

The impact of adjuvant treatment with external beam radiotherapy and vaginal brachytherapy on health-related quality of life in patients with early-stage endometrioid endometrial carcinoma — initial results of a prospective study

Adam Kluska^{1,2}, Malgorzata Moszynska-Zielinska³, Leszek Zytko³, Natalia Tracz¹, Bartlomiej Tomasik⁴, Anna Stanislawek³, Jolanta Luniewska-Bury¹, Jacek Fijuth^{2,3}, Leszek Gottwald^{2,3}

¹Department of Brachytherapy, Copernicus Memorial Hospital, Lodz, Poland

²Department of Radiotherapy, Chair of Oncology, Medical University of Lodz, Poland

³Department of Teleradiotherapy, Copernicus Memorial Hospital, Lodz, Poland

⁴Department of Biostatistics and Translational Medicine, Medical University of Lodz, Poland

ABSTRACT

Objectives: Our study evaluates the impact of adjuvant treatment with external beam radiotherapy (EBRT) combined with vaginal high-dose-rate brachytherapy (HDR BT) on health-related quality of life (HRQL) in patients with early-stage endometrioid endometrial carcinoma.

Material and methods: We assessed HRQL of patients based on the EORTC QLQ-C30 questionnaire, with endometrial cancer specific HRQL module — EORTC QLQ-EN24. From March 2019 to April 2020 we enrolled 20 patients with early-stage endometrioid endometrial carcinoma, qualified for adjuvant treatment after hysterectomy. We compared the scores measured with the questionnaires at the beginning and at the end of the treatment.

Results: There was a statistically significant decrease in the mean of global health status/quality of life assessed according to the EORTC QLQ-C30 scale, from 62.25 ± 13.12 at the beginning of the adjuvant radiotherapy to 55.85 ± 14.68 at the end of the treatment ($p = 0.047$). The mean appetite loss score was higher at the onset of the treatment as compared to its value after EBRT, 19.9 ± 27.33 vs 11.6 ± 19.52 ($p = 0.043$). Similarly to the mean constipation score, which was 29.85 ± 30.40 vs 11.6 ± 19.52 ($p = 0.013$). The mean diarrhoea symptom scale increased from 16.55 ± 20.16 to 56.75 ± 36.10 ($p = 0.001$). In the EORTC QLQ-EN24 scales, gastrointestinal symptoms scores were higher at the end of the treatment, (with the mean of 26.45 ± 22.76) as compared to 14.30 ± 16.52 at the beginning of EBRT ($p = 0.003$).

Conclusions: Patients who receive adjuvant radiotherapy have decreased quality of life during the treatment reporting more serious gastrointestinal symptoms. The potential risk of treatment-related toxicity should be taken into account during the treatment planning process in order to minimize the deterioration of HRQL.

Key words: health-related quality of life; endometrial carcinoma; endometrioid; radiotherapy

Ginekologia Polska 2022; 93, 3: 195–202

INTRODUCTION

Endometrial carcinoma is the fourth most common female carcinoma in Poland, with an incidence of 7.3% of all yearly registered malignant neoplasms in women. It causes 3.9% of cancer deaths in women in Poland [1]. Pathologically, endometrial carcinoma is divided into two main histological

and clinical subtypes: type I — endometrioid adenocarcinoma, which is more common and type II — non-endometrioid endometrial carcinoma [2]. Clinicopathological prognostic factors are staging, tumour histology, grading, lymphovascular space invasion (LVSI), depth of myometrial invasion, age and general condition of patients [3, 4]. After surgery,

Corresponding author:

Leszek Gottwald

Department of Radiotherapy, Chair of Oncology, Medical University of Lodz, Poland

e-mail: leszek.gottwald@umed.lodz.pl

Received: 25.05.2020 Accepted: 31.07.2020 Early publication date: 7.05.2021

This article is available in open access under Creative Commons Attribution-Non-Commercial-No Derivatives 4.0 International (CC BY-NC-ND 4.0) license, allowing to download articles and share them with others as long as they credit the authors and the publisher, but without permission to change them in any way or use them commercially.

in patients with type I endometrial carcinoma staged I B with risk factors and at stage II, radiotherapy is the adjuvant treatment of choice [5–8].

In numerous studies in oncological patients, the impact of adjuvant treatment on quality of life has been examined [9, 10]. In tumors localized in the pelvis, long term outcomes of quality of life after adding adjuvant radiotherapy show increase of adverse urinary and bowel symptoms and lower physical and role-physical functioning, even 15 years after treatment [9]. It is postulated that adjuvant treatment with vaginal high dose rate brachytherapy (HDR BT) provides better long-term health-related quality of life (HRQL) than external beam radiation therapy (EBRT) [10].

The HRQL can be measured using validated questionnaires. In patients with endometrial carcinoma, it can be done with the European Organization for Research and Treatment of Cancer (EORTC) core quality of life questionnaire (EORTC QLQ-C30) with Quality of Life Questionnaire-Endometrial Cancer module (EORTC QLQ-EN24) [11–13]. In the EORTC QLQ-C30 questionnaire, response scales ranging from 1 to 4 points for all items except for items 29 and 30 with response scales from 1 to 7 points. In the EORTC QLQ-EN24 module, response scales are used, all ranging from 1 to 4 points [12, 14].

