Survival of four different radical hysterectomy approaches for early-stage cervical cancer: a retrospective study

Nina Zhang[1], Xiangshu Jin[1], Wen Yang[1], Chenglei Gu[1], Li'an Li[1], Wensheng Fan[1], and Yuanguang Meng[1]

[1]Chinese PLA General Hospital

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Abstract

Objective This study compares survival of four different surgical approaches including ARH, LRH, RRH and VRH for early-stage cervical cancer in order to define the best effects and survivals for patients. Design Retrospective study. Setting The First Medical Center of the PLA General Hospital. Population 238 women diagnosed early-stage cervical cancer between January 2013 and December 2017 and followed up until September 2020. Methods All patients with early-stage cervical cancer were retrospective collected in the first medical center of the PLA general hospital. Disease free survival (DFS) and overall survival (OS) were calculated using Kaplan-Meier's method, and survival curves were compared using log-rank test. Main outcome measures Outcomes were the comparison of patients' DFS and OS between the four different radical hysterectomy approaches. Results The intraoperative blood loss and postoperative exhaust time of LRH, RRH and VRH groups are better than that in ARH group. The total 5-year OS was significant difference among the four groups. However, the difference of 5-year DFS was not statistically significant among the four groups. Furthermore, patients with early-stage cervical cancer had a significantly better DFS and OS in ARH and RRH groups than that in LRH and VRH groups. Conclusions This retrospective study demonstrated that both ARH and RRH obtained higher rate of 5-year DFS and 5-year OS compared with LRH and VRH for early-stage cervical cancer, and the survival outcomes between ARH and RRH were similar. Keywords Cervical cancer, ARH, LRH, RRH, VRH, survival.

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N Zhang,[a,1] X Jin,[a,1] W Yang,[a,1] C Gu,[a] L Li,[a] W Fan,[a,*] Y Meng[a,*]

a Department of Obstetrics and Gynaecology, the Seventh Medical Center of Chinese PLA General Hospital, Beijing, China

1 These authors contributed equally to this work.

***Corresponding Author**

Professor Yuanguang Meng, MD, PhD.

Department of Obstetrics and Gynaecology, the Seventh Medical Center of Chinese PLA General Hospital, Beijing, China

E-mail:*meng6512@vip.sina.com*

Wensheng Fan, MD.

Department of Obstetrics and Gynaecology, the Seventh Medical Center of Chinese PLA General Hospital, Beijing, China

E-mail: fanws99@163.com

Running title Survival of four different RH approaches

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Results The intraoperative blood loss and postoperative exhaust time of LRH, RRH and VRH groups are better than that in ARH group. The total 5-year OS was significant difference among the four groups. However, the difference of 5-year DFS was not statistically significant among the four groups. Furthermore, patients with early-stage cervical cancer had a significantly better DFS and OS in ARH and RRH groups than that in LRH and VRH groups.

Conclusions This retrospective study demonstrated that both ARH and RRH obtained higher rate of 5-year DFS and 5-year OS compared with LRH and VRH for early-stage cervical cancer, and the survival outcomes between ARH and RRH were similar.

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Tweetable abstract

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Introduction

Cervical cancer (CC) is one of the most important malignant tumors that threaten women's lives and health worldwide. There were approximately 570,000 new cases of CC worldwide in 2018 and 311,000 patients dying of the disease.[1, 2] About 90% of CC deaths occur in low- and middle-income countries, and the mortality rate is estimated 18 times that of developed countries.[3] The incidence of CC is 9.9/100,000 in developed countries, ranking 11th in the incidence of cancer, and the mortality is 3.3/100,000, ranking 9th in cancer-related mortality, while the incidence of CC is 15.7/100,000 in developing countries, ranking second in cancer incidence, with a mortality of 8.3/100,000, ranking third in cancer-related mortality.[4] Early-stage cervical cancer is usually asymptomatic and can be detected by screening on physical examination. Most outpatient patients have combined contact bleeding or abnormal vaginal bleeding and/or drainage.[5] Surgery and radiation therapy are preferred treatment for cervical cancer, and both treatments are thought to have similar survival outcomes.[6] However, patients with early-stage cervical cancer (2009 FIGO stage IA2-IB2) are usually treated with radical hysterectomy.[7]

