Surgery after Chemoradiation Therapy in Persistent/Recurrent locally advanced cervical cancer. Is Exenteration Always Necessary?

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Abstract

In cases of persistent or recurrent disease in locally advanced cervical cancer after chemoradiation therapy, surgery will be the last chance for survival, with pelvic exenteration representing the most used option. However, in cases of small central recurrences (<2 centimetres) limited to the cervix or vagina may be candidates for a less radical approach, specifically laparoscopic radical hysterectomy. This intervention has received little attention in the literature. The current article comprehensively outlines the rationale behind the management of these cases and discusses the existing literature. Indications for this approach must ensure that neighbouring organs such as the rectum or the bladder are not affected in the preoperative studies. The intention is to offer a less mutilating surgery than exenteration in cases of small persistent or recurrent disease.

Keywords: Cervical cancer; Chemoradiation therapy; Radical hysterectomy; Laparoscopy

Mini Review

Since 1999 chemoradiation therapy (CRT) has represented the standard treatment for locally advanced cervical cancer (LACC) [1,2]. However, about 30-50% of patients diagnosed with LACC will recur and ultimately die because of the disease [3]. Complete response after concurrent CRT and stage, are the two most important prognostic factors. The rate of residual disease after primary treatment increases in relation to the FIGO stage, and range between 35-61% [4-7]. It’s accepted that surgery is the only curative treatment for patients with recurrent or persistent pelvic cancer after CRT.

Although exenteration is the common surgical approach in post-radiation patients with isolated pelvic relapse, radical hysterectomy may be an option in carefully selected patients with small central recurrences (<2 cm) limited to the cervix or upper vagina [8]. (NCCN Guidelines Version 1.2018 Cervical Cancer). This treatment option has barely been published in literature [9-11]. In a series of 50 patients at Memorial Sloan-Kettering Center [10] that were operated on by laparotomy (radical hysterectomy, PIVER II, III), a 5-year survival rate of 90% was found in lesions smaller than 2 cm, versus 64% for bigger lesions. The high initial rates of serious postoperative complications (20-40%) with 26% of postoperative fistula [9], took to the practical abolishment of this technique. Most recent papers about completion surgery after CRT in LACC by laparotomy have had better results [5,12,13]. Perhaps, these improved results are due to the fact that surgeons tend to perform hysterectomy soon after CRT to avoid development of radiation-induced fibrosis. However, the role of this adjuvant surgery performed a few weeks after primary chemoradiation treatment (4-8 weeks) remain controversial [12-13] and the benefit to overall or disease free survival has never been demonstrated [14].

Ferrandina et al. [15] reported in a 362 consecutive LACC (FIGO stage IB2-IVA) patients submitted to laparotomic radical hysterectomy after CRT (interval to radical surgery around 6 weeks) a 25.7% postoperative complication rate. Classe et al. [16] showed that uretero vaginal fistulas occurred in 3.5%, whereas Toublul et al. [5] found a urinary fistula rate of 7.3% and 2 deaths linked to surgery. The literature describes radicality of the hysterectomy, residual disease and pelvic lymph node involvement as major risk factors for the occurrence of complications [5,17,18]. The effect of CRT on pelvic tissues had been proven to increase the difficulties of surgical dissection, due to an inflammation process, vascular fibrosis and firm adhesions. This effect promotes the loss of anatomical planes and determines an increased risk of morbidity.

Firm pelvic tissue fibrosis is documented in almost 50% of cases [19] and often involves the visco-uterine ligament and paracervix tissue. Due to these difficulties, a laparoscopic
Surgery after Chemoradiation Therapy in Persistent/Recurrent locally advanced cervical cancer is feasible with an acceptable rate of complications and oncological results. However, the main problem is how to determine certainly the presence of residual disease after CRT. Currently, there is no accurate method of detecting residual or recurrent disease after CRT, which makes it difficult to determine population of women who needs salvage surgery. Physical examination is the most often used method for diagnosis with sensitivity and specificity rates of 51 and 62% respectively [25]. Histological confirmation prior to surgery is difficult to achieve.

