

¹⁸F-FDG-PET/CT-guided intensity-modulated radiotherapy for 42 FIGO III/IV ovarian cancer: A retrospective study

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Abstract. The aim of the present study was to evaluate the curative effect of fludeoxyglucose-positron emission tomography/computed tomography (¹⁸F-FDG-PET/CT)-guided intensity-modulated radiotherapy (IMRT) for 42 patients with International Federation of Gynecology and Obstetrics (FIGO) stage III/IV ovarian cancer. Between January 2012 and December 2015, 42 patients with FIGO stage III/IV ovarian cancer who were treated with ¹⁸F-FDG-PET/CT-guided IMRT at the Department of Radiation Oncology were analyzed. A total of 21 patients who exhibited recurrence following surgery and 11 patients who were unable to tolerate or rejected surgery received 5-10 cycles of chemotherapy only. A total of 10 patients, who were either older (>70 years) or in poor general health were unable to undergo surgery and only received IMRT. The patients received a total radiation dose of 5,040 cGy (range, 4,500-5,500 cGy), with a dose fraction of 200 cGy/fx, administered a total of 10-14 times, 5 times/week, prior to being rested for half an hour to relocate lesions and undergoing a second round of radiotherapy for 10-14 cycles. The 1-, 2- and 3-year progression-free survival (PFS) rates of the patients were 66.7, 33.3 and 21.4%, respectively, and the median PFS time was 20.3 months. The 1-, 2- and 3-year local control rates of the patients were 90.5, 83.3 and 69.0%, respectively, and the 1-, 2- and 3-year overall survival (OS) rates were 73.8, 64.3 and 52.4%, respectively. According to the results of multivariate analysis using the Cox proportional hazards model, the Karnofsky performance status (KPS) score (1) was the only index associated with prognosis (P<0.003). The study concluded that for patients with advanced ovarian

cancer, particularly for patients unable to undergo surgery or chemotherapy, ¹⁸F-FDG PET/CT-guided IMRT is a safe and effective treatment method, and it may be considered as an equally effective treatment option. Furthermore, the results of the present study suggested that the KPS score of a patient is the only factor affecting the OS time.

Introduction

Ovarian cancer is one of the three major types of malignant tumor and is common in the female reproductive system. Approximately 70% of patients are diagnosed once the tumor has metastasized to the abdominal cavity outside of the reproductive organs, which represents International Federation of Gynecology and Obstetrics (FIGO) stage (2) III or IV disease, for which the respective 5-year overall survival (OS) rates are only ~31 and 13% (3,4). The mortality rate of malignant ovarian tumors is the highest among the gynecological malignant tumors, and has become a serious threat to the lives and health of women with primary tumors. Surgery is prioritized in order to cure ovarian cancer, and is supplemented by being combined with post-surgical chemotherapy. Tumor cells are successfully removed in ~45% of patients, and this is dependent on the tumor size and location, and the individual experience of the surgeons (5). The main cause of recurrent ovarian cancer remains unclear. Various types of consolidation therapy have been studied in a series of clinical trials, but none have been demonstrated to improve survival time in ovarian cancer (5-7).

Several studies (8,9) have introduced positron emission tomography/computed tomography (PET/CT)-guided intensity-modulated radiotherapy (IMRT) for the treatment of ovarian cancer. Du *et al* (8) demonstrated that use of fludeoxyglucose (¹⁸F-FDG)-PET/CT for ovarian cancer recurrence of retroperitoneal lymph nodes to design the IMRT plan can improve the accuracy of the gross tumor volume (GTV) sketch and improve the clinical therapeutic effect. Huang *et al* (9) reported the case of a 68-year-old female with ovarian cancer and a large abdominal metastasis (FIGO stage III), who did not undergo surgery, but received PET/CT imaging orientation-guided IMRT. The patient did not experience any significant acute or chronic radiation response. Subsequently, following 4 cycles of chemotherapy, all lesions disappeared, the cancer antigen (CA)-125, CA19-9 and carcinoembryonic antigen levels dropped to normal levels, and

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the patient experienced 3 years without recurrence. The present study retrospectively studied 42 patients with stage III or IV ovarian tumors using PET/CT-guided IMRT, and observed the curative effect and acute or chronic radiation reaction. Due to metastasis, only partial tumor resection was possible by surgery and chemotherapy, but certain patients experienced recurrence; furthermore, a number of patients refused surgery and chemotherapy.

Patients and methods

Patient characteristics. Between January 2012 and December 2015, 42 patients with FIGO stage III or IV ovarian cancer from the 323rd Hospital of the People's Liberation Army (Xi'an, China) underwent IMRT. There were 21 cases of recurrence following surgery (FIGO III or IV), and 11 patients were unable to tolerate or rejected surgery, and were therefore only treated with 5-10 cycles of chemotherapy of 105 mg cisplatin administered as a peritoneal perfusion, followed by 180 mg Taxol and 100 mg cisplatin (Table I). A total of 10 patients, who were either older (>70 years) or in poor general health were unable to undergo surgery and only received IMRT. All patients were pathologically diagnosed with ovarian cancer; 21 cases were diagnosed via postoperative pathology, and the remainder were differentially diagnosed using a detecting human epididymis protein 4 (HE4) and CA-125 in the serum, and auxiliary puncture lesion or abdominal cavity effusion gland cancer. Prior to radiotherapy the patients were systematically assessed through lab testing (blood and urine) and clinical imaging results to rule out any possible inflammation and bleeding. ¹⁸F-FDG-PET/CT examination was performed prior to radiotherapy positioning, and the staging and lesion size measurement. Patients were examined by ¹⁸F-FDG-PET/CT after 1 and 3 months of radiotherapy, and CA-125 and HE4 tumor markers were analyzed. The patients were treated with up to 6 cycles of chemotherapy depending on the curative effect and their systemic tolerance.

Radiotherapy. All patients underwent ¹⁸F-FDG-PET/CT simulation positioning, using PET/CT imaging with a standardized uptake value (SUV) of 3.0. The GTV, with an external expansion of 5 mm for the clinical target volume (CTV) boundary, the planning target volume (PTV) surrounding the CTV, which did not require amplification and the organs at risk, including the affected lymph nodes and areas of the liver, kidney, small intestine and bladder, were contoured for treatment planning purposes. Patients were treated with a median prescription dose of 5,040 cGy (range, 4,500-5,500 cGy) with a median dose/fraction of 200 cGy (range, 180-220 cGy), once daily, 5 times a week, for a total of 12-15 times over a period of 10-14 days, with a treatment break two times. The localization of the treatment was altered as the treatment progressed through repetitive PET/CT imaging. The plans were created to limit the volume receiving 40 Gy (V40) of the kidney, liver and small bowel to <30%, the V40 of the rectum to <60%, the V45 of the bladder to <50%, the V20 of the lung to <20% and the V25 of the heart to <25%.

