

# Fertility-sparing surgery for early-stage cervical cancer: does surgical approach have an impact on disease outcomes?



Kristin L. Bixel, MD; Jeffrey M. Fowler, MD

Historically, laparotomy was the preferred surgical approach for the management of gynecological malignancies. Laparoscopy was introduced in the early 1990s; however, gynecological oncologists were slow to incorporate standard laparoscopic techniques for radical and other complicated pelvic surgeries. This is likely due to the difficult and relatively long learning curve, limits of the technology (2-dimensional view; rigid instruments with limited articulation and rotation), poor ergonomics, longer operative times, and challenging patient factors such as obesity.<sup>1</sup>

The robotic platform offers several advantages over traditional laparoscopic methods including 3-dimensional vision, articulating instruments, motion scaling, and tremor filtration resulting in improved dexterity.<sup>2-4</sup> As a result, the robot has been increasingly used in gynecological oncology since its approval in 2005 and has been rapidly adopted for the surgical management of early stage cervical cancer in the United States.

Radical hysterectomy has been the cornerstone of surgical management of early-stage cervical cancer, and while the procedure results in excellent tumor control, it has been associated with significant morbidity.<sup>5-7</sup> Minimally invasive surgical (MIS) approaches (laparoscopic and robotic) to the radical hysterectomy were introduced in an effort to improve perioperative outcomes and decrease morbidity. Compared with the conventional open approach, MIS radical hysterectomy has been shown to decrease perioperative complications (blood loss, transfusion, infection, wound complications, pain), decrease length of hospital stay, and until recently believed to yield equivalent oncological outcomes.<sup>8-15</sup>

Two recent high-profile publications have left many reconsidering their surgical approach to the management of early-stage cervical cancer. A large, international, phase III study (the Laparoscopic Approach to Cervical Cancer [LACC] trial) found that women having MIS radical hysterectomy for early-stage cervical cancer had an increased risk of

recurrence and decreased overall survival compared with those undergoing open radical hysterectomy.<sup>16</sup> It is important to note that in this study nearly 85% of patients in the MIS arm underwent traditional laparoscopic surgery, which differs from the current practice pattern in the United States. Additionally, Melamed et al<sup>17</sup> published results from a cohort study utilizing data from the National Cancer Database (NCDB) and the Surveillance, Epidemiology, and End Results-18 registry. The authors found MIS radical hysterectomy to be associated with an increased risk of all-cause mortality compared with the open approach (5.3% in the laparotomy group compared with 9.1% in the MIS group at 4 years). Kim et al<sup>18</sup> contradict these findings in their retrospective study utilizing the Korean nationwide database. In this study, 6335 women were included, and laparoscopic radical hysterectomy was associated with improved perioperative outcomes and a better overall survival compared with the abdominal approach.

While there are several limitations to these studies, they have called into question the equivalency of oncological outcomes that was previously assumed or accepted and have made it clear that additional study is warranted.

Young women are disproportionately affected by cervical cancer, and thus, efforts have been made to pioneer uterus-sparing surgical techniques for those desiring future fertility. The use of fertility-sparing trachelectomy, regardless of surgical approach, has increased over time in the United States.<sup>19</sup> Although limited, evidence to date suggests oncological safety and favorable pregnancy outcomes following trachelectomy in reproductive-aged women with early stage cervical cancer.<sup>20-23</sup> Using the Surveillance, Epidemiology, and End Results database, Tseng et al<sup>22</sup> compared women with stage IBI cervical cancer treated with fertility preserving surgery (conization or trachelectomy with lymphadenectomy) with those having non-uterine-preserving surgical intervention. In this study, there was no difference in 5 year, disease-specific survival between the 2 groups (93% vs 94%).

The management of early-stage cervical cancer continues to evolve, with many options in regard to the radicality of the procedure and surgical technique; however, very few studies have compared outcomes with respect to surgical approach in women having fertility-preserving surgery for early-stage cervical cancer.<sup>24</sup> Those who have suggest a significant reduction in blood loss and length of stay for women having a MIS approach.<sup>20,21</sup> In addition, MIS results in less adhesion formation than traditional laparotomy,<sup>25,26</sup> which may be of particular importance when considering future fertility and obstetric outcomes.

From the Ohio State University Wexner Medical Center, Columbus OH.

Received March 18, 2019; accepted March 19, 2019.

The authors report no conflict of interest.

Corresponding author: Kristin L Bixel, MD. [Kristin.bixel@osumc.edu](mailto:Kristin.bixel@osumc.edu)

0002-9378/free

© 2019 Elsevier Inc. All rights reserved.

<https://doi.org/10.1016/j.ajog.2019.03.012>

➤ Related article, page 469.

