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ORIGINAL ARTICLE



# Outcome and safety analysis of endometrial cancer patients treated with postoperative 3D-conformal radiotherapy or intensity modulated radiotherapy

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**ABSTRACT**

**Background:** We sought to analyze the toxicity rates and the treatment outcomes in endometrial cancer (EC) patients treated with postoperative three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT).

**Material and methods:** The clinical data of 646 EC patients treated with postoperative adjuvant 3DCRT (265 patients, 41%) or with IMRT (381 patients, 59%) between April 2007 and August 2019 were retrospectively analyzed. The primary endpoints were treatment-related acute and late gastrointestinal (GI) and genitourinary (GU) toxicities. The secondary endpoints were LC and overall survival (OS) and disease-free survival (DFS).

**Results:** Median follow-up time was 37 months. The rates for acute GI and GU toxicities of any grade for the entire group were 55.6% and 46.8%, respectively. Acute grade $\geq$2 GI toxicity was significantly less in patients treated with IMRT compared to those treated with 3DCRT (11.0% vs. 19.2%, $p$=.004). However, no significant difference grade $\geq$2 GU toxicities was observed between the 3DCRT and IMRT groups (15.1% vs. 11.0%; $p$=.15). Acute grade $\geq$2 GI and GU toxicities were higher in patients receiving systemic chemotherapy, while paraaortic field irradiation increases only the risk of acute grade $\geq$2 GI toxicity. Estimated 3-year late grade $\geq$3 GI toxicity rates in the 3DCRT- and IMRT-treated patients were 4.6% and 1.9% ($p$= .03), respectively. The patients treated with adjuvant ChT had higher rates of late serious GI complications than those without adjuvant ChT. No significant difference in terms of survival and disease control was observed between the 3DCRT and IMRT treatment groups. No significant factor for LC was found in the multivariate analysis.

**Conclusion:** In this multicentric study involving one of largest patient population, we found that IMRT-treated EC patients showed comparable clinical outcomes but with a lower incidence of GI toxicities compared with those treated with 3DCRT.

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Endometrial carcinoma; three-dimensional conformal radiotherapy; intensity modulated radiotherapy; toxicity; survival

## Background

Endometrial cancer (EC) is the most common gynecological cancer and the fourth most common cancer in the female population [1]. Most EC patients are diagnosed at an early stage, and this disease has a good prognosis with a 5-year survival rate of 80–85% [2]. Postoperative external beam radiotherapy (RT) with or without vaginal cuff intracavitary brachytherapy (BRT) is administered in patients at intermediate to high risk for diminishing locoregional recurrence [3]. However, postoperative adjuvant pelvic RT exposes patients to potential risks, remarkably including gastrointestinal (GI) toxicity.

Although disease control is achieved efficiently with conformal RT, large volumes of the small intestines, rectum, bladder, and femoral heads receive most of the prescribed radiation dose with this technique, leading to increased risks for acute and late GI and genitourinary (GU) toxicities [4,5]. Intensity-modulated RT (IMRT) enables higher conformity than three-dimensional conformal RT (3DCRT), allowing the sculpting of dose away from normal organs. Since the beginning of the 2000s, IMRT tended to replace 3DCRT in gynecologic cancers, and its utilization rate increased from 1.5% in 2001 to 23.2% in 2007 [6].

Dosimetric studies showed that post-operative IMRT demonstrated highly conformal dose to target volumes as well as substantial sparing of surrounding normal tissues in patients with gynecological cancer [7,8]. A recent data in Cochrane Database support the finding that the use of IMRT for pelvic RT was more beneficial than the use of 3DCRT in terms of GI toxicity; however, the available data on the effect of IMRT on local control and survival are limited for tumors located in pelvic area [9]. Several studies demonstrated the feasibility of

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Supplemental data for this article can be accessed here.