The EORTC QLQ-C30 questionnaire is composed of both multi-item subscales and single-item measures. These in-

clude: five functional subscales (physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning), a global health status/QoL scale, three symptom subscales (fatigue, nausea and vomiting, pain) and six single symptom items (dyspnoea, insomnia, appetite loss, constipation, diarrhoea, financial difficulties). The EORTC QLQ-EN24 module is composed of 5 multi-item scales, from which four are used to assess lymphoedema, urological symptoms, gastrointestinal symptoms and body image. In addition, five single items are used to evaluate pain in the back and pelvis, tingling/numbness, muscular pain, hair loss, taste change [14]. The changes in HRQL parameters in patients with type I endometrial carcinoma is still not well defined.

The aim of our study was to prospectively assess the impact of adjuvant radiotherapy on HRQL in patients with type I endometrial carcinoma staged I–II treated at our institution. In this paper, we present preliminary results of our study.

MATERIAL AND METHODS

From March 2019 to April 2020, we enrolled 20 patients aged from 58 to 85 (mean 68.15 ± 6.43) years old with endometrioid endometrial carcinoma staged I–II in FIGO classification. All patients were after total abdominal hysterectomy (TAH). Lymphadenectomy of the pelvis was performed in 11 patients, seven patients had no lymphadenectomy, and

Table 1. Characteristics of patients in the study group

No.	Age [years]	histology	FIGO stage	Grading [G]	LVSI	TAH	PL — number of resected lymph nodes
1	63	Endometrioid	II	2	–	+	21
2	68	Endometrioid	I B	3	–	+	1
3	69	Endometrioid	I B	2	+	+	33
4	76	Endometrioid	I B	2	+	+	–
5	68	Endometrioid	I A	2	+	+	–
6	76	Endometrioid	I B	2	–	+	–
7	71	Endometrioid	I B	2	–	+	12
8	67	Endometrioid	I B	1	+	+	–
9	59	Endometrioid	I B	2	+	+	13
10	66	Endometrioid	I B	2	+	+	–
11	67	Endometrioid	II	2	–	+	22
12	62	Endometrioid	II	2	+	+	18
13	64	Endometrioid	II	2	+	+	5
14	85	Endometrioid	II	2	–	+	19
15	62	Endometrioid	I B	2	+	+	6
16	58	Endometrioid	I A	2	+	+	–
17	67	Endometrioid	II	1	No data	+	No data
18	72	Endometrioid	I B	2	+	+	10
19	69	Endometrioid	I B	2	No data	+	No data
20	77	Endometrioid	I B	2	No data	+	–

FIGO — The International Federation of Gynecology and Obstetrics; LVSI — lymphovascular space invasion; TAH — total abdominal hysterectomy; PL — pelvic lymphadenectomy

there was a lack of information about lymph node procedure in 2 patients. Detailed data are presented in Table 1. The patients were qualified for adjuvant radiotherapy. The treatment scheme involved the application of EBRT to postoperative bed in the pelvis and regional lymph nodes of a dose up to 44 Gy, fractionated at 2 Gy daily, five fractions a week in each patient. In EBRT, the irradiated area was marked according to the Radiation Therapy Oncology Group (RTOG) recommendations for adjuvant radiotherapy of endometrial carcinoma at stage I–II. It was not dependent on the number of resected histologically negative pelvic lymph nodes. During EBRT, vaginal HDR BT using vaginal stamps was implemented, fractionated at one application of 6 Gy or 7.5 Gy weekly for three weeks up to a total dose of 18 Gy or 22.5 Gy. The characteristics of the study group are presented in Table 2.

We assessed HRQL in the study group using the EORTC QLQ-C30 questionnaire [14] with endometrial cancer-specific HRQL module — EORTC QLQ-EN24 [12]. In both the EORTC QLQ-C30 and EORTC QLQ-EN24 questionnaires, the linear transformation was performed to standardize the raw score, so that scores ranged from 0 to 100; a higher score represented the higher intensity of symptoms. Baseline questionnaires were completed at the beginning of treatment and at the completion of EBRT. We compared scores measured with EORTC QLQ-C30 and EORTC QLQ-EN24 at the beginning and at the end of treatment. The first questionnaire was performed during the first week of treatment, before the first application of VBT, the questionnaire at the end of treatment was performed after the last application of VBT, during last three days of EBRT. Written informed consent to participate in the study was obtained from all patients.

All statistical analyses were performed using Statistica 13.1 software (Statsoft, Tulsa, OK, US). The Wilcoxon signed-rank test was used to compare HRQL scores at the beginning and at the end of treatment. The repeated measures ANOVA was used to compare changes in time of EORTC QLQ-C30 scales: global health status/quality of life, appetite loss, constipation, diarrhoea and EORTC QLQ-EN24 scales: gastrointestinal symptoms, urological symptoms and mean pain in the back and pelvis between subgroups. The „p” values below 0.05 were considered statistically significant. The study was approved by the Bioethics Commission of the Medical University of Lodz No. RNN/98/19/KE.

