



Review

Surgery for early stage cervical cancer: How radical should it be?

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HIGHLIGHTS

- Radical surgery for cervical cancer confers a significant risk of intra-operative and post-operative morbidity
- Treatment of early cervical cancer is evolving: non-radical surgery may be safe in some situations, including early adenocarcinoma
- Ongoing large, prospective trials will help define the best candidates for non radical surgery

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ABSTRACT

Objective. Less radical or non radical surgery for early-stage cervical cancer has been proposed to reduce morbidity while maintaining oncologic outcomes. Given that a standardized approach to conservative surgery is not yet available, we have summarized the literature on less radical surgery to better inform clinical practice.

Methods. MEDLINE R and MEDLINE in-process and non-indexed citations were searched from inception to April 14, 2013 to identify all English-language articles evaluating less-radical or non radical surgery for invasive cervical carcinoma. Articles including patients with squamous cell carcinoma, adenocarcinoma and adenosquamous carcinoma were included and a narrative review of the literature is presented.

Results. Radical surgery is associated with significant adverse effects in terms of urinary function, sexual function, and body image. Radical trachelectomy is an accepted fertility-sparing option, but still leads to morbidity from parametrectomy. The importance of the parametrectomy in patients with small early-stage tumors has been questioned recently, and many studies have found simple hysterectomy and simple trachelectomy can be safe in appropriately selected patients. Cone biopsy may be a fertility-sparing option in those patients with a very low risk of parametrial involvement. Neoadjuvant chemotherapy is also being investigated as a method to reduce the need for radical surgery. Sentinel lymph node biopsy is discussed as a method to reduce the morbidity while increasing the sensitivity of pelvic lymph node assessment in women with early cervical cancers. Finally, the treatment of early adenocarcinoma is addressed.

Conclusions. It appears many women with early-stage cervical cancer can be treated less radically than has been done in the past. Large prospective trials are underway to further define candidates for less-radical surgery.

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Introduction

Cervical cancer is the third most common malignancy in women worldwide [1]. While radical hysterectomy is an effective treatment in women with early stage cervical cancer (Stages IA1–IIA), with 5-year overall survival rates of 73.4%–97.5% [2–4], this procedure is not without morbidity. The risk of blood loss and transfusion, nerve or vascular injury, bladder and bowel dysfunction, fistula formation, lymphedema, and sexual dysfunction are significant [2,5–9].

In certain cases of early stage cervical carcinoma, the risk of parametrial involvement and lymph node metastases is accepted to be low. In the treatment of microinvasive squamous cell carcinoma, for instance, cone biopsy or simple hysterectomy has become an acceptable alternative [10,11]. While traditionally patients have received radical surgery for all but the smallest squamous cervical lesions [12], there is a movement towards less radical surgery in patients with 1A and small 1B cervical carcinoma.

Bergmark et al. [5] asked women whether they would be willing to make a ‘trade off’ of decreased morbidity at the cost of a slightly decreased survival. Ninety percent of women were not willing to make such a compromise. The question to be answered, therefore, appears to be whether a decrease in morbidity is possible in some patients without a compromise in oncologic outcome. While the GOG is currently evaluating physical function and quality of life in patients following non-radical surgery for early stage cervical cancer patients (IA1 with lymph-vascular space invasion (LVSI), IA2–IB1 ≤ 2 cm) this review is intended to evaluate the evidence in support of non-radical surgery in carefully selected patients.

Methods

MEDLINE R and MEDLINE in-process and non-indexed citations were searched from inception to April 14, 2013 to identify all English-language publications of less radical or non-radical surgery for invasive cervical carcinoma. No exclusions based on histology were embedded in the search strategy, however this review only addresses treatment of squamous cell carcinoma, adenocarcinoma and adenosquamous carcinoma. The search strategy incorporated appropriate controlled vocabulary and keyword searches including various terms for cervical carcinoma and combining these with terms for less radical surgery, including conization, cone biopsy, simple hysterectomy, simple trachelectomy, and nerve-sparing hysterectomy. In addition, the PubMed related articles feature was used to ensure all relevant articles were identified. Articles were separated into relevant categories and a narrative synthesis of the literature presented.