It is well known that radiation-induced morphologic changes continue also after finishing CRT with a risk of false positive findings in biopsies or cytology. Sensitivity of vaginal cytology is poor, probably due to radiation-induced dysmorphia. Imaging techniques have been included to improve the diagnosis of residual/persistent disease. The magnetic resonance image (MRI) is the standard imaging technique used. However, its accuracy in predicting response after CRT still is under debate because of the high risk of false positive results. Studies show sensitivities of 80%, specificities of 55% and positive and negative predictive values of 50 and 83%, respectively [26]. In the other hand, over the last few years, there has been an increase in the use of positron emission tomography/computed tomography (PET/TC) to detect residual or recurrent disease. Meta-analysis showed that the sensitivity and specificity of PET-CT for local regional recurrence were 0.82 (95% CI: 0.72–0.90) and 0.98% (95% CI: 0.96–0.99), respectively [27]. So, the use of PET-CT in local regional recurrent/persistent cervical cancer is not currently supported by published literature [28].

**Conclusion**

Indications for this approach, needs a positive preoperative biopsy and ensure that neighbouring organs such as the rectum or the bladder are not affected in the preoperative studies. The intention is to offer a less mutilating surgery than exenteration in cases of small persistent or recurrent central disease. Although radical hysterectomy is a valid option to avoid an exenteration in carefully selected cases, a multicentre prospectively study is needed.
References

1. McNeil C (1999) New standard of care for cervical cancer sets stage for next questions. J Natl Cancer Inst 91(6): 500-501.

2. Chemoradiotherapy for Cervical Cancer Meta-analysis Collaboration (CCCMAC) (2010) Reducing uncertainties about the effects of chemoradiotherapy for cervical cancer: individual patient data meta-analysis. Cochrane Database Syst Rev (1): CD008285.

3. Waggoner SE (2003) Cervical cancer. Lancet 361(9376): 2217-2225.

4. Houvenaeghel G, Lelièvre L, Gonzague Casabianca L, Buttarelli M, Moutardier V, et al. (2006) Long-term survival after concomitant chemoradiotherapy prior to surgery in advanced cervical carcinoma. Gynecol Oncol 100(2): 338-343.

5. Touboul C, Uzan C, Mauguen A, Gouy S, Roy A, et al. (2010) Prognostic factors and morbidities after completion surgery in patients undergoing initial chemoradiation therapy for locally advanced cervical cancer. Oncologist 15(4): 405-415.

6. Colombo PE, Bertrand MM, Gutowski M, Mourgogot A, Fabbro M, et al. (2009) Total laparoscopic radical hysterectomy for locally advanced cervical carcinoma (stages IIB, IIA and bulky stages IB) after concurrent chemoradiation therapy: surgical morbidity and oncological results. Gynecol Oncol 114(3): 404-409.

7. Hequet D, Marchand E, Place V, Fourchotte V, De La Rochefordiere A, Dridi S, et al. (2013) Evaluation and impact of residual disease in locally advanced cervical cancer after concurrent chemoradiation therapy: results of a multicenter study. Eur J Surg Oncol 39(12): 1428-1434.

8. Stanhope CR, Webb MJ, Podratz KC (1999) Pelvic exenteration for recurrent cervical cancer. Clin Obstet Gynecol 33(4): 897-909.

9. Rutledge S, Carey MS, Prichard H, Allen HH, Kocha W, et al. (1994) Conservative surgery for recurrent or persistent carcinoma of the cervix following irradiation: is exenteration always necessary? Gynecol Oncol 52(3): 353-359.

10. Coleman RL, Keeny ED, Freedman RS, Burke TW, Eifel PJ, et al. (1994) Radical hysterectomy for recurrent carcinoma of the uterine cervix after radiotherapy. Gynecol Oncol 55(1): 29-35.

11. Maneo A, Landoni F, Cormio G, Colombo A, Mangioni C (1999) Radical hysterectomy for recurrent or persistent cervical cancer following radiation therapy. Int J Gynecol Cancer 9(4): 295-301.

12. Houvenaeghel G, Lehevre L, Buttarelli M, Jaquemier J, Carcoppino X, et al. (2007) Contribution of surgery in patients with bulky residual disease after chemoradiation for advanced cervical carcinoma. Eur J Surg Oncol 33(4): 498-503.

13. Morice P, Uzan C, Zafani Y, Delpech Y, Gouy S, et al. (2007) The role of surgery after chemoradiation therapy and brachytherapy for stage IB2/II cervical cancer. Gynecol Oncol 107(1 Suppl 1): S122-S124.

