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Prospective analysis of the impact of adjuvant treatment with external beam radiation therapy and vaginal brachytherapy on health-related quality of life in patients with early-stage endometrioid endometrial carcinoma

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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: From March 2019 to February 2021, 60 patients were enrolled with early stage endometrioid endometrial carcinoma, and qualified to adjuvant treatment after hysterectomy. HRQL was assessed using the EORTC QLQ-C30 questionnaire, with the endometrial cancer-specific HRQL module EORTC QLQ-EN24. Questionnaires were completed in four timepoints during adjuvant radiotherapy.

Results: A significant decrease in mean global health status / quality of life ($p < 0.001$) and role functioning ($p = 0.028$) was noted, as assessed in EORTC QLQ-C30 scale. Among the EORTC QLQ-C30 symptoms scales, significant differences were noted in the fatigue scale ($p = 0.003$), pain scale ($p = 0.001$), constipation scale ($p < 0.001$) and diarrhea scale ($p < 0.001$) over time. The EORTC QRQ-EN24 analysis showed significant deterioration in the urological symptoms scale ($p < 0.001$), gastrointestinal symptoms scale ($p < 0.001$) and in the mean pain in back and pelvis scale ($p = 0.003$).

Conclusions: Adjuvant radiotherapy in patients with early-stage endometrioid endometrial cancer after hysterectomy is associated with worse quality of life, especially due to the toxicity of the treatment in relation to the gastrointestinal tract and urinary system.

Key words: endometrial carcinoma; radiotherapy; brachytherapy; quality of life

INTRODUCTION

In Poland, endometrial carcinoma is the fourth most common malignancy in women, with more than 6000 of new cases per year [1]. The most common location of gynaecological malignant neoplasms is the body of the uterus. Endometrial carcinoma is responsible for 95 % of these cases [2]. Pathologically, endometrial carcinoma is divided into two main histological and clinical subtypes: type I — endometrioid adenocarcinoma (80-90%) and type II — non-endometrioid endometrial carcinoma (10–20 % of cases) [3–5].

The main method of treating endometrial tumours is surgery [6]. After surgery, in patients with type I endometrial carcinoma staged I B with risk factors and at stage II, radiotherapy is the adjuvant treatment of choice [7]. Depth of myometrial invasion, cervical involvement, grading of the tumour, lymphovascular space invasion (LVSI), advanced age and general condition of the patient are clinicopathological risk factors [7, 8].

Health-related quality of life (HRQL) is a subjective assessment of the impact of both disease and treatment on the physical, psychological and social functioning of patients [9], and serves as one of the most important endpoints in contemporary Oncology. It is of crucial importance to prevent any worsening of HRQL in patients during radical treatment and to maintain the level of HRQL in those being given palliative care [9, 10].

In line with international recommendations, HRQL can be evaluated using validated and standardized questionnaires [11]. The most commonly-used tool for assessing general HRQL is European Organization for Research and Treatment of Cancer core questionnaire EORTC QLQ-C30, which is composed of five functional subscales, a global health

status/quality of life (QL) scale, three symptom subscales and six single symptom items [12]. As an addition to the core questionnaire, modules for particular localizations of cancer are also in use. For endometrial cancer it is the EN-24 module, introduced in 2010, comprising five multi-item scales and five single-item scales [13]. This module has only been used in a few studies so far; as such its results in patients with endometrioid endometrial carcinoma during adjuvant irradiation are still not well known [14, 15].

Objectives

The aim of our study was to prospectively assess the impact of adjuvant treatment with combined vaginal high dose-rate brachytherapy (HDR-BT) and external beam radiotherapy (EBRT) on HRQL in patients at stage I and II of type I endometrial carcinoma.

