Quality of life in endometrial cancer survivors: single institution experience in Slovakia

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Abstract
Background: To evaluate the association between body mass index (BMI) and quality of life among endometrial cancer survivors.

Methods: Women diagnosed with endometrioid endometrial cancer at the Slovakian university hospital between January 2010 and December 2018 were identified. Three hundred ninety women diagnosed with endometrial cancer were invited to participate. Quality of life was measured using 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. T-test was used to determine differences between groups.

Results: 337 (95.2%) women completed the questionnaire. 131 (38.8%) were pre-obese, 111 (32.9%) were class I and II obese and 29 (8.6%) were class III obese. Women with higher BMI experienced poorer physical, emotional and social functioning compared to normal weight and pre-obese patients (p < 0.05). Class I-III obese women had significantly more lymphoedema (59% v. 41%, p = 0.049) 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).

Conclusions: Class I-III obesity was associated with poorer quality of life in endometrial cancer survivors. Increasing BMI was inversely associated with QoL. Pre-obese and obese patients should be informed about greater incidence of pain, fatigue and dyspnea. Lifestyle changes (e.g., dietary interventions, physical activity) might reduce obesity and improve quality of life among endometrial cancer survivors.

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

Background
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]. Obesity and pre-obesity is serious public health problem. Degree of obesity and pre-obesity can be quantified by using the body mass index (BMI). Obesity is defined as a BMI of over 30, and pre-obesity 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 pre-obesity in 2014, and 13% obese [3]. In 2016, the age-standardized
adult prevalence of pre-obesity 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 pre-obese was 46.1% [5]. Among the women between 45 and 64 years old 23.3% were obese, and between 65 and 75 years old 33.7% were obese [6].

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].

The meta-analysis by Jenabi and Poorolajal showed 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 endometrial cancer survivors [9]. BMI is related to several HRQoL (Health-Related Quality of Life) outcomes and that BMI has an important contribution to HRQoL domains next to the contribution of comorbid 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 [10, 11]. In our study, we aimed to assess the association between BMI and the quality of life of endometrial cancer survivors using a validated quality of life questionnaire (EORTC 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 [2].

Current BMI (weight (kg)/[height (m)]2) was recorded and categorized according to the WHO: underweight (≤ 18.5 kg/m²), normal range (18.5–24.9 kg/m²), pre-obesity (25–29.9 kg/m²), class I and II obesity (≥ 30–39.9 kg/m²) and class III obesity (≥ 40 kg/m²) [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].
Statistical analysis
BMI was divided into four categories for analysis purposes: normal weight (< 24.9 kg/m²), pre-obesity (25–29.9 kg/m²), class I and II obesity (30–39.9 kg/m²) and class III obesity (> 40 kg/m²). Categorical outcomes were presented as percentages and frequencies, continuous outcomes as means with SD (standard 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 [15–17]. Hierarchical multiple regression analyses and univariate analyses were conducted to evaluate the relationship between patient reported outcomes as dependent 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, sociodemographic 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 endometrial endometrial cancer between January 2010 and December 2018, with 99 women being deceased at the time of the study and therefore excluded. 390 patients were invited to participate. Thirty-six patients were excluded for other types of histology (non-endometrioid). Out of the remaining 354 women, 337 (95.2%) completed the questionnaire. The analysis disclosed that higher BMI (> 25 kg/m²) 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/m²) 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 women had significantly worse physical, emotional and social functioning compared to normal weight and overweight participants [$p = 0.01$, $p = 0.010$, and $p = 0.033$, respectively]. Fatigue, pain and dyspnoea are the most common symptoms in class I-III 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/m²) was associated with lymphoedema, urologic and gastrointestinal symptoms, pain (back/pelvic and muscular/joint) and numbness/tingling (Table 3). Univariate linear regression analyses showed that higher levels of BMI were associated with lower levels of HRQoL (Table 3). After controlling for socio-

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demographic and clinical characteristics and number of comorbidities, physical function and vitality remained significantly associated with BMI. 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 lead to 7.9 points increase score in symptoms of lymphoedema, 2.4 points increase score in urologic symptoms, 1.9 points increase score in numbness/tingling symptoms, and 13.4 points decrease score in sexual problems. On the other hand it’s harder for patients with lymphoedema (f.e.) to stay fit because they hold more interstitial fluid in the body, which caused weight gain. This could be just a relation not a causality.

