European Journal of Gynaecological Oncology

Eur. J. Gynaecol. Oncol. **2022**; 43(1): 132–142
http://doi.org/10.31083/j.ejgo4301020

Review

Pelvic floor dysfunction in endometrial cancer patients after treatment. A literature review

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Academic Editor: Enrique Hernandez
Submitted: 3 October 2021 Revised: 19 December 2021 Accepted: 23 December 2021 Published: 15 February 2022

Abstract

Endometrial cancer (EC) survivors are increasing progressively. However, treating this disorder may detrimentally affect the pelvic organs, resulting in pelvic floor disorders (PFD): urinary incontinence, pelvic organ prolapse, and bowel dysfunction. The aim of this review is to investigate the prevalence of PFD in EC survivors following both surgical and nonsurgical treatments. The authors conducted a structured search in the following databases: MEDLINE, EMBASE, Global Health, The Cochrane Library, and Web of Science from inception until August 2021. The inclusion criteria were: (1) women with EC, (2) observational studies, (3) original data, (4) PFD result evaluation, and (5) the use of verified tools for the evaluation of PFD. The initial search found 590 articles for PFD and endometrial cancer. Only 10 of the studies were finally available for further analysis, including 1849 individuals with EC. In total, the incidence of UI increased from 7.6% to 20.8% after EC therapy. The incidence of stress and urge UI after treatment ranged from 23 to 74.3% and 20.8 to 71.4%, respectively. The prevalence of POP was as high as 13.6% in 638 EC survivors. The prevalence of fecal incontinence was 21% in 732 EC survivors. In conclusion, PFDs are common after endometrial cancer treatment. The lack of comparative studies between the type of EC and the type of treatment limits further exploration of the differences in PFD frequency among EC survivors and the variety of EC treatments.

Keywords: Endometrial cancer (survivors); Pelvic floor disorders; Urinary incontinence; Stress-urge urinary incontinence; Overactive bladder; Fecal incontinence

1. Introduction

Endometrial cancer (EC) is the most common gynecologic malignancy with a progressively growing incidence over the last decade [1,2]. This can be attributed to the increasing prevalence of obesity, the predominant modifiable risk factor for EC development, along with a parallel increase in a wide cluster of other common risk factors such as diabetes, metabolic syndrome, and smoking [3,4]. In addition, reduced fertility rates and menopausal hormone use (especially estrogen plus progestin formulations) may play a key role [5]. Another potential factor could be the reduced hysterectomy rates for non-malignant disorders observed in the last few years, which may increase the burden of women that may develop EC [6]. Women with this tumor have a generally good prognosis, with a five-year survival rate of approximately 81 percent of participants [7]. EC tumors are mainly well-differentiated and they are confined to the endometrium [8], which predicts an even better five-year survival rate (90%) [9].

All in all, the increase in EC prevalence along with improvements in treatment has led to a significant increase in EC survivors. In 2016, the number of EC survivors reached 755,000, making them the second-largest group of female cancer survivors in the United States [10]. Given the above-mentioned, improvements in the quality of life of these patients should be of paramount clinical relevance, but this has not been extensively evaluated. When selecting treatment options, it is important to take into consideration both the treatment's morbidity and its impact on quality of life. A wide range of therapeutic modalities are employed in EC therapy, all of which have the potential to influence the pelvic organs and cause pelvic floor symptoms: urinary incontinence (UI), pelvic organ prolapse (POP), and bowel disfaction (BD), whether used alone or in combination. In women with EC, the real prevalence of pelvic floor disorders (PFD) is unclear. The influence of EC treatment on the incidence of PFD has not been fully explored, and it is probable that it is mentioned relatively seldom with patients. Despite this, PFDs are prevalent, especially in older women, and have a major negative impact on quality of life [11]. A full literature evaluation on rates of PFD in women who have had EC treatment has not yet been completed.

The aim of this review was to explore the prevalence of PFD in EC survivors after surgical and non-surgical therapies.

2. Materials and methods

2.1 Search strategy and selection criteria

Following the Cochrane Handbook for Systematic Reviews of Interventions version 6.2 guidelines [12], we conducted a review of observational studies examining PFDs among EC survivors. For our purposes, we utilized the NCI definition of cancer survivor, which considers an individual a cancer survivor from the moment of diagnosis to the end of his or her life. A structured search of the following databases was performed by two of the authors (IT, TM): MEDLINE, EMBASE, Global Health, The Cochrane Library, and Web of Science from inception to August of 2021. The following MeSH and non-MeSH terms were used in combination: 'EC', 'PFD', 'POP', 'UI', 'stress urinary incontinence (SUI)', 'urge urinary incontinence (UUI)', overactive bladder (OB)', and 'fecal incontinence (FI)'. We also looked through the references of relevant articles to see if any publications on PFD had been published among EC survivors. Studies having outcomes other than PFD, as well as those that did not involve EC survivors, were omitted. All studies of any design, except Case reports, Case Series, Letters, Editorials, and Reviews were included. The population inclusion criteria were: (1) women diagnosed with EC, (2) observational studies, (3) original data collection, (4) PFD result evaluation, (5) the use of verified tools for the evaluation of PFD. We excluded pilot studies and studies of gynecologic cancer survivors that did not separately offer estimates for EC patients.

