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Quality of laparoscopic radical hysterectomy in developing countries: a comparison of surgical and oncologic outcomes between a comprehensive cancer center in the United States and a cancer center in Colombia

Rene Pareja[a], **Alpa M. Nick**[b], **Kathleen M. Schmeler**[b], **Michael Frumovitz**[b], **Pamela T. Soliman**[b], **Carlos A Buitrago**[a], **Mauricio Borrero**[a], **Gonzalo Angel**[a], **Ricardo dos Reis**[c], and **Pedro T. Ramirez**[b,*]

[a]Gynecology Oncology Unit, Instituto de Cancerología–Clínica las Américas, Medellín, Colombia

[b]Department of Gynecologic Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX, United States

[c]Department of Gynecologic Oncology, Universidade Federal Do Rio Grande do Sul, Porto Alegre, RS, Brazil

Abstract

Objective—To help determine whether global collaborations for prospective gynecologic surgery trials should include hospitals in developing countries, we compared surgical and oncologic outcomes of patients undergoing laparoscopic radical hysterectomy at a large comprehensive cancer center in the United States and a cancer center in Colombia.

Methods—Records of the first 50 consecutive patients who underwent laparoscopic radical hysterectomy at The University of Texas MD Anderson Cancer Center in Houston (between April 2004 and July 2007) and the first 50 consecutive patients who underwent the same procedure at the Instituto de Cancerología–Clínica las Américas in Medellín (between December 2008 and October 2010) were retrospectively reviewed. Surgical and oncologic outcomes were compared between the 2 groups.

Results—There was no significant difference in median patient age (US 41.9 years [range 23-73] vs. Colombia 44.5 years [range 24-75], P=0.09). Patients in Colombia had a lower median body mass index than patients in the US (24.4 kg/m^2 vs. 28.7 kg/m^2, P=0.002). Compared to patients treated in Colombia, patients who underwent surgery in the US had a greater median estimated

* To whom correspondence and reprint requests should be addressed. Department of Gynecologic Oncology, Unit 1362, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030. Phone: (713) 745-5498. Fax: (713) 792-7586. peramire@mdanderson.org..

Conflict of Interest
The authors have no conflicts to declare.

blood loss (200 mL vs. 79 mL, $P<0.001$), longer median operative time (328.5 min vs. 235 min, $P<0.001$), and longer postoperative hospital stay (2 days vs. 1 day, $P<0.001$).

Conclusions—Surgical and oncologic outcomes of laparoscopic radical hysterectomy were not worse at a cancer center in a developing country than at a large comprehensive cancer center in the United States. These results support consideration of developing countries for inclusion in collaborations for prospective surgical studies.

Introduction

Approximately 492,243 new cases of cervical cancer are diagnosed worldwide each year. Of these, 83% are diagnosed in developing countries [1]. The standard treatment for patients with early stage disease has been open radical hysterectomy. However, recently, an increasing number of centers are offering laparoscopic surgery as a routine approach to gynecologic malignancies. A number of reports have documented the safety and feasibility of laparoscopic radical hysterectomy [2-6].

Laparoscopic radical hysterectomy is currently being performed in both developed and in some developing countries. In many developing countries, hospitals provide limited or no training in laparoscopic surgery. Surgeons often teach themselves and embark on the practice of minimally invasive surgery with limited formal training.

Collaborations with centers throughout the world are becoming a more common goal of many academic centers in the United States [7]. At The University of Texas MD Anderson Cancer Center, surgeons from many developing countries are offered the opportunity to rotate with MD Anderson surgeons with support from Global Academic Programs, a division of MD Anderson's Center for Global Oncology [7]. In addition to providing developing-country surgeons with training and exposure to developed-world surgical practices, these rotations promote academic exchanges that often lead to joint research projects. In gynecology, studies are already under way in which institutions in the United States are conducting surgical trials in which patients are being accrued at institutions worldwide [8]. One potential concern with respect to multi-institutional gynecologic surgical trials, particularly those involving minimally invasive surgery, is that the quality of the technology in developing countries may not equal that in the US and that the technical skills of surgeons with no or only limited formal training in laparoscopic surgery may not equal that of surgeons trained in board-certified gynecologic oncology fellowship programs.

In an effort to determine whether collaborations for prospective surgical studies should include hospitals in developing countries, we retrospectively compared the surgical and oncologic outcomes of patients who underwent laparoscopic radical hysterectomy at MD Anderson, which is a large comprehensive cancer center in the United States, and a large hospital in Medellín, Colombia: Instituto de Cancerología—Clínica las Américas (ICCA). In addition, we evaluated the time required to register the first 50 patients at both institutions to help us predict the rate of accrual for future studies.

