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Survival outcomes of Stage IB cervical cancer treated with standard radical hysterectomy

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Summary

Objective: To determine risk factors of survival outcomes in patients with cervical cancer of Stage IB treated with standard hysterectomy (RH). *Materials Methods:* From February 2001 to November 2015, patients with cervical cancer of FIGO Stage IB were included, if they received RH of Class III or Type C1. Epidemiological and clinic-pathologic characteristics were compared to determine risk factors of overall survival (OS) and progression free survival (PFS). *Results:* Among 406 patients included, 371 (91.4%) had definite survival data, with recurrence rate and mortality of 17.2% and 9.4%. After a median follow-up of 48.5 (range 12-189) months, and ten-year PFS were 80% and 73%, and five- and ten-year OS were 88% and 84%, respectively. In multivariate analysis, patients with Stage IB2 (HR 2.0, 95% CI 1.2-3.2), positive vaginal margin (HR 9.2, 95% CI 2.6-33.0), or lymphatic metastasis (HR 2.0, 95% CI 1.1-3.6) had higher recurrence; patients with RH before year of 2011 (HR 2.8, 95% 1.3-6.0), Stage IB2 (HR 3.6, 95% CI 1.9-6.9) or lymphatic metastasis (HR 3.6, 95% CI 1.8-7.1) had higher mortality. Recurrent sites or post-recurrent treatment plans had no impact on the survival after recurrence. *Conclusion:* The prognosis of cervical cancer patients treated with RH by experienced physicians is favorable. Pathologic characters and experiences of surgeons are predictive factors of survival outcomes.

Key words: Cervical cancer; Radical hysterectomy; Recurrence; Mortality.

Introduction

Globally, cervical cancer is the third in incidence and fourth in mortality [1]. In China, cervical cancer has the highest incidence and mortality among female genital tract cancers [2]. Cervical cancer screening and HPV vaccine have significantly reduced the incidence and mortality of the disease, and the implementation of surgery, radiotherapy, and chemotherapy or their combinations rigorously following guidelines have further contributed to excellent survival outcomes. Surgeries, most of which consisting of radical hysterectomy (RH) and lymphadenectomy for early stage cervical cancers (IA2-IB2), have achieved similar survival outcomes compared with concurrent chemoradiotherapy (CCRT). There are various categories of RH and their modified types. Since Nezhat *et al.* [3] first reported laparoscopic RH (LRH) and dissection of pelvic lymph node in 1992, mini-invasive routes of surgeries have become the mainstream of surgical treatment. In a meta-analysis, Geetha and Nair reported higher complication morbidity in abdominal RH patients, including more blood loss and higher postoperative infectious morbidity, compared with LRH and robot-assisted RH [4]. The extensions of RH do rely on both the characters of disease and the experience of surgeons. One of the critical limitations of previous cohort reports about RH is the heterogeneity derived from different surgical types and surgeons. In this study the authors aimed to further clarify the survival outcomes of cervical cancer through a retrospective analysis of patients treated with RH in a tertiary teaching hospital, in particular all surgeries were performed by one physician (Dr. M. Wu) following relatively uniform surgical principles and extent.

Materials and Methods

This is a retrospective study conducted at Department of Obstetrics and Gynecology, Peking Union Medical College Hospital (PUMCH). The Institutional Review Board of PUMCH approved this study. The registration number is NCT03291236 (*clinicaltrials.gov*). All patients with cervical cancer Stage IB admitted to PUMCH from February 2001 to November 2015 were included, if they received RH of Class III or type C performed primarily by Dr. M. Wu. Follow-up was provided for all patients in outpatient clinics up to December 31, 2016. Recurrence was validated by imaging examination and/or biopsy. Mortality was confirmed by reviewing medical records and interviews of telephone or email.

The primary measurements of the study were overall survival (OS) and progression-free survival (PFS). Relevant epidemiological and clinico-pathologic factors of survival outcomes were determined by univariate and multivariate analysis.

Data of eligible patients were collected by searching and reviewing medical records. Inclusion criteria consisted of the following conditions: histopathologically proven primary cervical cancer; FIGO Stage IB diagnosed by pelvic examinations of two experienced physicians of gynecologic oncology; primary surgical physician was Dr. M Wu. Surgical procedures included RH of Class III or Type C.