Toxicity evaluation. Patients were monitored for acute and late toxicity using Common Terminology Criteria for Adverse Events (CTCAE) V4.03 (7,8) with data obtained by a radiation

Table I. Patient, tumor and treatment characteristics.

| Characteristics | Value |
|---------------------------------------|------------|
| Median age (range), years | 65 (45-86) |
| Histology, n (%) | |
| Epithelial tissue | 34 (81.0) |
| Mesenchyme | 5 (11.9) |
| Other | 3 (7.1) |
| KPS score, n (%) | |
| ≥70 | 25 (59.5) |
| <70 | 17 (40.5) |
| Peritoneal cavity effusion, n (%) | |
| Yes | 15 (35.7) |
| No | 27 (64.3) |
| Radiation dose (median, range) | 50 (30-60) |
| ≥50 Gy, n (%) | 24 (57.1) |
| <50 Gy, n (%) | 18 (42.9) |
| Stage, n (%) | |
| III | 26 (61.9) |
| IV | 16 (38.1) |
| Pro-surgery, n (%) | |
| No | 17 (40.5) |
| 1 | 14 (33.3) |
| ≥2 | 11 (26.2) |
| Pro-chemotherapy, n (%) | |
| Yes | 26 (61.9) |
| No | 16 (38.1) |
| Group, n (%) | |
| Surgery + chemotherapy + radiotherapy | 25 (59.5) |
| Chemotherapy + radiotherapy | 12 (28.6) |
| Radiotherapy | 5 (11.9) |

KPS, Karnofsky performance status.

oncologist from electronic hospital records. Patients were evaluated for disease status and for the appearance of acute and late toxicity according to their medical history, physical examination, and the aforementioned laboratory and radiological tests (8). Acute toxicities were defined as events occurring 28 days after radiotherapy completion, while late toxicities were defined as events occurring ≥28 days after radiotherapy completion. On average, patients were followed up by a radiation oncologist for 3 year following the completion of radiation therapy.

Statistical analysis. All patients were followed up for a total of 3 years, once every 6 months after radiotherapy. To evaluate the degree of improvement in the clinical symptoms of the patients, the KPS score, CA-125 levels, local control (LC) rate, disease progression, OS rate and ¹⁸F-FDG PET/CT findings were analyzed. Based on their re-examination, it was possible to determine the curative effect of radiotherapy. Statistical comparisons utilized univariate and the multivariate Cox proportional hazards model to evaluate the impact of clinical factors. The Kaplan-Meier method was used to derive actuarial

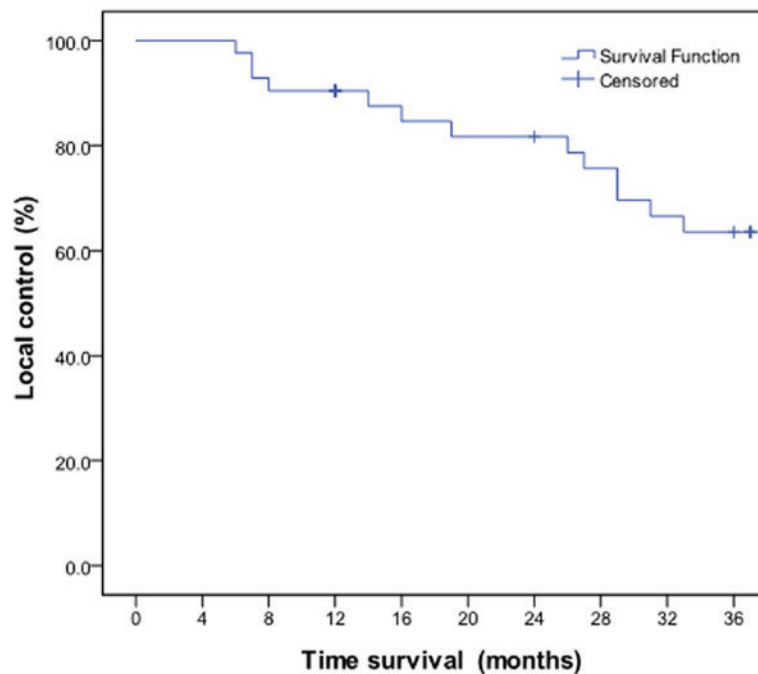


Figure 1. Kaplan-Meier plot showing 1-, 2- and 3-year local control rates of 90.5, 83.3 and 62.0%, respectively.

estimates of LC rate, progression-free survival (PFS) rate and OS rate, which were measured from the time between treatment and mortality. The survival data were analyzed using the log-rank test. Statistical tests were performed using SPSS 19 software (IBM Corporation, Armonk, NY, USA).

Results

Improvements in LCP, FS and OS rate. In the first follow-up year, no evident increase of the local lesions was observed in 38 patients with stable local lesions. Following 1 year follow-up, the follow-up intervals were 1.5, 2, 2.5 and 3 years. The 1-year LC rate was 90.5%, the 2-year LC rate was 83.3% and the 3-year LC rate was 62.0% (Fig. 1). The 1-, 2- and 3-year PFS rates were 66.7, 33.3 and 21.4%, respectively, and the median PFS time was 20.3 months (Fig. 2). The 1-, 2- and 3-year OS rates were 73.8, 64.3 and 52.4%, respectively (Fig. 3).

Lower incidence of acute and late toxicities. All the patients were observed for acute gastrointestinal or hematological reactions during radiation therapy, and the results revealed that 90.5% of the gastrointestinal reactions were less than level 2 (7,8) and that only 9.5% of gastrointestinal reactions were around level 3 (Table II). Although the lesions in the patients were indicated to be large and the distribution range to be wide, there were no symptoms of intestinal obstruction or intestinal bleeding. The gastrointestinal reaction was reversed by symptomatic treatment or at 3 days after the termination of radiotherapy. The acute toxicity of the blood was deemed to be acceptable; the hematological reaction in 92.9% of the patients was less than level 2, while that of 7.1% of the patients was around level 3 (Table III).

The incidence of side effects of late toxicity was only 42.9%, which was less than the percentage of level 2 gastrointestinal

reactions. The patients were able to tolerate the side effects and symptomatic treatment was used to alleviate them. No level 3 gastrointestinal side effects were reported. A total of 1/42 (2.4%) patients with hematological side effects was no more than level 3 (Table IV).

Multivariate analysis showing KPS score as an independent prognostic factor. Multivariate analysis was performed on KPS score, the total radiation dose administered to patients, Tumor-Node-Metastasis classification (10), peritoneal metastasis, and whether or not patients underwent chemotherapy or surgical treatment. The results suggested that KPS score was the only index associated with prognosis ($P < 0.003$). Patient age, tumor stage, radiotherapy dose, the presence of peritoneal cavity effusion and whether or not the patients underwent surgery or chemotherapy exhibited no clear association with prognosis.