MATERIAL AND METHODS

Sixty patients aged 42 to 85 years (median 67.00 ± 9.00) with endometrioid endometrial carcinoma staged I–II in The International Federation of Gynecology and Obstetrics (FIGO) classification after surgery were enrolled from March 2019 to February 2021. Total abdominal hysterectomy (TAH) was performed in all patients, and lymphadenectomy of the pelvis in 35 (58.33%). The patients were qualified for adjuvant radiotherapy (EBRT + vaginal HDR-BT) by multidisciplinary team, based on risk factors: FIGO stage, G3 tumor grade or presence of LVSI in histopathological report. The treatment scheme involved the application of EBRT to the postoperative bed in the pelvis and regional lymph nodes: the treatment intensity was up to 44 Gy, fractionated at 2 Gy daily, five fractions a week (Monday to Friday) 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. One patient finished EBRT at the dose of 32 Gy due to a severe course of coronavirus disease (COVID-19). 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 ($n = 48$) or 22.5 Gy ($n = 12$). The upper 3 cm of the vagina was treated with dose prescribed to 5 mm from the applicator surface. None of the patients received chemotherapy. The full characteristics of the study group are presented in Table 1.

HRQL was assessed in the study group using the EORTC QLQ-C30 questionnaire [14] with the EORTC QLQ-EN24 endometrial cancer-specific HRQL module [15]. The results of

both the EORTC QLQ-C30 and EORTC QLQ-EN24 questionnaires were subjected to linear transformation to standardize the raw score, so that scores ranged from 0 to 100; a higher score represented a higher intensity of symptoms. Baseline questionnaires were completed during the first week of treatment, before the first application of HDR-BT (time point 1), during the second (time point 2) and third week of treatment (time point 3) and after the final application of HDR-BT, during last three days of EBRT (time point 4). In all four time points HADS (Hospital anxiety and depression scale) and PSS-10 (Perceived stress scale) were also completed as well. The scores were used to evaluate psychological performance. 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 HRQL scores between all four timepoints for the whole study group, and to compare differences between subgroups. A p-value below 0.05 was considered statistically significant.

The study was approved by the Bioethics Commission of the Medical University of Lodz No. RNN/98/19/KE.

RESULTS

In the study group, among the EORTC QLQ-C30 functional scales, statistically significant changes over time were observed in mean functioning score (RF) and global health status/quality of life (QL). The mean values in the role functional scale were as follows: 76.80 ± 22.93 at the time point 1, 79.05 ± 23.25 and 79.43 ± 21.97 during radiotherapy and 73.50 ± 20.79 at the time point 4 ($p = 0.028$) (Fig. 1A). The mean values of the QL scale in time points from 1 to 4 were: 63.68 ± 17.46 , 60.52 ± 17.24 , 56.27 ± 16.99 , 56.40 ± 17.29 , respectively ($p < 0.001$) (Fig. 1B). No statistically significant changes were noted in other functional scales: physical functioning (PF) ($p = 0.335$), emotional functioning (EF) ($p = 0.054$), cognitive functioning (CF) ($p = 0.319$) and social functioning (SF) ($p = 0.863$) (Tab. 2).

On the other hand, statistically significant differences were noted in the fatigue scale (FA), pain scale (PA), constipation scale (CO) and diarrhea scale (DI) over time. The mean values of the FA scale at time points 1 to 4 were 33.53 ± 20.32 , 32.02 ± 18.89 , 36.35 ± 21.11 and 39.70 ± 22.29 , respectively ($p = 0.003$) (Fig. 1C). The mean values of the PA scale at time points 1 to 4 were 17.75 ± 20.02 , 18.27 ± 18.73 , 23.32 ± 22.79 and 27.17 ± 23.33 , respectively ($p = 0.001$) (Fig. 1D). The mean values of the CO scale at time points 1 to 4 were

24.35 ± 28.05, 13.85 ± 22.39, 12.18 ± 21.24 and 13.30 ± 22.32, respectively ($p < 0.001$) (Fig. 1E). The mean values of the DI scale at time points 1 to 4 were 14.35 ± 21.52, 29.37 ± 26.18, 42.77 ± 32.64 and 50.53 ± 33.44, respectively ($p < 0.001$) (Fig. 1F). No statistically significant changes were observed in the other EORTC QLQ-C30 scales: nausea and vomiting scale (NV) ($p = 0.961$), dyspnea scale (DY) ($p = 0.196$), insomnia scale (IN) ($p = 0.287$), appetite loss scale (AL) ($p = 0.080$), financial impact scale (FI) ($p = 0.580$). The results of the EORTC QLQ-C30 are presented in more detail in Table 2.

