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Class II versus Class III radical hysterectomy in early cervical cancer: An observational study in a tertiary center

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Abstract

Aims: The purpose of this observational study was to evaluate disease free survival (DFS), overall survival (OS), and local recurrence rate (LRR) in patients submitted to Class II RH compared with Class III RH in early FIGO stage cervical cancer (ECC).
Materials and methods: We investigated 127 patients with CC admitted to the National Cancer Institute of Milan from June 2001 to October 2011 treated with Class II RH, and compared them with 202 patients operated with Class III RH between March 1980 and March 2001. A total of 329 patients were collected.
Results: Median follow-up time was 91 months (IQ range:58–196). Five-year OS and DFS estimates were 89.5% (95%CI: 86.0–93.2%) and 85.6% (95%CI: 81.6–89.7%), respectively. Estimates of effect of surgical treatment (Class III RH versus Class II RH) on OS showed a HR of death = 3.38 (95%CI: 1.18–9.63, $P = 0.0228$), at univariable Cox analysis, and a HR = 3.08 (95%CI: 0.96–9.93; $P = 0.0595$) at multivariable analysis. For DFS, a HR of relapse = 2.51 (95%CI 1.10–5.72; $P = 0.0290$) comparing Class III vs Class II was found at multivariable analysis. Overall recurrence rate was 12.8%, whilst it was 16.3% for Class III and 7.1% for Class II respectively.
Conclusions: The present data suggest that the outcomes of Class II RH are comparable in terms of LRR and OS to those of Class III RH, according to literature data. The opportunity of extending the indication to all women with ECC needs further investigations. Clearer data are warranted by prospective controlled studies.

Keywords: Cervical cancer; Radical hysterectomy; Tailoring radicality; Overall/disease free survival; Recurrence rate

Introduction

Worldwide, cervical cancer (CC) is the third cancer affecting women and is the most frequent gynecologic cancer.[1] Five-year survival rates of more than 90% have been reported after Class III radical hysterectomy (RH) for early cervical cancer (ECC).[2] Due to this good 5-year survival rate, quality of life (QoL) issues for survivors have become increasingly considered.

The parametrectomy is the most technically difficult aspect of RH and is closely related to morbidity. Numerous modifications of Wertheim's surgical procedure have been proposed during the years, to improve feasibility and reduce side effects.[3]

During the last part of the 20th century, the morbidity of RH and the accumulating information on low risk for parametrial involvement in ECC led to more conservative approaches for cancer resection. Given that radicality is directly related to morbidity, the most obvious method for minimizing postoperative pelvic visceral dysfunction and improving QoL would be to reduce the extent of parametrial resection in patients with ECC. A new concept of

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modified RH or Class II RH has been developed in order to reduce morbidity without compromising the oncological outcome.

A randomized study demonstrated that Class II RH is superior to Class III RH in terms of morbidity, with equal results in terms of oncological outcome in patients with CC.[4] Recently, a trial comparing Class I to Class III RH on ECC has been published confirming that the reduction of radicality does not compromise the oncologic outcome.[5]

The purpose of this observational study was to evaluate disease free survival (DFS), overall survival (OS), and recurrence rate in patients with ECC who underwent Class II RH and to compare these data with a historical ECC control group in which Class III RH was performed.

Material and methods

After obtaining approval from the Institutional Review Board, all women who had undergone Class II or Class III RH for ECC were enrolled in this single center observational study. Patient information was gathered in a database held in our department. We compared prognosis in 127 patients treated with Class II RH between June 2001 and October 2011 with those of 202 patients submitted to Class III RH between March 1980 and March 2001. The patients submitted to surgery between 1996 and 2000 were not considered in this observational study because in this period, a modified RH, non includible in Class II or III RH, was performed.

Inclusion criteria were: histologically confirmed CC; clinically ECC (stage IA2-IB1-IIA1); eligibility for surgical treatment (RH); age distribution ranging between 18 years and 80 years; signed informed consent. Exclusion criteria were: other metachronous or synchronous neoplasia, presence of other severe co-morbidities, recurrent disease.

Patients were preoperatively evaluated with complete physical and gynecologic examination, routine blood and urine analysis, chest radiography, and magnetic resonance imaging since 2001. Cystoscopy, rectoscopy, or computed tomography were performed only on clinical indication. The stage of the disease was determined by using the Federation International of Gynecology and Obstetrics (FIGO) staging system.[6]

Gynecological examination was performed under anesthesia, when indicated. Clinical evaluation of the patients was performed jointly by at least two senior gynecologic oncologists; when there was disagreement the case was assigned to the earlier stage.

Surgical procedures were performed according to the operative guidelines described by Rutdlege, Piver et al.[7]

Class III RH was performed in all cases by laparotomy, whilst Class II RH either via laparotomy or laparoscopy. The main surgical steps of Class II RH are: the uterus, paracervical tissues, and upper vagina (1–2 cm) are removed after dissection of the ureters to the point of their entry to the bladder. The uterine arteries are ligated, and the medial half of the parametria and proximal uterosacral ligaments are resected. The main surgical steps of Class III RH are: en bloc removal of the uterus with the upper third of the vagina along with the paravaginal and paracervical tissues. The uterine vessels are ligated at their origin, and the entire width of the parametria is resected bilaterally. Removal of as much of the uterosacral ligaments as possible.

Systematic pelvic lymphadenectomy (PLN) was performed by skeletonizing vessels and removing lymph-node bearing fat tissue. A systematic PLN included the external, internal, interiliac, presacral, obturator, and common iliac nodes. Paraortic lymph node dissection was performed in presence of pelvic node metastases or of suspicious node/s in para-aortic area. When para-aortic lymphadenectomy was performed, it included paracaval, interaorto-caval and paraaortic lymph nodes up to the renal vessels.

The main difference in the surgical instrumentation between the two periods concerned the use of bipolar scissors and hemoclips in Class II group. In addition in the case group drains were not used routinely, whilst they were in the control group. Prophylactic antibiotics and antithrombotic therapy were administered pre-operatively to all the patients.

Transfusion rate, blood loss during surgery, operating time, and hospital stay were evaluated.

Pathologic assessment included histological type, infiltration of parametrium, resection margins, vaginal involvement, lymph vascular space invasion (LVSI), number of lymph nodes and lymph nodes status.

The criteria for adjuvant therapy in the Class III cohort were the following: patients received adjuvant radiotherapy in case of positive lymph node/s, parametrial or/and vaginal involvement or positive surgical resection margins (<5 mm). Most patients were submitted to adjuvant brachytherapy (BRT) regardless of pathologic factors on the specimens. In individual cases with multiple pelvic and para-aortic node metastases, platinum-based chemotherapy alone (3 patients) or CHT-RT (2 patients) were offered.

The criteria for adjuvant treatments in the Class II cohort were the following: patients received adjuvant concomitant CHT-RT in case of positive lymph node, parametrial or/and vaginal involvement or positive surgical resection margins (<5 mm). Patients received adjuvant radiotherapy in the presence of at least two of the following prognostic factors according to Sedlis'[8] criteria: large tumor diameter, cervical stromal invasion of more than 50% and LVSI. LVSI alone was not a criterium for adjuvant therapy. Radiotherapy included external pelvic irradiation with an 18-MV photon beam, using multiportal technique, with a single dose of 1.8–2 Gy at the isocenter and two or more portals treated daily. The total dose was 50 Gy in 5–6 weeks. A boost of 5–10 Gy was delivered to the positive pelvic nodes. In individual cases (5 patients) with multiple