RESULTS

There were no statistically significant differences in scores of the EORTC QLQ-C30 functioning scales (physical functioning, role functioning, emotional functioning, cognitive functioning, social functioning) between the onset of treatment and at the end of EBRT (Tab. 3). There was a sta-

Table 2. Characteristics of the study group

Age at enrollment [years]	
Median [years]	68.15 ± 6.43
< 60 years	2 (10%)
60–70 years	6 (30%)
> 70 years	12 (60%)
FIGO 2018 Stage	
FIGO IA	2 (10%)
FIGO IB	12 (60%)
FIGO II	6 (30%)
Histological grade	
Grade 1	2 (10%)
Grade 2	17 (85%)
Grade 3	1 (5%)
WHO performance score	
WHO 0	7 (35%)
WHO 1	12 (60%)
WHO 2	1 (5%)
Lymphadenectomy performed	
Yes	11 (55%)
No	7 (35%)
Missing data	2 (10%)
Median number of resected lymph nodes	14.55 ± 9.20
Adjuvant Treatment	
EBRT 44 Gy in 22 fractions	20 (100%)
Vaginal Brachytherapy 3 × 6 Gy	16 (80%)
Vaginal Brachytherapy 3 × 7.5 Gy	4 (20%)
Comorbidity	
Diabetes	6 (30%)
Hypertension	15 (75%)
BMI	
< 30	8 (40%)
> 30	12 (60%)

FIGO — The International Federation of Gynecology and Obstetrics; WHO — World Health Organization; EBRT — external beam radiotherapy

Table 3. Results of QLQ C-30 — functioning scales

EORTC functioning scales	Start of treatment Mean (± SD)	End of treatment Mean (± SD)	p value
Global health status/quality of life	62.25 (± 13.12)	55.85 (± 14.68)	0.047
Physical functioning	69 (± 15.47)	74.55 (± 13.02)	0.136
Role functioning	79.25 (± 22.08)	77.55 (± 14.42)	0.594
Emotional functioning	68.25 (± 20.29)	73.9 (± 17.07)	0.117
Cognitive functioning	77.55 (± 18.06)	81.75 (± 20.82)	0.154
Social functioning	76.75 (± 25.54)	73.25 (± 23.22)	0.423

EORTC — European Organization for Research and Treatment of Cancer; SD — standard deviation