The analysis of the EORTC QLQ-EN24 module showed significant changes from time point 1 to 4 in the urological symptoms scale (UR), gastrointestinal symptoms scale (GI) and in the mean pain in back and pelvis scale (BP). The mean values from points 1 to 4 were 23.05 ± 23.95, 21.75 ± 21.79, 25.97 ± 24.21 and 33.60 ± 28.14, respectively, in the urological symptoms scale (UR) ($p < 0.001$) (Fig. 2A), 14.43 ± 14.95, 17.82 ± 18.23, 20.32 ± 19.58 and 26.32 ± 20.25, respectively, in the gastrointestinal symptoms scale (GI) ($p < 0.001$) (Fig. 2B) and 25.97 ± 23.04, 26.53 ± 23.63, 28.73 ± 25.66 and 36.00 ± 27.74, respectively, in the mean pain in back and pelvis scale ($p = 0.003$) (Fig. 2C). No significant differences were noted in the lymphedema scale (LY) ($p = 0.598$), poor body image scale (PBI) ($p = 0.292$), tingling/numbness scale (TN) ($p = 0.252$), muscle pain scale (MP) ($p = 0.365$), hair loss scale (HL) ($p = 0.238$), taste change (TC) ($p = 0.171$). The exact data are presented in Table 3.

Subgroup comparison

In the NV scale, significant differences over time, from time point 1 to 4, were noted between the group with lymphadenectomy ($n = 35$) and without lymphadenectomy ($n = 22$). The mean values were 12.91 ± 20.23, 10.51 ± 18.07, 9.57 ± 18.65 and 11.06 ± 21.42 in the group with lymphadenectomy and 6.86 ± 13.29, 10.64 ± 15.00, 12.14 ± 15.52 and 10.64 ± 13.10 in the group without lymphadenectomy ($p = 0.047$) (Fig. 3A). Another significant difference between the two groups was observed in the TC scale of EORTC QLQ-EN24 module: 10.43 ± 22.50, 6.63 ± 15.71, 8.51 ± 16.78 and 9.46 ± 17.21 in the group with lymphadenectomy and 10.55 ± 18.88, 19.68 ± 26.62, 25.77 ± 32.50 and 21.14 ± 31.77 in the group without lymphadenectomy ($p = 0.002$) (Fig. 3B). No other statistically significant differences were noted between groups according to the lymphadenectomy procedure given in the EORTC QLQ-C30 and EN-24 questionnaires.

In the NV and PA scales of the EORTC QLQ-C30 questionnaire, significant differences from time points 1 to 4 were found between the group with diabetes ($n = 14$) and without diabetes ($n = 46$). Patients with diabetes had lower scores of NV scales with 1.21 ±

4.54, 3.64 ± 7.24 , 9.57 ± 12.56 and 8.43 ± 10.88 , respectively, when compared to patients without diabetes: 12.74 ± 19.29 , 11.98 ± 18.08 , 10.91 ± 18.32 and 11.30 ± 19.91 , respectively ($p = 0.012$) (Fig. 3C). At the beginning of treatment, patients with diabetes had a lower PA score (13.00 ± 16.09) compared to those without (19.20 ± 21.02). It rose more rapidly in the group with diabetes than the group without diabetes, with scores of 13.00 ± 16.09 at time point 2, 26.21 ± 22.42 at time point 3 and 32.21 ± 24.01 at the end of treatment; the respective scores were 19.87 ± 19.34 , 22.43 ± 23.08 and 25.63 ± 23.17 in the group without diabetes ($p = 0.041$) (Fig. 3D). No other statistically significant differences were noted between these groups in the EORTC QLQ-C30 and EN-24 questionnaires.