In light of these recent studies raising concern regarding the impact of surgical approach for radical hysterectomy on oncologic outcomes, Matsuo et al<sup>27</sup> analyzed the NCDB-evaluating trends in surgical approach, characteristics, and survival of women undergoing trachelectomy for stage IA2 to IB1 cervical cancer. Perhaps the most significant finding in this study is the rapid adoption of the MIS approach from 29.3% in 2010 to 75% in 2015. And of the 144 MIS patients included, 66.7% had robotic surgery.

This trend mirrors that seen in the surgical approach to radical hysterectomy in the United States and reflects the technical advantages of the robotic platform for performing these complicated procedures. When comparing patients by surgical approach, there were no significant differences in demographics or tumor characteristics with the exception of the year of diagnosis and regional location. And while not powered for this outcome, there was no significant difference in 4 year overall survival between the 2 groups (95.7% for the MIS group vs 92.3% for the laparotomy group).<sup>27</sup>

The strength of this study lies in the numbers. This is one of the largest studies to date examining the surgical approach and survival outcomes for patients undergoing trachelectomy for early-stage cervical cancer and provides reassurance regarding the safety of the MIS approach in this patient population.

There are, however, several limitations to a study of this nature, many of which the authors acknowledge. The NCDB is believed to include approximately 70% of all newly diagnosed cases of cancer in the United States. This is a broad sample, however certainly not all inclusive, and the available data points are limited, thereby restricting the analyses that can be performed. We lack information regarding surgeon experience, technique (radical vs simple), uterine-manipulating devices, and colpotomy type (abdominal vs vaginal), all of which may have an impact on the risk of disease recurrence. In addition, no data are available regarding perioperative morbidity, recurrence rates, disease-specific survival, or reproductive outcomes.

In the last 25 years, surgical management of cervical cancer has evolved from a one-size-fits-all approach of abdominal radical hysterectomy and pelvic lymphadenectomy to a more tailored approach factoring in tumor characteristics and patients desire for future fertility. Since Dargent's original description of the vaginal radical trachelectomy, continued efforts in tailoring fertility-sparing surgical techniques to tumor-associated prognostic factors to maintain oncological goals and optimize reproductive potential are part of an overall trend in more conservative management of lower-risk, early-stage cervical cancer.<sup>28</sup> Incorporation of minimally invasive surgical approaches is an important component of these surgical modifications, which contribute to minimizing the morbidity of the radical hysterectomy and trachelectomy.

Since the publication of the LACC trial, many gynecological oncologists have abandoned the MIS approach for the management of early-stage cervical cancer. While the data are

compelling, limitations must be recognized and further investigation is warranted before abandoning MIS for all patients with early-stage cervical cancer. It is difficult to generalize the results of the LACC trial to women with small tumors (<2 cm) because the risk of recurrence was very low and the study was not powered to detect differences in this subgroup. Most women considered for fertility-sparing surgery would fall into this better prognosis subgroup.

Additionally, there are several hypotheses as to why these differences in outcomes may have occurred including exposure of the tumor to the peritoneal cavity, degree of procedural radicality, the use of uterine manipulators, and the impact of carbon dioxide in minimally invasive surgery. We agree with Matsuo et al<sup>27</sup> that, given concerns about oncological outcomes in women undergoing MIS radical hysterectomy, further study to monitor outcomes in those undergoing MIS trachelectomy is required.

Are we comfortable accepting a one-size-fits-all surgical access approach for all patients with early invasive cervical cancer? Rather than eliminating MIS, we must be thinking about how we can improve outcomes by altering surgical technique and/or establishing improved selection criteria for patients who may benefit from a minimally invasive approach. ■

## REFERENCES

1. Shafer A, Boggess JF. Robotic-assisted endometrial cancer staging and radical hysterectomy with the da Vinci surgical system. *Gynecol Oncol* 2008;111(2 Suppl):S18–23.
2. Advincula AP, Wang K. Evolving role and current state of robotics in minimally invasive gynecologic surgery. *J Minim Invasive Gynecol* 2009;16:291–301.
3. Moorthy K, Munz Y, Dosis A, et al. Dexterity enhancement with robotic surgery. *Surg Endosc* 2004;18:790–5.
4. Truong M, Kim JH, Scheib S, Patzkowsky K. Advantages of robotics in benign gynecologic surgery. *Curr Opin Obstet Gynecol* 2016;28:304–10.
5. Landoni F, Maneo A, Colombo A, et al. Randomised study of radical surgery versus radiotherapy for stage Ib-IIa cervical cancer. *Lancet* 1997;350:535–40.
6. Brooks RA, Wright JD, Powell MA, et al. Long-term assessment of bladder and bowel dysfunction after radical hysterectomy. *Gynecol Oncol* 2009;114:75–9.
7. Landoni F, Colombo A, Milani R, et al. Randomized study between radical surgery and radiotherapy for the treatment of stage IB-IIA cervical cancer: 20-year update. *J Gynecol Oncol* 2017;28:e34.
8. Maggioni A, Minig L, Zanagnolo V, et al. Robotic approach for cervical cancer: comparison with laparotomy: a case control study. *Gynecol Oncol* 2009;115:60–4.
9. Park DA, Yun JE, Kim SW, Lee SH. Surgical and clinical safety and effectiveness of robot-assisted laparoscopic hysterectomy compared to conventional laparoscopy and laparotomy for cervical cancer: a systematic review and meta-analysis. *Eur J Surg Oncol* 2017;43:994–1002.
10. Sert BM, Boggess JF, Ahmad S, et al. Robo-assisted versus open radical hysterectomy: A multi-institutional experience for early-stage cervical cancer. *Eur J Surg Oncol* 2016;42:513–22.
11. Shah CA, Beck T, Liao JB, et al. Surgical and oncologic outcomes after robotic radical hysterectomy as compared to open radical