Use of radiotherapy results as an equally effective treatment option. Treatment was administered to patients who received three different treatment types: Surgery plus chemotherapy and radiotherapy (S+C+R; $n=12$), chemotherapy plus radiation therapy (C+R; $n=12$) and radiation therapy (R; $n=18$). The difference in OS time was not statistically significant ($P=0.637$), but the survival curves of the three groups were not identical (Fig. 4). However, radiotherapy resulted in a similar OS time to that achieved following surgery or chemotherapy. The OS times of patients in the peritoneal metastasis group were not statistically significantly different from those of patients without peritoneal metastasis ($P=0.059$; Fig. 5).

Radiotherapeutic effect in 3 typical patients

Case 1. In September 2012, a 59-year-old female presented with visible and diffusely distributed abdominopelvic lesions, a large area of peritoneal planting with abdominal cavity

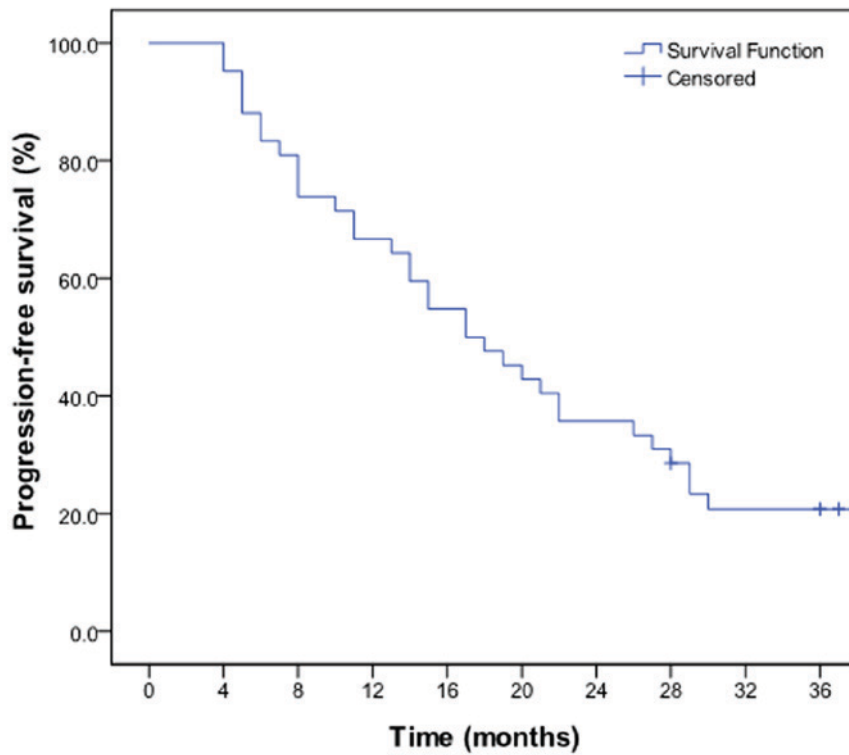


Figure 2. Kaplan-Meier plot showing 1-, 2- and 3-year PFS rates of 66.7, 33.3 and 21.4%, respectively, and a median PFS time of 20.3 months. PFS, progression-free survival.

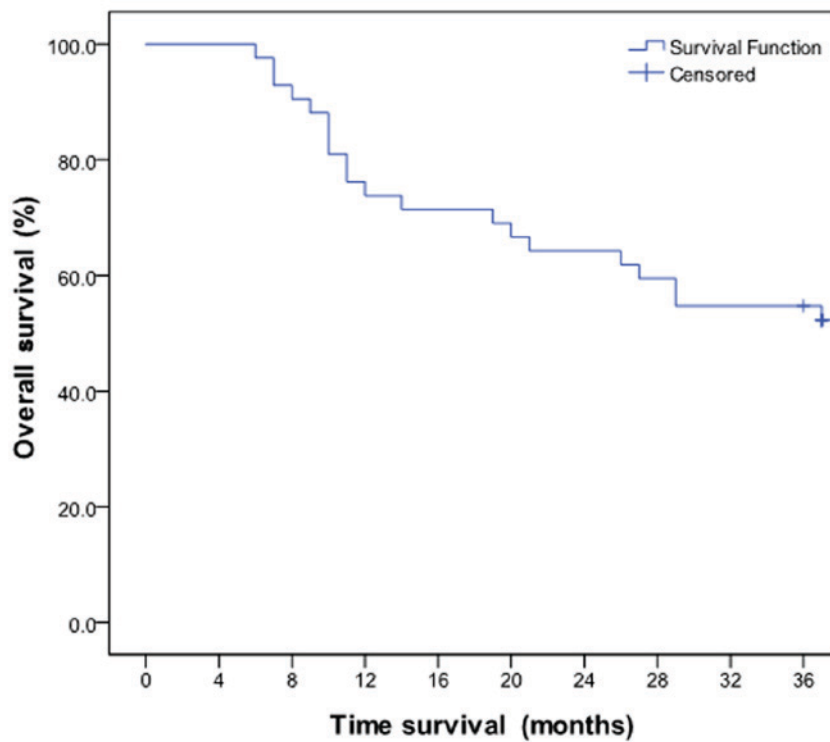


Figure 3. Kaplan-Meier plot showing 1-, 2- and 3-year overall survival rates of 73.8, 64.3 and 52.4%, respectively.

effusion in large quantities, and coronary heart disease, as shown in Fig. 6A, which lead to a refusal of surgery and chemotherapy. The patient underwent IMRT consisting of

a single 200-cGy fraction once daily, 5 times per week, for 14 cycles in total (the pulmonary lesions were not treated). Following the second treatment, the abdominopelvic lesions

Table II. Acute toxicities.

| Acute toxicities | Grade | |
|-------------------------|-----------|---------|
| | ≤2 | 3 |
| Gastrointestinal, n (%) | 38 (90.5) | 4 (9.5) |
| Hematological, n (%) | 39 (92.9) | 3 (7.1) |

Table III. Late toxicities.

| Late toxicities | Grade | |
|-------------------------|-----------|---------|
| | ≤2 | 3 |
| Gastrointestinal, n (%) | 18 (42.9) | 0 (0.0) |
| Hematological, n (%) | 24 (57.1) | 1 (2.4) |

became significantly smaller and exhibited reduced metabolism, while the heart was not targeted possibly due to the abscopal effect (Fig. 6B), while the pulmonary lesions were no longer present. Radiotherapy was continued 11 times, with a total dose of 50 Gy. From the third PET-CT review (Fig. 6C), the results revealed that the metabolism of the lesions, particularly the pulmonary lesions, had disappeared. This may have been caused by distant effects of the radiation.