The patients were divided into two groups according to body mass index (BMI): one group with BMI equal to or lower than 30 ($n = 29$) and BMI higher than 30 ($n = 31$). The only significant difference between the groups was found in the SF scale: the BMI ≤ 30 group had a lower score at the onset of treatment (69.62 ± 28.14), than the BMI > 30 group (76.94 ± 24.51). During treatment, the score rose in the first group with scores of 71.90 ± 26.41 at time point 2 and 76.48 ± 23.74 at time point 3 and lowered to 70.69 ± 26.57 at the end of treatment while in the second group it was 74.19 ± 23.48 , 69.35 ± 24.76 and 72.58 ± 25.23 , respectively ($p = 0.007$) (Fig. 3E). No other differences were observed between these two groups in the EORTC QLQ-C30 or EN-24 questionnaires.

DISCUSSION

The present study has several strengths. It used a prospective design, all the measurements were performed by the same examiner, and HRQL was assessed at predetermined four time points related to the treatment. In addition, the cohort comprised a homogeneous group of patients at stages I-II of endometrioid endometrial carcinoma, and all patients were treated according to the same protocol by a single medical team.

When planning adjuvant radiotherapy, both doses in target volumes and in organs at risk are considered and are guided by treatment protocol constraints. Maximal doses in the organs at risk, and the size of the irradiated volume correlate with a risk of acute and chronic toxicity, that mainly occur in gastrointestinal system and urinary tract [16]. Most common acute toxicity are diarrhea and frequent urination, whereas most typical late side effects from GI system are bowel inflammation, bleeding, fistulas and from urinary tract cystitis and incontinence [16–18]. Organs at risk dose constraints allow toxicity to be reduced to acceptable levels; however, even if all constraints are fulfilled, and treatment is conducted optimally, side effects can occur [17, 18]. Literature data suggests that dose escalation in

patients with endometrial carcinoma treated with adjuvant radiotherapy relates to higher risk of toxicity [19].

Despite the improvement of diagnostics and oncological treatment, a diagnosis of carcinoma arising from the female genital tract is a stressful situation influencing the quality of life of the patient [12, 20, 21]. Many studies have examined the changes in HRQL during adjuvant treatment in patients diagnosed with endometrial carcinoma [17, 20, 22]. However, these data are difficult to compare due to differences between therapies and the tools used to measure HRQL.

Although previous clinical trials in patients with endometrial carcinoma have examined the HRQL during treatment using EORTC questionnaires, none have used the EORTC QLQ-EN24 module for endometrial carcinoma employed in the present study. 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 [22]. Our findings confirm that changes in the quality of life occur during adjuvant radiotherapy in patients with type I endometrial carcinoma. Our results indicate a reduction in overall quality of life and role functioning, and higher values in the fatigue, pain, constipation and diarrhea symptom scales in the EORTC QLQ-C30 questionnaire. It also noted higher values in urological, gastrointestinal and pelvic pain symptom scales, measured by the EORTC QLQ-EN24 module.

The HRQL of patients with endometrial carcinoma was also studied in the PORTEC-2 and the PORTEC-3 trials. In the PORTEC-2, vaginal brachytherapy was compared with EBRT, and quality of life was assessed using EORTC QLQ-C30 with PR 25 (prostate cancer) and OV 28 (ovarian cancer) modules, as no EN-24 module was present at the time of trial. The results of the PORTEC-2 trial showed that vaginal brachytherapy alone provides better HRQL than EBRT [17]. In the PORTEC-3 trial, the EORTC QLQ-C30 with the cervix carcinoma module with chemotherapy and neuropathy subscales of the ovarian carcinoma module were used to assess the HRQL. Adjuvant chemotherapy given during and after pelvic radiotherapy related to higher patient-reported symptoms, as well as with decreased level of patient functioning and HRQL, compared with radiotherapy alone [18]. In our group, all patients were treated both with EBRT and HDR-BT and chemotherapy was not given to the patients, so no comparison was possible.