2.2 Study selection, data extraction, and quality assessment

Based on the specified qualifying criteria, two reviewers independently reviewed each paper by title and abstract. Two reviewers independently evaluated the full texts of qualifying papers for data extraction (IT, TM). Author, year of publication, study population, timing of PFD assessment, PFD assessed, PFD data collection method, number of patients included in final analyses, demographic characteristics (i.e., age, gender, and ethnicity), statistical analysis method, and outcomes were among the information extracted. Disagreements among the reviewers on research eligibility, data extraction, and quality assessment were addressed by consensus (Fig. 1).

3. Results

Our search revealed 590 references that assess PFD after an EC diagnosis. After removing 105 duplicates, we evaluated the titles and abstracts of 485 unique papers. Following an examination of the titles and abstracts, 51 publications were retrieved in their entirety [13–62], with 10 eventually qualifying for this study (Fig. 1) [13–22]. Most of the studies were retrospective cross-sectional, with the evaluation of PFD taking place at some point following the EC therapy; only 3 of them were prospective, and the overall quality of the studies was poor. All studies used English

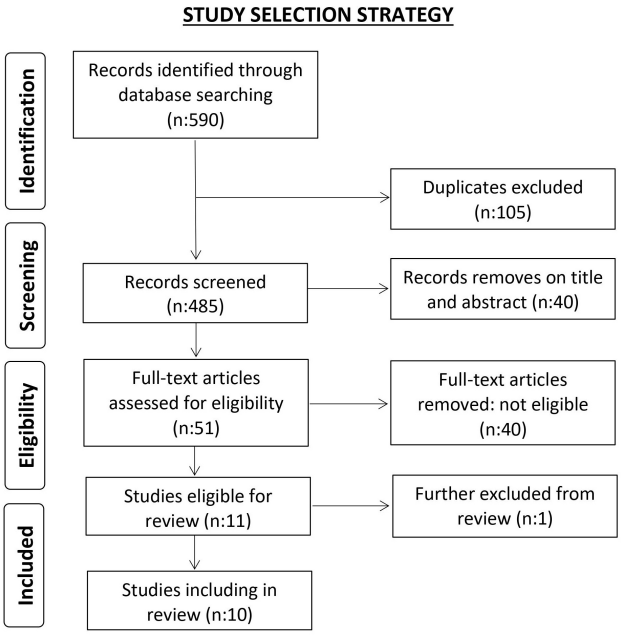

Fig. 1. The flow diagram of study search and selection.

as the language and were published in 2009 and afterwards.

Changes in PFD before and after therapy were reported only in 3 studies. Six studies exhibited PFD data only after EC therapy, and there was one study that presented the prevalence of PFD after EC diagnosis and before therapy. The impact of EC treatment on UI was evaluated in all the studies (n = 10); the impact of EC treatment on POP was evaluated in 4 studies; and the impact of EC treatment on FI was evaluated in 3 studies (Table 1, Ref. [13–22]). Treatment of endometrial malignancies may include various combinations of surgery, external beam radiotherapy, chemotherapy, and brachytherapy based on the extent of disease and other patient characteristics. Five of the studies focused on surgical therapy and four on drugs and radio therapy. The majority of articles comprised non-selected groups of EC patients, whereas 3 studies covered cases only in early stages (Stage I) (Table 1). The included studies' sample sizes ranged from 25 to 660 women with EC, and the majority of them employed more than one PFD evaluation. PFDs were assessed mainly via the completion of validated questionnaires. Table 2 provides the list of validated questionnaires that were used in the studies to assess various PFDs. The most frequently utilized PFD questionnaire was the International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms (ICIQ-FLUTS).

Overall, our results elicit information from 1849 patients with EC. The prevalence of PFDs was investigated in 1320 patients prior to treatment, and PFDs were evaluated in 1581 EC survivors after treatment. The mean age of the patients was 62.9 years, and the mean body mass index (BMI) was 31.8 kg/m^2 [12–22].

Table 1. List of studies included in review. Evaluation of PFDs before and after endometrial cancer treatment.