hysterectomy in the treatment of early cervical cancer. *J Gynecol Oncol* 2017;28:e82.

12. Shazly SA, Murad MH, Dowdy SC, et al. Robotic radical hysterectomy in early stage cervical cancer: a systematic review and meta-analysis. *Gynecol Oncol* 2015;138:457–71.

13. Wang Yz, Deng L, Xu HC, et al. Laparoscopy versus laparotomy for the management of early stage cervical cancer. *BMC Cancer* 2015;15:928.

14. Zanagnolo V, Minig L, Cardenas-Rebollo JM, et al. Robotic versus open radical hysterectomy in women with locally advanced cervical cancer after neoadjuvant chemotherapy: a single-institution experience of surgical and oncologic outcomes. *J Minim Invasive Gynecol* 2016;23:909–16.

15. Bogani G, Rossetti D, Ditto A, et al. Minimally invasive surgery improves short term outcomes of nerve-sparing radical hysterectomy in patients with cervical cancer: a propensity matched analysis with open abdominal surgery. *J Gynecol Oncol* 2019;30:e27.

16. Ramirez PT, Frumovitz M, Pareja R, et al. Minimally invasive versus abdominal radical hysterectomy for cervical cancer. *N Engl J Med* 2018;379:1895–904.

17. Melamed A, Margul DJ, Chen L, et al. Survival after minimally invasive radical hysterectomy for early-stage cervical cancer. *N Engl J Med* 2018;379:1905–14.

18. Kim JH, et al. Comparative effectiveness of abdominal versus laparoscopic radical hysterectomy for cervical cancer in the post-dissemination era. *Cancer Res Treat* 2018 Sep 11. <https://doi.org/10.4143/crt.2018.120> [Epub ahead of print].

19. Machida H, Mandelbaum RS, Mikami M, et al. Characteristics and outcomes of reproductive-aged women with early-stage cervical cancer: trachelectomy versus hysterectomy. *Am J Obstet Gynecol* 2018;219:461.e1–18.

20. Veira MA, Rendon GJ, Munsell M, et al. Radical trachelectomy in early-stage cervical cancer: a comparison of laparotomy and minimally invasive surgery. *Gynecol Oncol* 2015;138:585–9.

21. Nick AM, Frumovitz MM, Soliman PT, et al. Fertility sparing surgery for treatment of early stage cervical cancer vs robotic radical trachelectomy. *Gynecol Oncol* 2012;124:276–80.

22. Tseng JH, Aloisi A, Sonoda Y, et al. Long-term oncologic outcomes of uterine-preserving surgery in young women with stage IB1 cervical cancer. *Int J Gynecol Cancer* 2018;28:1350–9.

23. Bentivegna E, Maulard A, Pautier P, et al. Fertility results and pregnancy outcomes after conservative treatment of cervical cancer: a systematic review of the literature. *Fertil Steril* 2016;106:1195–211.

24. Bentivegna E, Gouy S, Maulard A, et al. Oncologic outcomes after fertility-sparing surgery for cervical cancer: a systemic review. *Lancet Oncol* 2016;17:e240–53.

25. Hackethal A, Sick C, Szalay G, et al. Intra-abdominal adhesion formation: does surgical approach matter? Questionnaire survey of south Asian surgeons and literature review. *J Obstet Gynaecol Res* 2011;37:1382–90.

26. Gutt CN, Oniu T, Schemmer P, et al. Fewer adhesions induced by laparoscopic surgery? *Surg Endosc* 2004;18:898–906.

27. Matsuo K, Chen L, Mandelbaum RS, et al. Trachelectomy for reproductive-aged women with early-stage cervical cancer: minimally invasive surgery versus laparotomy. *Am J Obstet Gynecol* 2019;220:469–70.e1-13.

28. Ramirez PT, Pareja R, Rendon GJ, et al. Management of low-risk early-stage cervical cancer: should conization, simple trachelectomy, or simple hysterectomy replace radical surgery as the new standard of care? *Gynecol Oncol* 2014;132:254–9.