Previous analyses of the HRQL in patients with type I endometrial carcinoma based on subgroups according to selected clinical parameters have yielded varying results. In the present study, the subgroup analysis showed differences in the EORTC QLQ-C30

questionnaire concerning BMI, lymphadenectomy status and the presence of diabetes: patients with diabetes had higher scores in the PA and the NV scales. However, Jareczek-Fossa et al. reported a lack of any relationship between toxicity of radiotherapy and diabetes [19]. In the present study, BMI higher than 30 related to worsening in the SF scale, as also noted by Nock et al. [23]. Additionally, our results indicate that pelvic lymphadenectomy was associated with differences in the NV and the TC scales. However, Foerster et al did not report any correlation between lymphadenectomy and the HRQL in endometrial carcinoma patients [24].

One limitation of our study was the small number of patients in the study group; therefore, any generalisation of our results into the whole population must be taken with care. Further prospective studies in larger populations are required to determine the impact of adjuvant radiation therapy (EBRT) on HRQL in patients with early-stage endometrioid endometrial carcinoma. They should also aim to identify the associated with poorer and improved HRQL in endometrial carcinoma patients to enable optimal individualization of treatment.

CONCLUSIONS

Adjuvant radiotherapy in patients with early-stage endometrioid endometrial cancer after hysterectomy is associated with poorer quality of life; this is mainly associated with the toxicity of the treatment in relation to gastrointestinal tract and urinary system.

Extended surgery, the presence diabetes and high BMI affect quality of life in patients with early-stage endometrioid endometrial cancer during adjuvant radiotherapy.

Conflict of interest

All authors declare no conflict of interest.

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Table 1. Characteristics of patients in the study group

Age of patients [years]	
Median [years ± InterQuartile Range (IQR)]	67 (IQR 61–70)

< 60 years old	10 (17%)
60–70 years old	35 (58%)
> 70 years old	15 (25%)
FIGO 2018 Stage	
FIGO IA	6 (10%)
FIGO IB	38 (63%)
FIGO II	16 (27%)
Histological grading	
Grade 1	8 (13%)
Grade 2	45 (75%)
Grade 3	7 (12%)
Overall Performance WHO	
WHO 0	28 (47%)
WHO 1	30 (50%)
WHO 2	2 (3%)
Lymphadenectomy performed	
Yes	35 (58%)
No	22 (37%)
Unknown	3 (5 %)
Median number of resected lymph nodes (n = 31)	11 (IQR 8–21)
Adjuvant Treatment	
EBRT 44 Gy in 22 fractions	59 (98%)
EBRT 32 Gy in 16 fractions	1 (2%)
VBT 3 × 6 Gy	48 (80%)
VBT 3 × 7.5 Gy	12 (20%)
Comorbidity	
Diabetes	2 (3%)
Hypertension	25 (42%)
Both — diabetes and hypertension	12 (20%)
None	21 (35%)
BMI	

< 30	28 (47%)
30–35	24 (40%)
> 35	8 (13%)
Adjuvant treatment mode	
Outpatient	48 (80%)
Inpatient	12 (20%)

IQR — ??; FIGO — The International Federation of Gynecology and Obstetrics; WHO — World Health Organization; EBRT — external beam radiotherapy; **VBT** — ???; BMI — body mass index

Table 2. Results of EORTC QLQ-C30 scale in all timepoints

EORTC QLQ-C30	Timepoint				p
	I	II	III	IV	Change over time
Global health status/quality of life scale (QL)	63.68 (± 17.46)	60.52 (± 17.24)	56.27 (± 16.99)	56.40 (± 17.29)	p < 0.001
Physical functioning scale (PF)	76.58 (± 15.88)	75.82 (± 17.34)	74.82 (± 18.02)	73.82 (± 17.63)	p = 0.335
Role functioning scale (RF)	76.80 (± 22.93)	79.05 (± 23.25)	79.43 (± 21.97)	73.50 (± 20.79)	p = 0.028
Emotional functioning scale (EF)	69.17 (± 19.16)	73.95 (± 19.06)	69.40 (± 21.73)	69.18 (± 19.04)	p = 0.054
Cognitive functioning scale (CF)	83.20 (± 20.45)	85.65 (± 20.23)	84.00 (± 20.81)	82.63 (± 21.58)	p = 0.319
Social functioning scale (SF)	73.40 (± 26.36)	73.08 (± 24.75)	72.80 (± 24.33)	71.67 (± 25.68)	p = 0.863
Fatigue scale (FA)	33.53 (± 20.32)	32.02 (± 18.89)	36.35 (± 21.11)	39.70 (± 22.29)	p = 0.003