### Discussion

Class I-III obesity was associated with poorer quality of life in endometrial cancer survivors. Increasing BMI was inversely associated with QoL. Pre-obese and obese patients should be informed about greater incidence of pain, fatigue and dyspnea.

### Table 1 Clinical characteristics of participants according to BMI categories

| Variable                | Normal BMI 18.5–24.9 | Pre-obese BMI 25–29.9 | Class I and II obese BMI 30–39.9 | Class III obese BMI ≥40 | P       |
|-------------------------|----------------------|-----------------------|----------------------------------|-------------------------|---------|
| 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 (0.6%)                |         |
| III-IV                  | 3 (4.5%)             | 5 (3.8%)              | 4 (3.6%)                         | 1 (1.4%)                |         |
| Grade                   |                      |                       |                                  |                         | 0.852   |
| I                       | 36 (54.5%)           | 69 (52.6%)            | 54 (48.6%)                       | 3 (67%)                 |         |
| 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               |                      |                       |                                  |                         | 0.041   |
| Surgery without LYA     | 55 (83.3%)           | 103 (78.6%)           | 81 (72.9%)                       | 28 (96.5%)              |         |
| Surgery + LYA           | 18 (27.2%)           | 38 (29%)              | 31 (27.1%)                       | 2 (6.8%)                |         |
| Surgery + RT            | 13 (19.6%)           | 29 (22.1%)            | 22 (19.8%)                       | 2 (6.8%)                | 0.374   |
| Recurrence              |                      |                       |                                  |                         | 0.461   |
| Yes                     | 5 (7.5%)             | 14 (10.6%)            | 1 (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 (8.2%)             | 10 (9%)                          | 3 (10.3%)               |         |
| 1–2 years               | 7 (10.6%)            | 13 (10.5%)            | 16 (14.4%)                       | 4 (13.7%)               |         |
| 2–3 years               | 12 (18.1%)           | 22 (17.7%)            | 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%)           | 13 (17.5%)            | 17 (15.3%)                       | 6 (20.6%)               |         |
| > 5 years               | 17 (25.7%)           | 32 (24.4%)            | 24 (21.6%)                       | 5 (17.2%)               |         |
| Comorbidity             |                      |                       |                                  |                         | 0.897   |
| No                      | 48 (72.7%)           | 30 (22.9%)            | 14 (12.6%)                       | 3 (10.3%)               |         |
| Yes                     | 18 (27.3%)           | 101 (77%)             | 97 (87.3%)                       | 26 (96.6%)              | < 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  |
| Arthritis               | 11 (16.6%)           | 45 (34.3%)            | 57 (51.3%)                       | 20 (68.9%)              | < 0.01  |

LYA lymphadenectomy, RT radiotherapy, FIGO endometrial cancer staging
In our study group of the endometrioid endometrial cancer survivors, 38.8% of patients were pre-obese, 32.9% were class I and II obese, and 8.6% were class III 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 [10]. In 2011, Fader et al. found 81% of patients with the type I of endometrial cancer were obese [18].

Increasing BMI score from class I to class III obesity was associated with a lower degree of physical,

