Quality of Life in Endometrial Cancer Survivors: A 10-year Experience from a Cancer Center in Slovakia

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ABSTRACT

The aim of this study is to evaluate the effect of body mass index (BMI) on quality of life among endometrial cancer survivors. Women diagnosed with endometrioid endometrial cancer at the Slovakian university hospital between January 2010 and December 2018 were identified. Quality of life was measured using the EORTC (European Organisation for Research and Treatment of Cancer) quality of life questionnaires (QLQ-C30 and QLQ-EN24). Univariate and multiple regression analyses were used to determine associations between BMI and quality-of-life outcome variables. 390 women diagnosed with endometrial cancer were invited to participate, 337 (95.2%) completed the questionnaire. Of all women, 131 (38.8%) were pre-obese, 111 (32.9%) were obese and 29 (8.6%) were morbidly obese. Women with increased BMI experienced poorer physical, emotional and social functioning. Obese and morbid obese women had significantly more lymphoedema (59% v. 41%, p=0.048) and dyspnea (73% v. 27%, p= 0.029), and experienced more fatigue (68% v, 32%, p= 0.036) and pain (65% v. 35%, p= 0.041). Obesity and morbid obesity was associated with poorer quality of life in endometrial cancer survivors. Lifestyle changes (e.g., dietary interventions, physical activity) might reduce obesity and improve quality of life among endometrial cancer survivors. Future studies are needed.

Keywords: Quality of life, Endometrial cancer, Obesity, Lymphoedema

INTRODUCTION

Endometrial cancer is the most common gynecological cancer in the Slovak Republic, with estimated 900 new cases annually.[1] Standardized incidence is 19.8/100,000 and mortality 9.5/100,000.[1] Analyzing the long-term national data by means of join-point regression, there is a continuous significant 3% average annual increase of standardized incidence of endometrial cancer without year-to-year fluctuations.[2]

One of the main reasons for this rise is the growing obesity epidemic.[3] Degree of obesity and overweightness can be quantified by using the body mass index (BMI). Obesity is defined as a BMI of over 30, and overweightness as BMI between 25 and 29.9.[3] Prevalence of worldwide obesity has more than doubled since 1980, with 39% of adults 18+ years and older being overweight in 2014, and 13% obese.[3] In 2016, the age-standardized adult prevalence of overweight and obesity was estimated to be 39.2% in women, affecting approximately 2.01 billion adults globally.[4] In the Slovak Republic in 2014 the proportion of adult females (18 years and older) who were considered to be overweight was 46.1%.[5] Among the women between 45-64 years old 23.3% were obese, and between 65-75 years old 33.7% were obese.[6]

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It is estimated that 5-6% of all cancers can be attributed to the combined effects of obesity and diabetes, which corresponds to nearly 800.000 new cases per year worldwide. In this context, 121.700 (38.4%) of 317.000 endometrial cancer cases are caused by these two risk factors.[7] The prognosis of patients with endometrial carcinoma is good, and the 5-year relative survival rate has reached 74.4% in Slovakia.[2]

A 2015 meta-analysis of 40 studies showed that compared to normal weight women. The relative risk and odds ratio for developing endometrial cancer in overweight women were 1.34 and 1.43, respectively. In obese women, the relative risk was 2.54 and the odds ratio was 3.33, confirming that the risk of endometrial cancer increases incrementally with increasing weight.[8]

Obesity has negative impact on quality of life in early stage endometrial cancer survivors. BMI has a important contribution to HRQoL domains next to the contribution of commorbid conditions, socio-demographic and clinical characteristics.[9] The association between quality of life and BMI seems evident. BMI level at which an important deterioration of quality of life occurs has not been identified nor established yet. Association with disease recurrence is questionable, but there is an association with all-caused mortality.[10,11] In our study, we aimed to assess the effect of BMI on the quality of life of endometrial cancer survivors using a validated quality of life questionnaire (EORTC QLQ-C30 and EORTC QLQ-EN24).

PATIENT and METHODS

Study Population

Women diagnosed with endometrial cancer that were treated at at the Slovakian university hospital between January 2009 and December 2018 were identified from the hospital information system. Women who had completed primary treatment were invited to participate in a department review of follow-up care. Eligible women were survivors of the endometrioid endometrial cancer. We included all stages/grades endometrial cancer patients and recurrent patients. We excluded women with other types of endometrial cancer or endometrial stromal tumors, a history of double primary malignancies, or those who had received treatment elsewhere. The women were sent a letter (personal, post, e-mail) accompanied by a patient satisfaction questionnaire and QLQ-C30 and QLQ-EN24 questionnaires. Consent was obtained at their review appointment.

