A retrospective study of stage IB node-negative cervical cancer treated with adjuvant radiation with standard pelvic versus central small pelvic fields

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Objective: To compare two types of postoperative radiation therapy (PORT) in early-stage, node-negative cervical cancer treated at Groote Schuur Hospital, Cape Town, South Africa.

Materials and methods: A retrospective observational study of patients with stage IB cervical cancer treated with radical surgery between 1984 and 2010. Node-negative patients regarded as at risk of pelvic recurrence received PORT, with or without concurrent cisplatin or additional vaginal brachytherapy. The PORT was given with either whole pelvis fields (WPF), or with central small pelvic fields (SPF). Data concerning indications for adjuvant therapy, treatment outcomes and grade 3–4 treatment-related toxicities, including leg lymphoedema, were extracted from clinical records.

Results: Thirty-one patients received WPF, and 56 SPF. The overall 5-year survival rate was 85%. No significant differences in survival rates were found between the WPF and SPF groups (log rank p = 0.67). Relapse patterns and the crude grade 3–4 treatment morbidity rates did not differ, although two patients in the WPF group (6%) died of treatment-related complications.

Conclusions: The expected benefit of PORT with SPF, which targets the cervical tumour bed and para-cervical tissues only, is a reduction in small bowel morbidity and lymphoedema. It is not possible to ascertain from this audit whether the SPF technique reduces complications, or that it increases out-of-field pelvic relapses. It seems unlikely that a randomised controlled trial will ever be performed, as a large sample size would be required. Comparisons of pooled SPF data with historical WPF controls seem the best option to establish the safety of this approach.

Key words: cervical cancer, postoperative radiotherapy, small pelvic field, stage IB

Introduction

Cervical cancer is the most common cancer in women in many developing countries.1 Due to inadequate screening programmes, late-stage presentations are common; at the authors’ institution, Groote Schuur Hospital (GSH), only 25% of patients present with early, surgically amenable stages.

Prior to the subdivision of stage IB by the Federation of Gynecology and Obstetrics (FIGO) in 2009,2 many of our patients with tumours > 4 cm underwent surgery. Since 2009, however, patients with stage IB1 cervical cancer are offered type 2 radical hysterectomy and bilateral pelvic lymphadenectomy, while primary concurrent chemoradiation (CRT) is recommended for those with stage IB2 in order to reduce the numbers requiring postoperative radiotherapy (PORT). Bilateral oophorectomies in premenopausal patients with adenocarcinoma were not routinely performed in the early years of this review.

The indications for PORT have varied over the years. Various studies conducted by the American Gynecology Oncology Group (GOG) have provided some clarity regarding the prognostic factors which portend an increased risk of pelvic relapse. The high-risk criteria are positive pelvic nodes, occult parametrial invasion or positive resection lines, for which adjuvant CRT is now a standard recommendation.3 Patients without these criteria but with combinations of ‘intermediate’ criteria have varying degrees of risk. We use the ‘GOG score’, as described by Delgado et al.,4 for these node-negative patients, since it is easier to apply in the clinic than a related set of GOG criteria known as the ‘Sedlis criteria’.5 Three factors are used to determine a patient’s risk score: tumour size, depth of cervical invasion and presence or absence of lympho-vascular invasion. A GOG score of > 120 was found by Delgado to predict a 40% recurrence rate. We recommend PORT for such patients. A weaker risk factor, not included by the GOG, includes uninvolved but close resection margins of < 5 mm.6,7

Radiation fields for PORT are standard whole pelvis fields (WPF). Since 1991, Hacker and colleagues have recommended a reduced volume, central pelvic field for those patients with a GOG score of > 120, with the aim of reducing morbidity (N. Hacker, personal communication 1991, though first published as a pilot study of 25 patients in 1999).8 We have used this ‘small pelvic field’ (SPF) method in our clinic since 1991.

This retrospective observational study was conducted to evaluate the outcome of our patients with stage IB node-negative cervical cancer treated with adjuvant PORT received with either WPF or SPF. Permission to perform the study was obtained from the hospital management and the Human Research Ethics Committee of the Faculty of Health Sciences, University of Cape Town (Ref 323/2015), with waiver of informed consent because data were collected retrospectively and anonymously.

