Editorial

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Who should be offered non-radical surgery for early-stage cervical cancer?

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See accompanying article by Yamazaki and colleagues on page 255.

Cervical cancer is the fourth most common cancer in women worldwide [1]. The standard treatment for early-stage cervical cancer such as the International Federation of Gynecology and Obstetrics (FIGO) stage IB is radical hysterectomy combined with bilateral pelvic lymph node assessment [2]. Radical trachelectomy is a safe alternative for young women who wish to preserve fertility [3]. The 5-year survival rate is excellent, ranging from 73.4% to 97.5% [4-6]. However, those radical procedures have significant morbidity, mainly as a result of the removal of the parametria. The parametrectomy is the most challenging part of the procedure and major complications have been reported such as blood loss, bladder and rectal dysfunction, sexual dysfunction, and fistula formation [7-12].

In recent years, the value of radical hysterectomy or trachelectomy in early-stage cervical cancer has been questioned. Parametrial involvement in early-stage cervical cancer with favorable prognostic factors can be as low as 1% [13-15]. Several reports have suggested that less radical surgery such as cervical conization, simple trachelectomy or simple hysterectomy with pelvic lymph node assessment is probably sufficient in well-selected early-stage cervical cancer to achieve excellent oncologic outcomes [16-19]. Reade et al. [13] recently summarized those reports and identified 476 women with early-stage cervical cancer managed with non-radical surgery. The reported recurrence rate was 1.5% and the rate of cancer-related death was 0.5%. Although level I evidence is still missing, this report suggests that non-radical surgery is probably a safe option in low-risk early-stage cervical cancer patients.

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Various retrospective studies have tried to identify which patients are at low-risk of parametrial involvement. Small tumor size, limited depth of invasion, negative lymph node status, and absence of lymphovascular space invasion (LVSI) are some of the prognostic factors associated with low-risk of parametrial involvement, however no consensus has yet been reached [14,20,21]. The caveat with those low-risk criteria is that pathologic assessment of the surgical specimens is required to confirm depth invasion, lymph node status, and the presence of LVSI.

To date, non-radical surgery has been offered to patients with small (<2 cm) cervical cancer with no evidence of radiological lymph node involvement. It remains unclear in which patients we may safely avoid a parametrectomy. We congratulate Dr. Yamazaki and colleagues [22] who have tried to answer this question in their retrospective cohort study titled "Pretreatment risk factors for parametrial involvement in FIGO stage IB1 cervical cancer." More specifically, they tried to identify preoperative factors that could help guide whether radical or non-radical surgery is required. They included 115 patients who underwent radical hysterectomy or trachelectomy for the management of FIGO stage IB1 cervical cancer. All patients included had a magnetic resonance imaging (MRI) done to confirm maximum tumor diameter, tumor volume, and size of pelvic lymph node. Serum concentrations of squamous cell carcinoma (SCC) antigen with a cut-off value of 1.5 ng/mL and serum cancer antigen 125 level with a cut-off value of 35 U/mL were obtained. Factors included on univariate analysis were histologic variant (SCC vs. non-SCC), maximum tumor diameter (<25 mm vs. ≥25 mm), pelvic lymph node enlargement (no vs. yes), volume index (<5,000 mm^3 vs. ≥5,000 mm^3), and tumor markers (negative vs. positive).

In their cohort, the reported rate of parametrial involvement and pelvic lymph node metastases was higher than one

might expect; 16% and 15%, respectively. Not surprisingly, they found that parametrial involvement was significantly associated with increasing MRI-based tumor diameter (p<0.001), tumor volume index (p<0.001) and positive tumor markers (p<0.001). Indeed, the rate of parametrial involvement was 1.5% for tumor diameter <20 mm compared to 80% for tumor diameter of 35 to 40 mm. Furthermore, 1.4% of tumor volume index <5,000 mm^3 had parametrial involvement compared to 75% for tumor volume index ≥30,000 mm^3. Only 5.6% of patients with negative tumor markers had parametrial involvement compared to 31% of those with positive tumor markers. None of the 53 patients with tumor diameter <25 mm, tumor volume index <5,000 mm^3 and negative tumor markers had parametrial involvement, which accounted for 47% of stage IB1 included in the study.

Yamazaki and colleagues' data add to the mounting evidence that non-radical surgery is feasible in well-selected low-risk early-stage disease. However we have to remain cautious when offering non-radical surgery to patients that meet their pretreatment low-risk criteria, keeping in mind that their results are based on a retrospective study of only 18 patients demonstrating parametrial invasion. Moreover, the pretreatment criteria identified on multivariate analysis had wide confidence intervals (despite significant p-value), and MRI measurements are subject to interobserver variability, further raising questions regarding the clinical value and widespread applicability of these results.

Two large prospective cohort studies and a non-inferiority randomized controlled trial are underway, and aim to evaluate whether non-radical surgery can reduce morbidity without compromising oncologic outcomes. Gynecologic Oncology Group (GOG) 278 is a multicenter prospective cohort study that is evaluating the physical function and quality of life before and after surgery in patients with stage I cervical cancer treated with non-radical surgery. It includes stage IA1 (LVSI present) and IA2–IB1 (≤2 cm) with negative radiologic scan of the abdomen and thorax for metastatic disease. MD Anderson Cancer Center is also conducting a prospective, international, multicenter cohort study evaluating the safety and feasibility of conservative surgery in women with early-stage cervical cancer. Finally, the Gynecologic Cancer Intergroup is conducting the SHAPE trial in which women with early-stage cervical cancer are randomized to radical hysterectomy or simple hysterectomy.