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All patients signed consents before surgeries. Surgical treatment consists of radical hysterectomy, bilateral salpingo-oophorectomy, pelvic lymphadenectomy, and para-aortic lymph node dissection (extension to the level of inferior mesenteric artery, and to the renal vein level when the metastasis was suspicious). For young patients with requirement of preserving ovaries, salpingectomy was undertaken along with suspension of the ovaries to the peritoneum at the level of the anterior superior spine. All surgical procedures were primarily performed by one surgeon (Dr. M. Wu) according to Class III or Meigs' surgeries of Piver-Rutledge-Smith classification [5] (before 2011) and later according to Type C1 of the Q-M classification [6] (after 2011). Type C1, i.e. nerve-sparing RH (NSRH), requires separation of two parts of the dorsal parametria: the medial part, which entails recto-uterine and recto-vaginal ligaments, and the lateral laminar structure, also called mesoureter, which contains the hypogastric plexus [6, 7]. Complications related with RH within three months were reviewed and collected in medical records as adverse events according to Common Terminology Criteria for Adverse Events (CTCAE) v4.03 [8]. All histological specimens underwent thorough pathologic examinations. Pathologic characteristics include pathologic subtypes, lymphovascular space invasion (LVSI), invasion depth of the stroma, lymphatic metastasis, involvement of uterus or parametrium, and status of vaginal margin.

Conization is performed in some patients to specify diagnosis or staging, followed by RH around 4-6 weeks later if diagnosis of Stage IB is validated. Neoadjuvant chemotherapy is given to partial patients with Stage IB2, LVSI in specimens of biopsy or conization. Regimens of neoadjuvant chemotherapy consist of palitaxel/carboplatin, palitaxel/cisplatin (in a cycle of 21 days) or fluorouracil/cisplatin (in a cycle of 28 days). Postoperative adjuvant therapies, including systematic chemotherapy, radiotherapy, CCRT or a combination of them, are provided for patients with risk factors of recurrence according to National Comprehensive Cancer Network (NCCN) guideline. Systematic chemotherapy has similar plans as neoadjuvant chemotherapy. CCRT consists of radiotherapy and concurrent chemotherapy of cisplatin or palitaxel if patient had hypersensitivity reaction to cisplatin. Radiotherapy consists of conventional external-bean fractionation and low-dose-rate (40-70 cGy/hr) brachytherapy. For metastasis to para-aortic lymph nodes, extending radiation therapy field is given to achieve curable treatment.

Patients proved to have recurrence accepted salvage therapy included surgeries (mainly of pelvic exenteration), radiotherapy (external-bean fractionation) or CCRT, systematic chemotherapy, or their combinations. Palliative care would be provided to all patients to relieve cancer-related symptoms, especially patients declining any aggressive treatment.

The software SPSS 23.0 was applied for the analysis of the differences of patients with and without recurrence and death, with $p < 0.05$ used to indicate statistical significance. The Kaplan-Meier method as univariate analysis and Cox proportional hazards regression model as multivariate analysis were used to determine the impact the clinic-pathologic characteristics on survival outcomes.

Results

A total of 406 patients with clinical Stage IB underwent RH during the study period, and 371 (91.4%) cases were included in the final analysis of survival outcomes. For all 406 patients, the median age, body mass index (BMI), and squamous cell carcinoma antigen (SCC-Ag) were 42 (range 21-65) years, 23.0 (range 17.6-39.1) kg/m^2, and 1.6 (range 0.3-18.2, n=191) ng/ml , and 85 (20.9%) cases accepted RH before menopause. One hundred and sixty-four cases of RH (40.4%) were performed before the year of 2011. Since 2011, all RH procedures (242 cases) belonged to NSRH and laparoscopy. Eighty-seven (21.4%) and 154 cases (37.9%) accepted conization and neoadjuvant chemotherapy before RH, respectively; 295 (72.7%) and 176 cases (43.3%) accepted NSRH and ovaries preservation, respectively. The median duration of RH, estimated blood loss, total and post-RH hospital stay were 200 (range 120-400) minutes, 300 (range 20-3800) ml, 14 (6-91) days, and ten (4-74) days. Adverse events of grade 3/4 occurred in 28 cases (6.9%). No perioperative mortality occurred.