Nausea and vomiting scale (NV)	10.05 (± 17.67)	10.03 (± 16.54)	10.60 (± 17.06)	10.63 (± 18.17)	p = 0.961
Pain scale (PA)	17.75 (± 20.02)	18.27 (± 18.73)	23.32 (± 22.79)	27.17 (± 23.33)	p = 0.001
Dyspnea scale (DY)	12.72 (± 20.41)	9.93 (± 17.61)	11.07 (± 20.03)	9.38 (± 17.39)	p = 0.196
Insomnia scale (IN)	29.92 (± 29.93)	28.27 (± 28.07)	28.17 (± 26.62)	33.18 (± 28.17)	p = 0.287
Appetite loss scale (AL)	14.38 (± 24.80)	18.27 (± 26.34)	21.07 (± 28.14)	21.07 (± 29.44)	p = 0.080
Constipation scale (CO)	24.35 (± 28.05)	13.85 (± 22.39)	12.18 (± 21.24)	13.30 (± 22.32)	p < 0.001
Diarrhea scale (DI)	14.35 (± 21.52)	29.37 (± 26.18)	42.77 (± 32.64)	50.53 (± 33.44)	p < 0.001
Financial impact scale (FI)	17.20 (± 24.98)	15.48 (± 21.65)	15.50 (± 22.53)	17.18 (± 25.69)	p = 0.580

Table 3. Results of EN24 scales in all timepoints

EORTC QLQ EN-24	Timepoint				p
	I	II	III	IV	Change over time
Lymphedema scale (LY)	18.90 (± 23.48)	19.70 (± 22.63)	17.72 (± 18.56)	20.48 (± 22.73)	p = 0.598
Urological symptoms scale (UR)	23.05 (± 23.95)	21.75 (± 21.79)	25.97 (± 24.21)	33.60 (± 28.14)	p < 0.001
Gastrointestinal symptoms scale (GI)	14.43 (± 14.95)	17.82 (± 18.23)	20.32 (± 19.58)	26.32 (± 20.25)	p < 0.001
Poor body image scale (PBI)	23.75 (± 26.82)	21.32 (± 23.58)	25.98 (± 27.97)	24.08 (± 26.09)	p = 0.292
Pain in back and pelvis scale (BP)	25.97 (± 23.04)	26.53 (± 23.63)	28.73 (± 25.66)	36.00 (± 27.74)	p = 0.003

Tingling/numbness scale (TN)	10.48 (± 17.81)	8.85 (± 18.25)	9.42 (± 19.50)	12.72 (± 22.17)	p = 0.252
Muscle pain scale (MP)	16.02 (± 22.49)	19.38 (± 24.03)	16.03 (± 24.89)	19.88 (± 26.14)	p = 0.365
Hair loss scale (HL)	12.73 (± 26.08)	13.82 (± 23.96)	14.37 (± 22.40)	16.57 (± 22.50)	p = 0.238
Taste change scale (TC)	9.95 (± 20.59)	11.08 (± 20.98)	14.42 (± 24.85)	13.27 (± 23.89)	p = 0.171