Laparoscopic surgery is the standard treatment for radical hysterectomy from 2014.[8] Subsequently, the NCCN recommended laparoscopic radical hysterectomy and robotic radical hysterectomy as the standard procedure for radical hysterectomy.[9]Nevertheless, in phase III the laparoscopic approach to cervical cancer (LACC) trial, minimally invasive surgery (MIS) was associated with lower rates of disease-free survival (DFS) and overall survival (OS) than open surgery among women with early-stage cervical cancer.[10, 11] These recent

findings are contradictory to the earlier referenced guidelines, which leads to widely controversial. Therefore, in this study we summarized the case data of cervical cancer patients in a single center for 5 years (January 2013 to December 2017), and evaluated survivals of four different surgical approaches including abdominal (ARH), laparoscopic (LRH), robotic-assisted (RRH) and vaginal (VRH) radical hysterectomy for early-stage cervical cancer in order to define benefits of the different radical hysterectomy approaches.

Methods

Patient enrollment

Patients with early-stage cervical cancer (Stage IA2-IB2) who were treated in the Department of Obstetrics and Gynaecology of the First Medical Center of the PLA General Hospital (PLAGH) were studied from January 2013 to December 2017. All enrolled patients were treated surgically, grouped according to different surgical approaches. Patients fully understood the advantages and disadvantages of various surgical treatments for cervical cancer before undergoing surgery, and voluntarily chose the surgical method.

Inclusion criteria

Patients with cervical cancer were diagnosed by cervical TCT, HPV, biopsy and/or conization. After examination by two (or more) gynecologists, patient was diagnosed as stage IA2, IB1, and IB2 using 2009 FIGO (International Federation of Obstetrics and Gynaecology) staging system.[12] No neoadjuvant therapy (chemotherapy or radiotherapy) was performed. The histologic types of pathology were squamous cell carcinoma, adenocarcinoma and adenosquamous cell carcinoma. Patients underwent radical hysterectomy which includes ARH, LRH, RRH and VRH with laparoscopic pelvic lymphadenectomy. Surgery, perioperative management, related clinical decision-making and postoperative follow-up were executed by the same medical team.

Exclusion criteria

We excluded patients with stage higher than IB2, those treated with neoadjuvant therapy (chemotherapy or radiotherapy), those who did not undergo intact radical hysterectomy, those who treated radical radiotherapy, those who were generally poor conditions or had severe diseases that could not tolerate anesthesia and surgery, those who had other malignant tumors or infectious diseases that were difficult to control, and those whose case data were incomplete.

Cohort selection

From January 2013 to December 2017, the First Medical Center of the PLA General Hospital diagnosed and treated 517 patients with stage IA2-IB2 of cervical cancer, and a total of 238 cases were screened to satisfy the above inclusion and exclusion criteria (Figure 1). Among them, 32 patients were included in ARH group, 61 patients were included in LRH group, 100 patients were included in RRH group, and 45 patients were included in VRH group.

Measures

General information includes age, body mass index (BMI), clinical stage, pathological type. Perioperative period indicators include intraoperative bleeding volume, operation time, blood transfusion rate, postoperative exhaust time, postoperative hospital stay, number of lymph node resection, number of positive lymph nodes, length of vaginal wall removal, hospitalization cost, major complications. We analyzed DFS and OS.

Follow-up

History and physical examination are recommended every 3 months for 1 year, every 6 months for another 2 years, and then annually. The tests include blood routine, biochemistry, tumor biomarkers, vaginal stump TCT and HPV, chest X-ray/chest CT, pelvic and abdominal CT/MRI or gynecological ultrasound, urinary ultrasound, hepatobiliary pancreas and retroperitoneal lymph node ultrasound, PET-CT/MRI examination when suspected recurrence.