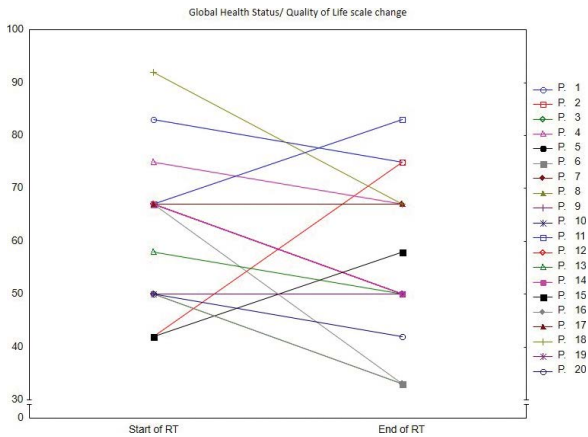


Figure 1. Global health status/Quality of life scale change; RT — radiotherapy

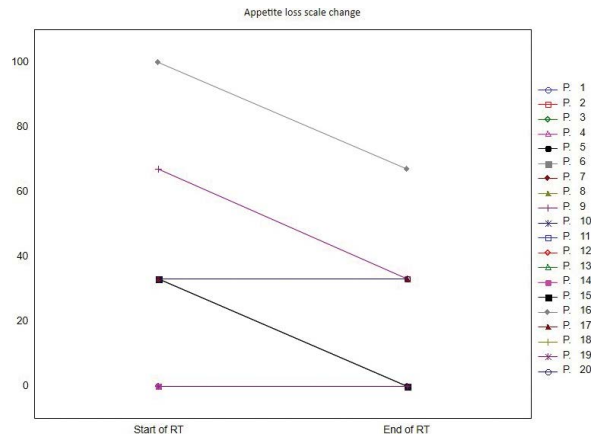


Figure 2. Change of appetite loss scale in time; RT — radiotherapy

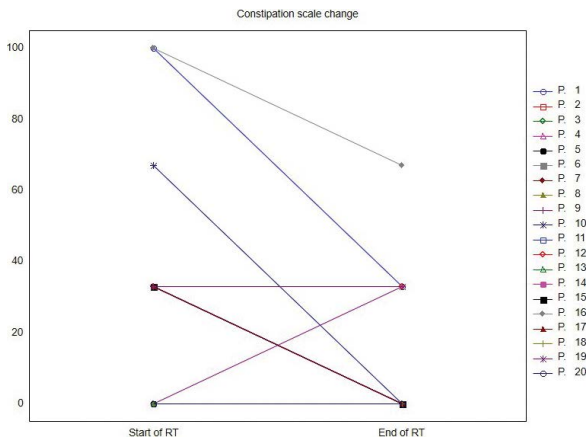


Figure 3. Change of constipation scale in time; RT — radiotherapy

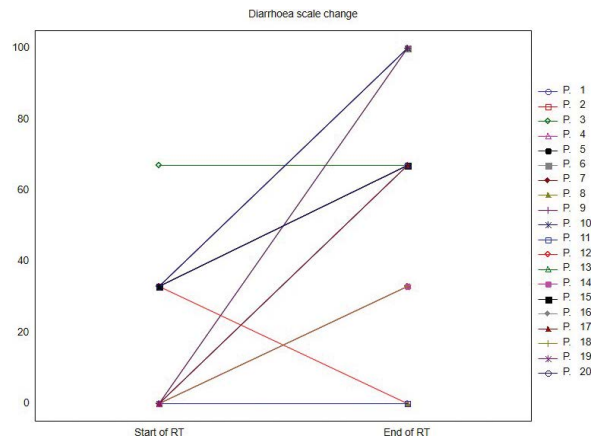


Figure 4. Change of diarrhoea scale in time; RT — radiotherapy

tistically significant decrease in mean of global health status/quality of life assessed in the EORTC QLQ-C30 scale, from 62.25 ± 13.12 at the beginning of adjuvant radiotherapy to 55.85 ± 14.68 at the end of treatment ($p = 0.047$) (Fig. 1).

In the EORTC QLQ-C30 symptoms scales, statistically significant differences between the onset and the end of treatment were found in three scales. Mean appetite loss score was higher at the onset of treatment than compared to its value after EBRT, 19.9 ± 27.33 vs 11.6 ± 19.52 ($p = 0.043$) (Fig. 2), similarly as the mean constipation score, 29.85 ± 30.40 vs 11.6 ± 19.52 ($p = 0.013$) (Fig. 3). Mean diarrhoea symptom scale increased from 16.55 ± 20.16 to 56.75 ± 36.10 ($p = 0.001$) (Fig. 4). There was no statistically significant difference between groups with lymphadenectomy performed and not performed in EORTC QLQ-C30 mean of global health status/quality of life, mean appetite loss scale score, mean constipation scale score and mean diarrhoea symptom scale score. Analysis of comorbidities also showed no differences between subgroups in those scales (Tab. 4). No statistically significant differences were found in other EORTC QLQ-C30 symptoms scales (Tab. 5).

In EORTC QLQ-EN24 symptoms scales, gastrointestinal symptoms scores were higher at the end of treatment, with a mean of 26.45 ± 22.76 than compared to 14.30 ± 16.52 at the beginning of EBRT ($p = 0.003$) (Fig. 5). No statistically significant differences were observed in mean urological symptoms score and mean pain in the back and pelvis score, however, the trend toward higher score was clear. The mean urological symptoms score was higher at the end of treatment 35.80 ± 31.50 compared to 25.05 ± 22.48 at the beginning ($p = 0.076$) (Fig. 6). The mean pain in the back and pelvis score at the beginning and after EBRT combined with HDR BT were 23.20 ± 21.89 and 34.85 ± 25.39 ($p = 0.103$), however subgroup analysis showed differences over time between subgroups with a medical history of diabetes mellitus (DM) and with no history of DM. No differences between patients with or without the medical history of DM were found in gastrointestinal symptoms scale and mean urological symptoms scale. There were no differences between subgroups with or with no medical history of hypertension or previously lymphadenectomy performed (Tab. 6). Lymphoedema symptom scale, poor