IMRT with reduced acute and late GI and GU toxicity rates [10–15]. However, only a few single-center studies involving a limited number of patients have compared the outcomes of 3DCRT and IMRT techniques in terms of survival and toxicity in EC patients [16,17]. There is no prospective study yet comparing the outcomes of 3DCRT and IMRT in the adjuvant treatment of EC patients.

In the absence of available prospective data, in this multi-institutional retrospective study, we sought to analyze the survival and toxicity outcomes of postoperative 3DCRT and IMRT in EC patients. In addition, the prognostic factors affecting the locoregional control (LC) and survival, as well as the predictive factors for acute and late GI and GU toxicities, were investigated.

## Material and methods

### Patient selection

The electronically stored clinical data for 646 patients with International Federation of Gynecology and Obstetrics (FIGO) stage I–III EC treated between April 2007 and August 2019 at four different university hospitals were retrospectively evaluated. All patients were surgically staged with total hysterectomy, bilateral salpingo-oophorectomy, and bilateral pelvic and/or paraaortic lymph node dissection. The FIGO staging system updated in 2009 was used. The inclusion criteria were as follows: patients with pathologically confirmed EC, patients without evidence of distant metastasis at diagnosis, and patients receiving a full course of external RT through 3DCRT or IMRT. The exclusion criteria were as follows: patients without pelvic and/or paraaortic lymph node dissection, patients treated with palliative RT doses, and patients receiving vaginal BRT only.

This study was approved by the Baskent University Institutional Review Board (project no.: KA19/45) and supported by the Baskent University Research Fund. This is an observational study, and the reporting of the study followed the EQUATOR Network's STROBE checklist.

### Treatment protocol

For RT planning, all patients had undergone computed tomography with comfortably full bladder with empty rectum. The clinical target volume (CTV) included the vaginal cuff and upper half of the vagina, regional lymph nodes including common, internal and external iliac lymph nodes, obturator, and the pre-sacral lymph nodes. The planning tumor volume (PTV) was created by adding a 1-cm margin around CTV. Para-aortic field starting from T12–L1 interspace is also added for patients with stage IIIC2 disease. In patients with gross lymphadenopathy, an additional boost dose of 9–16 Gy was added to this area. The organs at risk (OARs) included the rectum, sigmoid, bladder, and femoral heads. The rectum was delineated from anal verge to recto-sigmoid junction [18]. The femoral heads were contoured to the level of ischial tuberosities.

The dose was prescribed to PTV in accordance with International Commission on Radiation Units and Measurements (ICRU) 83 recommendations. The goal of treatment planning is to deliver at least 95% of the prescribed dose to 95% of the PTV, with a maximum dose not exceeding 107%. The 3DCRT was performed with four fields, and IMRT was performed with five to 10 beams with a step and shoot technique or with volumetric modulated arc method using helical tomotherapy. The dose constraints for rectum, sigmoid colon and bladder for patients treated with IMRT were maximal dose 45 Gy, median dose less than 40 Gy, and volume of organ receiving 40 Gy (V40 Gy) less than 40%. The V50 Gy of femoral heads should be less than 10%.

The vaginal vault BRT decision was left to the discretion of the treating physician and institutional protocol. Patients treated at Baskent University and Gelisim Hospital routinely had vaginal cuff BRT after completion of external RT, while other two institutions preferred to add vaginal vault BRT in case of cervical infiltration or positive surgical margin. The BRT dose was prescribed to a plane 5 mm deep to the vaginal mucosa. The equieffective dose in 2 Gy per fraction (EQD2) for 2 $cm^3$ of bladder and rectum is $\leq$90 Gy and $\leq$75 Gy, respectively, which was recommended by the American Brachytherapy Society [19].

The patients were treated according to their respective clinicians' practices and according to the admitting department's policies. The median total external RT dose was 50.4 Gy (range, 40–66.0 Gy), which was delivered daily at a fraction dose of 1.8 Gy (range, 1.8–2.0 Gy). The addition of vaginal cuff BRT was left to the discretion of the treating physician. The median total and fraction BRT doses for those who received vaginal BRT were 15 Gy (range, 12–28 Gy) and 4 Gy (range, 3–7 Gy), respectively.