Statistical analysis

SPSS 22.0 software was used for statistical analysis. The data are presented as means ±SD. One-way ANOVA was used for comparisons among the four groups. A two-sided P -value < 0.05 was considered statistically significant. The DFS and OS were graphing using GraphPad Prism 7.00, calculated using the Kaplan Meier method, and survival curves were compared using log-rank test.

Results

Comparison baseline of four different radical hysterectomy approaches

We identified 517 patients who underwent radical hysterectomy for early-stage cervical cancer during inclusion period. Of these, 238 patients (40.03%) were selected for primary analyses (Figure 1). The majority of the patients had stage IB1 disease (89.92%). Tumour characteristics are summarized in Table 1. The ARH group included 32 patients with mean age of 50.13 ± 8.89 years old and mean BMI of 25.42 ± 3.24 kg/m^2, of which 0 case (0.00%) for stage IA2, 31 cases (96.88%) for stage IB1, 1 case (3.13%) for stage IB2, 26 cases (81.25%) squamous cell carcinoma, 6 cases (18.75%) adenocarcinoma, 0 case (0.00%) adenosquamous carcinoma, and 16 cases (50.00%) received postoperative adjuvant therapy. Sixty-one patients were enrolled in the LRH group with 48.97 ± 8.59 years old of mean age, 24.06 ± 2.81 kg/m^2 of mean BMI, of which 5 cases (8.20%) for stage IA2, 52 cases (85.25%) for stage IB1, 4 cases (6.56%) for stage IB2, 49 cases (80.33%) squamous cell carcinoma, 11 cases (18.03%) adenocarcinoma, 1 case (1.64%) adenosquamous carcinoma, and 33 cases (54.10%) received postoperative adjuvant therapy. The RRH group included 100 patients with 48.64 ± 9.89 years old of mean age, 24.12 ± 3.50 kg/m^2 of mean BMI, of which 5 cases (5.00%) for stage IA2, 91 cases (91.00%) for stage IB1, 4 cases (4.00%) for stage IB2, 89 cases (89.00%) squamous cell carcinoma, 11 cases (11.00%) adenocarcinoma, 0 case (0.00%) adenosquamous carcinoma, and 55 cases (55.00%) received postoperative adjuvant therapy. The VRH group included 45 patients with 46.04 ± 8.16 years old of mean age, 24.15 ± 3.23 kg/m^2 of mean BMI, of which 3 cases (6.67%) for stage IA2, 40 cases (88.89%) for stage IB1, 2 cases (4.44%) for stage IB2, 40 cases (88.89%) squamous cell carcinoma, 4 cases (8.89%) adenocarcinoma, 1 case (2.22%) adenosquamous carcinoma, and 22 cases (48.89%) received postoperative adjuvant therapy. Whereas there was no statistical significance of the mean age, BMI, FIGO stage, histology and postoperative adjuvant therapy in the four groups ($P > 0.05$).

Comparison results of perioperative indices in four groups of cases

Then we compared characteristics of perioperative periods in the four groups. Our data showed that there was no significant difference in postoperative hospital stays, number of removed lymph nodes, number of positive lymph nodes and resected length of vagina in the four groups ($P > 0.05$), while the differences of mean surgery time, intraoperative blood loss, postoperative exhaust time and hospital cost were statistical significance ($P < 0.05$), which were summarized in Table 2.