Materials and methods

Study setting

All patients presenting with cervical cancer at GSH have a treatment recommendation made at a weekly multidisciplinary team meeting, which includes pathology review for postoperative cases. Current indications for PORT in node-negative early-stage
disease are: close (< 5 mm) or involved resection lines, histological parametrial invasion, or a GOG score of ≥ 120. Prior to 1991, the indications for PORT were less standardised.

The radiation portals for WPF radiation extend from L5/S1 to the inferior edge of the obturator foramina, and 1.5 cm lateral to the pelvic inlet, while the lateral portal borders are mid-symphysis pubis anteriorly and between S3 and S4 posteriorly. The SPF portals are centred on the cervical tumour bed, immediate para-cervical region, and upper third of the vagina. Three-dimensionally, the volume dimensions are typically 8 x 8 x 8 cm. Vaginal vault brachytherapy (VBT) is added if the vaginal resection lines are compromised, or as a result of physician preference.

External beam doses to the 'ICRU point' in the pelvis varied between 40 and 57 Gy over the study period (due to fractionation differences, all individual doses are expressed as linear quadratic equivalent dose to 2 Gy/fraction). The mean dose in the WPF group was 52.4 Gy and 51.4 Gy in the SPF group. Intracavitary brachytherapy (BT) was administered with low-dose radium sources prior to 1994, and subsequently with fractionated high dose rate (HDR) iridium. Since 2003, concurrent chemoradiation with weekly cisplatin was introduced (40 mg/m², capped at 60 mg per week, and a maximum of six weekly cycles).

Patients are followed up at three-monthly intervals for a year; thereafter, at longer intervals. The disease status, along with any treatment-related toxicities, is evaluated by clinical history and examination, or relevant investigations where indicated.

### Study methodology

A list of patients with stage IB cervical cancer, who underwent radical surgery followed by PORT during the period 1984 to 2010, was retrieved from a gynaecological oncology database. The following patients were excluded from further analysis: concurrent malignancy; lost to follow-up within one year after completion of treatment; small cell cancer of the cervix; and surgery less than type 2 radical hysterectomy and pelvic lymphadenectomy.

The data collected included the indications for adjuvant RT, treatment modalities applied, relapse patterns and complications, displayed as simple descriptive statistics. Treatment-related morbidities experienced 90 days or more after the completion of the treatment were considered to be late toxicities and graded according to the Radiation Therapy Oncology Group (RTOG) toxicity scores. Only grade 3 and 4 toxicities for gastrointestinal tract (GIT), bladder, bone and leg lymphoedema were documented.

Statistical calculations were made using Prism Graph pad (version 5.00; Graphpad software, San Diego, CA, USA). Overall survival (OS) was defined as the time from the initiation of treatment until the last follow-up or death. Patients were censored at last follow-up. Disease-free survival (DFS) was defined as the time from initiation of treatment until relapse (or last follow-up/death, if no relapse occurred). The five-year OS and DFS were estimated using the Kaplan–Meier method and the log rank test was performed to compare groups. Significance testing for groups of categorical variables was done with the chi-square test. A p-value of < 0.05 was significant.

### Results

Between 1984 and 2010, 373 patients who underwent radical surgery were found to be node-negative. Of the 94 who received additional therapy, 6 patients were excluded for small cell histology and 1 for follow-up less than one year. The remaining 87 form the study group; standard whole pelvis fields (WPF) were used in 31 and SPF in 56 patients. Histo-pathological characteristics are summarised in Table 1, treatment differences in Table 2 and outcomes in Table 3.

Neither the GOG scores, SPF nor CRT were used in the early part of the study period; Table 2 shows that the indications for PORT