Materials and Methods

After approval was obtained from the Institutional Review Boards at MD Anderson and ICCA, a retrospective chart review was conducted of the first 50 consecutive women who underwent laparoscopic radical hysterectomy at MD Anderson (between April 2004 and July 2007) and the first 50 consecutive women who underwent laparoscopic radical hysterectomy at ICCA (between December 2008 and October 2010). No women who underwent robotic-assisted radical hysterectomy were included. The difference in surgery dates for the patients included in this study reflects our intent to compare the initial experiences of the surgeons at the 2 institutions. To be included in this study, patient not only had to have undergone laparoscopic radical hysterectomy but also had to have histopathologic confirmation of early-stage (1A2-1B2) cervical cancer or stage II endometrial cancer.

MD Anderson is an academic tertiary referral center that specializes in oncologic care. The Department of Gynecologic Oncology includes 17 full-time faculty gynecologic oncologists. Approximately 1,400 new patients are evaluated annually in the Gynecologic Oncology Center, while an additional 350 new patients are treated annually at outreach hospitals. Of the patients seen each year at MD Anderson and outreach hospitals, approximately 25 patients have early stage cervical cancer and are considered surgical candidates. At the time of this study, 5 of the gynecologic oncologists at MD Anderson performed laparoscopic radical hysterectomy, and for each of these surgeons, laparoscopic radical hysterectomy was a skill acquired after fellowship. The first laparoscopic radical hysterectomy at MD Anderson was performed in April 2004.

ICCA is the largest cancer center in Colombia, with approximately 70,000 outpatient visits per year. There are 3 gynecologic oncologists in the Department of Obstetrics and Gynecology, and at the time of this study, all 3 performed laparoscopic radical hysterectomy. Approximately 700 new patients are seen annually in the gynecologic oncology service. Approximately 280 new cervical cancer patients are seen annually, and of these, approximately 60 patients have early-stage disease suitable for surgical management. At the time of this study, 3 of the gynecologic oncologists had formal training in laparoscopy, and 1 of them had spent 3 months as an observer in the Department of Gynecologic Oncology at MD Anderson. The first laparoscopic radical hysterectomy at ICCA was performed in December 2008.

Demographic, clinical, and perioperative characteristics of each patient population were analyzed using descriptive statistics. Categorical variables were summarized using frequencies and percentages. The Fisher exact test was used to compare differences between MD Anderson and ICCA. Continuous variables were summarized as the mean with standard deviation and/or the median and range, and the Mann-Whitney rank sum test was used for comparisons between MD Anderson and ICCA. Missing data were coded as “unknown.” Statistical analysis was performed using XL-STAT v2011 (Belmont, MA). All *P* values were 2-sided, and *P* values <0.05 were considered statistically significant.

Results

The time to accrue the first 50 patients at MD Anderson was 39 months, and the time to accrue the first 50 patients at ICCA was 22 months. There was no significant difference between institutions with respect to median age at diagnosis (MD Anderson 41.9 years vs. ICCA 44.5 years, P=0.09). Patients from ICCA had a lower median body mass index than patients from MD Anderson (24.4 kg/m^2 vs. 28.7 kg/m^2, P=0.002) (Table 1).

At each institution, the majority of patients undergoing laparoscopic radical hysterectomy had a diagnosis of cervical cancer (ICCA 94%, MD Anderson 90%). Among patients with cervical cancer, more patients at MD Anderson had cervical adenocarcinoma (44%), and more patients at ICCA had squamous cell carcinoma (61%) (P=0.04). There was no significant difference in median tumor size between patients at the 2 institutions, and the majority of tumors measured less than 1 cm.

The median estimated blood loss during laparoscopic radical hysterectomy was greater at MD Anderson than at ICCA (200 mL vs. 79 mL, P<0.001). The greater blood loss in the MD Anderson group resulted in a higher rate of intraoperative or postoperative transfusions (10% at MD Anderson compared to 0% at ICCA), although the difference was not statistically significant (P=0.06). Patients at MD Anderson also had longer median operative time (328.5 min vs. 235 min, P<0.001) and a higher rate of conversion to laparotomy (6% vs. 0%, P=0.24). Two patients underwent conversion because of a vascular injury, and these were 2 of the 5 patients who required intraoperative or postoperative blood transfusion. Five patients at MD Anderson and none at ICCA underwent lymphatic mapping. Twelve patients at MD Anderson and none at ICCA underwent a frozen section evaluation. The frozen section evaluations at MD Anderson were performed either for suspicious lymph nodes or for a frozen conization.