Data Collection

Baseline and clinical characteristics such as age and date of diagnosis, disease stage (according to International Federation of Gynecology and Obstetrics), grade, treatment, time from the diagnosis, and other characteristics had been collected from the patients' medical records.[12] We determined the extend of surgery according to Mayo algorithm and we used frozen section routinely. All the patients undergo CT or MRI scan (pelvic, abdominal, retroperitoneal) and CT chest scan preoperative.

Current BMI (weight (kg)/[height (m)]^2) was recorded and categorized according to the WHO: underweight (≤ 18.5 kg/m^2), normal range (18.5-24.9 kg/m^2), overweight (25-29.9 kg/m^2), obese (≥ 30-39.9 kg/m^2) and morbidly obese (≥ 40 kg/m^2).[3]

Measures

Quality of life was measured using the EORTC QLQ-C30 and QLQ -EN24 questionnaires. Items 1-28 of the EORTC QLQ-C30 and all 54 items of the QLQ-EN24 are rated on a 4-point scale from 1 to 4 (i.e., "not at all" to "very much"). Items 29 and 30 of the QLQ-C30 are rated on a 7 point scale from 1 to 7 (i.e., "very poor" to "excellent).

The EORTC QLQ-C30 (Version 3.0) is an instrument well-validated for measuring global quality of life in cancer patients.[13] This questionnaire measures 5 domains of global QOL (i.e., physical, role, cognitive, emotional, & social) and 3 symptom scales (i.e., fatigue, pain, nausea and vomiting).[14] Higher scores for global quality of life and functional scales represent higher level of quality of life and functioning. Conversely, higher scores for symptom scales and items represent clinically significant symptomatology.[15]

The EORTC QLQ-EN24 is an instrument developed for quality of life in women with endometrial cancer. It is comprised of 13 domains including lymphoedema, urologic problems, gastro-intestinal problems, body image, sexual/vaginal problems, back/pelvic pain, tingling/numbness, muscular/joint pain, hair loss, taste change, sexual interest, sexual activity and sexual enjoyment.[16] Scores are transformed into a scale from 0 to 100 where higher scores indicate more symptoms, except for the final three sex-related questions. Here, the higher scores represent higher levels of functioning.[16]

Ethical issues (including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the author.

Statistical Analysis

BMI was divided into four categories for analysis purposes: normal weight (< 24.9 kg/m^2), overweight (25-29.9 kg/m^2), obese (30-39.9 kg/m^2) and morbid obese (> 40 kg/m^2). Categorical outcomes were presented as percentages and frequencies, continuous outcomes as means with SD (standart deviation) and baseline and clinical data were compared using nonparametric tests for continuous data. Fischer's exact test and Pearson's chi-squared test were used for categorical variables. The EORTC-C30 and the EORTC QLQ-EN24 data were analyzed according to scoring procedures. The linear transformation into 0 to 100 scales was used.[15,16,17] Hierarchical multiple regression analyses and univariate analyses were conducted to evaluate the relationship between patient reported outcomes as depent variables and independent variables. The analysis was used to evaluate primary associations between BMI and quality of life outcomes. The insertion of BMI data into the model was the first step of analysis, the second step was entering comorbidity, sociodemograpic and clinical characteristics. The data were analysed using SPSS statistics program version 20.0. P-values were regarded as significant if p< 0.05, and tests were two-sided.

RESULTS

A total of 489 women were diagnosed with endometrioid endometrial cancer between January 2009 and December 2018, with 99 women being deceased at the time of the study and therefore excluded. 390 patients were invited to participate. Women with unknown BMI were excluded. 36 patients were excluded for other types of histology (non-endometrioid). Out of the remaining 354 women, 337 (95.2%) completed the questionnaire. 32 women had recurrent disease. Time interval between diagnosis and recurrence was 34 months. Some of them have been undergone treatment in the time of data collection. Their weight classification is classified in Table 1. They are very heterogenous group and association between recurrence, BMI and QoL were not study separately.

