Gynecologic Oncology 132 (2014) 624–627

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Non-radical surgery for small early-stage cervical cancer. Is it time?

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HIGHLIGHTS

- Non-radical surgery achieves excellent oncologic outcomes in low-risk early-stage cervical cancer.
- Non-radical surgery is associated with minimal perioperative complications.
- Ongoing large, prospective trials will determine whether non-radical surgery reduces morbidity without compromising oncologic outcomes.

ARTICLE INFO

Article history:
Received 22 November 2013
Accepted 18 January 2014
Available online 27 January 2014

Keywords:
Cervical cancer
Non-radical surgery
Cone biopsy
Hysterectomy

ABSTRACT

Objectives. Non-radical surgery has been proposed in women with early-stage cervical cancer to reduce morbidity. Our objective was to evaluate the outcomes of women with early-stage cervical cancer treated with non-radical surgery.

Methods. Between March 1991 and July 2013, 51 women with early-stage cervical cancer underwent simple hysterectomy or cone biopsy. All patients had assessment of pelvic lymph nodes. Patient demographics, stage, perioperative complications, pathology findings and disease-free interval were collected prospectively.

Results. Twenty-six women had squamous cell carcinoma (SCC), 22 adenocarcinoma (AC) and 3 adenosquamous (AS) carcinoma. Thirty women were FIGO stage 1A1, 8 women IA2, and 13 women 1B1. Twenty-two (43%) and 29 (57%) women underwent simple hysterectomy and cone biopsy respectively. Median measurable tumor size was 10 mm (range 2–11), and median depth of invasion was 2.0 mm (range 0.1–12 mm). Lymphovascular space invasion (LVSI) was present in 18 women (35%). Surgical margins were negative in all women. Two women received adjuvant chemoradiation (one had deep stromal invasion with LVSI, and one had two micrometastases to pelvic nodes). Forty-nine women (96%) had their Foley catheter removed on the day of surgery or post-operative day 1. No intraoperative or postoperative complications occurred and the median blood loss was 100 ml. Median follow-up was 21 months (range 1–112). None of the 51 women developed a recurrence during follow-up (95% CI: 0–6%).

Conclusion. Non-radical surgery in appropriately selected early-stage cervical cancer patients results in a low complication rate and excellent oncologic outcomes. This approach seems to be a reasonable option in well-selected patients.

Introduction

Cervical cancer is the third most common cancer in women worldwide [1]. Approximately 530,000 women are newly diagnosed with cervical cancer each year and 275,000 die from it [1]. Nonetheless, cervical cancer among women with access to an organized cervical cancer screening program is uncommon and often diagnosed at an early curable stage [2]. The International Federation of Gynecology and Obstetrics (FIGO) defines early-stage cervical cancer as FIGO stage IA or IB1. Radical hysterectomy combined with bilateral pelvic lymph node dissection remains the standard treatment for women with early-stage disease, [3] resulting in excellent 5-year overall survival rates ranging from 73.4 to 97.5% [4–6]. Radical trachelectomy with bilateral pelvic lymph node dissection in early-stage disease results in comparable overall survival and recurrence-free survival to radical hysterectomy and this approach is considered a standard of care for the management of early-stage cervical cancer in women who desire preservation of fertility [7].

Parametrectomy is the most challenging part of a radical hysterectomy or radical trachelectomy and is responsible for the majority of surgical complications such as significant blood loss, bladder and bowel dysfunction, fistula formation, and sexual dysfunction [4,8–16]. Several reports have shown that the risk of parametrial involvement is less than 1% in women with favorable prognostic factors [17–23]. Therefore, the radicality of surgery should be carefully considered in patients with low-risk early-stage cervical cancer. A parametrectomy might not be warranted if the risk of parametrial involvement is very low. Several small retrospective series have demonstrated the feasibility of non-

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0090-8258/$ – see front matter
http://dx.doi.org/10.1016/j.ygyno.2014.01.037

radical surgery for the management of early-stage cervical cancer, and have reported favorable oncologic outcomes with a cumulative recurrence rate of 1.5% and cancer-related death of 0.5% [14,17,24–29]. However, due to the need to detect small differences in recurrence and survival, larger prospective studies (randomized if feasible) are needed to confirm whether non-radical surgery can safely reduce morbidity while maintaining oncologic outcomes, and to further clarify the appropriate patient population for non-radical surgery.

Will non-radical surgery ever become the new gold standard for women with low-risk early-stage disease? Two large prospective cohort studies and a non inferiority trial are currently underway, and aim to evaluate whether non-radical surgery can reduce morbidity without compromising oncologic outcomes [30–32]. At our center, non-radical surgery has been offered to appropriate low-risk early-stage cervical cancer patients for the past 12 years, and outcomes have been recorded in a prospective database. The objective of this study was to characterize the patients and tumor characteristics, and evaluate the outcomes of women with early-stage cervical cancer treated with non-radical surgery.