There were 277 (68.2%) and 129 (31.8%) cases of Stage IB1 and IB2. The median diameters of tumors were 3.0 (range 1.0-7.0) cm. Squamous carcinoma, adenoma, and adenosquamous carcinoma were seen in 336 (82.8%), 55 (13.5%), and 15 (3.7%) cases. Grade 1, 2, and 3 were seen in 203 (50.0%), 145 (35.7%), and 58 (14.3%) cases. Invasion depth of < 1/3, 1/3-2/3, and > 2/3 of the stroma were seen in 180 (44.3%), 115 (28.3%), and 111 (27.3%) cases. One hundred and sixty-two (39.9%), 331 (81.5%), 24 (5.9%), three (0.7%), and 54 (13.3%) cases had positive LVSI, involvement of the uterine, involvement of the parametrium, positive vaginal margin, and metastasis to LN, respectively. After RH, 217 cases (53.4%) accepted adjuvant treatment, including 209 cases of radiotherapy (18 cases) or CCRT (191 cases), and 35 cases of systematic chemotherapy.

Among 371 patients with definite survival outcomes, 70 (17.2%) had recurrence proved by imaging or pathologic examinations. Median PFS was 45.8 (range 6-189) months, five- and ten-year PFS were 80% and 73%, respectively.

Among 70 patients with recurrence, there were 50 cases (71.4%) of local recurrence in pelvic cavity and 20 cases (28.6%) with distant metastasis. Distant metastasis involved lung (15 cases), bone (four cases), liver (three cases), mediastinal lymph nodes (three cases), supraclavicular lymph nodes (two cases), brain (one case), and sites not specifically stated (one case). After recurrence, 65 patients (92.9%) accepted salvage treatment: ten accepted surgeries for recurrence and metastasis lesions dissection, with or without adjuvant therapies, 12 accepted CCRT, 24 accepted CCRT and systematic chemotherapy, 11 patients had radiotherapy plus chemotherapy, three and five patients had chemotherapy and radiotherapy respectively. Five of 70 patients (7.1%) accepted palliative care only to relieve recurrence-related symptoms.

In univariate analysis (Table 1), stage IB2 ($p = 0.003$), larger tumor sizes ($p = 0.006$), deeper invasion of stroma ($p = 0.037$), involvement of parametrium ($p = 0.001$), positive vaginal margin ($p < 0.001$), and LN metastasis ($p = 0.001$) resulted in higher recurrence. In multivariate analysis, Stage IB2 (HR 2.0, 95% CI 1.2-3.2, $p = 0.005$), positive vaginal margin (HR 9.2, 95% CI 2.6-33.0, $p = 0.001$), and