Clinical Characteristics

Table 1 represents the clinical characteristics of normal, overweight, obese and morbid obese women. The mean age of the women participating in the study was 65.8 years (SD 7.8 years). The mean age of normal weight patients was similar to morbidly obese patients, and lower compared to overweight and obese patients. Overweight and obese women were significantly older than other women at the time of diagnosis. The majority (91%) of women were diagnosed with early stage (FIGO I) endometrial cancer. About half of the patients suffered from grade I endometrial cancer at diagnosis. All survivors were post treated and had undergone surgery. The majority of patients had surgical procedure without lymphadenectomy and about one-quarter of the survivors received radiotherapy. Normal weight and overweight patients underwent more frequent lymphadenectomy [p= 0.041]. The majority of patients were overweight (38.8%) or obese (32.9%). Mean BMI of overweight patients was 29.1 and mean BMI of obese patients was 34.1. Twenty nine (8.6%) were morbidly obese (mean BMI 43.8, maximum 56). Patients in higher BMI categories reported more comorbidities [p < 0.01]. The following comorbid conditions were associated with higher BMI: diabetes, hypertension and arthrosis. Approximately one tenth [normal weight, n= 5 (7.5%), overweight, n= 14 (10.6%),

Table 1. Clinical characteristics of participans according to BMI categories

	Normal BMI 25-29.9 N= 66 (19.5%)	Overweight BMI 30-39.9 N= 131 (38.8%)	Obese BMI ≥40 N= 111 (32.9%)	Morbid obese N= 29 (8.6%)	p
Variable	**N**	**N**	**N**	**N**	
Age (mean, SD)	62.4 (7.5)	68.3 (6.9)	69.8 (6.9)	62.7 (9.9)	< 0.01
FIGO					0.041
I	57 (86.3%)	119 (90.8%)	105 (94.5%)	26 (89.6%)	
II	6 (9%)	7 (5.3%)	2 (1.8%)	2 (6.8%)	
III-IV	3 (4.5%)	5 (3.8%)	4 (3.6%)	1 (3.4%)	
Grade					0.852
I	36 (54.5%)	69 (52.6%)	54 (48.6%)	18 (62%)	
II	25 (37.8%)	54 (41.2%)	50 (45%)	9 (31%)	
III	5 (7.5%)	8 (6.1%)	7 (6.3%)	2 (6.8%)	
Treatment					
Surgery without LYA	55 (83.3%)	103 (78.6%)	81 (72.9%)	28 (96.5%)	
Surgery + LYA	11 (16.7%)	28 (21.4%)	30 (27.0%)	2 (6.9%)	0.041
Surgery + RT	7 (10.6%)	20 (15.6%)	22 (19.8%)	2 (6.9%)	0.374
Recurrence					0.461
Yes	5 (7.5%)	14 (10.6%)	11 (9.9%)	2 (6.8%)	
No	61 (92.4%)	117 (89.3%)	100 (90%)	27 (93.1%)	
Time since diagnosis					0.897
<1 year	5 (7.5%)	10 (7.6%)	10 (9%)	3 (10.3%)	
1-2 years	7 (10.6%)	19 (14.5%)	16 (14.4%)	4 (13.7%)	
2-3 years	12 (18.1%)	22 (16.7%)	21 (18.8%)	5 (17.2%)	
3-4 years	13 (19.6%)	25 (19%)	23 (20.7%)	6 (20.6%)	
4-5 years	12 (18.1%)	23 (17.5%)	17 (15.3%)	6 (20.6%)	
>5 years	17 (25.7%)	32 (24.4%)	24 (21.6%)	5 (17.2%)	13
Comorbidity					
No	48 (72.7%)	30 (22.9%)	14 (12.6%)	3 (10.3%)	
Yes	18 (27.2%)	101 (77%)	97 (87.3%)	26 (89.6%)	< 0.01
Type of comorbidities					
Diabetes	6 (9%)	18 (13.7%)	31 (27.9%)	14 (48.2%)	< 0.01
Hypertension	15 (22.7%)	63 (48%)	68 (61.2%)	21 (72.4%)	< 0.01
Arthrosis	11 (16.6%)	45 (34.3%)	57 (51.3%)	20 (68.9%)	< 0.01

LYA= lymphadenectomy; RT= radiotherapy

obese, n= 11 (9.9%) and morbid obese, n= 2 (6.8%) of patients had recurrent disease. The median time to recurrence was 15 months (range 7-48). There was no significant effect of obesity on recurrent disease.