Additionally, the mean surgery time in ARH group was less than that in RRH group [(182.31 ± 55.75) vs (212.32 ± 57.13) min, $P = 0.013$], the VRH group was less than the ARH group, LRH group and RRH group, respectively [(139.11 ± 36.54) vs (182.31±55.75) & (184.34 ± 35.31) & (212.32 ± 57.13) min, $P < 0.01$]. Intraoperative blood loss in ARH group was more than that in LRH group, RRH group and VRH group, respectively [(712.50 ± 407.59) vs (224.43 ± 191.89) & (109.80 ± 92.98) & (216.67 ± 176.78) ml, $P< 0.01$], while RRH group was less than LRH group and the VRH group, respectively ($P < 0.01$ and $P = 0.027$). Postoperative exhaust time in LRH group was less than that in ARH group [(1.85 ± 0.70) vs (2.28±0.77) day, $P = 0.013$], whereas there was no significant difference among other groups ($P> 0.05$). Hospital cost in RRH group was more than that in ARH group, LRH group and VRH group, respectively [(6.66 ± 1.32) vs (4.54 ± 1.21) & (3.71 ± 1.41) & (3.12 ± 1.09) $\times 10^4$,$P < 0.01$], while ARH group was more than LRH group and VRH group, respectively ($P = 0.021$ and $P < 0.01$).

Comparison of survivals in four different surgical approaches

The mean follow-up time of all patients was 1697 days (range 1302 to 2055 days), and the interquartile spacing between 25% and 75% was 1290 days and 2054 days, and the median follow-up time was 1639 days

(4.49 years), which 5-year DFS was 89.00% (95% CI 88.21%-89.81%), and 5-year OS was 91.13% (95% CI 90.07%-92.20%). Five-year DFS of ARH was 96.88%, 5-year DFS of LRH was 81.99% (95% CI 83.21%-86.56%), 5-year DFS of RRH was 91.38% (95% CI 93.03%-94.48%), and 5-year DFS of VRH was 87.27% (95% CI 87.85%-91.47%). The total DFS curve of the four groups using Log-rank test was no significant difference (P= 0.061) (Figure 2A). However, DFS in LRH group was shorter than that in ARH group (P = 0.0294) (Figure S1A). DFS in RRH group was better than that in LRH group (P = 0.0442) (Figure S1D).

Furthermore, 5-year OS of ARH was 96.88% (95% CI 96.38%-97.37%), 5-year OS of LRH was 82.45% (95% CI 87.17%-92.00%), 5-year OS of RRH was 94.18% (95% CI 96.95%-97.23%), and 5-year OS of VRH was 91.49% (95% CI 95.42%-96.74%). The total OS curve of the four groups using Log-rank test was statistically significant (P = 0.015) (Figure 2B). Additionally, OS in LRH group was shorter than that in ARH group (P = 0.0305) (Figure S2A). OS in RRH group was better than that in LRH group (P = 0.0055) (Figure S2D). Nevertheless, the difference between other groups was not statistically significant ($P > 0.05$).

Discussion

Main findings

This study analyzed clinical data of early-stage cervical cancer treated by four different surgical approaches (ARH, LRH, RRH and VRH groups) in a single center of our hospital for 5 years, and we noted that the difference of DFS was not statistically significant among the four groups. However, LRH and VRH were associated with shorter OS than ARH and RRH. Therefore, this study showed that not all the survival outcome indicators of MIS are inferior to ARH, RRH can obtain similar survival outcome as the ARH. Furthermore, the intraoperative blood loss and postoperative exhaust time of the three MIS are better than that in ARH. The intraoperative blood loss in RRH is the least, but hospital cost is highest.

Strengths and limitations

The standard approach for radical hysterectomy is open abdominal approach. According to the Guidelines, radical hysterectomy could be performed via open surgery and MIS. However, recent retrospective reviews and prospective observational studies demonstrated that MIS were associated with lower rate of DFS and OS than open surgery for cervical cancer patients. Controversially, robotic-assisted MIS obtained similar oncologic outcomes compared with open surgery. Therefore, the clinical advantages of robotic-assisted MIS for the treatment of cervical cancer remain to be confirmed. This study is the first retrospective analysis to compare clinical characteristics and survivals of ARH, LRH, RRH and VRH simultaneously in a single center by the same medical team. Based on our study results, we demonstrated that both ARH and RRH obtained higher rate of 5-year DFS and 5-year OS compared with LRH for early-stage cervical cancer, and the survival outcomes between ARH and RRH were similar.