The chemotherapy regimen commenced within 2–3 weeks of surgery depending on histopathological findings, and it mainly included carboplatin (area under curve of 5 or 6) and paclitaxel (175 $mg/m^2$), which were administered every 21 days. The sequence of adjuvant chemotherapy and RT was determined using the difference between the time to initiation of adjuvant chemotherapy and RT.

### Toxicity analysis

The patients were monitored in every three months for the first two years, every six months until year five, and annually thereafter. Complete physical and gynecologic examinations were periodically performed, as well as routine complete blood cell counts, serum biochemical testing, and chest X-rays. However, biopsies were reserved for suspicious lesions. Treatment-related acute and late GI and GU toxicities were analyzed. The acute toxicities were graded weekly during treatment period by treating physicians. Acute and late toxicities were defined as any event occurring within and beyond 90 days from the start of RT, respectively. Treatment toxicities were assessed according to the 'Common Terminology Criteria for Adverse Events' version 4.0. Late toxicity was

scored according to 'Late effects of normal tissues-Subjective Objective Management Analytic'. To avoid underreporting of toxicities subject to reporting bias, only grade ≥2 acute toxicities and grade ≥3 late GU and GI toxicities are reported.

### Statistical analysis

All statistical analyses were performed using a standard software (SPSS version 20; SPSS Inc. (IBM), Chicago, IL, USA). The primary endpoints were acute and late GI and GU toxicities. The secondary endpoints were disease-free survival (DFS), LC, and overall survival (OS). The time to death or progression was defined as the period from the date of diagnosis to the date of death or to the time when the first clinical or imaging evidence of disease recurrence was obtained. Locoregional relapse is defined as the recurrence located within the RT fields. The Chi-square test or Student's *t*-test was used to analyze the differences between the 3DCRT and IMRT arms in terms of clinical and pathological factors. The LC, OS, and DFS were calculated using the Kaplan–Meier method. Univariate and multivariate analyses were performed using the Cox proportional hazards model. A $p$ value of $<.05$ indicated statistical significance.

## Results

### Patient characteristics

Of the 646 patients analyzed, 381 patients (59%) were treated with IMRT and 265 patients (41%) were treated with 3DCRT. The tumor and patient characteristics in the IMRT and 3DCRT arms were equally distributed (Table 1). The median age in the entire cohort was 61 years (range, 26–88 years). Nearly, two-thirds of the patients had endometrioid adenocarcinoma histology, and the majority (272 patients, 43.4%) had stage III disease. Vaginal cuff BRT was used in 72.4% of the patients, and 43.2% received adjuvant chemotherapy, wherein paclitaxel and carboplatin were administered with a median of four cycles (range, 2–6) to most of the patients (88.7%). The median numbers for dissected and metastatic lymph nodes for the entire group were 36 (range, 5–162 nodes) and 2 (range, 1–61 nodes), respectively.

### Toxicity

No treatment-related deaths were observed in the cohort. The rates for acute GI toxicities of any grade for the entire group were 55.6%. The incidences of grade I, grade II, and

**Table 1.** Patient and tumor characteristics of the entire cohort and of the patients treated with three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT).