Quality of Life

The quality of life outcomes of endometrial cancer survivors are presented as the mean scores (+/-SD) according to BMI categories (Table 2). The overall quality of life of survivors was the lowest among morbid obese women, and the highest among nor-

Table 2. Outcomes of QLQ-C30 questionnaires of participans accordings to BMI categories

	Normal BMI 18.5-24.9 N= 66	Overweight BMI 25-29.9 N= 131	Obese BMI 30-39.9 N= 111	Morbid obese BMI ≥40 N= 29	Univariate analysis	Multivariate analysis	BMI < 40 versus BMI ≥ 40
Variable	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**p**	**p**	**p**
Global quality of life	80 (19)	76 (18)	75 (23)	69 (25)	0.081	N/A	N/A
Functional scales							
Physical functioning	86 (18)	81 (18)	81 (17)	64 (27)	0.003	0.001	0.001
Role functioning	88 (21)	83 (25)	84 (26)	79 (32)	0.061	0.009	0.051
Emotional functioning	90 (17)	85 (15)	78 (14)	71 (29)	0.035	0.003	0.010
Cognitive functioning	90 (15)	88 (15)	89 (20)	83 (29)	0.082	0.053	0.059
Social functioning	92 (20)	88 (14)	76 (13)	74 (27)	0.007	0.021	0.033
Symptom scales							
Fatigue	20 (19)	23 (21)	25 (23)	29 (25)	0.082	N/A	0.036
Nausea and vomiting	4 (8)	5 (9)	7 (15)	7 (16)	0.071	N/A	0.051
Pain	12 (20)	18 (26)	26 (28)	26 (30)	0.081	N/A	0.041
Dyspnoea	10 (18)	16 (20)	23 (30)	26 (33)	0.009	N/A	0.029
Insomnia	27 (29)	22 (29)	19 (20)	18 (22)	0.211	N/A	0.054
Appetite loss	7 (12)	5 (14)	4 (12)	4 (15)	0.891	N/A	0.079
Constipation	15 (24)	10 (20)	10 (21)	12 (20)	0.121	N/A	0.089
Diarrhoea	4 (11)	4 (12)	7 (14)	9 (14)	0.076	N/A	0.079
Fainancial difficulties	5 (15)	7 (24)	6 (13)	6 (18)	0.641	N/A	0.082

N/A= not applicable

mal weight women, but there was no significant difference by their BMI status [p= 0.081].

Patients with increased BMI (≥ 25 kg/m^2) had significantly worse physical, emotional and social functioning [p= 0.003, p= 0.035, and p= 0.007, respectively]. The multiple regression analysis by clinical characteristics (age, stage, grade and recurrence) showed the same statistical significance [p= 0.001, p= 0.003 and, p= 0.021 respectively].

Women with higher BMI (≥ 25 kg/m^2) experienced significantly more fatigue, pain and dyspnoea [p= 0.082, p= 0.081 and p= 0.009]. The role functioning and cognitive functioning did not vary significantly among the BMI categories. Other symptom distress scores did not show significant association with BMI categories.

Obese and morbidly obese women had significantly worse physical, emotional and social functioning compared to normal weight and overweight participans [p= 0.01, p= 0.010, and p= 0.033, respectively]. Fatigue, pain and dyspnoea are the most common symptoms in obese and morbidly obese women [p= 0.036, p= 0.041, and p= 0.029, respectively].

Our results are related to participant responses on the questionnaire. The analysis disclosed that higher BMI (≥ 25 kg/m^2) was asociated with lymphoedema, urologic and gastrointestinal symptoms, pain (back/pelvic and muscular/joint) and numbness/tingling (Table 3). Higher scores of lymphoedema, urologic and gastrointestinal symptoms, body image, sexual problems, pain (back, pelvic, muscular, joint), tingling and numbness and hair loss represent higher level of symptoms. Higher score of sexual interest, activity and enjoyment represent a higher level of satisfaction. BMI was inversely associated with sexual problems. A 10 point increase in the BMI score led to 7.9 points increase score in symptoms of lymphoedema, 2.4 points increase

Table 3. Outcomes of QLQ-EN24 questionnaires of participans accoridng to BMI categories, linear regression and multivariate analysis.

	Normal BMI 18.5-24.9 N= 66	Overweight BMI 25-29.9 N= 131	Obese BMI 30-39.9 N= 111	Morbid obese BMI ≥40 N= 29	Univariate analysis	Multivariate analysis
Variable	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Beta BMI**	**Beta BMI, adjusted model**
Lymphoedema	14 (22)	19 (23)	25 (23)	33 (29)	1.1	0.79
Urologic	28 (20)	23 (19)	25 (19)	29 (19)	0.37	0.24
Gastro-intestinal	15 (18)	18 (18)	18 (21)	21 (20)	0.29	0.11
Body image	10 (20)	6 (18)	8 (16)	8.5 (15)	0.03	-0.12
Sexual problems	34 (20)	25 (20)	20 (21)	22 (25)	-1.00	-1.34
Pain (back, pelvic)	21 (25)	22 (28)	30 (29)	29 (31)	0.48	0.05
Numbness/tingling	15 (20)	18 (22)	21 (25)	24 (26)	0.49	0.19
Pain (muscular, joint)	26 (22)	29 (22)	33 (29)	38 (29)	0.49	-0.03
Hair loss	7 (12)	8 (20)	10 (13)	8 (11)	0.14	0.07
Taste change	5 (13)	6.8 (15)	10 (14)	7.8 (15)	-0.32	-0.22
Sexual interest	17 (20)	18 (16)	16 (15)	12 (20)	-0.22	-0.12
Sexual activity	16 (20)	15 (16)	17 (14)	14 (17)	-0.19	-0.14