Table 1. — *Survival analysis for risk factors of recurrence and mortality.*

	PFS		OS	
	HR (95% CI)	*p*	HR (95% CI)	*p*
Surgical years		0.777		0.014
Before 2011	Reference		Reference	
After 2011	0.9 (0.6-1.6)		0.4 (0.2-0.8)	
Age (every year)	1.0 (1.0-1.0)	0.362	1.0 (1.0-1.0)	0.415
Menopause		0.591		0.872
No	Reference		Reference	
Yes	1.2 (0.6-2.1)		1.1 (0.5-2.3)	
Gravidity	0.8 (0.7-1.0)	0.077	1.0 (0.8-1.2)	0.956
Parity	1.0 (0.8-1.2)	0.767	1.1 (0.9-1.4)	0.421
BMI (every kg/m^2)	0.9 (0.8-1.0)	0.204	1.0 (0.8-1.1)	0.473
SCC (every ng/ml)	1.1 (1.0-1.1)	0.110	1.1 (1.0-1.2)	0.095
Conization		0.201		0.135
No	Reference		Reference	
Yes	0.6 (0.3-1.3)		0.4 (0.1-1.3)	
Preoperative neoadjuvant CT		0.256		0.466
No	Reference		Reference	
Yes	1.3 (0.8-2.1)		1.3 (0.7-2.4)	
Surgical routes		0.433		0.050
Laparoscopy	Reference		Reference	
Laparotomy	1.2 (0.7-2.1)		2.0 (1.0-4.0)	
NSRH		0.796		0.043
No	Reference		Reference	
Yes	0.9 (0.6-1.6)		0.5 (0.3-1.0)	
Preservation of ovaries		0.190		0.265
No	Reference		Reference	
Yes	0.7 (0.4-1.2)		0.7 (0.3-1.3)	
Duration of RH procedure	1.0 (1.0-1.0)	0.281	1.0 (1.0-1.0)	0.795
EBL (every ml)	1.0 (1.0-1.0)	0.671	1.0 (1.0-1.0)	0.372
Grade 3/4 complications*		0.387		0.063
No	Reference		Reference	
Yes	1.4 (0.6-3.3)		2.4 (1.0-6.3)	
FIGO Stage		0.003		< 0.001
IB1	Reference		Reference	
IB2	2.0 (1.3-3.3)		4.0 (2.1-7.6)	
Pathologic subtype		0.123		
Squamous carcinoma	Reference		Reference	0.850
Adenocarcinoma	1.2 (0.6-2.4)	0.632	1.7 (0.2-12.5)	0.596
Adenosquamous carcinoma	2.4 (1.0-5.6)	0.042	1.5 (0.2-13.5)	0.712
Diameter of tumor (every 10 mm)	1.2 (1.1-1.5)	0.006	1.4 (1.1-1.7)	0.007
Differentiation		0.294		0.810
G1	Reference		Reference	
G2	1.3 (0.8-2.2)	0.290	1.0 (0.5-2.1)	0.913
G3	1.7 (0.8-3.5)	0.147	1.4 (0.5-3.7)	0.520
Invasion depth of stroma		0.037		0.350
< 1/3	Reference	Reference		
> 1/3 but < 2/3	1.6 (0.8-2.9)	0.146	1.2 (0.5-2.8)	0.613
> 2/3	2.1 (1.2-3.8)	0.010	1.7 (0.8-3.7)	0.154
LVSI		0.038		0.630
No	Reference		Reference	
Yes	1.6 (1.0-2.6)		1.2 (0.6-2.2)	
Uterine involvement		0.911		0.799
No	Reference		Reference	
Yes	1.0 (0.6-1.9)		1.1 (0.5-2.5)	
Parametrial involvement		0.001		0.025
No	Reference		Reference	
Yes	3.0 (1.6-5.6)		2.7 (1.1-6.5)	
Positive vaginal margin		<0.001		0.001
No	Reference		Reference	
Yes	16.7 (5.1-54.8)		10.7 (2.5-45.4)	
Metastasis to LN 0.001 < 0.001				
No	Reference		Reference	
Yes	2.5 (1.4-4.3)		3.5 (1.7-6.9)	
Postoperative adjuvant therapy		0.937		0.361
No	Reference		Reference	
Yes	1.0 (0.6-1.6)		1.4 (0.7-2.6)	
Recurrence				0.046
No			Reference	
Yes			3447.0 (1.1-10371042.2)	
Recurrent sites				0.377
Local recurrence			Reference	
Distant metastasis			1.4 (0.7-2.7)	
Treatment after recurrence				0.319
Salvage treatment			Reference	
Palliative care			1.7 (0.6-4.8)	

** These complications and their severity were defined as adverse events happened within three months after RH according to Common Terminology Criteria for Adverse Events (CTCAE) v4.03.*

LN metastasis (HR 2.0, 95% CI 1.1-3.6, $p = 0.017$) were independent risk factor of higher recurrence.

Among 371 patients with definite survival outcomes, explicit death related to recurrence occurred in 38 (9.4%) patients. Median OS was 48.5 (range 12-189) months, five- and ten-year OS were 88% and 84%, respectively.

In univariate analysis (Table 1), RH before year of 2011 ($p = 0.014$), laparotomy ($p = 0.050$), non-NSRH ($p = 0.043$), Stage IB2 ($p < 0.001$), larger tumor sizes ($p = 0.007$), involvement of parametrium ($p = 0.025$), positive vaginal margin ($p = 0.001$), LN metastasis ($p < 0.001$), and recurrence ($p = 0.046$) resulted in higher mortality. In multivariate analysis, RH before year of 2011 (HR 2.8, 95% 1.3-6.0, $p = 0.010$), Stage IB2 (HR 3.6, 95% CI 1.9-6.9, $p < 0.001$), and LN metastasis (HR 3.6, 95% CI 1.8-7.1, $p < 0.001$) were independent risk factor of higher mortality.

The median period from recurrence to death was 7.5 (range 2-23) months. Four in five (80.0%) patients of palliative care and 34 in 65 patients (52.3%) of salvage treatment died of recurrence. In univariate analysis, recurrent sites (local *vs.* distant, $p = 0.870$) or post-recurrent treatment (salvage treatment *vs.* palliative care, $p = 0.970$) had no impact on the survival outcomes after recurrence.