Table 4. EORTC QLQ C-30 — differences between groups

EORTC QLQ-C30 scales	Questionnaire timepoints		p value		
	Start of treatment Mean (\pm SD)	End of treatment Mean (\pm SD)	Changes over time	Difference between groups	Difference between groups over time
Global health status/quality of life scale					
Lymphadenectomy performed					
Yes (n = 11)	62.27 (\pm 15.95)	59.82 (\pm 14.86)	0.039	0.402	0.130
No (n = 7)	63.29 (\pm 9.53)	48.86 (\pm 14.21)			
Diabetes mellitus					
Yes (n = 6)	65.5 (\pm 8.24)	58.33 (\pm 17.55)	0.105	0.483	0.889
No (n = 14)	60.86 (\pm 14.78)	54.79 (\pm 13.87)			
Hypertension					
Yes (n = 15)	60.13 (\pm 14.52)	55.53 (\pm 16.35)	0.056	0.430	0.382
No (n = 5)	68.6 (\pm 3.58)	56.8 (\pm 9.31)			
Appetite loss symptoms scale					
Lymphadenectomy performed					
Yes (n = 11)	15.09 (\pm 22.91)	9 (\pm 15.41)	0.014	0.423	0.290
No (n = 7)	28.43 (\pm 35.61)	14.29 (\pm 26.30)			
Diabetes mellitus					
Yes (n = 6)	26.07 (\pm 29.75)	16.57 (\pm 21.64)	0.056	0.092	0.592
No (n=14)	5.5 (\pm 13.47)	0			
Hypertension					
Yes (n = 15)	22.13 (\pm 29.98)	13.27 (\pm 21.05)	0.063	0.518	0.775
No (n = 5)	13.2 (\pm 18.07)	6.6 (\pm 14.76)			
Constipation symptoms scale					
Lymphadenectomy performed					
Yes (n = 11)	30.09 (\pm 27.68)	12 (\pm 16.65)	0.011	0.867	0.945
No (n = 7)	28.57 (\pm 40.55)	9.57 (\pm 25.32)			
Diabetes mellitus					
Yes (n = 6)	27.67 (\pm 25.15)	5.5 (\pm 13.47)	0.007	0.599	0.662
No (n = 14)	30.79 (\pm 33.23)	14.21 (\pm 21.51)			
Hypertension					
Yes (n = 15)	30.93 (\pm 32.03)	13.27 (\pm 21.05)	0.011	0.644	0.864
No (n = 5)	26.6 (\pm 27.97)	6.6 (\pm 14.76)			
Diarrhoea symptom scale					
Lymphadenectomy performed					
Yes (n = 11)	18.09 (\pm 22.90)	51.55 (\pm 34.64)	< 0.001	0.792	0.768
No (n = 7)	18.86 (\pm 17.64)	57.29 (\pm 41.82)			
Diabetes mellitus					
Yes (n = 6)	11 (\pm 17.04)	50 (\pm 54.77)	< 0.001	0.455	0.923
No (n = 14)	18.93 (\pm 21.50)	59.64 (\pm 26.86)			
Hypertension					
Yes (n = 15)	15.47 (\pm 21.29)	55.6 (\pm 37.17)	< 0.001	0.722	0.989
No (n = 5)	19.8 (\pm 18.07)	60.2 (\pm 36.56)			

EORTC — European Organization for Research and Treatment of Cancer; SD — standard deviation

Table 5. Results of QLQ C-30 — symptoms scales

EORTC symptoms scales	Start of treatment Mean (± SD)	End of treatment Mean (± SD)	p value
Fatigue	40.4 (± 22.72)	38.15 (± 20.65)	0.514
Nausea and vomiting	14.2 (± 17.29)	12,55 (± 17.85)	0.784
Pain	22.4 (± 17.22)	28.3 (± 21.70)	0.197
Dyspnoea	19.95(± 25.17)	13.25 (± 19.88)	0.138
Insomnia	45.0 (± 37.97)	41.55 (± 28.48)	0.433
Appetite loss	19.9 (± 27.33)	11.6 (± 19.52)	0.043
Constipation	29.85 (± 30.40)	11.6 (± 19.52)	0.013
Diarrhoea	16.55 (± 20.16)	56.75 (± 36.10)	0.001
Financial difficulties	11.6 (± 19.52)	13.3 (± 22.71)	0.423

EORTC — European Organization for Research and Treatment of Cancer; SD — standard deviation

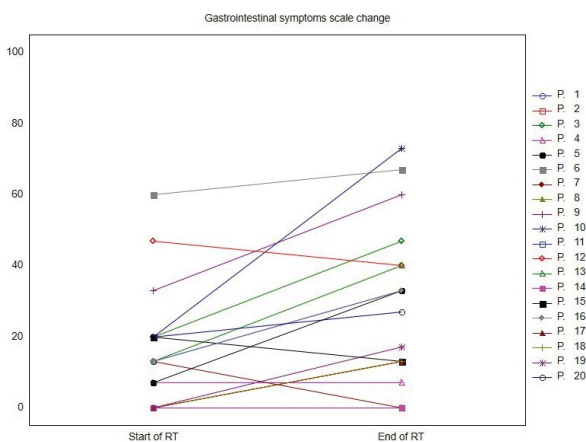


Figure 5. Change of urological symptoms scale in time; RT — radiotherapy

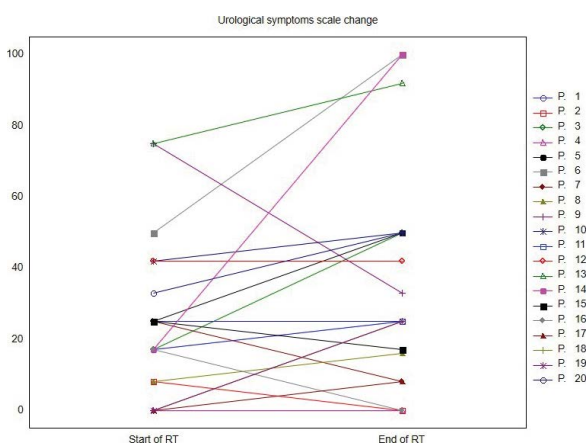


Figure 6. Change of gastrointestinal symptoms scale in time; RT — radiotherapy

body image scale, tingling/numbness scale, hair loss scale, taste change scale showed no differences. The exact data of scales from EORTC QLQ-C30 and EORTC QLQ-EN24 modules are presented in Tables 3–7.