Case 2. In August, 2012, the second case was that of an 84-year-old female presenting with abdominal pain, diarrhea and emaciation, and pathologically diagnosed primary ovarian cancer, metastases and obstruction in the ascending colon, caused by an incomplete ileus and diagnosed by colonoscopy (Fig. 7A). Due to the age, poor health and poor heart function of the patient, surgery and chemotherapy were not possible. Therefore, the patient underwent local IMRT with a single dose of 200 cGy, 5 times per week, up to a total of 4,800 cGy. Following radiotherapy, the PET/CT scan revealed that all the lesions had disappeared, and that the complete remission of symptoms had been achieved (Fig. 7B). However, the patient succumbed to gastric cancer three years later.

Case 3. In August, 2013, the third case was that of a 58-year-old female with ovarian cancer, who at 22 months post-surgery underwent four cycles of chemotherapy following multiple abdominal and multiple intrahepatic metastases (Fig. 8A). The patient was treated with local IMRT at a single dose of 200 cGy/day, 5 times per week, for a total of 13 cycles (total, 4,600 cGy). Following IMRT, the PET/CT scan revealed that the multiple abdominal tumors had mostly disappeared, with one residual lesion due to the low radiation dose (Fig. 8B).

Discussion

The ¹⁸F-FDG-PET/CT technique demonstrates high diagnostic value for the identification of primary ovarian cancer in patients who present with a pelvic mass of unknown origin. PET/CT has been identified as a useful method for

Table IV. Multivariate analysis using Cox's proportional hazard model.

| Variable | SE | P-value | HR | 95% CI | |
|-----------------------|-------|--------------|-------|--------|-------|
| | | | | Min | Max |
| KPS | 0.531 | 0.003 | 0.203 | 0.072 | 0.575 |
| Age | 0.480 | 0.728 | 1.182 | 0.461 | 3.030 |
| TNM | 0.526 | 0.426 | 1.520 | 0.542 | 4.263 |
| Peritoneal metastasis | 0.559 | 0.545 | 1.403 | 0.469 | 4.201 |
| Surgery | 0.307 | 0.132 | 1.589 | 0.870 | 2.903 |
| Chemotherapy | 0.622 | 0.712 | 1.258 | 0.372 | 4.261 |
| Dose | 0.665 | 0.693 | 1.300 | 0.353 | 4.788 |

KPS, Karnofsky performance status; Tumor-Node-Metastasis; SE, standard error; HR, hazard ratio; CI, confidence interval.

detecting recurrence in individuals with increased serum levels of CA-125 and no findings on CT, or in those with normal levels of CA-125 and recurrence detected by CT that was performed due to clinical symptoms. PET/CT, detecting recurrence in patients, demonstrated the value of qualitative diagnosis, improving the diagnosis of ovarian cancer. In the present study, PET/CT-guided IMRT in patients with recurrent ovarian cancer improved the delineation of GTV and reduced the likelihood of treatment that is not targeted correctly to the tumor location, and therefore improved the clinical outcome. Certain studies have suggested that standard CT for radiation treatment planning (RTP), which is acquired during free breathing but lacks measures for compensating for the breathing motion, results in deformation and misplacement of tumor locations. In certain cases, fluoroscopy or slow CT can provide a general impression of the breathing motion, but these approaches are not considered to be sufficient for RTP procedures. As free breathing occurs during PET, the resultant images are blurred according to the breathing motion and thus provide a good impression of the tumor shape and location (11,12). In the most common RTP scenario, where 3DCT and 3D PET scans are acquired, a respiratory expanded GTV approach is recommended. Furthermore, PET-CT can aid in distinguishing between the active and necrotic portions in mixed cystic and solid lesions. However, the target area with PET-CT is larger compared with CT as indicated in the present study. The aforementioned finding correspond with the findings reported by Mundt *et al* (13). In the present study of patients with stage III or IV disease, the majority of the patients had numerous, widely distributed lesions, a large volume flow rate and an irregular shape, thus the outline of the GTV was difficult to determine. A PET/CT SUV value of 3.0 was set for the GTV border, with a 5 mm surrounding boundary for the CTV, while the PTV boundary was no more than that for the CTV. The PTV target area should be in close proximity to tumor edge, in order to reduce the ray radiation to normal tissue area. Following 12-15 treatments with radiotherapy, the patients rested for 10-14 days, prior to PET/CT localization and redesign, and a repeat of the treatment, due to the following

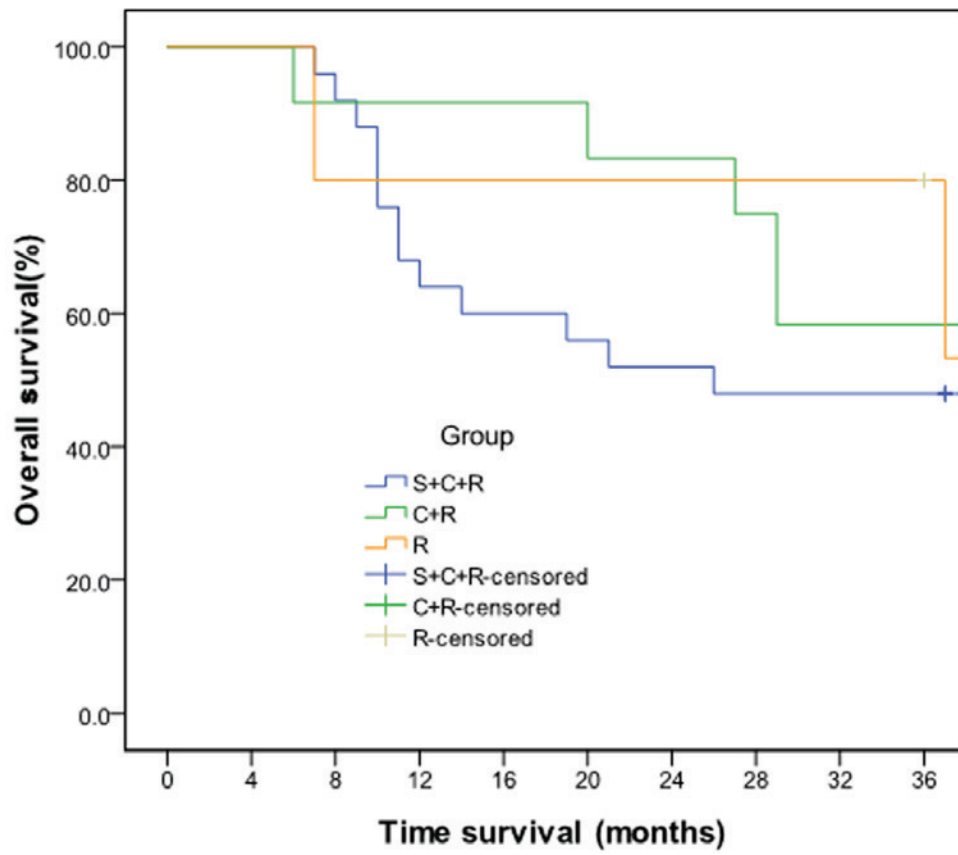


Figure 4. Kaplan-Meier plot of cumulative survival rates comparing different treatments among S+C+R, C+R and R groups (P=0.637). S, surgery; C, chemotherapy; R, radiotherapy; cum, cumulative.