| Characteristics | Entire cohort ($n = 646$) (%) | IMRT ($n = 381$) (%) | 3DRT ($n = 265$) (%) | $p$ |
|---|---|---|---|---|
| Age | | | | |
| <60 years | 288 (44.6) | 163 (42.8) | 125 (47.2) | .30 |
| ≥60 years | 358 (55.4) | 218 (57.2) | 140 (52.8) | |
| Histology | | | | |
| Endometrioid | 431 (66.7) | 259 (68.0) | 172 (64.9) | .45 |
| Non-endometrioid | 215 (33.3) | 122 (32.0) | 93 (35.1) | |
| Grade | | | | |
| I | 127 (20.3) | 76 (20.6) | 51 (19.8) | .95 |
| II | 227 (36.3) | 132 (35.8) | 95 (37.0) | |
| III | 272 (43.4) | 161 (43.6) | 111 (43.2) | |
| LVSI | | | | |
| Yes | 329 (56.8) | 197 (56.0) | 132 (58.1) | .61 |
| No | 250 (43.2) | 155 (44.0) | 95 (41.9) | |
| Myometrial invasion | | | | |
| No | 13 (2.1) | 4 (1.1) | 9 (3.5) | .09 |
| <1/2 | 169 (26.7) | 105 (27.9) | 64 (25.1) | |
| ≥1/2 | 450 (71.2) | 268 (71.1) | 2812 (71.4) | |
| Cervical glandular invasion | | | | |
| Yes | 169 (28.5) | 95 (25.7) | 74 (33.2) | .11 |
| No | 424 (71.5) | 275 (74.3) | 149 (66.8) | |
| Cervical stromal invasion | | | | |
| Yes | 275 (44.9) | 168 (45.3) | 107 (44.2) | .42 |
| No | 338 (55.1) | 203 (54.7) | 135 (55.8) | |
| Stage | | | | |
| I–II | 296 (45.8) | 170 (44.6) | 126 (47.5) | .47 |
| III | 350 (54.2) | 211 (55.4) | 139 (52.5) | |
| Lymph node metastasis | | | | |
| Negative | 396 (613) | 230 (60.4) | 166 (62.6) | .64 |
| Pelvic | 170 (26.3) | 100 (26.2) | 70 (26.4) | |
| Pelvic and para-aortic | 80 (12.4) | 51 (13.4) | 29 (10.9) | |
| Radiotherapy field | | | | |
| Pelvic | 562 (87.0) | 328 (86.1) | 234 (88.3) | .48 |
| Pelvic and para-aortic | 84 (13.0) | 53 (13.9) | 31 (11.7) | |
| Vaginal BRT | | | | |
| Yes | 468 (72.4) | 283 (74.3) | 185 (69.8) | .21 |
| No | 178 (27.6) | 98 (25.7) | 80 (30.2) | |
| Adjuvant chemotherapy | | | | |
| Yes | 279 (43.2) | 174 (45.7) | 105 (39.6) | .15 |
| No | 367 (56.8) | 207 (54.3) | 160 (60.4) | |

LVSI: lymphovascular space invasion; BRT: brachytherapy.

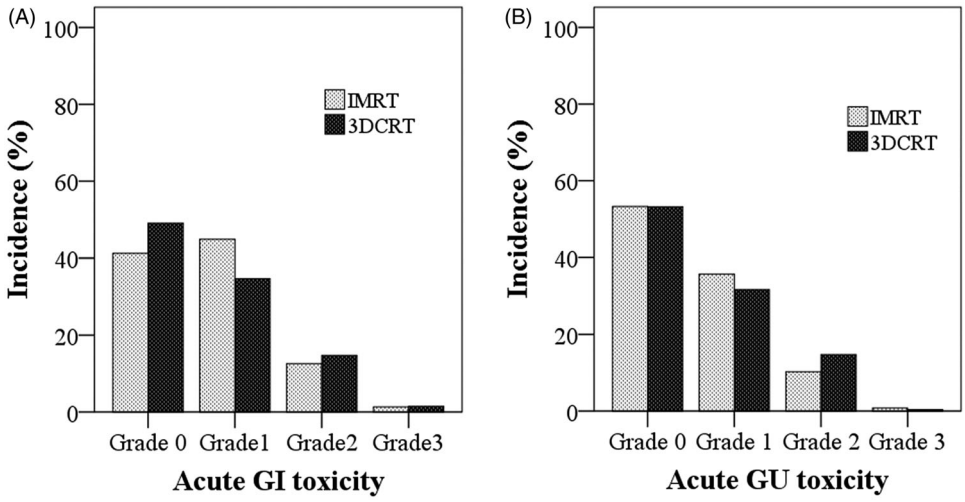


**Figure 1.** Bar graphics demonstrating the incidence of (A) acute gastrointestinal (GI) toxicity and (B) acute genitourinary (GU) toxicity.