Discussion

The recurrence rate of cervical cancers was reported to be 25%-61% [9]. According to a previous GOG study, lymphatic metastasis, positive surgical margin, and parametrial involvement were high-risk factors related to prognosis outcomes; factors like tumor size, LVSI, deep invasion of cervical interstitial tissue, and pathologic subtypes could be grouped into middle-risk factors [10]. High-risk factors or combined middle-risk factors could increase the recurrence rate [11], especially the distant recurrence rate [12], and thus impair the survival outcomes. It was reported that the five-year OS dropped to 50%-70% when a tumor expresses one or more factors in pelvic lymph node metastasis, LVSI, deep invasion of stroma, parametrial involvement, vaginal margin involvement, non-squamous histological subtype, advanced stage, and tumor size > 4 cm [13]. The prognosis of early cervical cancers with multiple high-risk factors could be comparable to the prognosis of advanced cervical cancers [14]. Postoperative adjuvant therapy are provided for patients with different sorts of risk factors for better outcomes [15]. Risk factors related with the prognosis of patients after RH still remain thoroughly unclear, especially due to the heterogeneity of patients cohort, surgical methods, and physicians.

The present authors reported a series of patients with RH performed primarily by one physician, which guaranteed the homogeneity of the study and reduced potential bias from methodology. Data from this study not only validated conclusions about prognosis factors related with cervical cancer in previous reports, but also provided some new information for RH procedures, including surgical routes, NSRH, and treatment after recurrence. In this study, involvement of parametrium had no obvious impact on the survival outcomes due to the selection of patients confined to Stage IB. Status of vaginal margin also had no role in the OS due to limited sample with positive margin and appreciable staging before RH. However, in the present study the year of surgery (before and after 2011) had significant impact on OS, which was adjusted by surgical routes (laparotomy *vs.* laparoscopy) and NSRH. Previous study showed high-volume surgeons have fewer postoperative medical complications, shorter lengths of stay, and lower transfusion requirements, while hospital volume appears to have only a minor influence on outcomes after radical hysterectomy [16]. The progression of prognosis with surgical years indicates the development of experience, skill, and case amount of the one surgeon, which needs more studies to clarify. High-quality surgery requiring intensive skill and experiences is critical for the survival of patients.

The present multivariate analysis found no risk factors related with survival after recurrence in patients with cervical cancers. It did not necessarily signify a weakened effect of salvage treatment, for they indeed released some patients' complaints, although the five-year OS and PFS have kept low in most studies. In patients with isolated LN recurrence after RH treatment, salvage CCRT or RT resulted in a maximum five-year OS of 30% [17, 18]. Tempfer *et al.* also suggested that the response rate of chemotherapy in patients with distant recurrence was poor, they recommended CCRT, surgery, including pelvic exenteration, and palliative chemotherapy for patients in different conditions, but the treatment of patients after recurrence still remains challenging [19]. However, the number of death cases in this study was small, which limited its weight in final results. Whether salvage treatment and recurrence condition have influence on the survival of patients with recurrence needs further discussion.

The main limitations of this study consisted of recall bias and selection bias as a retrospective study. Moreover, the collection of surgery cases included in this study had spanned 14 years, and the changes of individual experience and skills of the surgeon was also part of the bias, which all need further exploration in prospective study. The authors also failed to include property patients' life qualities, and the size of recurrence cohort is small, and it is premature to draw any conclusion about risk factor of survival after recurrence.

In conclusion, the survival outcomes of cervical cancer after RH by experienced physicians were favorable, suggesting consistent high quality of surgery and comprehensive control of the disease have been the crucial management of cervical cancer in carefully selected and evaluated patients. Pathologic characters and physician's experiences were an independent factor related to survival outcomes. Survival after recurrence is poor, and salvage

therapy and palliative care had similar effects about mortality.

References

[1] Jemal A., Bray F., Center M.M., Ferlay J., Ward E., Forman D.: "Global cancer statistics". *CA Cancer J. Clin.,* 2011, *61*, 69.

[2] Chen W., Zheng R., Baade P.D., Zhang S., Zeng H., Bray F., *et al.*: "Cancer statistics in China, 2015". *CA Cancer J. Clin.,* 2016, *66*, 115.

[3] Nezhat C.R., Burrell M.O., Nezhat F.R., Benigno B.B., Welander C.E.: "Laparoscopic radical hysterectomy with paraaortic and pelvic node dissection". *Am. J. Obstet. Gynecol.,* 1992, *166*, 864.