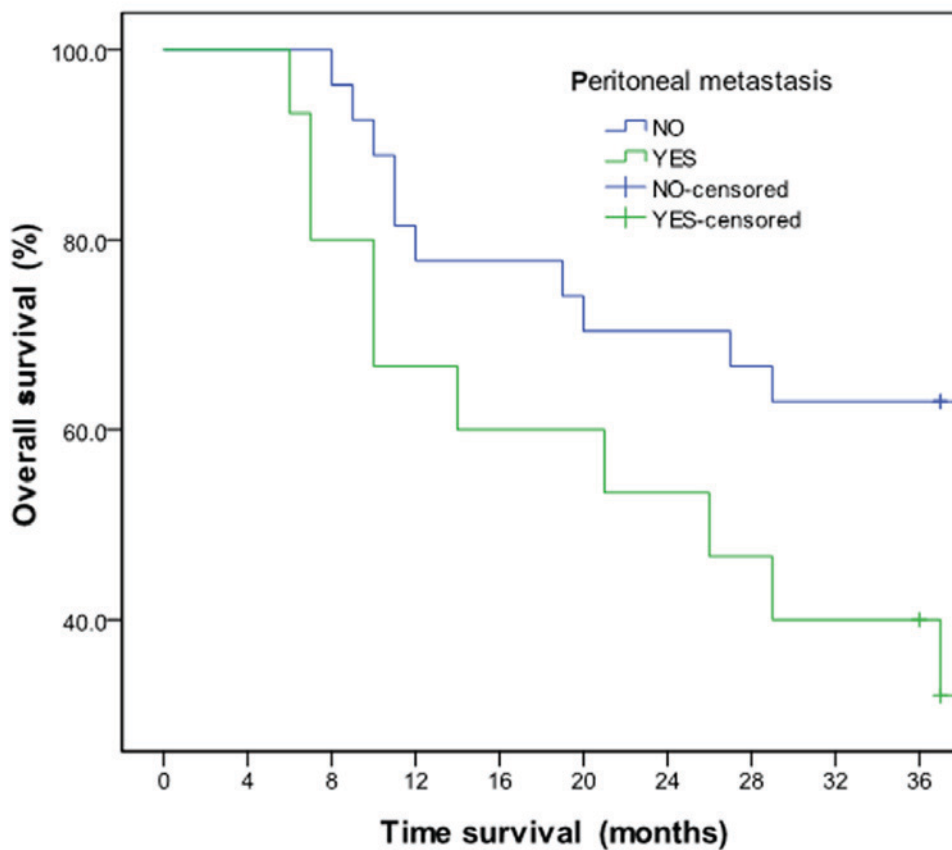


Figure 5. Kaplan-Meier plot comparing cum survival rates between patients with and without peritoneal metastasis (P=0.059).

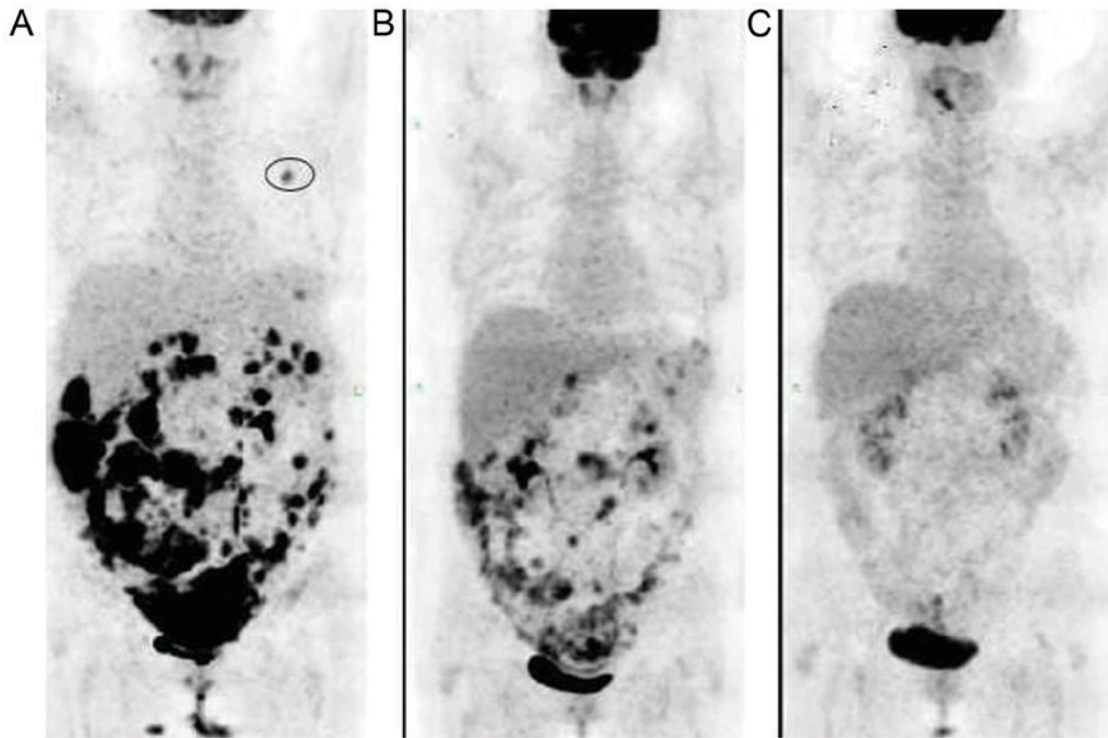


Figure 6. PET/CT scans of a 59-year-old female (A) prior to treatment, and following the (B) second and (C) third treatment. The results revealed that the metabolism of the lesions, particularly the pulmonary lesions (indicated by the oval), had disappeared.