### Table 1: Histo-pathological characteristics

| Factor | All patients, n = 87 (%) | WPF, n = 31 (%) | SPF, n = 56 (%) |
|--------|------------------------|----------------|----------------|
| Histology: | | | |
| Squamous | 72 (83) | 26 (84) | 46 (82) |
| Adenocarcinoma | 8 (9) | 3 (10) | 5 (9) |
| Adeno-squamous | 7 (8) | 2 (6) | 5 (9) |
| Tumour size (cm): | | | |
| < 2 | 4 (5) | 0 | 4 (7) |
| 2-4 | 45 (51) | 14 (45) | 31 (55) |
| > 4-6 | 34 (39) | 15 (49) | 19 (34) |
| > 6-8 | 4 (5) | 2 (6) | 2 (4) |
| Tumour grade: | | | |
| 1 | 1 (1) | 1 (3) | 0 |
| 2 | 59 (68) | 17 (55) | 42 (75) |
| 3 | 25 (29) | 12 (39) | 13 (23) |
| NS | 2 (2) | 1 (3) | 1 (2) |
| Resection line (mm): | | | |
| < 2 | 33 (38) | 14 (46) | 19 (34) |
| 2-5 | 28 (32) | 6 (19) | 22 (39) |
| > 5 | 16 (18) | 5 (16) | 11 (20) |
| Involved | 10 (12) | 6 (19) | 4 (7) |
| Lympho-vascular space inv.: | | | |
| Positive | 47 (54) | 17 (55) | 30 (54) |
| Negative | 39 (45) | 13 (42) | 26 (46) |
| NS | 1 (1) | 1 (3) | 0 |
| Vaginal cuff length (mm): | | | |
| ≤ 3 | 9 (10) | 3 (10) | 6 (11) |
| > 3 | 71 (82) | 27 (87) | 44 (78) |
| Involved | 2 (2) | 1 (3) | 1 (2) |
| NS | 5 (6) | 0 | 5 (9) |
| Parametrial invasion: | | | |
| No | 71 (82) | 21 (68) | 50 (89) |
| Yes | 14 (16) | 9 (29) | 5 (9) |
| NS | 2 (2) | 1 (3) | 1 (2) |
| GOG score: | | | |
| < 120 | 24 (28) | 7 (23) | 17 (30) |
| ≥ 120 | 50 (57) | 11 (35) | 39 (70) |
| Not evaluable | 13 (15) | 13 (42) | 0 |

Note: 'GOG score = Gynecologic Oncology Group (Delgado) score.'
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Survival rates were similar for the two groups (Figures 1 and 2). The DFS of patients with GOG score > 120 and who received SPF was 86.9%. There was no difference in grade 3–4 small bowel morbidity. Two patients (6%) in the WPF group died from treatment complications compared with none in the SPF group. The median follow-up period of surviving patients was 100 months.

Discussion

Our study involves relatively small numbers of patients and suffers the limitations of a retrospective audit of patients managed over a long period of time, with changing treatment indications and methods. Comparisons between treatments can at best reveal trends only. Outside of a randomised study, only serious, grade 3–4 treatment-related complications are likely to be recorded routinely. Furthermore, the patients in the Delgado study, on which the GOG score is based, all underwent para-aortic lymphadenectomies, and all had squamous cancers.4 Our patient cohort is different (includes adeno- and adeno-squamous cancers, did not have para-aortic nodal dissections) and has not been externally validated with the GOG score. The interpretation of depth of invasion is also made more complicated by prior cone biopsies, and one should preferably have a dedicated pathologist to interpret the various parameters used in determining the GOG score.10 It remains a useful guide, nevertheless, for allocating risk of pelvic relapse in our node-negative patients. A further weakness of our study is that relatively more patients in the SPF group received CRT than RT (43%, vs. 16% in the WPF group), though the significance of this

Table 2: Treatment characteristics

| Factor                          | All patients, \(n = 87\) (%) | WPF, \(n = 31\) (%) | SPF, \(n = 56\) (%) |
|--------------------------------|-------------------------------|---------------------|---------------------|
| Indication for PORT 1          |                               |                     |                     |
| Resection line (< 5 mm)        | 17 (19)                      | 3 (10)              | 14 (25)             |
| Local factors 2                | 1 (1)                        | 0                   | 1 (2)               |
| GOG score alone                | 4 (5)                        | 0                   | 4 (7)               |
| Local factors + resection line | 31 (36)                      | 24 (77)             | 7 (12)              |
| GOG score + resection line     | 34 (39)                      | 4 (13)              | 30 (54)             |
| RT vs. CRT 3                   |                               |                     |                     |
| RT only                        | 58 (67)                      | 26 (84)             | 32 (57)             |
| CRT                            | 29 (33)                      | 5 (16)              | 24 (43)             |
| External beam dose             |                               |                     |                     |
| ≤ 50 Gy                        | 21 (24)                      | 5 (16)              | 16 (29)             |
| > 50 Gy                        | 66 (76)                      | 26 (94)             | 40 (71)             |
| Vaginal brachytherapy          |                               |                     |                     |
| Not done                       | 27 (32)                      | 3 (10)              | 24 (43)             |
| Low dose-rate                  | 30 (34)                      | 24 (77)             | 6 (11)              |
| High dose-rate                 | 30 (34)                      | 4 (13)              | 26 (46)             |

Notes: 1PORT = postoperative radiotherapy. 2Local factors = used prior to GOG score era – depth of invasion, grade, size. 3CRT = concurrent chemo-radiation.