There are several limitations in this study. First of all, we collected 517 patients to analysis the oncological outcomes of different radical hysterectomy approaches. However, based on the inclusive and exclusive criteria, we excluded approximate half of the whole data, which might decrease credibility of this result. Another major limitation was that each group enrolled different number of cases, especially ARH group (n=32) and RRH group (n=100), leading to deficiency of results on statistical difference.

Interpretation

Radical hysterectomy is the standard procedure for the treatment of early-stage cervical cancer (FIGO 2009 IA2-IB stage). Since researchers reported the first case of laparoscopic radical cervical cancer,[13] laparoscopic surgery and robotic surgery have been widely used in the treatment of cervical cancer patients and have been reported in many relevant clinical studies.[14-16] Most studies focus on perioperative conditions such as intraoperative blood loss, postoperative hospital stay, postoperative exhaust time, and survival outcomes. Previous retrospective analysis results have shown that neither laparoscopic approach nor robotic-assisted laparoscopic approach reduces patients' 5-year progression free survival (PFS) and OS compared with abdominal approach.[17, 18] The LACC trial provided a definitive comparison of MIS and ARH including 631

patients with early-stage cervical cancer in 33 medical centers worldwide, and the results showed no significant difference in the occurrence of intraoperative complications and serious adverse events in the two groups. Additionally, 4.5-year PFS and 3-year OS in MIS group were significantly lower than that in ARH, and the recurrence rate of early-stage cervical cancer patients who underwent MIS (15.6% robotic surgery) was approximate four times of ARH.[19] Nevertheless, controversies remain as to whether bias in the study due to case selection, surgeon level and duration of recruited time. Whether the heterogeneity of the two MIS approaches had an impact on the conclusions is worth pondering. A multicenter study from Canada included 958 cases of cervical cancer in 10 years (2006-2016) (including 485 cases in the open surgery group and 473 cases in the MIS group), and 5-year follow-up showed that the open surgery group was significantly better than the MIS group. However, the laparoscopic surgery accounted for 89.6% of the MIS group and 10.4% of robotic surgery.[20] A retrospective study from China analyzed the complications of open surgery (n=12956) and laparoscopic surgery (n=5491) from 2004 to 2015, and the results showed that the incidence of intraoperative and postoperative complications in laparoscopic surgery was significantly higher than that of open surgery (5.55% vs 2.76%).[21] Therefore, NCCN, FIGO, and ESGO have updated their guidelines and unanimously recommended ARH as the standard surgical modality for patients with early-stage cervical cancer.[22-24] On the contrary, clinical data from the Memorial Sloan Kettering Cancer Center showed that there was no significant difference in survival outcomes from MIS (90% robotic surgery) and open surgery for patients with cervical cancer, while complication rates for MIS were significantly reduced.[25] Another study of 1125 cervical cancer patients in Denmark from 2005 to 2017, of which 595 were MIS (94.9% robotic surgery), showed that the 5-year disease-specific survival rate (95.9% vs.94.1%) and recurrence rate (6.3% vs.8.2%) in the MIS group were non-inferior compared with the control group.[26] A meta-analysis related to robotic surgery, laparoscopic surgery, and open surgery for cervical cancer showed that robotic surgery had advantages over open surgery in terms of bleeding, duration, lymphadenectomy, average hospital stays, and complications intra- and post- operation.[27]

Currently, an international multicenter randomized control trial (Robot-Assisted Approach to Cervical Cancer, NCT03719547) evaluate the efficacy of robotic surgery and open surgery is underway in China.[28] In addition, although there is limited research on vaginal surgery for cervical cancer, it is still one of surgical treatment options for patients with early-stage cervical cancer. Thus, in this study we analyzed the clinical data of patients with early-stage cervical cancer who underwent ARH, LRH, RRH and VRH in a single center by the same medical team for 5 years, compared the perioperative indicators and survival outcomes.

