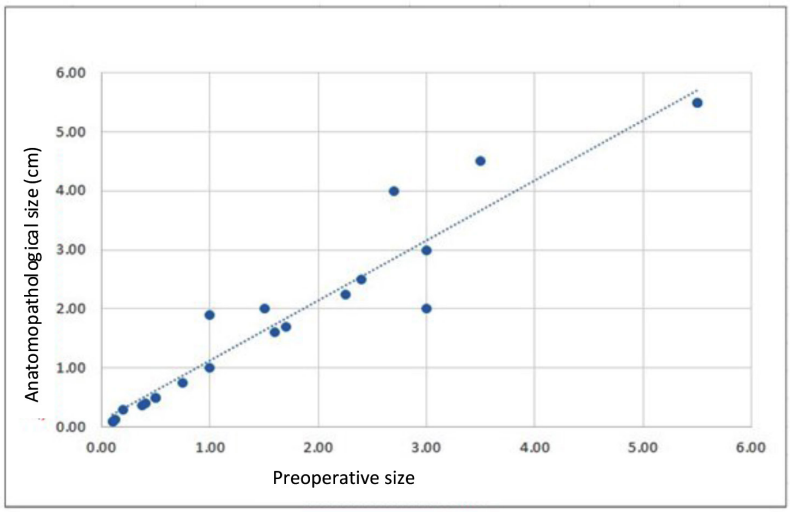

Figure 4. Correlation of pre and postoperative tumor size.

power to respond to this statement. The same result was found in the database analysis (the hazard ratio for deaths was statistically similar between the two surgical approaches).

Currently, laparotomy is the standard approach for all procedures that include RH (grade A), and MIS is an acceptable approach for lymph node staging (grade B). According to the last update of the ESGO/ESTRO/ESP guidelines[3] for the management of patients with CC, MIS may be considered in low-risk tumors (< 2 cm and free margins after conization) in high-volume centers that meet the ESGO quality criteria for surgery.

This is why, in our study, we designed two groups considering a tumor size cutoff of 2 cm and avoiding the possible main risk factors for tumor spread (the use of a uterine manipulator and/or intracorporeal colpotomy without the presence of CO_2). The objective of our study was not to compare the two surgical approaches but to perform a description and assess the oncological safety of both considering tumor size as the point of choice. Most laparoscopic/robotic patients had tumors smaller than 2 cm (0.4 [0.1-1.5]) and most had pre-operative conizations (60%) as protective maneuvers, whereas patients operated *via* a hybrid approach had tumors over 2 cm (2.3 [0.8-3.0]).

It is very important to consider the tumor size estimation method[12]. In our current practice, tumor size is evaluated pre-operatively by clinical examination, pelvic MRI, and/or conization for better triage. We conclude that the pre-operative study was carried out correctly because only 7.7% had a change in FIGO stage.

After a follow-up period of 32 months (21-50), neither group presented recurrence. These results are comparable with the laparotomic arm of the LACC trial. We conclude that tumor size plays an important clinical role in determining the type of surgical approach to perform and avoiding possible risk factors of tumor fragmentation and spread, without compromising the radicality of the surgery. These are key considerations for improving patient survival. Our data demonstrate overall safety and no differences in complication rates between the two surgical approaches. Our study, in agreement with others published, suggests that laparoscopy or robotics may be a safe oncological surgical approach for women with tumors smaller than 2 cm[13].

The hybrid surgical technique appears to be a safe technique for larger tumors (> 2 cm). It achieves good oncological results with the advantages of a similar recovery to the exclusively laparoscopic approach, avoiding laparotomy in the case of pelvic nodal involvement, and with the advantage of, in these cases, being able to initiate adjuvant treatment early.

Lymph node metastasis was not included in CC staging until the 2018 International Federation of Gynecology and Obstetrics (FIGO) classification[14]. Importantly, it informs about worse prognosis and facilitates treatment adaptation.

The use of the MIS for SLN biopsy resulted in the upgrade of FIGO IIIC1/IIIC2 and the avoidance of a midline laparotomy in 13.3% (4/30) of patients. In this way, these patients benefited from a rapid recovery and were able to start adjuvant treatment with ChRT 7-10 days after surgery (the main factor for improving survival).

The use of a hybrid tracer (ICG-^{99m}Tc-nanocoloid) for SLN biopsy is feasible and safe in early-stage CC. This tracer avoids the lymphography typically observed with ICG alone, provides a high detection rate (96.1%) with high bilateral detection (88.5%), and combines the benefits of both tracers: it makes it easier to identify the lymph node *via* the fluorescent signal of ICG and ^{99m}Tc provides preoperative images that enhance the search for sentinel nodes in atypical locations (15.4%).