DISCUSSION

When planning EBRT, doses in organs at risk (OARs) are being calculated and approved. Maximal doses to organs and dose-volumetric histograms correlate with the risk of acute and late radiation toxicity [15]. Dose constraints, maximal doses in OARs or maximal volume of OARs that are irradiated up to particular doses, allow to control toxicity at reasonable levels [16]. Even in appropriate planned and carried radiotherapy, symptoms of acute and late radiation toxicity can be observed. Our results show that in endometrial carcinoma patients after surgery, during adjuvant radiotherapy, changes in the HRQL occurred. We found the highest differences in symptoms scales regarding gastrointestinal symptoms and diarrhoea.

The HRQL is measured in many oncological clinical trials comparing the use of adjuvant treatment and its escalation [9, 10, 17]. It allows us to better identify potential factors that worsen and improve HRQL and to prognose and calculate the impact of treatment on HRQL. Appropriate prognosis of changes in the HRQL allows for optimal modification of the treatment in an individual patient [9, 10, 17].

The reports describing the influence the mode of surgery on the HRQL in endometrial carcinoma patients are present in the literature. The authors confirmed that minimally invasive surgery (robotic, laparoscopic) not only shortens postoperative period but also results in a better quality of life of patients compared to open surgery [18].

The HRQL was also reported in many trials regarding adjuvant radiotherapy in endometrial carcinoma patients. The EORTC QLQ-C30 questionnaire to assess the HRQL was used in many well-known trials [10, 17], but the EORTC QLQ-EN24 module for endometrial carcinoma patients is a relatively new tool with only a few trials reported recently [11, 19]. In the PORTEC-1 trial, comparing the use of EBRT with no adjuvant treatment, EBRT was associated with long-term urinary and bowel symptoms and lower physical and role-physical functioning [9]. The results of the PORTEC-2 trial showed that vaginal brachytherapy alone provides better HRQL than EBRT. In the PORTEC-2 for HRQL analysis, like in our study, the EORTC QLQ-C30 questionnaire was used, but no endometrial cancer aimed module was available at that time, so some symptoms scales were used from PR25 (prostate cancer module) and OV28 (ovarian cancer module) [10]. In the PORTEC-3 trial, HRQL was measured with EORTC QLQ-C30 with the cervix carcinoma module with chemotherapy and neuropathy subscales of the ovarian carcinoma module. This analysis of HRQL in that trial showed, that adjuvant chemotherapy given during and after pelvic radiotherapy relates to higher patient-reported symptoms, as well as with decreased level of patient functioning and HRQL compared with radiotherapy alone [17].

Table 6. EORTC QLQ-EN24 — differences between groups

EORTC QLQ-EN24 scales	Questionnaire timepoints		p value		
	Start of treatment Mean (\pm SD)	End of treatment Mean (\pm SD)	Changes over time	Difference between groups	Difference between groups over time
Gastrointestinal symptoms scores					
Lymphadenectomy performed					
Yes (n = 11)	14.45 (\pm 15.19)	23.55 (\pm 21.23)	0.006	0.443	0.394
No (n = 7)	18.14 (\pm 19.84)	34.29 (\pm 27.52)			
Diabetes mellitus					
Yes (n = 6)	14.5 (\pm 23.61)	27.33 (\pm 33.68)	0.006	0.934	0.903
No (n = 14)	14.21 (\pm 13.57)	26.07 (\pm 17.90)			
Hypertension					
Yes (n = 15)	13.67 (\pm 16.40)	24.2 (\pm 22.07)	0.003	0.555	0.440
No (n = 5)	16.2 (\pm 18.67)	33.2 (\pm 26.10)			
Urological symptoms score					
Lymphadenectomy performed					
Yes (n = 11)	29.64 (\pm 24.82)	37.91 (\pm 32)	0.143	0.851	0.736
No (n = 7)	25 (\pm 18.06)	38 (\pm 35.70)			
Diabetes mellitus					
Yes (n = 6)	20.83 (\pm 21.67)	36 (\pm 35.30)	0.085	0.813	0.638
No (n = 14)	26.86 (\pm 23.37)	35.71 (\pm 31.17)			
Hypertension					
Yes (n = 15)	26.13 (\pm 23.53)	37.73 (\pm 34.13)	0.175	0.638	0.811
No (n = 5)	21.8 (\pm 21.07)	30 (\pm 24.12)			
Pain in back and pelvis score					
Lymphadenectomy performed					
Yes (n = 11)	21.09 (\pm 22.45)	39.27 (\pm 29.23)	0.086	0.952	0.297
No (n = 7)	28.43 (\pm 23.05)	33.14 (\pm 19.34)			
Diabetes mellitus					
Yes (n = 6)	33.17 (\pm 21.19)	27.67 (\pm 25.15)	0.238	0.846	0.040
No (n = 14)	18.93 (\pm 21.50)	37.93 (\pm 25.78)			
Hypertension					
Yes (n = 15)	19.8 (\pm 16.73)	35.4 (\pm 26.70)	0.240	0.598	0.228
No (n = 5)	33.4 (\pm 33.50)	33.2 (\pm 23.69)			

EORTC — European Organization for Research and Treatment of Cancer; SD — standard deviation

The significance of HRQL decrease during any treatment proposed to patients is relevant in clinical practice. In our analysis, despite a small group of patients, the impact of combined EBRT and HDR BT on HRQL is clear. What is more, further enrollment to our study may allow us to find dosimetric and clinical risk factors linked to decreases HQRL during adjuvant treatment.