score in urologic symptoms, 1.9 points increase score in numbness/tingling symptoms, and 13.4 points decrease score in sexual problems.

We compare QoL between patient group of lymphadenectomy and the patient group of lymphadenectomy plus radiotherapy. There were 71 women who underwent pelvic lymphadenectomy and 51 women who underwent adjuvant radiotherapy. Patients who were treated with radiotherapy reported 6 points higher on the EORTC-EN24 gastrointestinal symptom scale and 7 points higher on diarrhea, but differences were not clinically nor statistically significance. Ten percent of women who received adjuvant radiotherapy reported to have had "quite a bit" or "very much" diarrhea, compared to six percent women who received no radiotherapy respectively two percent of women who received brachytherapy only. Gastrointestinal and diarrhea symptoms were highest among women who received radiotherapy.

DISCUSSION

In our study group of the endometrioid endometrial cancer survivors, 38.8% of patients were overweight, 41.5% were obese, and 8.6% were morbidly obese. Von Gruenigen et al. in their study in 2006 found, that 24 % of patients in the early stages of endometrial cancer were overweight, 41 % were obese, and 12 % morbidly obese.[17] Fader et al. reported that 16 % of patients were overweight and 50 % were obese.[18] In 2011, Fader et al. found 81% of patients with the type I of endometrial cancer were obese.[19]

In our study, deterioration in the quality of life was found based on changes in the values of the monitored parameters in each domain of the functional scale. An increased BMI (≥ 25 kg/m^2) score was associated with a lower degree of physical, emotional, and social functioning. Among the morbidly obese patients, this association was statistically significant. Similar findings can also be found in previous studies.[9,19-20] Fatigue, pain, and dyspnea were more often associated with higher BMI (≥

25 kg/m^2). A similar relationship was observed in other studies, confirming association between BMI and poorer physical functioning.[9,19,20,22] While several authors report a positive correlation between diarrhoea and morbid obesity, we have not found such association.[20,23] In our study, morbidly obese patients reported significantly worse scores in terms of social functionality. While Smits et al. found the same correlation; other authors have failed to do so.[9,19-21] Emotional functioning was significantly worse in our sample among patients with BMI ≥ 40. The role functioning domain in our study showed no changes, which is in contradiction with another study.[20]

The explanation of reduced physical functionality can be found in limited mobility, usually present comorbidity, and somewhat poor physical endurance.[20] Obese people are often discriminated against in social situations, therefore their social interactions may be limited.[14,24] The question is whether there is a social discrimination in a religious society.[25] Christianity is the predominant religion in Slovakia and the average religion rate in Slovakia was 75.5%.[26] Spiritual well-being and religiosity tend to be associated with better quality of life, including better quality perception and satisfaction with health care.[27] Increased perception of pain, feeling of isolation, hopelessness and anger is evident in case of religious patients with insufficient access to adequate spiritual care.[28] The environment of faith can improve the scores of some functional scales in the area of quality of life in many communities.[28]

Smits et al. published a review article and a meta-analysis, which showed statistically significant differences in the domains of physical functioning, social functioning and role functioning in obese women with endometrial cancer compared to women of normal weight.[29] Changing lifestyle, improving physical activity, reducing weight and improving dietary habits is a key way to improve the quality of life.[30] Patients with endometrial cancer face a lifelong challenge to change their lifestyle and reduce their weight.[30,31] Von Gruenigen et al. reported that only 12% of patients were able to reduce their weight, only 30% of patients achieved at least 5% weight reduction due to exercise and dietary changes.[33] It appears that 5% weight reduction significantly reduces the presence of comorbidities.[33]