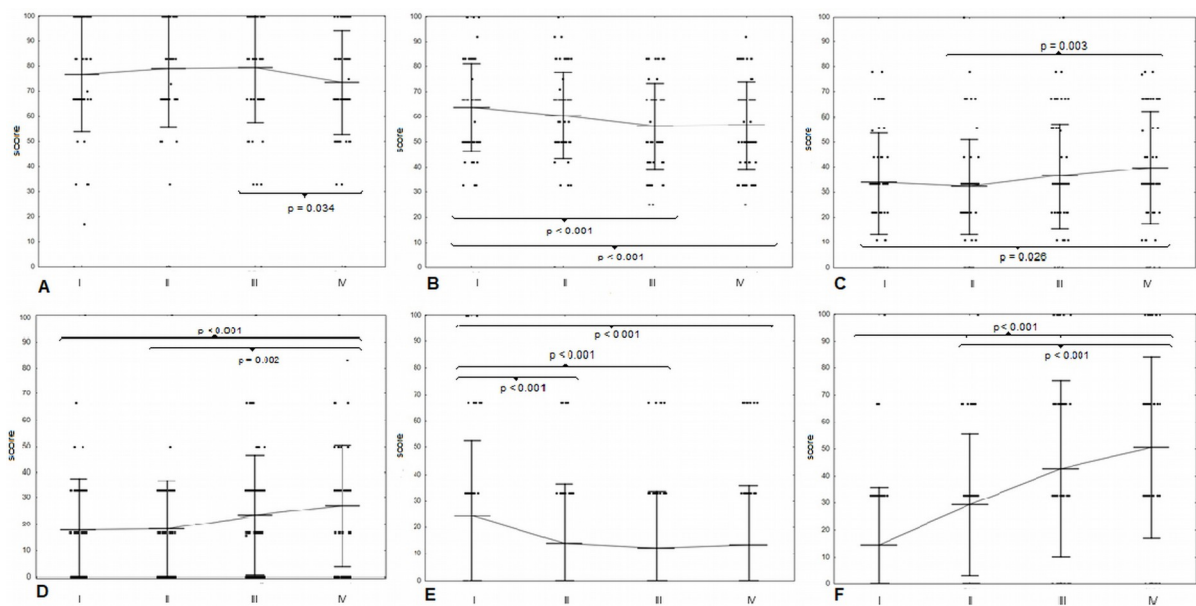


Figure 1. Analysis of scores of EORTC QLQ C-30 scales at the beginning (timepoint 1), during (timepoints 2 and 3) and at the end of adjuvant radiotherapy (timepoint 4). Points are singular observations, horizontal line is mean, whiskers are standard deviation; **A.** Role functioning scale (RF) scale scores (p = 0.028); **B.** Quality of life scale (QL) scale scores (p < 0.001); **C.** Fatigue scale (FA) scores (p = 0.003); **D.** Pain scale (PA) scores (p = 0.001); **E.** Constipation scale (CO) scores (p < 0.001); **F.** Diarrhea scale (DI) scores (p < 0.001)

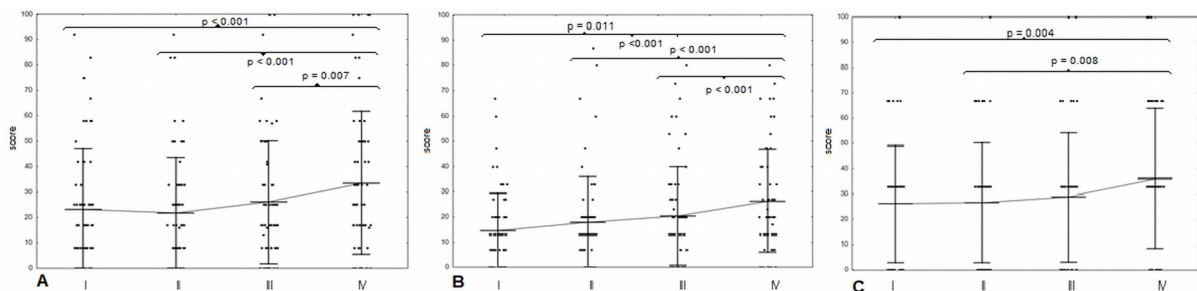


Figure 2. Analysis of score of EORTC QLQ EN-24 module scales at the beginning (timepoint 1), during (timepoints 2 and 3) and at the end of adjuvant radiotherapy (timepoint