CONCLUSIONS

Patients who receive adjuvant radiotherapy have decreased quality of life during treatment with higher reported gastrointestinal symptoms.

The potential risk of treatment-related toxicity should be considered during the treatment planning process in order to minimize the deterioration of HRQL.

Table 7. Results of EN-24 — symptoms scales

EORTC symptoms scales	Start of treatment Mean (\pm SD)	End of treatment Mean (\pm SD)	p value
Lymphoedema	29.95 (\pm 25.23)	28.20 (\pm 23.58)	0.529
Urological symptoms	25.05 (\pm 22.48)	35.80 (\pm 31.50)	0.076
Gastrointestinal symptoms	14.30 (\pm 16.52)	26.45 (\pm 22.76)	0.003
Poor body image	26.35 (\pm 26.23)	27.3 (\pm 22.41)	0.753
Pain in back and pelvis	23.20 (\pm 21.89)	34.85 (\pm 25.39)	0.103
Tingling/numbness	13.2 (\pm 16.59)	9.9 (\pm 15.51)	0.463
Muscular pain	18.2 (\pm 20.09)	19.85 (\pm 19.87)	0.917
Hair loss	11.65 (\pm 22.40)	16.55 (\pm 20.16)	0.735
Taste change	11.65 (\pm 22.40)	13.25 (\pm 19.88)	0.944

EORTC — European Organization for Research and Treatment of Cancer;
SD — standard deviation

Acknowledgments

None.

Conflict of interests

The authors declare that they have no conflict of interests.

