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M.L. is supported by an award from the NIH/ORWH Building Interdisciplinary Research Careers in Women's Health (BIRCWH), NIH K12HD043441.

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## Minimally invasive surgery for early-stage cervical cancer: is the uterine manipulator a risk factor?



**TO THE EDITORS:** We read with great interest the study by Matsuo et al<sup>1</sup> highlighting the minimally invasive surgery (MIS)/MIS trachelectomy for reproductive women with early-stage cervical cancer. Given the results of recent reported studies that demonstrated decreased survival with MIS, the authors discuss the use of uterine manipulators as well as vaginal colpotomy as potential factors affecting tumor spread following MIS.

An uncommon variant of cervical adenocarcinoma is the villoglandular adenocarcinoma (VGA). VGA generally presents as an exophytic mass arising from the endocervical canal. It occurs mostly in young women and has an excellent prognosis. In a systematic literature review (unpublished data) from 1989 to 2018, we found 8 reported recurrences in 231 patients treated surgically for VGA of the cervix (FIGO stage Ia–Ib1). All 8 cases were histologically well differentiated pure VGA and had neither lymphovascular space invasion nor lymph node involvement. The recurrence sites were in 5 cases: episiotomy scar (n = 1), pelvic wall (n = 2), vaginal vault (n = 2). The primary treatment was open surgery. A recent case series (n = 15) reported 3 intraabdominal metastases: 2 in the ovary and 1 in the liver.<sup>2</sup> The 3 patients were treated through MIS.

This intraabdominal metastasis of VGA is remarkable because VGA has an unusually favorable prognosis. Was there a residual tumor in the endocervical canal? In all 15 cases, VGA was diagnosed after a punch biopsy. Only with uncertain tumor was a conization conducted. Among potential reasons for the inferior oncological outcomes in

patients with cervical cancer who underwent MIS than in women who underwent open surgery, the routine use of a uterine manipulator might increase the propensity for tumor spillage intraperitoneally after colpotomy under laparoscopic vision.<sup>3</sup>

Another conceivable mechanism is the hematogenous tumor cell spread intraoperatively because of the continuous mechanical manipulation of the cervix, potentially leading to an influx of tumor cells into veins and lymphatic vessels. The unavoidable damage of the tumor and its vasculature during surgery leads to a shedding of tumor cells into the blood circulation. The level of circulating cancer cells is a strong predictor of tumor recurrence.<sup>4</sup>

Given the uncertainty of the oncological safety of uterine manipulators in patients with cervical cancer, their use should be limited to patients with removed tumors. A pretherapeutic large loop excision with tumor-free margins may be an indispensable prerequisite for the use of manipulators during MIS if open surgery is not an option. ■

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The authors report no conflict of interest.

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#### REPLY



We appreciate the comments and insights by Dietl et al regarding our recent study.<sup>1</sup> The authors expressed their concern regarding uterine manipulator use during minimally invasive radical hysterectomy for early-stage cervical cancer as a risk factor for tumor spillage and dissemination. Several previous studies may support their hypothesis. First, uterine manipulator use during minimally invasive radical hysterectomy for early-stage cervical cancer was associated with increased risk of tumor surface disruption (45% vs 13%) and artificial parametrial tumor carryover (65% vs 29%) compared with laparotomy (both,  $P < .05$ ).<sup>2</sup> Second, albeit statistically not significant, there is a trend towards an increased risk of recurrence with the use of a uterine or vaginal manipulator during minimally invasive radical hysterectomy for early-stage cervical cancer: 0% for no manipulator use vs 7–11% for vaginal or uterine manipulator use ( $P = .119$ ).<sup>3</sup>

Although interpretation is limited by the small sample size and methodologic limitations of the data, these studies suggest that direct contact against the tumor in uterine cervix may be associated with iatrogenic tumor spread with manipulation. To avoid such an event, some surgeons advocate a specific surgical technique by concealing the tumor with vaginal cuff closure at the beginning of surgery, followed

by a placement of a uterine corpus-holding device inserted through the posterior vaginal fornix.<sup>4</sup> Although this “no-look no-touch technique” may reduce tumor disruption, whether the technique mitigates the risk associated with minimally invasive hysterectomy remains unknown.

Although our findings that compare minimally invasive and open trachelectomy appear reassuring, overall mortality rates were low, significantly limiting the power of our study to detect differences in survival between the groups. Furthermore, we were unable to assess manipulator use or disease recurrence.<sup>1</sup> Further study of the mechanisms underlying the increased risk of death that is associated with minimally invasive radical hysterectomy and techniques to mitigate that risk are ongoing; the use of minimally invasive techniques in the treatment of cervical cancer should be approached with caution. ■

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J.D.W. is a consultant for Tesaro and Clovis Oncology and receives research funding from Merck; K.M. has an honorarium, Chugai, textbook editorial, Springer, investigator meeting attendance expense, VBL therapeutics. A.M. reports no conflict of interest.

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