**Table 2.** The prevalence of acute grade 2 or higher gastrointestinal (GI) and genitourinary (GU) system, and grade 3 or higher chronic toxicities according to treatment characteristics.

| | Grade ≥2 acute GI toxicity | | Grade ≥2 acute GU toxicity | | Grade ≥3 chronic GI toxicity | |
|---|---|---|---|---|---|---|
| Covariate | *n* (%) | *p* | *n* (%) | *p* | *n* (%) | *p* |
| Age (years) | | | | | | |
| <60 | 39 (13.5) | .65 | 35 (12.2) | .72 | 11 (3.8) | .57 |
| ≥60 | 54 (15.1) | | 47 (13.1) | | 18 (5.0) | |
| Radiotherapy technique | | | | | | |
| 3DCRT | 51 (19.2) | .004 | 40 (15.1) | .15 | 18 (6.8) | .02 |
| IMRT | 42 (11.0) | | 42 (11.0) | | 11 (2.9) | |
| Radiotherapy field | | | | | | |
| Pelvis | 66 (11.7) | <.001 | 73 (13.0) | .73 | 27 (4.8) | .41 |
| Pelvis and paraaortic | 27 (32.1) | | 9 (10.7) | | 2 (2.4) | |
| Vaginal BRT | | | | | | |
| Yes | 63 (13.5) | .43 | 61 (13.0) | .13 | 17 (3.6) | .10 |
| No | 19 (10.7) | | 32 (18.0) | | 12 (6.7) | |
| Systemic chemotherapy | | | | | | |
| Yes | 73 (26.2) | <.001 | 49 (17.6) | .002 | 21 (7.5) | .002 |
| No | 20 (5.4) | | 33 (9.0) | | 8 (2.2) | |

grade III acute GI toxicity were 40.7%, 13.5%, and 1.4%, respectively for entire cohort (Figure 1(A)). A total of 51 (19.2%) and 42 (11.0%) patients in the 3DCRT and IMRT groups, respectively, had acute grade ≥2 GI toxicity ($p = .004$). Grade III acute GI toxicity was observed in four patients treated with IMRT and in five patients treated with 3DCRT. Pelvic and paraaortic field irradiation and the adjuvant ChT significantly increased the acute grade ≥2 GI toxicity rates (Table 2).

For entire cohort, 46.8% of patients had acute GU toxicities of any grade, 34.1% had grade I, 12.1% had grade II, and 0.6% had grade III toxicities (Figure 1(B)). No significant difference in grade ≥2 GU toxicities was observed between the 3DCRT and IMRT groups (15.1% vs. 11.0%; $p = .15$). Grade III acute GU toxicities were observed in three patients treated with IMRT and one patient receiving 3DCRT. Acute grade ≥2 GU toxicity rate was higher in patients receiving adjuvant ChT than in patients without adjuvant ChT. Vaginal BRT had no significant impact on grade ≥2 acute GU toxicity (18.0% vs. 13.0%, $p = .15$).

Late serious grade ≥3 toxicity was observed in 29 patients (4.5%). All serious late complications were associated with the GI system, and no case of grade ≥3 chronic GU was observed. The 3-year late grade ≥3 GI toxicity rates in the 3DCRT- and IMRT-treated patients were 4.6% and 1.9% ($p = .03$), respectively (Figure 2). The patients treated with adjuvant ChT had higher rates of late serious GI complications than those without adjuvant ChT (7.5% vs. 2.2%; $p = .002$).