So who is the ideal candidate for non-radical surgery? While we wait for level 1 or 2 evidence, few would argue that non-radical surgery seems to be a safe option in women with predefined low-risk small early-stage cervical cancer. It is the specific criteria and definitions that are the subject of debate, and continue to remain open to interpretation and local jurisdictional philosophies.

CONFLICT OF INTEREST

Dr. Covens is the PI for GOG 278. Dr. Bouchard-Fortier has no conflict of interests to report.

REFERENCES

1. International Agency for Research on Cancer. GLOBOCAN 2008 v1.2, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 10 [Internet]. Lyon, FR: International Agency for Research on Cancer; 2010 [cited 2015 Sep 23]. Available from: http://globocan.iarc.fr.
2. Pecorelli S, Zigliani L, Odicino F. Revised FIGO staging for carcinoma of the cervix. Int J Gynaecol Obstet 2009;105:107-8.
3. Beiner ME, Hauspy J, Rosen B, Murphy J, Laframboise S, Nofech-Mozes S, et al. Radical vaginal trachelectomy vs. radical hysterectomy for small early stage cervical cancer: a matched case-control study. Gynecol Oncol 2008;110:168-71.
4. Covens A, Rosen B, Murphy J, Laframboise S, DePetrillo AD, Lickrish G, et al. Changes in the demographics and perioperative care of stage IA(2)/IB(1) cervical cancer over the past 16 years. Gynecol Oncol 2001;81:133-7.
5. Quinn MA, Benedet JL, Odicino F, Maisonneuve P, Beller U, Creasman WT, et al. Carcinoma of the cervix uteri. FIGO 26th Annual Report on the Results of Treatment in Gynecological Cancer. Int J Gynaecol Obstet 2006;95 Suppl 1:S43-103.
6. Comerci G, Bolger BS, Flannelly G, Maini M, de Barros Lopes A, Monaghan JM. Prognostic factors in surgically treated stage IB-IIB carcinoma of the cervix with negative lymph nodes. Int J Gynecol Cancer 1998;8:23-6.
7. Bergmark K, Avall-Lundqvist E, Dickman PW, Henningsohn L, Steineck G. Lymphedema and bladder-emptying difficulties after radical hysterectomy for early cervical cancer and among population controls. Int J Gynecol Cancer 2006;16:1130-9.
8. Sood AK, Nygaard I, Shahin MS, Sorosky JI, Lutgendorf SK, Rao SS. Anorectal dysfunction after surgical treatment for cervical cancer. J Am Coll Surg 2002;195:513-9.
9. Trimbos JB, Franchi M, Zanaboni F, Velden J, Vergote I. 'State of the art' of radical hysterectomy; current practice in European oncology centres. Eur J Cancer 2004;40:375-8.
10. Wenzel L, DeAlba I, Habbal R, Kluhsman BC, Fairclough D, Krebs LU, et al. Quality of life in long-term cervical cancer survivors. Gynecol Oncol 2005;97:310-7.
11. Frumovitz M, Sun CC, Schover LR, Munsell MF, Jhingran A, Wharton JT, et al. Quality of life and sexual functioning in cervical cancer survivors. J Clin Oncol 2005;23:7428-36.
12. Benedetti-Panici P, Maneschi F, D'Andrea G, Cutillo G, Rabitti C,

 http://dx.doi.org/10.3802/jgo.2015.26.4.243

Congiu M, et al. Early cervical carcinoma: the natural history of lymph node involvement redefined on the basis of thorough parametrectomy and giant section study. Cancer 2000;88:2267-74.
13. Reade CJ, Eiriksson LR, Covens A. Surgery for early stage cervical cancer: how radical should it be? Gynecol Oncol 2013;131:222-30.
14. Frumovitz M, Sun CC, Schmeler KM, Deavers MT, Dos Reis R, Levenback CF, et al. Parametrial involvement in radical hysterectomy specimens for women with early-stage cervical cancer. Obstet Gynecol 2009;114:93-9.
15. Stegeman M, Louwen M, van der Velden J, ten Kate FJ, den Bakker MA, Burger CW, et al. The incidence of parametrial tumor involvement in select patients with early cervix cancer is too low to justify parametrectomy. Gynecol Oncol 2007;105:475-80.
16. Bouchard-Fortier G, Reade CJ, Covens A. Non-radical surgery for small early-stage cervical cancer. Is it time? Gynecol Oncol 2014;132:624-7.
17. Pluta M, Rob L, Charvat M, Chmel R, Halaska M Jr, Skapa P, et al. Less radical surgery than radical hysterectomy in early stage cervical cancer: a pilot study. Gynecol Oncol 2009;113:181-4.
18. Biliatis I, Kucukmetin A, Patel A, Ratnavelu N, Cross P, Chattopadhyay S, et al. Small volume stage 1B1 cervical cancer: Is radical surgery still necessary? Gynecol Oncol 2012;126:73-7.
19. Rob L, Pluta M, Strnad P, Hrehorcak M, Chmel R, Skapa P, et al. A less radical treatment option to the fertility-sparing radical trachelectomy in patients with stage I cervical cancer. Gynecol Oncol 2008;111(2 Suppl):S116-20.
20. Covens A, Rosen B, Murphy J, Laframboise S, DePetrillo AD, Lickrish G, et al. How important is removal of the parametrium at surgery for carcinoma of the cervix? Gynecol Oncol 2002;84:145-9.
21. Wright JD, Grigsby PW, Brooks R, Powell MA, Gibb RK, Gao F, et al. Utility of parametrectomy for early stage cervical cancer treated with radical hysterectomy. Cancer 2007;110:1281-6.
22. Yamazaki H, Todo Y, Okamoto K, Yamashiro K, Kato H. Pretreatment risk factors for parametrial involvement in FIGO stage IB1 cervical cancer. J Gynecol Oncol 2015;26:255-61.