Methods

All patients diagnosed with early-stage cervical cancer and treated with non-radical surgery at the Sunnybrook Health Sciences Centre between March 1991 and July 2013 were identified. Eligibility evolved over the 20 year time span of this study, but in general included patients with a histologic diagnosis of squamous cell carcinoma (SCC), adenocarcinoma (AC), or adenosquamous cell carcinoma (AS) of the cervix, stage IA1 with positive lymphovascular space invasion (LVSI) or non-SCC histology, stage IA2, or stage IB1 of any grade with inner 2/3 cervical stromal invasion (≤10 mm). Surgery included simple hysterectomy or cone biopsy depending on patient's desire for future fertility. Furthermore, all patients underwent a concomitant assessment of pelvic lymph nodes with either a bilateral pelvic lymphadenectomy or bilateral sentinel lymph node biopsy. Patients were all managed by members of the Division of Gynecologic Oncology at our tertiary-care cancer regional center.

Candidates for non-radical surgery were selected based on FIGO stage and tumor factors, and informed written consent was obtained from all patients. Definitions of maximal tumor dimension, LVSI, depth of tumor invasion, maximum depth of invasion, blood loss, operative time, intraoperative and postoperative complications have been previously defined [4]. All surgical specimens were examined by a subspecialist gynecologic pathologist.

Data on patient demographics, clinical stage, perioperative complications, pathology findings and disease-free interval were collected prospectively in a computerized database (Medlog, Crystal Bay, Nevada). Patients had a follow-up visit scheduled 3–4 weeks after surgery, followed by every 4 months for 2 years, followed by every 6 months for 3 years. At each follow-up visit, a history and physical examination including cervical smear and colposcopic assessment for patients managed by cone biopsy were performed.

Descriptive statistics were used for patient characteristics. Recurrence-free survival was calculated from the date of the surgery to the date of last follow-up or the date of recurrence.

Results

A total of 51 patients were diagnosed with early-stage cervical cancer and treated with simple hysterectomy, or cone biopsy and concomitant bilateral pelvic lymphadenectomy or sentinel lymph node biopsy between March 1991 and July 2013. The median age at diagnosis was 34 years (range 19–77). Patient and tumor characteristics are shown in Table 1, while intraoperative and postoperative outcomes are shown in Table 2.

Table 1
Patient and tumor characteristics.

Variable	#
Number of patients	51
Median age, range (years)	34 (19–77)
Histology subtypes	
SCC	26 (51%)
AC	22 (43%)
AS	3 (6%)
FIGO stage	
1A1	28 (55%)
1A2	10 (20%)
1B1	13 (25%)
LVSI present	18 (35%)
Median measurable tumor size, range (mm)	10 (2–11)
Median max. depth of invasion, range (mm)	
SCC	2 (0.6–12)
AC	2 (0.1–4.5)
AS	2 (1.7–4.0)
Positive margin status	0 (0%)

SCC: Squamous cell carcinoma; AC: Adenocarcinoma; AS: Adenosquamous carcinoma; LVSI: Lymphovascular space invasion.

Twenty-two patients (43%) underwent simple hysterectomy with assessment of the pelvic lymph nodes. Cone biopsy with pelvic lymph node assessment was performed in 29 patients (57%). Twenty-nine patients underwent complete pelvic lymph node dissection (with or without sentinel lymph node biopsy) while 22 patients had sentinel lymph node biopsy only. The majority of patients had SCC (51%) or AC (43%) histology, while 6% had AS histology. Twenty-eight patients (55%) were FIGO stage 1A1, 10 patients (20%) were stage IA2, and 13 patients (25.5%) were stage 1B1. Nine of FIGO stage IA1 disease had LVSI present and 15 of FIGO stage IA1 had non-SCC histology.

Median measurable tumor size was 10 mm (range 2–11). LVSI was present in 18 patients (35%). The median depth of invasion was 2.0 mm (range 0.6–12), 2.0 mm (range 0.1–4.5) and 2.0 mm (range 1.7–4.0) for women with SCC, AC, or AS histologies respectively. Surgical margins were negative for carcinoma in all women.

Forty-nine patients (96%) had their Foley catheter removed on the day of surgery or post-operative day 1. Two patients experienced urinary retention requiring a delay in the removal of their Foley catheter (2 and 5 days after surgery). There were no intraoperative or postoperative complications and the median blood loss was 100 ml (range 50–1200) (Table 2).

Two patients (4%) required adjuvant chemoradiation. One had deep stromal invasion of at least 8 mm on cone biopsy with LVSI present. She was still alive without recurrence at her last follow-up 6 months after surgery. The other patient had two micrometastases to pelvic lymph nodes and was alive without a recurrence at her last follow-up 21 months after surgery.

Median follow-up is 21 months (range 1–112). None of the 51 women with early-stage cervical cancer have recurred (95% CI: 0–6%).

Table 2
Intraoperative and postoperative outcomes.

Variable	#
Procedure	
Simple hyst + PND	22 (43%)
Cone biopsy + PND	29 (57%)
Median surgical time (min), range (min)	90 (45–180)
Median blood loss (ml), range (ml)	100 (50–1200)
Complications	
Intraoperative	0 (0%)
Postoperative	0 (0%)
Removal of Foley catheter by post-op day 1	49 (96%)
Median follow-up, range (months)	21 (1–112)
Recurrence	0 (0%)

Hyst: Simple hysterectomy; PND: Pelvic lymph node assessment.