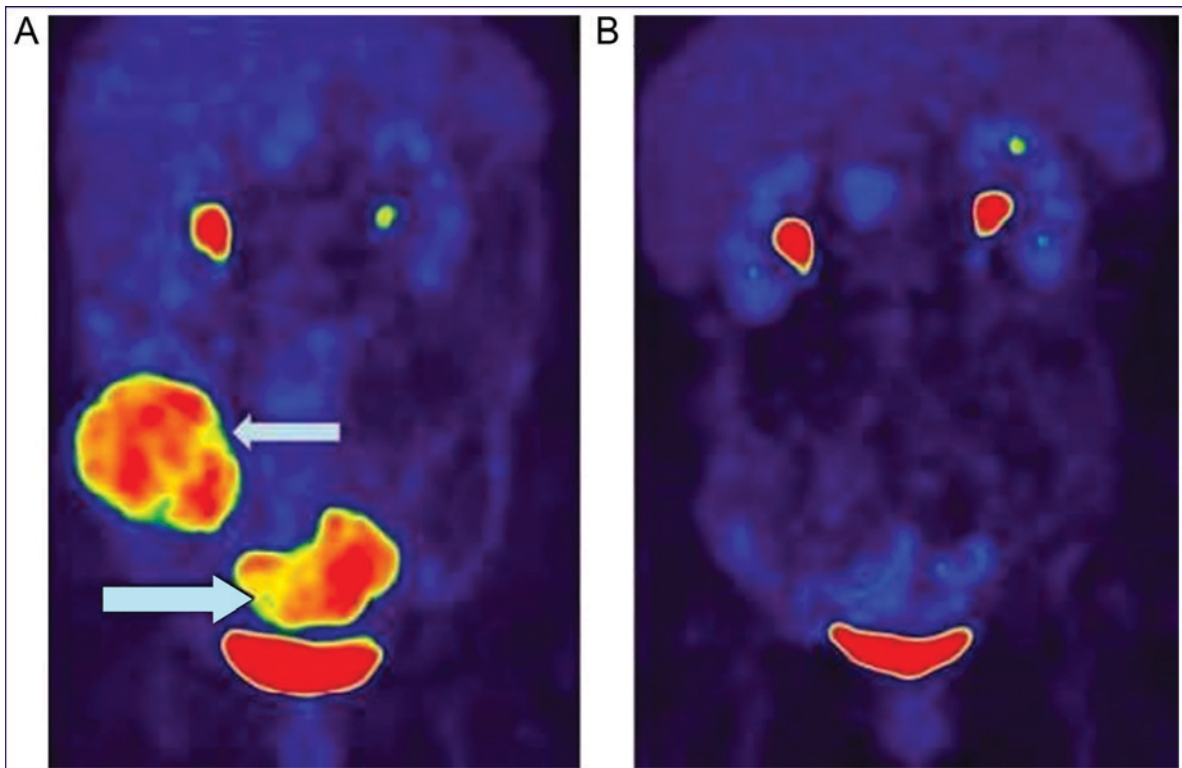


Figure 7. PET/CT scans of an 84-year-old female patient. (A) Patient was pathologically diagnosed with primary ovarian cancer (\rightarrow), and metastases and obstruction in the ascending colon, caused by an incomplete ileus and diagnosed by colonoscopy (\leftarrow). (B) Following radiotherapy, the PET/CT scan revealed that all the lesions had disappeared, and that the complete remission of symptoms had been achieved. PET/CT, positron emission tomography/computed tomography.

reasons: i) a number of the older patients underwent surgery or chemotherapy multiple times, due to poor physical condition, more lesions and a wide metastasis distribution. A number

of patients with primary peritoneal tumors indicated more metastases with large ascites and a larger radiotherapy volume, causing normal tissue to receive a relatively large quantity of

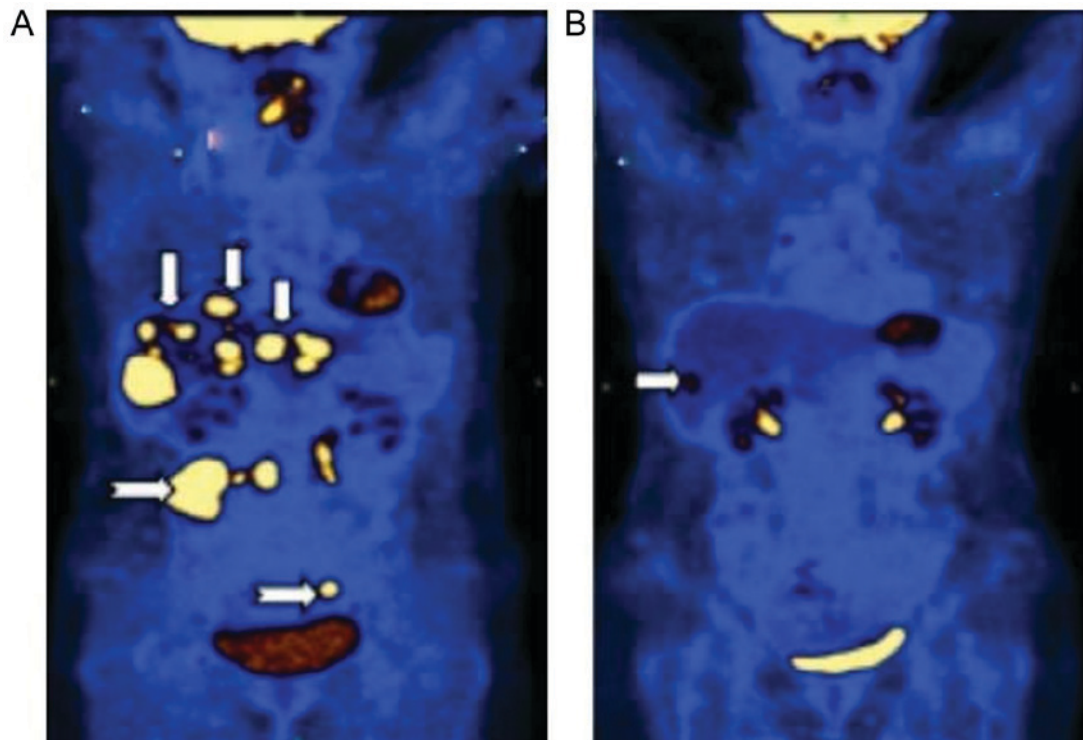


Figure 8. Positron emission tomography/computed tomography scans of (A) a 58-year-old female with ovarian cancer, who at 22 months post-surgery underwent four cycles of chemotherapy following multiple abdominal and multiple intrahepatic metastases. (B) Following intensity-modulated radiotherapy, the multiple abdominal tumors had mostly disappeared, with one residual lesion due to the low radiation dose.

radiation. In addition, the prolonged treatment interval could reduce the acute toxicity of the gastrointestinal system and the blood caused by the radiotherapy; ii) after resting, the majority of patients exhibited significantly smaller lesions, abdominal lesions and ascites volume, and the location changed and iii) in a small number of patients, following PET/CT positioning, novel lesions appeared, and repeating treatment could improve the effects of the original treatment

In cases of peritoneal metastasis with a large amount of ascites, an abdominal cavity drainage tube was used for various durations according to the tolerance of the patient. To ensure the location of the metastasis accurately, we treated patients with peritoneal effusion prior to radiotherapy, following a 1-2 cm incision to release the peritoneal effusion. The use of the drainage tube process was smooth and all patients successfully completed radiotherapy.