The patients on our study responded to questions in the EORTC QLQ-questionnaire EN24 that take into account comorbidity, clinical and sociodemographic parameters. Our study found a positive relationship between BMI increase and, higher incidence of lymphedema in particular, urological disorders, fatigue, and pain. The incidence of lymphedema is positively associated with increased BMI (≥ 30 kg/m^2) (59% v 41%, p= 0.048). Oldenberg et al. and Beesley et al. reported similar conclusions.[9,34] Oncogynecological patients are at increased risk of developing lymphedema partly due to lymphadenectomy or radiation therapy and this risk rises with increasing BMI.[35-37] The incidence of lymphedema is associated with a poor quality of life.[38] Many patients refuse an exercise as a part of their rehabilitation program, thus aggravating existing difficulties and comprehensive rehabilitation has a positive effect on the potential development and treatment of lymphedema.[39] Mizrahi et al. reported that only 19% of patients are physically active, the most common reason for lack of physical activity is fatigue (37.8%), irregular exercise (34.7%), the lack of self-discipline (32.6%) and procrastination (27.4%).[40]

Fatigue is a common symptom of cancer. It is often unrecognized and untreated, and a specific questionnaire is required to correctly identify this symptom.[41] The etiology in cancer is unclear, although obesity is a co-responsible factor in its development.[41] Fatigue or exhaustion usually prevents patients from improving their health by regular exercise.

We found out that increasing BMI is associated with a decrease in sexual / vaginal problems. This result is consistent with the authors of another study.[9] On one hand, the vaginal dryness is a common condition in postmenopausal women; on the other hand the fatty tissue produces a certain amount of estrogen, which particularly alleviates this problem in the case of obese patients.[42] Becker et al. published a study in which they found that adjuvant vaginal brachytherapy does not have a negative impact on the quality of life of patients with endometrial cancer.[43] The side effects of brachytherapy are dryness

of the vagina, pain in the vagina, stenosis or shortening of the vagina.[43]

The change in sexual activity in relation to BMI change is unclear. Respondents often consulted their responses in the questionnaire with health care workers or they do not answer at all. Among the 339 participants, 256 (75.5%) did not answer on questions related sexual behavior. Gao et al. found that 68.6% of endometrial cancer survivors had sexual dysfunction, and 55.9% reported no sexual intercourse after the surgery, respectively the average time of first sexual intercourse after the surgery was at 10 months (range, 6-60 months).[44]

The use of adjuvant radiotherapy and lymphadenectomy can have a tremendous impact on QoL. This was the reason for comparing QoL between the group of patients with lymphadenectomy and the group of patients with lymphadenectomy and radiotherapy, but the differences were ultimately not clinically or statistically significant. This is partly consistent with what was found in a previous study by van de Poll-Franse et al.[45] Women receive pelvic lymphadenectomy without clinically relevant better QoL or minor symptoms compared to women who have received radiotherapy or were not adjuvant at all. Patients with external radiotherapy experienced higher gastrointestinal symptoms than women receiving only brachytherapy. Our statement is strongly limited by the results obtained in a small group of patients.

The strength of our study include the use of internationally recognized and validated quality of life questionnaires, the use of a specific questionnaire for patients with endometrial carcinoma, the high response rate, and the size of the studied cohort. All patients included in the study were followed in our oncogynecological center and regularly participated in the follow-up. 337 (95.5%) patients out of 354 returned the completed questionnaire. The response rate was significantly higher compared to other studies, which documents an excellent collaboration within our department, as well as high patients satisfaction with the follow-up care after the primary treatment finalization.[9,21,22]

The limitation of this study include: cross-sectional study with the data collected at different times after the termination of primary treatment (3 months to 8 years), absence of specific questionnaires for the incidence of e.g. depression or fatigue, and the inability to accurately identify the causality between BMI and the outcomes reported by the patients. The sample of morbidly obese patients with endometrial cancer was small. Results may be generalized to Slovakian women with endometrial cancer.

Conclusion

The results of our study suggest that obesity is one of the greatest health threats and has a negative impact on quality of patients' lives. The most significant study finding was the negative impact reflected in the decline on physical, emotional and social functioning. Lymphedema is a major complication of lymphadenectomy among women with endometrial cancer, especially those with morbid obesity. We have not been reckonning the influence of belief and religiousity in our group, it opens the door to conducting research in specific areas of cancer care. Furthermore, an increasing trend of morbid weight gain and related diseases is alarming particularly in light of the rising health care costs. Prospective studies that evaluate this effect are needed.