4). Points are singular observations, horizontal line is mean, whiskers are standard deviation; **A.** Urological symptoms scale (UR) scores ($p < 0.001$); **B.** Gastrointestinal symptoms scale (GI) scores ($p < 0.001$); **C.** Pain in back and pelvis scale (BP) scores ($p = 0.003$)

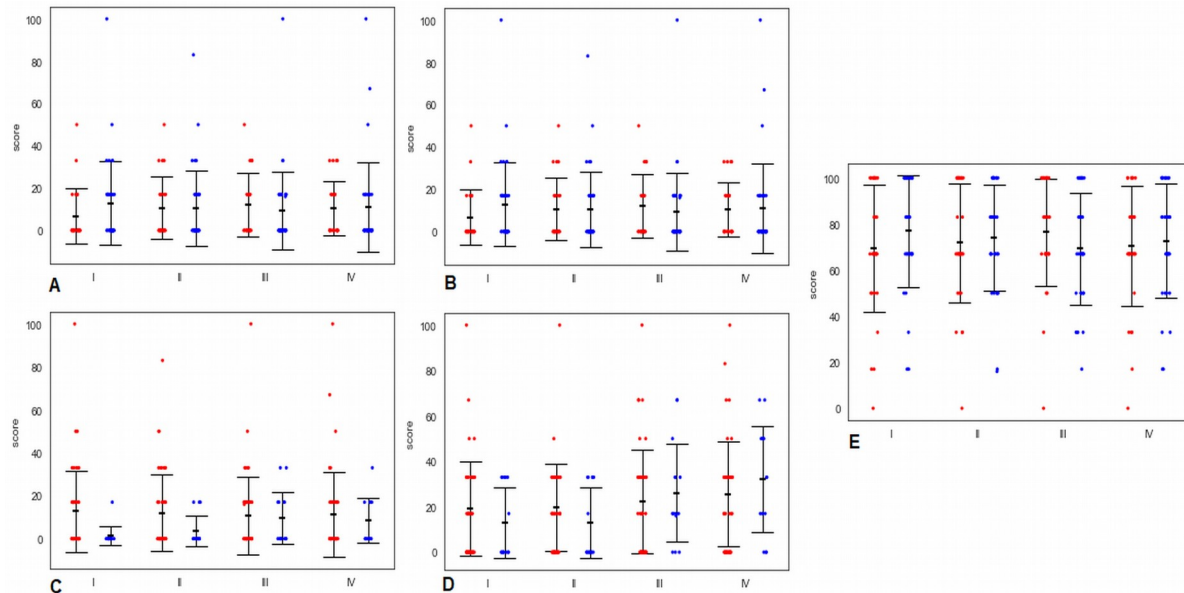


Figure 3. Analysis of changes of scale scores in all four timepoints of subgroups. Points are singular observations, horizontal line is mean, whiskers are standard deviation; **A.** Nausea and vomiting scale (NV) scores in groups with ($n = 35$) or with no lymphadenectomy ($n = 22$) during surgery, red — no lymphadenectomy, blue — lymphadenectomy performed ($p = 0.047$); **B.** Taste change scale (TC) scores in groups with ($n = 35$) or with no lymphadenectomy ($n = 22$) during surgery, red — no lymphadenectomy, blue — lymphadenectomy performed ($p = 0.002$); **C.** Nausea and vomiting scale (NV) scores in groups with DM in medical history ($n = 14$) and with no DM diagnosed ($n = 46$), red — no DM, blue — DM in medical history of patient ($p = 0.012$); **D.** Pain scale (PA) scores in groups with DM in medical history ($n = 14$) and with no DM diagnosed ($n = 46$), red — no DM, blue — DM in medical history of patient ($p = 0.041$); **E.** Social functioning scale (SF) scores in groups with obesity ($n = 31$) and with BMI lower or equal 30 ($n = 29$), red — BMI lower or equal 30, blue — BMI higher than 30 ($p = 0.007$); BMI — body mass index