Results

Morbidity of radical surgery for cervical cancer

The first series of radical hysterectomy in the treatment of cervical cancer was reported by Ernst Wertheim in 1912 [13]. This was followed by the series of Meigs [14]. The radical hysterectomy today is commonly categorized by amount of parametria resected (or class), with class III (radical) hysterectomy, typically employed in cases of IB or IIA disease and class II (modified radical) hysterectomy offered primarily to patients with stage IA2 disease.

Compared to the class I or non-radical hysterectomy, the risks of blood loss and transfusion, nerve or vascular injury, bladder/bowel

dysfunction, fistula formation, lymphedema, and sexual dysfunction associated with radical or modified radical hysterectomy are considerably increased. A median blood loss of 600–2100 ml with transfusion rates of 23% has been reported in large series [2,15]. Long-term voiding dysfunction may occur in up to 40–42% of patients [15,16]. Bladder dysfunction may include incomplete bladder emptying and the use of straining to micturate in 16–25% of patients [5,16], with a median of 7 days to complete bladder emptying [2]. These figures rise when adjuvant radiotherapy is employed [17]. Bowel dysfunction may include constipation in 9–18% of patients [5,18], and fecal or flatal incontinence in 33% [18], with manometric evidence of dysfunction [19]. The risk of fistula formation is 1–6.7% [15,20–23]. Lymphedema has been documented in 3–19% of patients, depending on criteria used for diagnosis [5–8]. The incidence of sexual dysfunction ranges from 19–36% [5,9].

Sexual dysfunction may take the form of decreased arousal (31%) [24], inadequate lubrication (10–55%) [6,9,25,26], vaginal shortening (25–29%) [6,15,25], dyspareunia (18–42%) [6,24,26], decreased sensation of the labia and thighs (71%) [6] and decreased genital swelling (36%) [9]. The distress associated with sexual dysfunction in women following treatment for cervical cancer is twice that of controls with similar sexual dysfunction [9] and 25–66% of patients have little interest in, or are unsatisfied with sex [6,25,26], or have increased anxiety regarding sexual performance (53%) [26].

While the majority of patients (91%) resume sexual activity following surgery for early stage cervical cancer [25], there is a decrease in frequency of intercourse reported [25], and decreased quality of life in women with diminished sexual functioning [24]. This is in addition to the loss of fertility after radical hysterectomy in the proportion of women of childbearing age.

Radical trachelectomy

Fertility preservation through the use of radical vaginal trachelectomy in patients with early cervical carcinoma was first described by Dargent [27]. Over the last 20 years, radical trachelectomy has also been performed abdominally through open [28], laparoscopic [29,30] and robotic [31–33] approaches, although the vaginal approach is the most commonly reported and has resulted in the highest number of successful pregnancies [34]. Regardless of approach, radical trachelectomy removes the cervix with contiguous parametria and upper vaginal cuff, and preserves the uterine corpus and adnexae. It is combined with an assessment of the pelvic lymph nodes. In general, radical trachelectomy is only recommended for tumors measuring ≤ 2 cm, as the risk of recurrence appears to increase in larger tumors [35,36]. A matched case–control study compared 90 women undergoing radical vaginal trachelectomy to 90 women undergoing radical hysterectomy, and controlled for age, tumor size, histology, grade, depth of invasion, LVSI, pelvic node metastases and adjuvant therapy [37]. There was no difference in the 5-year recurrence free or overall survival between groups [37]. Another retrospective study demonstrated no difference in recurrence or survival rates in women undergoing radical vaginal trachelectomy (n = 118) compared to radical vaginal hysterectomy (n = 139) after adjusting for age, tumor size, histology, LVSI, and pelvic node metastases [35]. Together, these two studies suggest radical trachelectomy has similar oncologic outcomes to radical hysterectomy in patients with tumors measuring 2 cm or less who desire fertility preservation.

Fertility rates vary after radical trachelectomy, but have been reported to be between 41% and 70% [38–40]. Fertility may be impaired

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