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REFERENCES

1. National Health Information Center, National Cancer Registry of Slovakia. Cancer incidence in the Slovak Republic 2010, NHIC, Bratislava, 2017. http://www.nczisk.sk/Documents/publikacie/analyticke/incidencia_zhubnych_nadorov_2010.pdf (Access date: 1/15/2019).
2. Ondrusova M, Psenkova M. Epidemiology of selected female genital organs malignancies. Onkologia (Bratisl.) 8: 350-354, 2013.
3. WHO. Obesity and overweight Fact sheet Updated October 2017. http://www.who.int/mediacentre/factsheets/fs311/en/ (Access date: 1/15/2019).

4. NCD Risk Factor Collaboration. Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128•9 million children, adolescents, and adults. Lancet. 2017. http://dx.doi.org/10.1016/S0140-6736(17)32129-3 (Access date: 1/15/2019).

5. Eurostat. Statistics Explained. 2014. http://ec.europa.eu/eurostat/statisticsexplained/ (Access date: 1/15/2019).

6. Eurostat. Statistics Explained. 2008. http://ec.europa.eu/eurostat/documents/2995521/5032782/3-24112011-BP-EN.PDF/831f0ca4-7105-4045-9e25-604141ef5108 (Access date: 1/15/2019).

7. Pearson-Stuttard J, Zhou B, Kontis V, et al. Worldwide burden of cancer attributable to diabetes and high body-mass index: a comparative risk assessment. 2017. http://www.thelancet.com/pb/assets/raw/Lancet/pdfs/S2213858717303662.pdf (Access date: 1/15/2019).

8. Jenabi E, Poorolajal J. The effect of body mass index on endometrial cancer: a meta-analysis. Public Health 129: 872-880, 2015.

9. Oldenburg CS, Boll D, Nicolaije KA, et al. The relationship of body mass index with quality of life among endometrial cancer survivors: a study from the population-based PROFILES registry. Gynecol Oncol 129: 216-221, 2013.

10. Fader AN, Arriba LN, Frasure HE, et al. Endometrial cancer obesity: epidemiology, biomarkers, prevention and survivorship. Gynecol Oncol 114: 121-127, 2009.

11. Arem HPY, Pelser C, Ballard-Barbasch R, et al. Prediagnosis body mass index, physical actvity and mortality in endometrial cancer patients. J Natl Cancer Inst 105, 342-349, 2013.

12. Amant F, Mirza MR, Koskas M, et al. Cancer of the corpus uteri. FIGO cancer report 2015. Int J Gynecol Obstet 131: S96-S104, 2015.

13. Giesinger JM, Kieffer JM, Fayers PM, et al. Replication and validation of higher order models demonstrated that a summary score for the EORTC QLQ-C30 is robust. J Clin Epidemiol 69: 79-88, 2016.

14. 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 85: 365-376, 1993.

15. Fayers P, Aaronson NK, Bjordal K, et al. The EORTC QLQ-C30 Scoring Manual. 3rd ed, Brussels, Belgium: European Organisation for Research and Treatment of Cancer, 2001: 1-427.

16. Greimel E, Nordin A, Lanceley A, et al. 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 47: 183-190, 2011.

17. von Gruenigen VE, Tian C, Frasure H, et al. Treatment effects, disease recurrence, and survival in obese women with early endometrial carcinoma: a Gynecologic Oncology Group study. Cancer 107: 2786-2791, 2006.

18. Fader AN, Arriba LN, Frasure HE, et al. Endometrial cancer and obesity: epidemiology, biomarkers, prevention and survivorship. Gynecol Oncol 114,:121-127, 2011.

19. Fader AN, Frasure HE, Gil KM, et al. Quality of life in endometrial cancer survivors: what does obesity have to do with it? Obstet Gynecol Int. 2011. http://dx.doi.org/10.1155/2011/308609 (Access date: 1/15/2019).

20. Smits A, Lopes A, Das N, et al. The impact of BMI on quality of life in obese endometrial cancer survivors: Does size matter? Gynecol Oncol 132: 137-141, 2014.

21. Courneya KS, Karvinen KH, Campbell KL, et al. Associations among exercise, body weight, and quality of life in a population-based sample of endometrial cancer survivors. Gynecol Oncol 2: 422-430, 2005.

22. Basen-Engquist K, Scruggs S, Jhingran A, et al. Physical activity and obesity in endometrial cancer survivors: associations with pain, fatigue, and physical functioning. Am J Obstet Gynecol 200: e1-8, 2009.

