



Feasibility of robotic radical hysterectomy after neoadjuvant chemotherapy in women with locally advanced cervical cancer

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Abstract

Objective: To evaluate the safety and feasibility of robotic radical hysterectomy (RRH) in women with locally advanced cervical cancer (LACC) after neoadjuvant chemotherapy (NACT).

Material and methods: A retrospective comparative longitudinal observational study was performed in 30 patients with LACC FIGO stage IB2–IIB who underwent RRH after NACT between February 2008 and September 2014. This group was compared with a cohort of 176 patients underwent RRH with cervical cancer FIGO stage IA2–IB1 in the same period of time.

Results: Patients' age, BMI, ASA score, comorbidity, and previous abdominal surgery, was similar between groups. FIGO stage significantly differed between groups; 29 (96.6%) of patients had FIGO stage IB2 in NACT group and 163 (92.6%) were FIGO stage IB1 in women without NACT, $p < 0.001$. Type of RRH was also significantly different between groups. Type C1 RRH was significantly more common in NACT group, $p = 0.015$. Mean (SD) tumor size was significantly bigger in NACT, 27.0 (13.7) mm versus 20.9 (9.0) mm in early stage versus LACC, respectively. $p = 0.023$. Mean (SD) surgical time was significantly longer in NACT group (307.8 (40.2) min versus 277.4 (45.4) min, $p = 0.001$). Estimated blood loss and length of the hospital stay were similar between groups. There were no significant differences in terms of intraoperative and postoperative complications.

Conclusions: RRH after NACT in women with LACC seems to be safe and feasible. These results need to be confirmed in studies with a larger patients sample.

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Keywords: Robotic radical hysterectomy; Abdominal radical hysterectomy; Cervical cancer; Neoadjuvant chemotherapy; Complications

Introduction

Over 35% of women with cervical cancer are diagnosed at locally advanced stage of disease, which include stage IB2–IIB.¹ Despite the fact that concurrent chemoradiation is recommended as standard of treatment based on randomized clinical studies,² results of a meta-analysis have shown similar oncological outcomes by using

platinum-based neoadjuvant chemotherapy (NACT) followed by radical hysterectomy in women with locally advanced cervical cancer (LACC).³

Over a decade ago, robotic surgery emerged as a technological evolution of laparoscopy in gynecological surgery, especially for complex procedures such as radical hysterectomy that requires an extensive dissection of parametrial tissues involving the ureter, bladder, rectum and autonomic nerves.⁴

Moreover, it has been postulated that such a procedure can become more complex after NACT that might increase the difficulties of tissue's dissection due to a desmoplastic reaction after chemotherapy.^{5,6}

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However, there is very little information regarding the feasibility of robotic surgery after neoadjuvant chemotherapy in patients with gynecological cancer.⁷ Therefore, the aim of this study was to evaluate the safety and feasibility of robotic radical hysterectomy (RRH) in women with LACC after platinum-based NACT.

Patients and methods

After the Institutional Review Board approval was obtained, a retrospective comparative longitudinal observational study was performed at Gynecology Department of the European Institute of Oncology in Milan, Italy. The study group was composed of all women with cervical cancer FIGO stage IB2–IIB who underwent RRH after NACT between February 2008 and September 2014. The control group included a cohort of consecutive patients who had undergone RRH without NACT for FIGO stage IA2–IB1 cervical cancer during the same period of time.

Criteria to undergo RRH were: tumor size ≤ 4 cm, most common histology types, and absence of medical conditions that would be a contraindication to minimally invasive surgery. Charts were abstracted and the analyzed data included: baseline patient characteristics, clinical FIGO stage, intra-operative results, length of hospital stay (LOS), final histology diagnosis, postoperative bladder function as well as post-operative complications. Operating time was defined from the beginning of skin incision to completion of skin closure. The 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 from grade I to IV.**⁸ They were recorded at the time of the hospital stay, in case of re-admission or at the first post-operative check (within 8 weeks after surgery).

LACC included patients with FIGO stage IB2, IIA or IIB cervical cancer. They received 3 courses of neo-adjuvant chemotherapy: paclitaxel, epirubicine and cisplatin (TEP) regimen in case of squamous histology and Paclitaxel, ifosfamide and cisplatin (TIP) regimen in case of adenocarcinoma histology. Radical hysterectomy and pelvic lymphadenectomy were performed in patients with adequate tumor response. Five gynecologic oncologists performed surgeries.

Surgical technique

RRH was performed as described elsewhere⁹ by using the *Da Vinci* surgical robot system S and Si (da Vinci[®], Surgical System, Intuitive Surgical Inc., CA, USA). Type B radical hysterectomy, as defined by classification of Querleu/Morrow,⁴ was performed in patients with FIGO stage IA2 or IB1 with a tumor size less or equal to 2 cm. Patients with FIGO stage IB1 with tumor larger than

2 cm, or in patients with FIGO stage IB2 who were previously treated with neo-adjuvant chemotherapy underwent Type C1 radical hysterectomy.

Postoperative care

Most patients remained in the hospital until post-operative day number 3 in order to undergo voiding trials. If post voiding residual volume was more than 100 mL for 3 consecutive times, then patients were instructed to self-catheterization until the adequate post voiding residual volume was achieved. If patients were unable to perform this task, they were discharged with a Foley catheter in place and scheduled for another voiding trial in 7 days.

Statistical analysis

Kolmogorov–Smirnov with Lilliefors correction was used to evaluate the normal distribution of the data of the collected variables. Whereas frequencies and proportions were used as summary statistics for categorical variables, Mean and standard deviation were used for the continuous. By using a χ^2 -based proportion test as implemented in R, Yates correction, or Fisher exact test the categorical variables among groups (NACT vs no NACT) were compared; for continuous variables, either a two-tailed *t*-test when the normality and homogeneity of variance assumptions were met, or the non-parametric Mann–Whitney's U test, was used. In all statistical tests a confidence interval (CI) of 95% and $p < 0.05$ was considered as significant differences. Statistical analysis was performed using the IBM SPSS version 20.0 program.

Results

Patients' characteristics

A total of 30 patients who had undergone RRH after NACT for LACC were compared with 176 patients who had undergone RRH for early stage cervical cancer without previous NACT. Age, body mass index (BMI), comorbidity, and number of previous abdominal surgeries were similar in both groups of patients. As it was expected, the FIGO stage of disease was statistically different between groups; 29 (96.6%) patients were FIGO stage IB2 in NACT group, while 163 (92.6%) patients were FIGO stage IB1 in non-NACT group, $p \leq 0.001$ (Table 1).

Intra-operative characteristics

The intra-operative characteristics are shown in Table 2. The mean (SD) operative time was significantly longer in NACT group [307.8 (40.2) versus 277.4 (45.4), $p \leq 0.001$]. EBL and LOS were similar in both groups. The type of radical hysterectomy was significantly different between groups, $p \leq 0.05$. Similar incidence of intra-operative complications

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