Table 3: Outcomes

| Factor                          | All patients, \(n = 87\) (%) | WPF, \(n = 31\) (%) | SPF, \(n = 56\) (%) |
|--------------------------------|-------------------------------|---------------------|---------------------|
| Relapse:                        |                               |                     |                     |
| None                            | 73 (84)                       | 25 (80)             | 48 (85)             |
| Central                         | 3 (3)                         | 2 (6)               | 1 (2)               |
| Pelvic sidewall                 | 1 (1)                         | 0                   | 1 (2)               |
| Distal                          | 10 (12)                       | 4 (14)              | 6 (11)              |
| Current status:                 |                               |                     |                     |
| Alive – clear                   | 61 (70)                       | 17 (55)             | 44 (79)             |
| Dead – cancer                   | 12 (14)                       | 5 (16)              | 7 (12)              |
| Dead – treatment                | 2 (2)                         | 2 (6)               | 0                   |
| Dead – unrelated (> 1 year)     | 9 (11)                        | 4 (13)              | 5 (9)               |
| Lost to follow up               | 3 (3)                         | 3 (10)              | 0                   |
| Grade 3–4 complications:        |                               |                     |                     |
| None                            | 71 (82)                       | 23 (76)             | 48 (85)             |
| Vaginal stenosis                | 7 (8)                         | 2 (6)               | 5 (9)               |
| Bladder                         | 4 (5)                         | 2 (6)               | 2 (4)               |
| Small bowel                     | 2 (2)                         | 1 (3)               | 1 (2)               |
| Large bowel                     | 1 (1)                         | 1 (3)               | 0                   |
| Bone                            | 1 (1)                         | 1 (3)               | 0                   |
| Lymphoedema                     | 1 (1)                         | 1 (3)               | 0                   |

differed between the two techniques (\(p\)-values not shown). Survival rates were similar for the two groups (Figures 1 and 2). The DFS of patients with GOG score > 120 and who received SPF was 86.9%. There was no difference in grade 3–4 small bowel morbidity. Two patients (6%) in the WPF group died from treatment complications compared with none in the SPF group. The median follow-up period of surviving patients was 100 months.

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difference is uncertain, since the role of CRT in patients with intermediate risk criteria is unknown.\textsuperscript{11}

Despite these limitations, our purpose was primarily to report our experience with adjuvant radiation using WPF, as compared with SPF, in the treatment of early-stage, node-negative cervical cancer. The questions posed were as follows: is it safe to substitute the standard radiation fields for smaller central pelvic fields, and does this reduce complications? We found no differences in survival rates, or relapse pattern, between the two approaches after median follow-up of 100 months. Theoretically, in-transit tumour emboli in lymphatic channels on the pelvic sidewalls or in the common iliac regions may not be well covered by SPF. One patient with adenocarcinoma in the SPF group had lateral pelvic relapse, but in her ovary, not in the lymphatic area. Furthermore, the DFS of our 39 patients treated with SPF for GOG scores $> 120$ was 86.9\%, compared with 60\% for patients with scores of $> 120$ who did not receive PORT in the Delgado study.\textsuperscript{4} Our findings suggest that PORT with SPF has merit and is safe.

There is a potential for a reduction in complications using the SPF technique as far as small bowel and lymphoedema of the lower extremities are concerned; this is because of less bowel exposure to radiation in the upper pelvis, and of the lymphatics on the pelvic sidewalls.

There were very few instances of lymphoedema recorded in our study, with only one case in the WPF group and none in the SPF group. Central organs such as the vagina, rectum or bladder, however, would not be spared by SPF and our results indicate that the two techniques resulted in similar incidences of grade 3–4 morbidity for these organs. Two patients in the WPF group died from treatment complications: one from bladder damage and the other from small bowel damage; the latter could be attributed to the volume of bowel exposed, or to a hypo-fractionated RT schedule used in the early part of the study period.