23. Eslick GD. Gastrointestinal symptoms and obesity: a meta-analysis. Obes Rev 13: 469-479, 2012.

24. National Institutes of Health (1998). Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults - the evidence report NHLBI Obesity Education Initiative Expert Panel on the identification, evaluation, and treatment of obesity in adults. https://www.ncbi.nlm.nih.gov/books/NBK2003/

25. Cline KMC, Ferraro KF. Does religion increase the prevalence and incidence of obesity in adulthood? J Sci Study Relig 45: 269-281, 2006.

26. Slovak Republic: Population and Housing Census (2011). Results in multidimensional tables. https://census2011.statistics.sk/tabulky.html (Access date: 1/15/2019).

27. Astrow AB, Wexler A, Texeira K, et al. Is failure to meet spiritual needs associated with cancer patients' perceptions of quality of care and their satisfaction with care? J Clin Oncol 25: 5753-5757, 2007.

28. Narayanasamy A. The impact of empirical studies of spirituality and culture on nurse education. J Clin Nurs 15: 840-851, 2006.

29. Smits A, Lopes A, Bekkers R, et al. Body mass index and the quelity of life of endometrial camcer survivors – a systematic review and meta-analysis. Gynecol Oncol 137: 180-187, 2015.

30. Blanchard CM, Courneya KS, Stein K. Cancer survivors' adherence to lifestyle behavior recommendations and associations with health-related quality of life: results from the American Cancer Society's SCS-II. J Clin Oncol 26: 2198-2204, 2008.

31. Beesley VL, Eakin EG, Janda M, et al. Gynecological cancer survivors' health behaviors and their associations with quality of life. Cancer Causes Control 19: 775-782, 2008.

32. von Gruenigen VE, Waggoner SE, Frasure HE, et al. Lifestyle challenges in endometrial cancer survivorship. Obstet Gynecol 117: 93-100, 2011.

33. von Gruenigen V, Frasure H, Kavanagh MB, et al. Survivors of uterine cancer empowered by exercise and healthy diet (SUCCEED): a randomized controlled trial. Gynecol Oncol 125: 699-704, 2012.

34. Beesley V, Janda M, Eakin E, et al. Lymphedema after gynecological cancer treatment: prevalence, correlates, and supportive care needs. Cancer 109: 2607-2614, 2007.

35. Graf N, Rufibach K, Schmidt AM, et al. Frequency and risk factors of lower limb lymphedema following lymphadenectomy in patients with gynecological malignancies. Eur J Gynaecol Oncol 34: 23-27, 2013.

36. Konno Y, Todo Y, Minobe S, et al. A retrospective analysis of postoperative complications with or without para-aortic lymphadenectomy in endometrial cancer. Int J Gynecol Cancer 21: 385-390, 2011.

37. Achouri A, Huchon C, Bats AS, et al. Complications of lymphadenectomy for gynecologic cancer. Eur J Surg Oncol 39: 81-86, 2013.

38. Rowlands IJ, Beesley VL, Janda M, et al. Quality of life of women with lower limb swelling or lymphedema 3-5 years following endometrial cancer. Gynecol Oncol 133: 314-318, 2014.

39. Do JH, Choi KH, Ahn JS, et al. Effects of a complex rehabilitation program on edema status, physical function, and quality of life in lower-limb lymphedema after gynecological cancer surgery. Gynecol Oncol 147: 450-455, 2017.

40. Mizrahi D, Naumann F, Broderick C, et al. Quantifying physical activity and the associated barriers for women with ovarian cancer. Int J Gynecol Cancer 25: 577-583, 2015.

41. Barton DL, Soori GS, Bauer BA, et al. Pilot study of Panax quinquefolius (American ginseng) to improve cancer related fatigue: a randomized, double-blind, dose-finding evaluation: NCCTG trial N03CA. Support Care Cancer 18: 179-187, 2010.

42. Repse-Fokter A, Takac I, Fokter SK. Postmenopausal vaginal atrophy correlates with decreased estradiol and body mass index and does not depend on the time since menopause. Gynecol Endocrinol 24: 399-404, 2008.

43. Becker M, Malafy T, Bossart M, et al. Quality of life and sexual functioning in endometrial cancer survivors. Gynecol Oncol 121: 169-173, 2011.

44. Gao H, Xiao M, Bai H, et al. Sexual function and quality of life among patients with endometrial cancer after surgery. Int J Gynecol Cancer 2: 608-612, 2017.

45. van de Poll-Franse LV, Pijnenborg JMA, Boll D, et al. Health related quality of life and symptoms after pelvic lymhadenectomy or radiotherapy vs. no adjuvant regional treatment in early-stage endometrial carcinoma: A large population-based study. Gynecol Oncol 127: 153-160, 2012.

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