### *Treatment outcomes*

The median follow-up times for the entire cohort and survivors were 37 months (range, 3–157 months) and 44 months (range, 5–167 months), respectively. The median follow up was longer for the 3DCRT-treated patients (70 months, range 3–157 months) than for those treated with IMRT (29 months, range 3–88 months). At final follow-up, 487 patients (75.4%) were alive (46 [7.1%] with disease) and 159 patients (24.6%) died (133 [20.6%] with disease; 26 [4.0%] due to other causes).

Of the 646 patients analyzed, 187 (28.9%) displayed disease progression; of them, 135 (20.9%) had distant metastases, 22 (3.4%) had locoregional recurrences, and 30 (4.6%)

showed both locoregional and distant metastasis during the last visit. The 3-year LC rate was 91.1%. No significant difference in LC was observed between the IMRT- and 3DCRT-treated patients (3-year LC, 91.6% vs. 90.7%; $p = .91$) (Figure 3(A)). In the univariate analysis, age, histology, tumor grade, lymphovascular invasion, and lymph node status were the significant prognostic factors for LC (Suppl. 1). Meanwhile, myometrial invasion and vaginal cuff BRT had borderline significance for LC. We did not find any statistically significant factor for LC in the multivariate analysis (Suppl. 2).

The 3-year OS and DFS rates were 79.0% and 71.5%, respectively. The 3-year OS rate was 82.0% in the IMRT group and 76.1% in the 3DCRT group ($p = .18$), and the 3-year DFS rates for the IMRT- and 3DCRT-treated patients were 71.2% and 70.9% ($p = .95$), respectively (Figure 3(B,C)). In the univariate analysis, age, histology, tumor grade, lymphovascular invasion, myometrial invasion, cervical stromal invasion, FIGO stage, lymph node status, and adjuvant chemotherapy were the significant prognostic factors for OS and DFS (Suppl. 1). Adjuvant BRT was significantly correlated with improved OS, and it demonstrated a borderline significance for DFS. Advanced age, non-endometrioid histology, ≥1/2 myometrial invasion, presence of cervical stromal invasion, and lymph node metastasis were independent predictors for worse OS and DFS in the multivariable analysis (Suppl. 2).

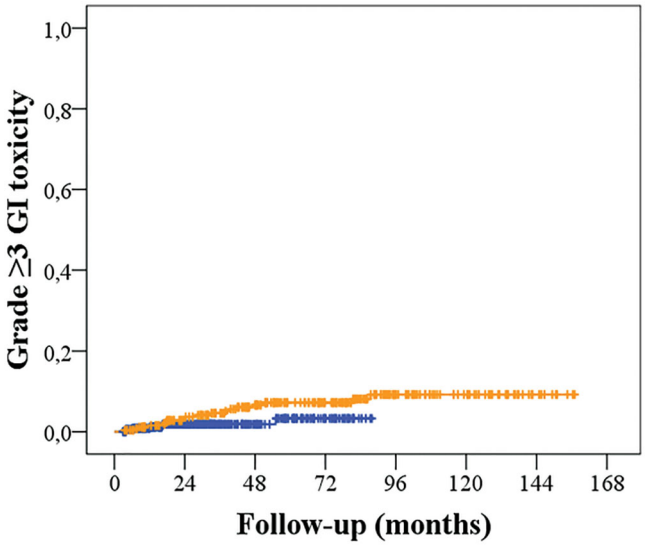


**Figure 2.** The grade 3 or higher gastrointestinal (GI) toxicity incidence in patients treated with IMRT (blue line) and 3DCRT (yellow line).

## Discussion

In this multicentric study involving a large cohort, we found that the IMRT-treated patients had lower incidence of grade ≥2 acute GI toxicities and grade ≥3 late GI toxicities than the 3DCRT-treated patients. Adjuvant ChT significantly increased the incidence of grade ≥2 acute GI and GU toxicities and grade ≥3 late GI toxicities. IMRT was not inferior to 3DCRT in terms of survival and recurrence in the adjuvant treatment of EC patients. No significant factor for predicting LC rates was found in multivariate analysis. Advanced age, non-endometrioid histology, myometrial invasion by more than 50%, presence of cervical stromal invasion, and lymph node metastasis were the independent predictors for worse OS and DFS, consistent with previous findings [3,5,14,20,21].