The choice of radiation dose and the sensitivity of the ovarian tumors to radiotherapy are associated with FIGO stage III and IV ovarian cancer, a large tumor volume and a wide distribution. According to the results of LC, OS and PFS analysis, as well as multivariate analysis with adverse effects of treatment and tolerance to treatment, the effect of treatment in patients in the present study resulted in little improvement compared with the effect of surgery and/or chemotherapy.

De Meerleer *et al* (14) studied patients with FIGO stage III and IV postoperative residual or recurrent ovarian cancer using whole abdominopelvic radiotherapy (WAPRT) in the palliative treatment of chemotherapy-resistant ovarian cancer with bulky peritoneal disease. All patients exhibited disease, including gastrointestinal obstruction or an incomplete ileus. A dose of 33 Gy was prescribed, to be delivered in 22 fractions of 1.5 Gy

to the abdomen and pelvis. Delivery of whole abdomen pelvic RT using IMAT offers palliation therapy in cases of peritoneal metastatic ovarian cancer. WAPRT can resolve intestinal obstructions for at least 3 months, suggesting that a total of 33 Gy WAPRT is effective and safe. Rochet *et al* (15-17) reported a similar study regarding lesion-involved field irradiation. Brown *et al* (18) studied involved field radiation therapy for locoregionally recurrent ovarian cancer, for which the total dose of the local lesion was ≥ 45 Gy and the median dose was 59.2 Gy (range, 45-68.2 Gy). Definitive IFRT can yield excellent LC, protracted disease-free intervals and even complete remission in carefully selected patients. RT should be considered as a tool in the curative management of locoregionally recurrent ovarian cancer. In a study undertaken by Chundury *et al* (19), the total median radiation dose was 5,040 cGy (range, 4,500-7,000 cGy). The results revealed an association between using IMRT for recurrent chemorefractory ovarian cancer and good LC and limited radiation-associated toxicity. Future studies should be performed to determine the subpopulation that will most benefit from IMRT, and to assess whether other techniques, such as stereotactic body radiotherapy, may be suitable.

The present study reported that the 1-, 2- and 3-year LC rates were 90.5, 83.3 and 69.0%, respectively. Chundury *et al* (19) reported similar results, but 18.2% of the patients exhibited relatively mild disease (FIGO stage I or II), with a small lesion range. According to the results of slow side radiation reactions, which revealed no more than level 3 gastrointestinal reactions and a small number of patients with level 3 blood toxicity, we hypothesized that a mean total radiation dose of 5,000 cGy to patients with FIGO stage III and IV ovarian cancer is feasible and effective.

The present study demonstrated that disease progression in patients was first identified in the appearance of new lesions in areas that had not been treated with radiotherapy, including the liver capsule, peritoneum and pelvic cavity. Therefore, systemic chemotherapy drugs or abdominal cavity perfusion chemotherapy is required for the majority of patients presenting with abdominal cavity effusion while undergoing radiotherapy. According to the study by Dembo *et al* (20) in 1979, the 5-year OS rate in patients with stage I-III ovarian cancer treated by radiotherapy was 58%, and the 5-year OS rate of the patients treated with chlorambucil plus pelvic RT was 41%. In 2010, the 3-year OS rate of neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer was recorded to be ~48% (21). In the present study, the 3-year OS rate of patients treated with radiotherapy was 52.4% (22/42 patients), which was similar to the results found by Brown *et al* and Chundury *et al* (18,19); however, the present study enrolled patients with late-stage disease as follows: 15/42 patients (35.7%) with peritoneal metastasis and peritoneal effusion, 12/42 patients (28.6%) who refused surgery and opted for chemotherapy plus radiotherapy, and 5/42 patients (11.9%) who were unable to tolerate surgery or chemotherapy and opted for radiotherapy. In general, the causes of the positive curative effect, resulting from radiotherapy, were associated with the PET/CT localization design scheme. Although the survival analysis of three groups (S+C+R, C+R and R) revealed no statistically significant differences, the results suggested that patients who did not undergo surgery exhibited a good survival trend. The good survival trend may be associated with chemotherapy or surgery, or the patient's health condition. According to the survival analysis of patients with or without peritoneal metastasis and effusion, although no statistically significant differences were observed, survival was improved in patients without peritoneal metastasis or effusion. Of the various factors assessed in the patient survival analysis, it was revealed that KPS was the only factor associated with survival. For the PET/CT-guided IMRT in the treatment of patients with advanced ovarian cancer, the general condition of the patient is important.

The current study presented the case of a 59-year-old female with diffusely distributed abdominal pelvic visible lesions who was treated with ¹⁸F-FDG PET/CT-guided IMRT, and in whom the metabolism of the lesions dissipated and the peritoneal effusion completely subsided (Fig. 6). The health condition of the patient was poor and due to abdominal metastasis, the patient was unable to undergo surgery. In addition, she did not wish to receive chemotherapy, due to the severe adverse effects. Although this was a specific case, the present study did reveal that patients unable to undergo surgery and chemotherapy should be enrolled in future studies. The fact that the pulmonary lesions also disappeared without treatment may be associated with the abscopal effect. For the two other selected cases from the present study, namely an elderly patient unable to tolerate surgery (Fig. 7) and a 58-year-old female with ovarian cancer, who at 22 months post-surgery underwent four cycles of chemotherapy following abdominal multiple metastasis and multiple intrahepatic metastasis (Fig. 8), PET/CT-guided IMRT obtained a good curative effect and significantly prolonged the survival time. Therefore, this

approach should be trialed as a treatment option and future studies should incorporate a larger number of cases.

For patients with advanced ovarian cancer, ¹⁸F-FDG-PET/CT-guided IMRT is a safe and effective treatment method, particularly for patients unable to undergo surgery and chemotherapy. Furthermore, the KPS score was the only factor significantly associated with the OS time. To verify this result, the number of cases should be increased to perform randomized controlled prospective studies in future.

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Availability of data and materials

All data generated or analyzed during this study are included in this published article.

Authors' contributions

YD contributed to the study design, data collection and writing of the manuscript. XL contributed to data collection and data analysis. XLL and YM contributed to data analysis and interpretation of data, TY and WL performed the follow-up of patients and were responsible for chemotherapy scheduling. SH contributed to the study design, data analysis, interpretation of data, writing of the manuscript and revision of the manuscript. All authors read and approved the final manuscript.