Conclusion

In this retrospective study, we demonstrated that there was no statistical significance of the mean age, BMI, FIGO stage, histology and postoperative adjuvant therapy among ARH, LRH, RRH and VRH groups. Five-year DFS in LRH group was shorter than that in ARH and RRH groups. The total 5-year OS curve of the four groups was statistically significant. Additionally, 5-year OS in ARH and RRH groups was better than that in LRH group. The survival outcomes between ARH and RRH were similar for patients with early-stage cervical cancer.

Disclosure of interests

The authors declare no conflict of interest.

Contribution to authorship

YM and WF were involved in the study conception and design. NZ and CG were participated in data collection and analysis. XJ and WY drafted and approved this article. LL revised the article critically. All authors have read and approved the manuscript for publication.

Details of ethics approval

Ethics approval was not applicable.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Disease free survival (DFS)

Figure S2. Overall survival (OS)

References

1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018 Nov;68(6):394-424.

2. Olawaiye AB, Baker TP, Washington MK, Mutch DG. The new (Version 9) American Joint Committee on Cancer tumor, node, metastasis staging for cervical cancer. CA Cancer J Clin. 2021 Jul;71(4):287-98.

3. Cohen PA, Jhingran A, Oaknin A, Denny L. Cervical cancer. Lancet. 2019 Jan 12;393(10167):169-82.

4. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin. 2015 Mar;65(2):87-108.

5. Arbyn M, Weiderpass E, Bruni L, de Sanjose S, Saraiya M, Ferlay J, et al. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. Lancet Glob Health. 2020 Feb;8(2):e191-e203.

6. Noguchi T, Zaitsu M, Oki I, Haruyama Y, Nishida K, Uchiyama K, et al. Recent Increasing Incidence of Early-Stage Cervical Cancers of the Squamous Cell Carcinoma Subtype among Young Women. International journal of environmental research and public health. 2020 Oct 12;17(20).

7. Liontos M, Kyriazoglou A, Dimitriadis I, Dimopoulos MA, Bamias A. Systemic therapy in cervical cancer: 30 years in review. Crit Rev Oncol Hematol. 2019 May;137:9-17.

8. Basaran D, Leitao MM, Jr. The Landmark Series: Minimally Invasive Surgery for Cervical Cancer. Annals of surgical oncology. 2021 Jan;28(1):204-11.

9. Koh WJ, Greer BE, Abu-Rustum NR, Apte SM, Campos SM, Cho KR, et al. Cervical Cancer, Version 2.2015. J Natl Compr Canc Netw. 2015 Apr;13(4):395-404; quiz

10. Ramirez PT, Frumovitz M, Pareja R, Lopez A, Vieira M, Ribeiro R, et al. Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer. The New England journal of medicine. 2018 Nov 15;379(20):1895-904.

11. Melamed A, Margul DJ, Chen L, Keating NL, Del Carmen MG, Yang J, et al. Survival after Minimally Invasive Radical Hysterectomy for Early-Stage Cervical Cancer. The New England journal of medicine. 2018 Nov 15;379(20):1905-14.

12. Pecorelli S. Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium. Int J Gynaecol Obstet. 2009 May;105(2):103-4.

13. Nezhat C, Nezhat F, Burrell MO, Benigno B, Welander CE. Laparoscopic radical hysterectomy with paraaortic and pelvic node dissection. Am J Obstet Gynecol. 1994 Feb;170(2):699.

14. Nam JH, Kim JH, Kim DY, Kim MK, Yoo HJ, Kim YM, et al. Comparative study of laparoscopico-vaginal radical hysterectomy and abdominal radical hysterectomy in patients with early cervical cancer. Gynecologic oncology. 2004 Jan;92(1):277-83.

15. Rodriguez J, Rauh-Hain JA, Saenz J, Isla DO, Rendon Pereira GJ, Odetto D, et al. Oncological outcomes of laparoscopic radical hysterectomy versus radical abdominal hysterectomy in patients with early-stage

cervical cancer: a multicenter analysis. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2021 Apr;31(4):504-11.