Five patients (10%) at MD Anderson and 4 patients (8%) at ICCA suffered an intraoperative complication. At MD Anderson, there were 2 cystotomies and 3 vascular injuries. Both cystotomies were repaired laparoscopically. Two of the 3 patients with vascular injuries required conversion to laparotomy. At ICCA, 3 patients suffered cystotomies, and all of these were repaired laparoscopically. One patient had an external iliac vein injury, which was also repaired laparoscopically.

The median length of hospital stay after laparoscopic radical hysterectomy was shorter at ICCA than at MD Anderson (1 day vs. 2 days, P<0.001).

The median number of pelvic lymph nodes removed was lower at MD Anderson than at ICCA (11 vs. 20, P<0.001). Fourteen patients (28%) at MD Anderson and 15 patients (30%) at ICCA suffered a postoperative complication. At MD Anderson, these were urinary tract infection in 4 patients (8%), deep venous thrombosis or pulmonary embolism in 3 patients (6%), febrile morbidity in 4 patients (8%), and 1 case each of atelectasis, peripheral neuropathy, and hypoxemia (2% each). At ICCA, the postoperative complications were cuff dehiscence in 3 patients (6%), vesicovaginal fistula in 2 patients (4%), bladder atony in 3 patients (6%), urinary tract infection in 3 patients (6%), and 1 case each of pelvic abscess, port site herniation, deep venous thrombosis, and lymphedema of right lower extremity (2%

each). There was no significant difference in the rate of postoperative complications between the 2 institutions (*P*=0.65). A greater proportion of patients at ICCA underwent reoperation (10% vs. 0%), although the difference was not statistically significant (*P*=0.06). The reasons for reoperation in these 5 patients were cuff dehiscence in 3 patients, pelvic abscess in 1 patient, and port-site herniation in 1 patient.

A higher proportion of patients at ICCA underwent adjuvant therapy (38% vs. 28%), although this difference was not statistically significant (*P*=0.40). At ICCA, 6 cervix cancer patients received radiation therapy and chemotherapy because of positive pelvic nodes, and 11 cervix cancer patients received radiation and chemotherapy because of cervical invasion >50%. Two endometrial cancer patients received radiation therapy postoperatively because of myometrial invasion >50%. At MD Anderson, 1 patient received vaginal cuff brachytherapy secondary to a stage II clear cell carcinoma of the uterus. Four patients with cervical cancer underwent postoperative pelvic radiotherapy for positive pelvic lymph nodes (n=2), poorly differentiated histology with lymph-vascular space invasion and deep cervical stromal invasion (n=1), or parametrial disease (n=1). Nine patients were treated with postoperative pelvic radiotherapy with concurrent chemotherapy for deep cervical stromal invasion (n=4) or positive pelvic lymph nodes (n=5).

The surgeries were performed by 5 different surgeons at MD Anderson and 3 different surgeons at ICCA. Twenty-five (50%) of the cases at MD Anderson and 46 (92%) of the cases at ICCA were performed by a single surgeon.

At the time of this analysis, the median follow-up time was 41 months (range, 0.9 to 75.5) at MD Anderson and 12 months (range, 3.7 to 23.9) at ICCA. There had been 2 recurrences at MD Anderson and none at ICCA. One patient was diagnosed with pelvic recurrence and liver metastases 11 months after radical hysterectomy. She was initiated on palliative combination chemotherapy with carboplatin and paclitaxel and died of disease 6 months later. The second patient presented 3 months after radical hysterectomy with recurrent disease and died of disease 8 months after the hysterectomy.

Discussion

In our cohort, we found that surgical and oncologic outcomes in patients undergoing laparoscopic radical hysterectomy were not inferior at a referral center in a developing country compared to a large comprehensive cancer center in the United States. To our knowledge, this is the first study to compare the results from 2 centers in different countries and specifically focus on radical hysterectomy.

We found no differences between the 2 centers with respect to the age of the patients at diagnosis or tumor size and stage. Not unexpectedly, given the higher prevalence of cervical cancer in Colombia, we found that the time required to accrue the first 50 patients was much faster in Colombia than in the United States. This fact underscores the value of international collaborations in planning for future studies in patients with diseases with a low prevalence in the United States, such as cervical cancer.