Ethics statement and consent to participate

The present study was approved by the 323 Hospital of People's Liberation Army Ethics Board (approval no., LZ323-003-89; XI'an, China). Consent to participate was obtained from all patients.

Patient consent for publication

The patients provided written informed consent for publication.

Competing interests

The authors declare that they have no competing interests.

References

1. Rudolf F, Joaquim LC, Vieira C, Bjerregaard-Andersen M, Andersen A, Erlandsen M, Sodemann M, Andersen PL and Wejse C: The Bandim tuberculosis score: Reliability and comparison with the Karnofsky performance score. *Scand J Infect Dis* 45: 256-264, 2013.
2. Kosary CL: FIGO stage, histology, histologic grade, age and race as prognostic factors in determining survival for cancers of the female gynecological system: An analysis of 1973-87 SEER cases of cancers of the endometrium, cervix, ovary, vulva, and vagina. *Semin Surg Oncol* 10: 31-46, 1994.
3. Poveda A: Advanced ovarian cancer: Update, remarks and conclusions on optimal therapy. *Int J Gynecol Cancer* 10: 57-60, 2000.

4. Stuart G, Avall-Lundqvist E, du Bois A, Bookman M, Bowtell D, Brady M, Casado A, Cervantes A, Eisenhauer E, Friedlaender M, *et al*: 3rd international ovarian cancer consensus conference: Outstanding issues for future consideration. *Ann Oncol* 8 (Suppl 16): viii36-viii38, 2005.
5. Ozols RF: Treatment goals in ovarian cancer. *Int J Gynecol Cancer* 1 (Suppl 15): S3-S11, 2005.
6. Heintz AP, Odicino F, Maisonneuve P, Quinn MA, Benedet JL, Creasman WT, Ngan HY, Pecorelli S and Beller U: Carcinoma of the ovary. FIGO 6th annual report on the results of treatment in gynecological cancer. *Int J Gynaecol Obstet* 1 (Suppl 95): S161-S192, 2006.
7. Ozols RF: Update on gynecologic oncology group (GOG) trials in ovarian cancer. *Cancer Invest* 2 (Suppl 22): S11-S20, 2004.
8. Du XL, Jiang T, Sheng XG, Li QS, Wang C and Yu H: PET/CT scanning guided intensity-modulated radiotherapy in treatment of recurrent ovarian cancer. *Eur J Radiol* 81: 3551-3556, 2012.
9. Huang S, Dang Y, Li F, Wei W, Ma Y, Qiao S and Wang Q: Biological intensity-modulated radiotherapy plus neoadjuvant chemotherapy for multiple peritoneal metastases of ovarian cancer: A case report. *Oncol Lett* 9: 1239-1243, 2015.
10. Deng J, Zhang R, Pan Y, Wang B, Wu L, Jiao X, Bao T, Hao X and Liang H: Comparison of the staging of regional lymph nodes using the sixth and seventh editions of the tumor-node-metastasis (TNM) classification system for the evaluation of overall survival in gastric cancer patients: Findings of a case-control analysis involving a single institution in China. *Surgery* 156: 64-74, 2014.
11. Lindner H, Willich H and Atzinger A: Primary adjuvant whole abdominal irradiation in ovarian carcinoma. *Int J Radiat Oncol Biol Phys* 19: 1203-1206, 1990.
12. Sorbe B and Swedish-Norgewian Ovarian Cancer Study Group: Consolidation treatment of advanced (FIGO stage III) ovarian carcinoma in complete surgical remission after induction chemotherapy: A randomized, controlled, clinical trial comparing whole abdominal radiotherapy, chemotherapy, and no further treatment. *Int J Gynecol Cancer* 13: 278-286, 2003.
13. Mundt AJ, Lujan AE, Rotmensch J, Waggoner SE, Yamada SD, Fleming G and Roeske JC: Intensity-modulated whole pelvic radiotherapy in women with gynecologic malignancies. *Int J Radiat Oncol Biol Phys* 52: 1330-1337, 2002.
14. De Meerleer G, Vandecasteele K, Ost P, Delrue L, Denys H, Makar A, Speleers B, Van Belle S, Van den Broecke R, Fonteyne V and De Neve W: Whole abdominopelvic radiotherapy using intensity-modulated arc therapy in the palliative treatment of chemotherapy-resistant ovarian cancer with bulky peritoneal disease: A single-institution experience. *Int J Radiat Oncol Biol Phys* 79: 775-781, 2011.
15. Rochet N, Jensen AD, Sterzing F, Munter MW, Eichbaum MH, Schneeweiss A, Sohn C, Debus J and Harms W: Adjuvant whole abdominal intensity modulated radiotherapy (IMRT) for high risk stage FIGO III patients with ovarian cancer (OVAR-IMRT-01)-Pilot trial of a phase I/II study: Study protocol. *BMC Cancer* 7: 227, 2007.
16. Rochet N, Kieser M, Sterzing F, Krause S, Lindel K, Harms W, Eichbaum MH, Schneeweiss A, Sohn C and Debus J: Phase II study evaluating consolidation whole abdominal intensity-modulated radiotherapy (IMRT) in patients with advanced ovarian cancer stage FIGO III-The OVAR-IMRT-02 Study. *BMC Cancer* 11: 41, 2011.
17. Rochet N, Lindel K, Katayama S, Schubert K, Herfarth K, Schneeweiss A, Sohn C, Harms W and Debus J: Intensity-modulated whole abdomen irradiation following adjuvant carboplatin/taxane chemotherapy for FIGO stage III ovarian cancer: Four-year outcomes. *Strahlenther Onkol* 191: 582-589, 2015.
18. Brown AP, Jhingran A, Klopp AH, Schmeler KM, Ramirez PT and Eifel PJ: Involved-field radiation therapy for locoregionally recurrent ovarian cancer. *Gynecol Oncol* 130: 300-305, 2013.
19. Chundury A, Apicelli A, DeWees T, Powell M, Mutch D, Thaker P, Robinson C, Grigsby PW and Schwarz JK: Intensity modulated radiation therapy for recurrent ovarian cancer refractory to chemotherapy. *Gynecol Oncol* 141: 134-139, 2016.
20. Dembo AJ, Bush RS, Beal FA, Bean HA, Pringle JF and Sturgeon JF: The princess margaret hospital study of ovarian cancer: Stage I, II and asymptomatic III presentations. *Cancer Treat Rep* 63: 249-254, 1979.
21. Vergote I, Tropé CG, Amant F, Kristensen GB, Ehlen T, Johnson N, Verheijen RH, van der Burg ME, Lacave AJ, Panici PB, *et al*: Neoadjuvant chemotherapy or primary surgery in stage IIIC or IV ovarian cancer. *N Engl J Med* 363: 943-953, 2010.



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