16. Lee EJ, Kang H, Kim DH. A comparative study of laparoscopic radical hysterectomy with radical abdominal hysterectomy for early-stage cervical cancer: a long-term follow-up study. Eur J Obstet Gynecol Reprod Biol. 2011 May;156(1):83-6.

17. Cao T, Feng Y, Huang Q, Wan T, Liu J. Prognostic and Safety Roles in Laparoscopic Versus Abdominal Radical Hysterectomy in Cervical Cancer: A Meta-analysis. J Laparoendosc Adv Surg Tech A. 2015 Dec;25(12):990-8.

18. Wang YZ, Deng L, Xu HC, Zhang Y, Liang ZQ. Laparoscopy versus laparotomy for the management of early stage cervical cancer. BMC cancer. 2015 Nov 24;15:928.

19. Frumovitz M, Obermair A, Coleman RL, Pareja R, Lopez A, Ribero R, et al. Quality of life in patients with cervical cancer after open versus minimally invasive radical hysterectomy (LACC): a secondary outcome of a multicentre, randomised, open-label, phase 3, non-inferiority trial. Lancet Oncol. 2020 Jun;21(6):851-60.

20. Cusimano MC, Baxter NN, Gien LT, Moineddin R, Liu N, Dossa F, et al. Impact of surgical approach on oncologic outcomes in women undergoing radical hysterectomy for cervical cancer. Am J Obstet Gynecol. 2019 Dec;221(6):619 e1- e24.

21. Liang C, Liu P, Cui Z, Liang Z, Bin X, Lang J, et al. Effect of laparoscopic versus abdominal radical hysterectomy on major surgical complications in women with stage IA-IIB cervical cancer in China, 2004-2015. Gynecologic oncology. 2020 Jan;156(1):115-23.

22. Committee FGO. FIGO statement on minimally invasive surgery in cervical cancer. Int J Gynaecol Obstet. 2020 Jun;149(3):264.

23. Koh WJ, Abu-Rustum NR, Bean S, Bradley K, Campos SM, Cho KR, et al. Cervical Cancer, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2019 Jan;17(1):64-84.

24. Querleu D, Cibula D, Concin N, Fagotti A, Ferrero A, Fotopoulou C, et al. Laparoscopic radical hysterectomy: a European Society of Gynaecological Oncology (ESGO) statement. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2020 Jan;30(1):15.

25. Brandt B, Sioulas V, Basaran D, Kuhn T, LaVigne K, Gardner GJ, et al. Minimally invasive surgery versus laparotomy for radical hysterectomy in the management of early-stage cervical cancer: Survival outcomes. Gynecologic oncology. 2020 Mar;156(3):591-7.

26. Jensen PT, Schnack TH, Froding LP, Bjorn SF, Lajer H, Markauskas A, et al. Survival after a nationwide adoption of robotic minimally invasive surgery for early-stage cervical cancer - A population-based study. European journal of cancer. 2020 Mar;128:47-56.

27. Jin YM, Liu SS, Chen J, Chen YN, Ren CC. Robotic radical hysterectomy is superior to laparoscopic radical hysterectomy and open radical hysterectomy in the treatment of cervical cancer. PloS one. 2018;13(3):e0193033.

28. Falconer H, Palsdottir K, Stalberg K, Dahm-Kahler P, Ottander U, Lundin ES, et al. Robot-assisted approach to cervical cancer (RACC): an international multi-center, open-label randomized controlled trial. International journal of gynecological cancer : official journal of the International Gynecological Cancer Society. 2019 Jul;29(6):1072-6.

Figure legends

Figure 1. The CONSORT (Consolidated Standards of Reporting Trials) diagram. Patients with early-stage cervical cancer who underwent radical surgery from January 2013 to December 2017.

Figure 2. (A) Disease free survival (DFS). (B) Overall survival (OS).

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