REFERENCES

- Didkowska J, Wojciechowska U, Czaderny K, et al. Cancer in Poland in 2017, 2019, Polish National Cancer Registry. <http://onkologia.org.pl/k/baza-on-line/> (2020-05-25).
- Bokhman JV. Two pathogenetic types of endometrial carcinoma. *Gynecol Oncol.* 1983; 15(1): 10–17, doi: [10.1016/0090-8258\(83\)90111-7](https://doi.org/10.1016/0090-8258(83)90111-7), indexed in Pubmed: [6822361](https://pubmed.ncbi.nlm.nih.gov/6822361/).
- Creasman WT, Morrow CP, Bundy BN, et al. Surgical pathologic spread patterns of endometrial cancer. A gynecologic oncology group study. *Cancer.* 1987; 60(Suppl 8): 2035–2041, doi: [10.1002/1097-0142\(19901015\)60:8+<2035::aid-cncr2820601515>3.0.co;2-8](https://doi.org/10.1002/1097-0142(19901015)60:8+<2035::aid-cncr2820601515>3.0.co;2-8), indexed in Pubmed: [3652025](https://pubmed.ncbi.nlm.nih.gov/3652025/).
- Gadducci A, Cavazzana A, Cosio S, et al. Lymph-vascular space involvement and outer one-third myometrial invasion are strong predictors of distant haematogeneous failures in patients with stage I-II endometrioid-type endometrial cancer. *Anticancer Res.* 2009; 29(5): 1715–1720, indexed in Pubmed: [19443392](https://pubmed.ncbi.nlm.nih.gov/19443392/).
- Colombo N, Creutzberg C, Amant F, et al. ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: diagnosis, treatment and follow-up. *Ann Oncol.* 2016; 27(1): 16–41, doi: [10.1093/annonc/mdv484](https://doi.org/10.1093/annonc/mdv484), indexed in Pubmed: [26634381](https://pubmed.ncbi.nlm.nih.gov/26634381/).
- Creutzberg C, Putten Wv, Koper P, et al. PORTEC Study Group. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomised trial. *The Lancet.* 2000; 355(9213): 1404–1411, doi: [10.1016/s0140-6736\(00\)02139-5](https://doi.org/10.1016/s0140-6736(00)02139-5).
- Kong A, Johnson N, Kitchener HC, et al. Adjuvant radiotherapy for stage I endometrial cancer: an updated Cochrane systematic review and meta-analysis. *J Natl Cancer Inst.* 2012; 104(21): 1625–1634, doi: [10.1093/jnci/djs374](https://doi.org/10.1093/jnci/djs374), indexed in Pubmed: [22962693](https://pubmed.ncbi.nlm.nih.gov/22962693/).
- Wortman BG, Creutzberg CL, Putter H, et al. PORTEC Study Group. Ten-year results of the PORTEC-2 trial for high-intermediate risk endometrial carcinoma: improving patient selection for adjuvant therapy. *Br J Cancer.* 2018; 119(9): 1067–1074, doi: [10.1038/s41416-018-0310-8](https://doi.org/10.1038/s41416-018-0310-8), indexed in Pubmed: [30356126](https://pubmed.ncbi.nlm.nih.gov/30356126/).
- Nout RA, van de Poll-Franse LV, Lybeert MLM, et al. Long-term outcome and quality of life of patients with endometrial carcinoma treated with or without pelvic radiotherapy in the post operative radiation therapy in endometrial carcinoma 1 (PORTEC-1) trial. *J Clin Oncol.* 2011; 29(13): 1692–1700, doi: [10.1200/JCO.2010.32.4590](https://doi.org/10.1200/JCO.2010.32.4590), indexed in Pubmed: [21444867](https://pubmed.ncbi.nlm.nih.gov/21444867/).
- Nout RA, Putter H, Jürgenliemk-Schulz IM, et al. Five-year quality of life of endometrial cancer patients treated in the randomised Post Operative Radiation Therapy in Endometrial Cancer (PORTEC-2) trial and comparison with norm data. *Eur J Cancer.* 2012; 48(11): 1638–1648, doi: [10.1016/j.ejca.2011.11.014](https://doi.org/10.1016/j.ejca.2011.11.014), indexed in Pubmed: [22176868](https://pubmed.ncbi.nlm.nih.gov/22176868/).
- Stukan M, Zalewski K, Mardas M, et al. Independent psychometric validation of European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Endometrial Cancer Module (EORTC QLQ-EN24). *Eur J Cancer Care (Engl).* 2018; 27(1), doi: [10.1111/ecc.12639](https://doi.org/10.1111/ecc.12639), indexed in Pubmed: [28058740](https://pubmed.ncbi.nlm.nih.gov/28058740/).
- Greimel E, Nordin A, Lanceley A, et al. EORTC Quality of Life Group. Psychometric validation of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Endometrial Cancer Module (EORTC QLQ-EN24). *Eur J Cancer.* 2011; 47(2): 183–190, doi: [10.1016/j.ejca.2010.08.014](https://doi.org/10.1016/j.ejca.2010.08.014), indexed in Pubmed: [20851597](https://pubmed.ncbi.nlm.nih.gov/20851597/).
- Leppert W, Gottwald L, Forycka M. Clinical practice recommendations for quality of life assessment in patients with gynecological cancer. *Prz Menopauzalny.* 2015; 14(4): 271–282, doi: [10.5114/pm.2015.56539](https://doi.org/10.5114/pm.2015.56539), indexed in Pubmed: [26848300](https://pubmed.ncbi.nlm.nih.gov/26848300/).
- Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst.* 1993; 85(5): 365–376, doi: [10.1093/jnci/85.5.365](https://doi.org/10.1093/jnci/85.5.365), indexed in Pubmed: [8433390](https://pubmed.ncbi.nlm.nih.gov/8433390/).
- Stanic S, Mayadev JS. Tolerance of the small bowel to therapeutic irradiation: a focus on late toxicity in patients receiving para-aortic nodal irradiation for gynecologic malignancies. *Int J Gynecol Cancer.* 2013; 23(4): 592–597, doi: [10.1097/IGC.0b013e318286aa68](https://doi.org/10.1097/IGC.0b013e318286aa68), indexed in Pubmed: [23615570](https://pubmed.ncbi.nlm.nih.gov/23615570/).
- Bentzen SM, Constine LS, Deasy JO, et al. Quantitative Analyses of Normal Tissue Effects in the Clinic (QUANTEC): an introduction to the scientific issues. *Int J Radiat Oncol Biol Phys.* 2010; 76(Suppl 3): S3–S9, doi: [10.1016/j.ijrobp.2009.09.040](https://doi.org/10.1016/j.ijrobp.2009.09.040), indexed in Pubmed: [20171515](https://pubmed.ncbi.nlm.nih.gov/20171515/).
- de Boer SM, Powell ME, Mileskin L, et al. PORTEC study group. Toxicity and quality of life after adjuvant chemoradiotherapy versus radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): an open-label, multicentre, randomised, phase 3 trial. *Lancet Oncol.* 2016; 17(8): 1114–1126, doi: [10.1016/S1470-2045\(16\)30120-6](https://doi.org/10.1016/S1470-2045(16)30120-6), indexed in Pubmed: [27397040](https://pubmed.ncbi.nlm.nih.gov/27397040/).
- Ferguson SE, Panzarella T, Lau S, et al. Prospective cohort study comparing quality of life and sexual health outcomes between women undergoing robotic, laparoscopic and open surgery for endometrial cancer. *Gynecol Oncol.* 2018; 149(3): 476–483, doi: [10.1016/j.ygyno.2018.04.558](https://doi.org/10.1016/j.ygyno.2018.04.558), indexed in Pubmed: [29681461](https://pubmed.ncbi.nlm.nih.gov/29681461/).
- Papathemelis T, Scharl S, Hipp M, et al. Quality of life and oncological outcome in endometrial cancer patients after vaginal brachytherapy: comparison of two dosing schemes. *Arch Gynecol Obstet.* 2019; 299(2): 507–514, doi: [10.1007/s00404-018-4951-x](https://doi.org/10.1007/s00404-018-4951-x), indexed in Pubmed: [30357499](https://pubmed.ncbi.nlm.nih.gov/30357499/).