We noted that the ICCA group had shorter operative times and less blood loss than the MD Anderson group. Furthermore, the lymph node counts were higher at ICCA. In interpreting these findings, one must consider that at ICCA, cases were performed by faculty surgeons with the assistance of another faculty member, whereas at MD Anderson, all cases are teaching cases and include participation by a fellow trainee. In addition, it is possible that the higher number of cases performed within the same time frame at ICCA allowed for more consistency in results. Furthermore, the rates of intraoperative frozen section and lymphatic mapping were also higher in the patients at MD Anderson, and these factors may have contributed to the longer operative times at MD Anderson. We found no differences between the 2 centers in the rates of intraoperative or postoperative complications or in the rates of conversion to open surgery or reoperation. Similarly, there were no differences between the 2 centers in the rate of postoperative adjuvant treatment or the recurrence rate. We did note that the severity of the postoperative complications between the two institutions was different, with a higher rate of vaginal cuff dehiscence and vesico-vaginal fistulae at ICCA. These findings may have been attributed to more frequent use of monopolar energy by their group; however, since that time, their tools and techniques have evolved to reflect those used by the team at MD Anderson.

We recognize that our study is limited by several factors. First, it was a retrospective study limited to 2 institutions, and our findings may not be applicable to other similar institutions. Second, because the study was retrospective, there was not a uniform standard for intraoperative and postoperative management (e.g., criteria for blood transfusions or hospital discharge) or for postoperative adjuvant therapy. Third, processing of the lymph node tissue by pathologists could have led to differences in results, and no central review of pathology was performed. Lastly, the indications for postoperative adjuvant therapy might differ between the 2 institutions.

In summary, our results show that quality and surgical principles for laparoscopic radical hysterectomy were similar between a large cancer center in the US and a large cancer hospital in the developing world and raised no major concerns with regard to the reproducibility of the procedure at the developing-country institution. These findings support the concept that conducting multi-institutional international surgical studies including countries in the developing world is feasible. We do recognize that many challenges remain in order to implement and complete prospective randomized international surgical trials such as issues related to cost, central pathology review, data gathering, and regulatory requirements. It should also be emphasized that strict criteria must be implemented in order to assure equivalency of surgical technique. MD Anderson is currently conducting a number of prospective surgical trials in collaboration with other countries where cervical cancer is more prevalent [8, 9]. We encourage other countries to consider future collaborations in order to advance the field of gynecologic oncology surgery and to provide their patients with uniform surgical care.

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Highlight

1. Collaborative prospective trials in developing countries using minimally invasive surgery in gynecologic oncology are safe and feasible
2. Laparoscopic radical hysterectomy results between a tertiary cancer center in the United States and a developing country are comparable
3. Accrual to surgical trials evaluating laparoscopic radical hysterectomy may be faster in developing countries.

Table 1

Comparison of patient demographics and perioperative variables (univariate analysis)

Characteristic	ICCA (n = 50)	MD Anderson (n = 50)	*P* value
Median age at diagnosis, years (range)	44.5 (24-75)	41.9 (23-73)	0.09
Median BMI, kg/m^2 (range)	24.4 (18.6-34.2)	28.7 (18.4-45.1)	0.002*
Median tumor size, cm (range)	0 (0-3.5)	0 (0-5)	0.28
Median operative time, min (range)	235 (160-375)	329 (185-510)	<0.001*
Median estimated blood loss, mL (range)	79 (15-400)	200 (25-2000)	<0.001*
Perioperative transfusion, no. of pts. (%)	0 (0)	5 (10)	0.06
Median no. of pelvic LNs removed (range)	20 (9-53)	11 (2-32)	<0.001*
Median hospital stay, days (range)	1 (1-2)	2 (1-6)	<0.001*
Intraoperative complication, no. of pts. (%)	4 (8)	5 (10)	1.00
Postoperative complication, no. of pts. (%)	15 (30)	14 (28)	0.65
Postoperative VTE, no. of pts. (%)	1 (2)	3 (6)	0.29
Conversion to open surgery, no. of pts. (%)	0 (0)	3 (6)	0.24
Reoperation, no. of pts. (%)	5 (10)	0 (0)	0.06
Postoperative adjuvant treatment, no. of pts. (%)	19 (38)	14 (28)	0.40
Recurrence, no. of pts. (%)	0 (0)	2 (4)	0.49
Disease site, no. of pts. (%)			
Cervical	47 (94)	45 (90)	0.72
Endometrial	3 (6)	5 (10)	
Histologic subtype of patients with cervical cancer, no. of pts. (%)			
Adenocarcinoma	15 (31)	22 (44)	0.04**
Squamous	30 (61)	18 (36)	

BMI, body mass index; ICCA, Instituto de Cancerología—Clínica las Américas; LN, lymph node; pts., patients; VTE, venous thromboembolism.

*Comparison using Mann Whitney Rank Sum Test

**Comparison using Fisher's exact test