### Table 2 Outcomes of QLQ-C30 questionnaires of participants according to BMI categories

| Variable                  | Normal BMI 18.5–24.9 | Pre-obese BMI 25–29.9 | Class I and II obese BMI 30–39.9 | Class III obese BMI ≥40 | Univariate analysis | Multivariate analysis |
|---------------------------|-----------------------|------------------------|----------------------------------|-------------------------|---------------------|----------------------|
| N = 66                    | N = 131               | N = 111                | N = 29                           |                         |                     |                      |
| Global quality of life    | Mean (SD)             | Mean (SD)              | Mean (SD)                        | Mean (SD)               | 0.081               | N/A                  |
| Functional scales         |                       |                        |                                  |                         |                     |                      |
| Physical functioning      | 86 (18)               | 81 (18)                | 81 (17)                          | 64 (27)                 | 0.003               | 0.011                |
| Role functioning          | 88 (21)               | 83 (25)                | 84 (26)                          | 79 (32)                 | 0.061               | 0.008                |
| Emotional functioning     | 90 (17)               | 85 (15)                | 78 (14)                          | 71 (29)                 | 0.035               | 0.003                |
| Cognitive functioning     | 90 (15)               | 88 (15)                | 89 (20)                          | 83 (29)                 | 0.82                | 0.053                |
| Social functioning        | 92 (20)               | 88 (14)                | 76 (13)                          | 74 (27)                 | 0.030               | 0.021                |
| Symptom scales            |                       |                        |                                  |                         |                     |                      |
| Fatigue                   | 20 (19)               | 23 (21)                | 25 (23)                          | 29 (25)                 | 0.82                | N/A                  |
| Nausea and vomiting       | 4 (8)                 | 5 (9)                  | 7 (15)                           | 7 (16)                  | 0.071               | N/A                  |
| Pain                      | 12 (20)               | 18 (26)                | 26 (28)                          | 26 (33)                 | 0.081               | N/A                  |
| Dyspnoea                  | 10 (18)               | 16 (20)                | 23 (30)                          | 26 (33)                 | 0.009               | N/A                  |
| Insomnia                  | 27 (29)               | 22 (29)                | 19 (20)                          | 4 (15)                  | 0.891               | N/A                  |
| Appetite loss             | 7 (12)                | 5 (14)                 | 4 (12)                           | 4 (15)                  | 0.891               | N/A                  |
| Constipation              | 15 (24)               | 10 (20)                | 10 (21)                          | 12 (20)                 | 0.121               | N/A                  |
| Diarrhoea                 | 4 (11)                | 4 (12)                 | 7 (15)                           | 9 (14)                  | 0.076               | N/A                  |
| Financial difficulties    | 5 (15)                | 7 (24)                 | 6 (13)                           | 6 (18)                  | 0.641               | 0.082                |

N/A not applicable

In our study group of the endometrioid endometrial cancer survivors, 38.8% of patients were pre-obese, 32.9% were class I and II obese, and 8.6% were class III 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 [10]. In 2011, Fader et al. found 81% of patients with the type I of endometrial cancer were obese [18].

Increasing BMI score from class I to class III obesity was associated with a lower degree of physical,
emotional, and social functioning. Similar findings can also be found in previous studies [9, 18–21]. Fatigue, pain, and dyspnea were more often associated with higher BMI (≥ 25 kg/m²). A similar relationship was observed in other studies, confirming association between BMI and poorer physical functioning [9, 18, 19, 21]. While several authors report a positive correlation between diarrhoea and morbid obesity, we have not found such association [19, 22]. In our study, class III 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, 18–20]. Emotional functioning was significantly worse in our sample among patients with BMI ≥ 40. The role functioning domain in our study showed no association, which is in contradiction with another study [19].

In our study, women with higher BMI experienced poorer physical functioning. Rossi et al. published that physically active endometrial cancer survivors reported higher QoL and lower BMI. Our results are consistent with the results of the study by Rossi et al. Their data suggest that a physically active lifestyle has a benefit in socioculturally diverse endometrial cancer survivors [23].

The explanation of reduced physical functionality can be found in limited mobility, usually present comorbidity, and somewhat poor physical endurance [15]. Obese people are often discriminated against in social situations, therefore their social interactions may be limited [19, 24]. The question is whether there is 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 particularly alleviate this problem in the case of obese patients [29]. 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%) [30].

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 cosubstantial 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 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, 20, 21].

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.

Comorbidities were significantly different in the four BMI groups. This fact can have impact on the quality of life. We suggest that the impact of comorbidities should be considered in future studies.

We have not been reckoning the influence of belief and religiosity in our group, it opens the door to conducting research in specific areas of cancer care. Furthermore, an increasing trend in body weight gain and related diseases is alarming particularly in light of the rising health care costs. Prospective studies that evaluate this effect are needed.

Conclusions

Obesity is one of the greatest health threats and has negative impact on quality of patients’ lives. Obese women have significantly more dyspnea, fatigue and pain. Lymphedema is a major complication of lymphadenectomy among women with endometrial cancer, especially those with class III obesity. Women with increased BMI experienced poorer physical, emotional and social functioning compared to normal weight and pre-obese patients.

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Author’s contributions

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Availability of data and materials

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Ethics approval and consent to participate

The author declare that he has received Ethics committee approval (The Ethics Committee of Faculty Hospital in Nitra, Slovakia).

Consent for publication

Not applicable.

Competing interests

The author declare he have no competing interests.

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