Following the initial report on SPF by the Australian group,\textsuperscript{6} there have been other publications on using reduced pelvic field PORT, mainly from Asian centres. Thus, Hong et al.\textsuperscript{12} described a retrospective review of 228 patients of whom 65\% received what the report termed ‘low pelvic RT’; this has similar dimensions to WPF, with the exception that the upper border is 1 cm above the inferior edge of the sacroiliac joints to the inferior of the obturator foramina, and 1–1.5 cm medial to the true pelvic inlet. The protocol was of no adjuvant RT if the GOG score < 40, SPF if the GOG score was in the range 40–120, and WPF if the score was $> 120$. Four field plans were used, delivering 45–50.4 Gy. All patients received additional HDR vaginal brachytherapy, 10 Gy in two fractions. PORT was administered to 61 patients (36 SPF, 25 WPF). The overall DFS was 98.2\% after five years. Lymphoedema was mild (grade 1–2) and significantly fewer instances were reported in the SPF group, presumably because the lateral pelvic lymphatics were less exposed to RT than in the WPF group. Chronic GI complications were also surprisingly low (one patient in each group, both grade 1 severity).

Hacker and co-workers, who first proposed the SPF technique, in 2013 published their group’s results of 93 cervical cancer patients with stage IB2.\textsuperscript{14} Their policy is to use a primary surgical approach in order to avoid the vaginal complications of high-dose brachytherapy in these bulky tumours if primary CRT is given. Adjuvant therapy was required in 79.6\% of patients, which consisted of SPF for a GOG score of $> 120$ (31\% of patients), and WPF for high-risk criteria in 48.6\%. No vaginal brachytherapy was used. It was not possible to extrapolate the outcome of the SPF group from the paper, although 85\% of all the node-negative patients (SPF, or no RT) were alive at five years. Late RT complications of grade 3–4 severity were seen in only 3 of 74 patients, which was a remarkable outcome.

A final publication on SPF in early cervical cancer was from China. The authors, Yi et al.,\textsuperscript{13} describe using an SPF method since the 1970s. They compared 364 node-negative patients treated with adjuvant SPF with 29 treated with WPF RT. The average portal size was 12 x 10 cm for SPF, in comparison with 16 x 18 cm for the WPF. A median dose of 48 Gy was delivered, with vaginal BT boost of 6 Gy x 2 if cuff margins were < 5 mm. In the SPF cohort 9.3\% recurred, the pattern in these 34 patients being intra-pelvic in 19 instances, extra-pelvic in 13 and mixed in two patients. Both acute and chronic treatment-related diarrhoea was less common in the SPF group, while lymphoedema rates were similar in both groups. Survival rates were also similar. The authors conclude that the SPF adjuvant technique is beneficial in node-negative early-stage cervical cancer as it reduces bowel morbidity. They note that the SPF approach does not appear in North American treatment guidelines, and recommend a randomised controlled trial to resolve the issue.

The SPF technique is recommended, however, in a gynaecological oncology textbook co-authored by Prof. Hacker.\textsuperscript{18} The use of SPF has also been reported in Europe, though for high-risk, node-negative endometrial cancers, which significantly reduced gastro-intestinal morbidity (De Jong et al., Groningen).\textsuperscript{19}

