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Original Article

Robotic Versus Open Radical Hysterectomy in Women With Locally Advanced Cervical Cancer After Neoadjuvant Chemotherapy: A Single-institution Experience of Surgical and Oncologic Outcomes

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ABSTRACT **Study Objective:** To compare the surgical and oncologic outcomes of robotic radical hysterectomy (RRH) versus laparotomy in women with locally advanced cervical cancer (LACC) after neoadjuvant chemotherapy (NACT).

Setting: Oncology referral center.

Design: A retrospective comparative observational study was performed in 30 patients with LACC Fédération Internationale de Gynécologie et d'Obstétrique stage IB2-IIB who underwent RRH after NACT between February 2008 and December 2014. This group was compared with a cohort of 44 patients with similar characteristics who underwent abdominal radical hysterectomy after NACT (Canadian Task Force classification II2).

Patients: Patients with LACC FIGO stage IB2-IIB.

Interventions: A retrospective comparative observational study.

Measurements and Main Results: The mean (standard deviation [SD]) operative time was significantly longer in the robotic group (307.8 minutes [40.2] vs 233.7 minutes [61.9], $p \leq .001$). On the contrary, the mean (SD) estimated blood loss was significantly lower in the robotic group (111.0 mL [69.6] vs 286.9 mL [159.1], $p \leq .001$), and length of stay was significantly shorter (4.1 [2.4] days vs 5.8 days [3.3], $p = .015$). The incidence of intraoperative and early and late complications was not statistically significantly different between the 2 groups. The mean (SD) follow-up of patients was 35.6 months (28.4) and 43.7 months (23.2) in the open and robotic groups, respectively ($p = .137$). The disease recurrence rate (27.2% vs 20%) was similar between the 2 groups; sites and types of recurrences were also similar. Kaplan-Meier survival analysis for median progression-free survival and median overall survival were not statistically different comparing cohorts by surgery type.

Conclusions: RRH after NACT in women with LACC is associated with similar perioperative and oncologic outcomes to open procedure. These results require further investigation to establish a more robust conclusion. Journal of Minimally Invasive Gynecology (2016) 23, 909–916 © 2016 AAGL. All rights reserved.

Keywords: Abdominal radical hysterectomy; Complications; Locally advanced cervical cancer; Neoadjuvant chemotherapy; Robotic radical hysterectomy

Patients with locally advanced cervical cancer (LACC), defined as Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) stage IB2-IIB, III, and IVA, represent about one third of women with this disease; the recommended standard of treatment is concomitant chemoradiotherapy (CT-RT) following a National Cancer Institute alert in 1999 [1,2].

However, over the last few decades, particularly in Europe and South America, survival benefits seem to be associated with neoadjuvant chemotherapy (NACT) followed by radical surgery compared with conventional exclusive radiotherapy, as shown by the results of a meta-analysis published by Ye et al [3].

In the past, abdominal radical hysterectomy (ARH) with pelvic lymphadenectomy has been considered the standard of treatment for women with early-stage cervical cancer,

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even more so for patients who had received NACT for LACC. In the last 2 decades, laparoscopic radical hysterectomy was incorporated in the surgical field of gynecologic oncology as an alternative that offers the advantages of minimal invasive surgery (MIS) without apparent compromise of the surgical and oncologic outcomes [4]. However, this technique is still technically challenging with a significant learning curve; therefore, it has not gained widespread use.

In 2005, robotic surgery was approved as a technological evolution of laparoscopy in gynecologic surgery, providing surgeons with a greater range of instrument movements, decreased tremor, enhanced dexterity, and improved 3-dimensional visualization. These advantages enable surgeons to overcome some of the limitations of traditional laparoscopy, especially in cases of complex procedures such as radical hysterectomy [5–7], which can become even more difficult because of increased difficulties in tissue dissection as a consequence of a desmoplastic reaction after NACT [8,9].