[4] Geetha P., Nair M.K.: "Laparoscopic, robotic and open method of radical hysterectomy for cervical cancer: A systematic review". *J. Minim. Access. Surg.,* 2012, *8*, 67.

[5] Piver M.S., Rutledge F., Smith J.P.: "Five classes of extended hysterectomy for women with cervical cancer". *Obstet. Gynecol.,* 1974, *44*, 265.

[6] Cibula D., Abu-Rustum N.R., Benedetti-Panici P., Kohler C., Raspagliesi F., Querleu D., *et al.*: "New classification system of radical hysterectomy: emphasis on a three-dimensional anatomic template for parametrial resection". *Gynecol. Oncol.,* 2011, *122*, 264.

[7] Querleu D., Morrow C.P.: "Classification of radical hysterectomy". *Lancet Oncol.,* 2008, *9*, 297.

[8] "Common Terminology Criteria for Adverse Events (CTCAE) v4.03 Available at: http://evs.nci.nih.gov/ftp1/CTCAE/

[9] Howlader N, Noone AM, Krapcho M, Neyman N., Aminou R., Waldron W., et al.: "SEER Cancer Statistics Review, 1975-2012". National Cancer Institute. Bethesda, MD". Available at: www.seer.cancer. gov

[10] Sedlis A., Bundy B.N., Rotman M.Z., Lentz S.S., Muderspach L.I., Zaino R.J.: "A randomized trial of pelvic radiation therapy versus no further therapy in selected patients with stage IB carcinoma of the cervix after radical hysterectomy and pelvic lymphadenectomy: A Gynecologic Oncology Group Study". *Gynecol. Oncol.,* 1999, *73*, 177.

[11] Ryu S.Y., Park S.I., Nam B.H., Cho C.K., Kim K., Kim B.J., *et al.*: "Is adjuvant chemoradiotherapy overtreatment in cervical cancer patients with intermediate risk factors?". *Int. J. Radiat. Oncol. Biol. Phys.,* 2011, *79*, 794.

[12] Matsuo K., Mabuchi S., Okazawa M., Kawano M., Kuroda H., Kamiura S., *et al.*: "Clinical implication of surgically treated early-stage cervical cancer with multiple high-risk factors". *J. Gynecol. Oncol.,* 2015, *26*, 3.

[13] Peters W.A., 3rd, Liu P.Y., Barrett R.J., 2nd, Stock R.J., Monk B.J., Berek J.S., *et al.*: "Concurrent chemotherapy and pelvic radiation therapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early-stage cancer of the cervix". *J. Clin. Oncol.,* 2000, *18*, 1606.

[14] Fagundes H., Perez C.A., Grigsby P.W., Lockett M.A.: "Distant metastases after irradiation alone in carcinoma of the uterine cervix". *Int. J. Radiat. Oncol. Biol. Phys.,* 1992, *24*, 197.

[15] Delgado G., Bundy B., Zaino R., Sevin B.U., Creasman W.T., Major F.: "Prospective surgical-pathological study of disease-free interval in patients with stage IB squamous cell carcinoma of the cervix: a Gynecologic Oncology Group study". *Gynecol. Oncol.,* 1990, *38*, 352.

[16] Wright J.D., Lewin S.N., Deutsch I., Burke W.M., Sun X., Herzog T.J.: "The influence of surgical volume on morbidity and mortality of radical hysterectomy for cervical cancer". *Am. J. Obstet. Gynecol.,* 2011, *205*, 225.e221.

[17] Chou H.H., Wang C.C., Lai C.H., Hong J.H., Ng K.K., Chang T.C., *et al.*: "Isolated paraaortic lymph node recurrence after definitive irradiation for cervical carcinoma". *Int. J. Radiat. Oncol. Biol. Phys.,* 2001, *51*, 442.

[18] Jeon W., Koh H.K., Kim H.J., Wu H.G., Kim J.H., Chung H.H.: "Salvage radiotherapy for lymph node recurrence after radical surgery in cervical cancer". *J. Gynecol. Oncol.,* 2012, *23*, 168.

[19] Tempfer C.B., Beckmann M.W.: "State-of-the-Art Treatment and Novel Agents in Local and Distant Recurrences of Cervical Cancer". *Oncol. Res. Treat.,* 2016, *39*, 525.

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