Treatment toxicities and quality of life are a particular concern for EC patients [22–24]. Several retrospective [7,10,14–17] and prospective studies [13,15] have demonstrated the feasibility of IMRT for EC patients on the basis of favorable acute GI toxicity rates and comparable treatment outcomes. He *et al.* [10], a 1.6% rate of acute grade 3 GI toxicity in 128 EC patients was treated with IMRT. In a series of 47 patients with EC treated by adjuvant RT using IMRT and vaginal cuff BRT, Beriwal et al. [14] reported only one case of grade 3 GI toxicity. Ta et al. [16] demonstrated lower incidence of acute grade 3 GI toxicity in patients treated with IMRT compared to patients treated with 3DCRT (10.6% vs. 5.4%). However, the difference was not significant which may be explained by the sample size and low number of events. Chen et al. [17] found that four (11.1%) patients had grade 3 or greater acute GI toxicity in patients treated with conventional RT, whereas four (6.2%) patients had grade 3 or greater acute GI toxicity in the IMRT group. In a phase II RTOG 0418 trial, 28% of the 43 patients had acute GI toxicities, and only three patients had grade 3 GI toxicity [13]. The phase II RTCMIENDOMETRE trial, 27% of the 49 patients treated with pelvic IMRT developed acute grade ≤2 or GI toxicity, and no grade 3 or higher toxicity was reported [11]. The present study is one of the largest retrospective studies reporting on toxicity related to 3DCRT and IMRT in EC patients, and the results demonstrated that patients treated

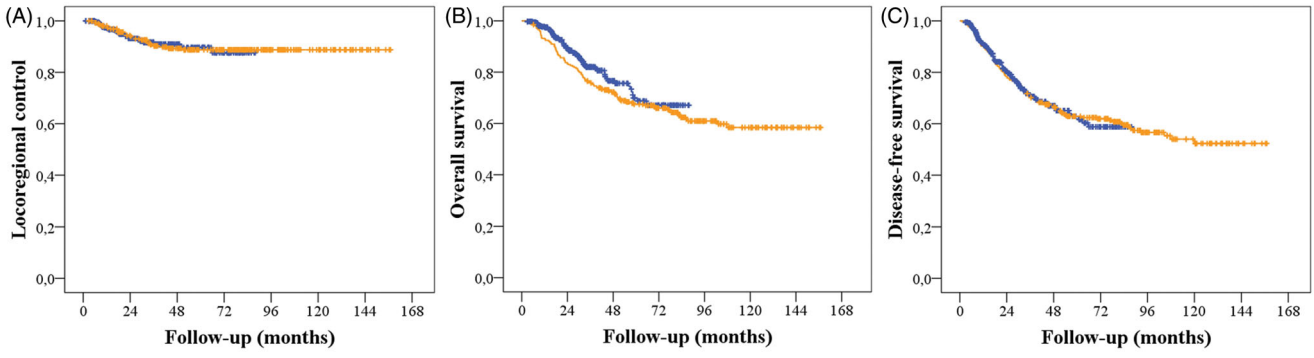


**Figure 3.** Kaplan–Meier's patient survival estimates: (A) locoregional control, (B) overall, and (C) disease-free survival in patients treated with IMRT (blue line) and 3DCRT (yellow line).

with pelvic IMRT had significantly lower incidence of grade ≥2 acute GI toxicity than those treated with 3DCRT. Furthermore, pelvic and paraaortic field irradiation and adjuvant chemotherapy significantly increased the acute grade ≥2 GI toxicity, consistent with the findings reported in the literature [22,25].