14. Kokka F, Bryant A, Brockbank E, Powell M, Oram D (2015) Hysterectomy with radiotherapy or chemotherapy or both for women with locally advanced cervical cancer. Cochrane Database Syst Rev (4): CD010260.

15. Ferrandina G, ERCOLI A, FAGOTTI A, Fanfani E, Gallotta V, et al. (2014) Completion surgery after concomitant chemoradiation in locally advanced cervical cancer: a comprehensive analysis of pattern of postoperative complications. Ann Surg Oncol 21(5): 1692-1699.

16. Classe JM, Rauch P, Rodier JF, Morice P, Stoeckle E, et al. (2006) Surgery after concurrent chemoradiotherapy and brachytherapy for the treatment of advanced cervical cancer: morbidity and outcome: results of a multicenter study of the GCCGCC (Groupe des Chirurges de Centre de Lucre Contre le Cancer). Gynecol Oncol 102(3): 523-529.

17. Ferrandina G, Margariti PA, Smaniotto D, Pettrillo M, Salerno MG, et al. (2010) Long-term analysis of clinical outcome and complications in locally advanced cervical cancer patients administered concomitant chemoradiation followed by radical surgery. Gynecol Oncol 119(3): 404-410.

18. Chereau E, DE LA Hosseraye C, Ballester M, Monnier L, Rouzier R, et al. (2013) The role of completion surgery after concurrent radio chemotherapy in locally advanced stages IB2-IIIB cervical cancer. Anticancer Res 33(4): 1661-1666.

19. Gallotta V, Ferrandina G, Chiatera V, Fagotti A, Fanfani F, et al. (2015) Laparoscopic Radical Hysterectomy after Concomitant Chemoradiation in Locally Advanced Cervical Cancer: A Prospective Phase II Study. J Minim Invasive Gynecol 22(5): 877-883.

20. Lambaudie E, Narducci F, Bannier J, Jauffret C, Pouget N, et al. (2010) Role of robot-assisted laparoscopy in adjuvant surgery for locally advanced cervical cancer. Eur J Surg Oncol 36(4): 409-413.

21. Morice P, Rouanet P, Roy A, Romestaing P, Houvenaeghel G, et al. (2012) Results of the GYNeco 02 study, an FNCLCC phase III trial comparing hysterectomy with no hysterectomy in patients with a (clinical and radiological) complete response after chemoradiation therapy for stage IB2 or II cervical cancer. Oncologist 17(1): 64-71.

22. Zygooris D, Kotsopoulos IC, Chalvatzas N, Maltaris T, Kartsiounis V, et al (2013) Laparoscopic pan-aortic and pelvic lymphadenectomy and radical hysterectomy in a patient with cervical cancer, six months after primary chemoradiation. Eur J Gynaecol Oncol 34(5): 484-486.

23. Reyes Clarat A, Martin Jiménez À, Robles Gourley A, Llull Gomila M, Martinez Canto MC, et al. (2016) Feasibility of laparoscopic radical hysterectomy after chemoradiation therapy in persistent locally advanced cervical cancer. Gynecol Surg 13: 405-492.

24. Rotman M, Aziz H, Choi KN (1989) Radiation damage of normal tissues in the treatment of gynaecological cancers. Front Radiat Ther Oncol 23: 349-366.

25. Lavoue V, Voguet L, Bertel C, Mebah H, Willaume D, et al. (2011) Place of surgery before and after concurrent chemoradiotherapy for locally advanced cervical carcinoma: A retrospective study of 102 cases. J Gynecol Obstet Biol Reprod (Paris) 2011 40(1): 11-21.

26. Vincens E, Balleguier C, Roy A, Uzan C, Zaenski E, et al. (2008) Accuracy of magnetic resonance imaging in predicting residual disease in patients treated for stage IB2/II cervical carcinoma with chemoradiation therapy: correlation of radiologic findings with surgicopathologic results. Cancer 113(8): 2158-2165.

27. Chu Y, Zheng A, Wang F, Lin W, Yang X, et al. (2014) Diagnostic value of 18F-FDG-PET or PET-CT in recurrent cervical cancer: a systematic review and meta-analysis. Nucl Med Commun 35(2): 144-150.

28. Meads C, Davenport C, Malysiak S, Kowalska M, Zapalska A, et al. (2014) Evaluating PET-CT in the detection and management of recurrent cervical cancer: systematic reviews of diagnostic accuracy and subjective elicitation. BJOG 121(4): 398-407.