As shown in Table II, when compared to important studies using the hybrid tracer and following the MSKCC algorithm, we display a higher global and bilateral detection rate[15-17].

SLN mapping during surgical staging in early-stage CC has become a common practice and is integrated into surgical guidelines. Approximately 70-80% of SLNs are located at the external iliac vessels and obturator fossa[18,19]. In our study, 19.2% of SLNs were in these uncommon areas with a high rate (50%) of positive nodes.

Patients with metastatic SLNs in atypical locations had a positive LVSI and larger tumors (mean: 2.65 cm) than those with negative SLN (mean: 2 cm). We could hypothesize that these results could be due to the larger tumor volumes clogging the lymphatic vessels[20].

There are other theories to explain unusual drains, such as additional lymphatic drainage in larger tumors, the usual lymphatic channels being obstructed by cancer cells, and the main drainage deviating to less common channels or uncommon SLNs were mainly related to the surgeon's experience.

Our surgical experience with the help and supervision of nuclear medicine and the possibility of having pre-surgical SPECT-CT helps us localize these nodes. We encourage gynecological

surgeons to explore uncommon areas to improve the localization of the true sentinel node.

Clinically, considering that the parametrium is a clear lymphatic tissue and a key point of lymphatic drainage of the cervix, the rationale for surgical treatment in CC is complete parametrectomy. Parametrectomy allows the removal of occult disease at the same time as resection of the primary cervical tumor and as a part of the pelvic lymphadenectomy. Lymph nodes were found in the cardinal ligament and, less commonly, in the cervicovesical and sacrouterine ligaments. Complete parametrectomy and accurate parametria analysis may account for a better lymphatic study.

Some authors reported positive SLNs in the parametria area in 4.4% of cases, concluding that the presence of a significant percentage of parametrial lymph nodes may be clinically useful[20].

In our study, we reported one negative SLN in the lateral parametrial. This patient also presented a negative SLN in the obturator fossa. Another patient presented a positive lymph node with macrometastasis (3 mm) detected during the final pathology analysis of the uterus at the lateral parametria. She had bilateral lymphatic drainage with a negative SLN.

Parametrial involvement can be due to invasion of the primary tumor from the cervical lesion or nodal involvement through lymphatic drainage.

If suspected, by clinical examination or radiological imaging, parametrial invasion is considered a locally advanced tumor (at least FIGO IIB) and, therefore, the treatment of choice is ChRT. Rarely, but with a significant percentage, parametrial involvement may be due to a positive parametrial lymph node.

Published series describe positive parametrial nodes in up to 22.5% of cases, 80% of which had positive pelvic nodes. The five-year survival rate decreases with any type of parametrial involvement and positive pelvic lymph nodes (56%) compared with patients whose parametria is disease-free (84%)[21]. Survival is being discussed in the case of positive parametrial nodes without pelvic node involvement as they could correspond more to FIGO stage IIB than IIIC1 with a worse prognosis.

Given the findings and the actual evidence, we must offer our patients a new standard of care, consisting of an open approach for RH, and only offer MIS in the context of a clinical trial. If risk recurrence factors are identified and eliminated in present and future studies, MIS could be considered again if the evidence warrants it.

The sample size of our work might be considered small given the low incidence of CC nowadays and that it is a unicentric study. This new approach can encourage further investigation into surgical strategies, and within specialized centers, adequate patient selection and good surgical skills could avoid the complete abandonment of laparoscopy.

Conclusions

The hybrid tracer (ICG-^{99m}Tc) provided a high detection rate and offered the advantages of the two tracers combined. The use of MIS for SLN avoids performing a laparotomy in cases in which nodes are affected and benefits from a rapid recovery and early start of adjuvant treatment.

Initial data show that hybrid surgery could be a good option for treating CC with larger tumors (> 2 cm), without compromising oncological safety.

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Authors' Contributions

Amengual Vila J: investigation, data curation, Software, and writing.
Torrent Colomer A: Conceptualization, Methodology, supervision, and review.
Cordoba O: Visualization and reviewing.
Sampol Bas C: Methodology, supervision and review.
Quintero Duarte A, Ruiz Coll MJ, Rioja Merlo J: reviewing.

Conflict of Interest

The authors have no conflict of interest to declare.

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Ethics Approval

This study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of the Balearic Islands (IB 4954/22 PI; IB 4955/22 PI).

Informed Consent

All subjects gave their informed consent for inclusion before participating in the study.

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