An increasing number of publications have shown the feasibility and efficacy of robotic radical hysterectomy (RRH) to treat women with early-stage cervical cancer, and experience with this procedure is ever growing [10–18]. Studies have shown that RRH has an equal or even shorter operative time, lower blood loss, and a shorter length of hospitalization, with similar or a higher number of lymph nodes collected than ARH [12,13].

However, there is very little information regarding the feasibility and safety of robotic surgery after neoadjuvant chemotherapy in patients with gynecologic cancer [19]. Therefore, the objective was to compare the surgical and oncologic outcomes of RRH versus ARH in patients with LACC after NACT.

Patients and Methods

After institutional review board approval was obtained, a retrospective comparative observational study was performed at the Gynecology Department of the European Institute of Oncology, Milan, Italy, in 30 patients with LACC FIGO stage IB2-IIB who underwent RRH after NACT between February 2008 and December 2014. This group was compared with a cohort of 44 consecutive patients who underwent ARH during the same period of time.

Inclusion criteria for choosing the robotic approach after NACT were not strict but mostly included the following: tumor size $\leq$3 cm, most common histotypes (squamous and adenocarcinoma), and absence of medical conditions that would be a contraindication to MIS. Before neoadjuvant treatment, patients underwent a computed tomographic scan of the chest, abdomen, and pelvis and magnetic resonance imaging of the pelvis that was repeated at completion of chemotherapy to confirm the response. Charts were abstracted, and the analyzed data included baseline patients' characteristics, clinical FIGO stage, intraoperative results, length of hospital stay (LOS), final histology diagnosis, postoperative bladder function, and intra- and postoperative complications. Operative time was defined from the beginning of skin incision to the completion of skin closure. Estimated blood loss (EBL) was calculated by the difference in the total amounts of suctioned and irrigation fluids. Major complications were defined as those requiring a return to the operating room, prolonged hospital stay, or medical attention after discharge from the hospital. Complications were classified as intraoperative or early ($\leq$1 month after surgery) or late ($>$1 month after surgery) postoperative complications recorded at the time of the hospital stay, in case of readmission, or at the first postoperative check (within 8 weeks after surgery) and were graded from I to IV according to the Clavien-Dindo classification [20].

LACC included patients with FIGO stage IB2, IIA, or IIB cervical cancer. They received 3 courses of 3 weeks of NACT (a paclitaxel, epirubicin, and cisplatin regimen in case of adenocarcinoma histology and a paclitaxel, ifosfamide, and cisplatin regimen in case of squamous histology) [21,22]. After clinical and radiologic evaluation to confirm the response after NACT, radical hysterectomy and pelvic lymphadenectomy were performed within 4 weeks from the last chemotherapy cycle. Para-aortic lymphadenectomy is usually not performed unless there are suspicious nodes at the time of surgery either in the pelvis or the para-aortic area to define the upper limits of the radiation field.

Tumor responses were evaluated according to the Response Evaluation Criteria in Solid Tumors [23], and only patients with a complete response or partial response defined as at least a 30% decrease in the measurement of the longest diameter were selected for surgery. Five gynecologic oncologists performed both robotic and abdominal surgeries. Adjuvant treatment was administered based on the presence of risk factors for recurrence in the final pathology findings such as positive nodes, parametrial involvement, or close surgical margins.

Surgical Technique

All RRHs were performed using the da Vinci Si System (Intuitive Surgical Inc, Sunnyvale, CA). The available instruments have evolved over the years, and surgeries are currently performed using 3 instruments: Maryland fenestrated bipolar forceps (da Vinci, Surgical System; Intuitive Surgical Inc., CA), monopolar curved scissors, and Prograsp forceps (Cadier). Central docking between the patient's legs was used. All 4 robotic arms were used; 1 assistant trocar was placed in the left upper abdominal quadrant, and initial access was obtained at the umbilicus using the open Hasson technique.

RRH was performed as described by Magrina et al [24]. Patients who had a significant reduction in tumor size to less than 2 cm after NACT underwent radical hysterectomy type B as defined by the classification of Querleu and Morrow [25]; otherwise, type C1 radical hysterectomy was performed in women with a reduction in tumor size to less than 4 cm but $>$2 cm.