While IMRT is evidently beneficial in acute and late GI toxicities compared with 3DCRT owing to the dosimetric advantages of IMRT on intestinal doses, little data are available to verify the effect of IMRT on GU toxicity [11,16]. In the RTCMIENDOMETRE trial, the rate of grade 2 acute GU toxicity was 19% [11]. Ta et al. [16] reported only 2.7% of acute grade 2 GU toxicity. However, factors including age, stage, tumor grade, and treatment with BRT or chemotherapy may affect the risk for GU toxicities [26]. Although previous studies demonstrated the dosimetric advantages of IMRT over 3DCRT in terms of bladder doses [27], we could not find any predictive factor for increased risk of acute grade ≥2 GU toxicity except for adjuvant chemotherapy. Furthermore, although vaginal cuff BRT increases the risk of acute grade ≥2 GU toxicity, the difference reaches close to the level of significance.

In this current study, we demonstrated that IMRT significantly decreases the rate of grade ≥3 chronic GI toxicity, in agreement with Foerster et al. [28] that reported a significant decrease in chronic intestinal symptoms using IMRT. Ta et al. [16] reported only one patient with late GI toxicity of grade 3, and no case of grade ≥2 chronic GU toxicity. He et al. [10] found that 5-year actuarial rates of late grade 3 GI and GU toxicity rates of 3.2% and 0.0%, which were in parallel with our findings. Together with RT technique, we found that systemic chemotherapy increases risk of late grade ≥3 GI toxicity.

With the advent of highly conformal irradiation techniques, the initial dosimetric studies had observed a significant reduction in small bowel dose that may potentially diminish GI toxicities [8,16,27,29]. The 3-year LC rate of 91.1% reported in this large cohort should reassure clinicians that adjuvant IMRT is not inferior in efficacy compared with 3DCRT, and also consistent with previous findings [7,11–17]. Furthermore, recent studies comparing IMRT and 3DCRT did not find any significant difference in survival between these treatment modalities [16,17]. In the current study, despite the different follow-up duration, we did not find any significant difference in survival and LC between the 3DCRT- and IMRT-treated patients. In our multivariate analysis, age, non-endometrioid histology, rate of myometrial invasion, cervical stromal invasion, and lymph node status were the independent factors for both DFS and OS [11,13,16]. By contrast, no significant factor for LC was found in multivariate analysis.

The present study clearly had limitations primarily due to its retrospective nature. First, appreciation of overall toxicity may be confounded because toxicity analysis was performed retrospectively based on patient charts. We could only analyze acute GI and GU, whereas hematological toxicities or pelvic bone insufficiency fractures seen as late complications were not taken into account. Second, different long-term follow-up durations for the two treatment groups may have inherently biased the treatment outcomes and long-term toxicities, even though no differences in survival and LC were noted between the groups. Despite these limitations, our findings showed that the IMRT-treated patients displayed decreased incidence of acute and late GI toxicities compared with the 3DCRT-treated patients. Moreover, our findings are important in demonstrating that pelvic IMRT does not significantly differ with 3DCRT in terms of tumor control and survival. The current study involved a relatively large and a more homogenous study population, which included patients treated with hysterectomy and pelvic and/or paraaortic lymph node dissection.

## Conclusion

In this multicentric study involving one of largest patient populations, we found that IMRT is as effective as 3DCRT in terms of survival and disease control in EC patients. The most notable advantage of IMRT over 3DCRT was the reduction in acute grade ≥2 and late grade ≥3 GI toxicities. Paraaortic field irradiation and adjuvant ChT also increased the incidence of grade ≥2 acute GI and GU toxicities and grade ≥3 late GI toxicities. Although the IMRT-treated EC patients showed comparable clinical outcomes but with a lower incidence of GI toxicities compared with those treated with 3DCRT, a large prospective and randomized study is warranted to compare the efficacy and safety of these two techniques in EC patients.

## Disclosure statement

All authors declare no conflicts of interest related to this article.

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