In conclusion, the concept of using reduced pelvic fields in treating early-stage cervical cancer was intuitively introduced into adjuvant radiotherapy protocols, mainly in Australia and Asia, in an attempt to improve the therapeutic ratio. The usage of SPF at Groote Schuur Hospital followed the Australian approach. Unfortunately, the SPF concept has never been tested in a multi-institution RCT, which could clarify whether morbidity is truly reduced, and recurrences not increased by this method. Nevertheless, from our audit and the reported retrospective studies in the literature, the SPF approach appears to be safe and worthy of ongoing exploration, though the chances of being tested in an RCT seem remote, as a large sample size will be required. Retrospective comparisons of SPF vs. WPF outcome data, or a matched historical case-control study, are possibilities for the continued study of the SPF method.
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References
1. Cervical Cancer: Estimated Incidence, Mortality and Prevalence Worldwide in 2012. [cited 2017, July 1]. Available from: http://globocan.iarc.fr/old/FactSheets/cancers/cervix-new.asp
2. Pecorelli S, Zigliani L, Odicino F. Revised FIGO staging for carcinoma of the cervix. Int J Gynaecol Obstet. 2009;105(2):107–8. https://doi.org/10.1016/j.ijgo.2009.02.009
3. Peters WA 3rd, Liu PY, Barrett RJ 2nd, 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. 2009;18(8):1606–13. https://doi.org/10.1200/JCO.2009.18.8.1606
4. Delgado G, Bundy B, Zaino R, et al. 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. 1999;73(3):352–7. https://doi.org/10.1006/gyno.1999.5387
5. Sedlis A, Bundy BN, Rotman MZ, et al. 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(2):177–83. https://doi.org/10.1006/gyno.1999.5387
6. Viswanathan AN, Lee H, Hanson E, et al. Influence of margin status and radiation on recurrence after radical hysterectomy in Stage IB cervical cancer. Int J Radiat Oncol Biol Phys. 2006;65(5):1501–7. https://doi.org/10.1016/j.ijrobp.2006.03.010
7. Estape RE, Angioli R, Madrigal M, et al. Close vaginal margins as a prognostic factor after radical hysterectomy. Gynecol Oncol. 1998;68(3):229–32. https://doi.org/10.1006/gyno.1998.4960
8. Kridelka FJ, Berg DO, Neuman M, et al. Adjuvant small field pelvic radiation for patients with high risk, stage IB lymph node negative cervix carcinoma after radical hysterectomy and pelvic lymph node dissection. A pilot study. Cancer. 1999;86(10):2059–65.
9. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the radiation therapy oncology group (RTOG) and the European organization for research and treatment of cancer (EORTC). Int J Radiat Oncol Biol Phys. 1995;31(5):1341–6. https://doi.org/10.1016/0360-3016(95)0060-C
10. Allam M, Feely C, Millan D, et al. Depth of cervical stromal invasion as a prognostic factor after radical surgery for early stage cervical cancer. Gynecol Oncol. 2004;93(3):637–41. https://doi.org/10.1016/j.ygyno.2004.02.020
11. Biewenga P, van der Velden J, Mol BW, et al. Prognostic model for survival in patients with early stage cervical cancer. Cancer. 2011;117(4):768–76. https://doi.org/10.1002/cncr.v117.4
12. Hong J, Tsai C, Lai C, et al. Postoperative low-pelvic irradiation for stage I-IIA cervical cancer patients with risk factors other than pelvic lymph node metastasis. Int J Radiat Oncol Biol Phys. 2002;53(5):1284–90. https://doi.org/10.1016/S0360-3016(02)02831-6
13. Ohara K, Tsunoda H, Nishada M, et al. Use of small pelvic field instead of whole pelvic field in postoperative radiotherapy for node-negative, high-risk stage I and II cervical squamous cell carcinoma. Int J Gynecol Cancer. 2003;13:170–6.
14. Ohara K, Tsunoda H, Satoh T, et al. Use of the small pelvic field instead of the classic whole pelvic field in postoperative radiotherapy for cervical cancer: Reduction of adverse events. Int J Radiat Oncol Biol Phys. 2004;60(1):258–64. https://doi.org/10.1016/j.ijrobp.2004.02.023
15. Yeo RMC, Chia YN, Namuduri RPD, et al. Tailoring adjuvant therapy for stage IB-IIA node negative cervical carcinoma after radical hysterectomy and pelvic lymph node dissection using the GOG score. Gynec Oncol. 2011;123(2):225–9. https://doi.org/10.1016/j.ygyno.2011.06.040
16. Hacker NF, Barlow EL, Scurry J, et al. Primary surgical management with tailored radiation for stage IB2 cervical cancer. Obstet Gynecol. 2013;121(4):765–72. https://doi.org/10.1097/AOG.0b013e3182887836
17. Yi O, Cao X, Wang Y, et al. Small-pelvic field postoperative radiotherapy benefit for early-stage cervical cancer patients without pelvic lymph node metastasis. J Comput Theor Nanosci. 2016;13(1):528–33. https://doi.org/10.1166/jctn.2016.4836
18. Berek JS, Hacker NF. Berek and Hacker’s Gynecologic Oncology. 6th ed. Philadelphia, PA: Wolters Kluver; 2015.
19. de Jong RA, Pras E, Boozen HM, et al. Less gastrointestinal toxicity after adjuvant radiotherapy on a small pelvic field compared to a standard pelvic field in patients with endometrial carcinoma. Int J Gynecol Cancer. 2012;22(7):1177–86. https://doi.org/10.1097/IGC.0b013e31826302dd

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