Study, Year	Endometrial Cx Stage	Type of treatment	n	Mean age (years)	Mean BMI (Kg/m^2)	Pre-treatment					Post-treatment				
						SUI	OAB	UI	POP	FI	SUI	OAB	UI	POP	FI
1 Higgs *et al.* 2017 [13]	Stage I	(A) Abd (B) Lap TH and BSO	381 (A = 195, B = 186)	62.8 (A = 62.6 ± 10.9, B = 63.0 ± 9.5)	N/A	-	-	31/381 (A = 11/195 B = 20/186)	23/381 (A = 9/195, B = 14/186)	21/381 (A = 7/195, B = 14/186)	-	-	18/207 (A = 10/102, B = 8/105)	4/207 (A = 2/102, B = 2/105)	10/207 (A = 1/102, B = 9/105)
2 Lipetskaia *et al.* 2019 [14]	Stage I	Robotic-assisted LH (A) with L/N dissection (B) without	74 (A = 37, B = 37)	59 ± 11 (A = 60.0 ± 11.0, B = 58.0 ± 11.0)	39.0 ± 11.0 (A = 37.2 ± 9.0, B = 41.3 ± 12.0)	-	-	17/74	-	-	-	-	22/74 (A = 11/37, B = 10/37)	-	-
3 Zi etek-Strobl *et al.* (2020) [15]	Stage I-IV	TAH+ BSO or TH with pelvic L/N dissection or RH ± adjuvant oncological therapy	83	59.1 ± 12.1	26.7 ± 5.56	-	-	-	-	-	-	-	33/83	41/83	-
4 Bernard *et al.* (2017) [16]	Stage I, II	TAH+ BSO and adjuvant RT, BT with or without external-beam RT	111	69.4 ± 5.7	30.4 ± 4.5	-	-	0/111	-	-	-	-	11/111	-	-
5 Nosti *et al.* 2012 [17]	Stage IB	extra fascial TAH+ BSO with or without L/N sampling	25	62.0 ± 12.0	32	-	-	-	-	-	-	-	19/25	11/25	-
6 De Boer *et al.* 2015 [18]	Stage I	(A) EBRT, (B) VBT	202 (A = 89, B = 113)	67.7 (A = 67.1, B = 68.1)	N/A	-	-	-	-	-	-	-	83/202 (A = 36, B = 47)	-	37/202 (A = 21, B = 16)
7 Segal *et al.* 2017 [19]	Stage I-IV	Abd or lap or robotic TAH+ BSO (A) with RT (B) without	149 (A = 62, B = 87)	63.4 (A = 64.0, B = 63.0)	30 (A = 30.3, B = 30.8)	-	-	-	-	-	34/149 (A = 13, B = 21)	31/149 (A = 8, B = 23)	68/149 (A = 30, B = 38)	7/149 (A = 4, B = 3)	70/149 (A = 28, B = 42)

Table 1. Continued.

	Study, year	Endometrial Cx Stage	Type of treatment	n	Mean age (years)	Mean BMI (Kg/m^2)	Pre-treatment SUI	Pre-treatment OAB	Pre-treatment UI	Pre-treatment POP	Pre-treatment FI	Post-treatment SUI	Post-treatment OAB	Post-treatment UI	Post-treatment POP	Post-treatment FI
8	De Boer *et al*. 2016 [20]	Stage IA grade; stage IB grade 3; stage II, stage IIIA, IIIB (parametrial invasion), IIIC; serous or clear cell stage IA (with invasion), IB, II, or III	(A) CRT, (B) RT alone, (1) Grade 2, (2) Grade 3–4	660 (A = 32, B = 333, 1 = 99, 2 = 274)	62.2 (A = 62.5, B = 61.9)	N/A	-	-	17/660 (A = 12, B = 5, 1 = 16, 2 = 1)	-	-	-	-	19/660 (A = 9, B = 10, 1 = 17, 2 = 2)	-	-
9	Erekson *et al*. 2009 [21]	Stage I-IV	Any surgical treatment (A) no Adjuvant RT (B) Adjuvant RT	70 (A = 45, B = 25)	60.1 ± 12.1 (A = 60.0 ± 12.9, B = 60.2 ± 10.5)	33.5 ± 9.8 (A = 32.7 ± 9.5, B = 34.7 ± 10.2)	-	-	-	-	-	52/70 (A = 31, B = 21)	50/70 (A = 30, B = 20)	56/70	-	-
10	Bretschneider *et al*. 2016 [22]	Stage I-IV	Before treatment	94	58.1 ± 13.3	33.6 ± 8.8	27/94	23/94	35/94	-	3/94	-	-	-	-	-
Total				1849	62.9	31.97	27/94 (28.7%)	23/94 (24.5%)	100/1320 (7.6%)	23/381 (6.0%)	21/381 (5.5%)	86/219 (39.3%)	81/219 (37.0%)	329/1581 (20.8%)	63/464 (13.6%)	117/558 (21.0%)

Cx, Cancer; Abd, abdominal; Lap, laparoscopic; TH, total hysterectomy; TAH, total abdominal hysterectomy; BSO, bilateral salpingectomy and oophorectomy; L/N, lymph node; RT, radiotherapy; VBT, vaginal brachytherapy; EBRT, external beam radiation therapy; CRT, chemoradiotherapy; RH, radical Wertheim-Meigs hysterectomy.

Table 2. Questionnaires used in the assessment of patient-reported outcomes.

Questionnaire	Abbreviation	Constructs measured	Studies using questionnaire n (%)
International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms	ICIQ-FLUTS	Evaluating female lower urinary tract symptoms and impact on quality of life (QoL)	3 (30)
International Consultation on Incontinence Questionnaire - Urinary Incontinence	ICIQ-UI	A questionnaire for evaluating the frequency, severity and impact on quality of life (QoL) of urinary incontinence	1 (10)
Pelvic Floor Distress Inventory-20	PFDI-20	This Questionnaire will ask if there are certain bowel, bladder, or pelvic symptoms and how much they bother over the last 3 months	2 (20)
Pelvic Floor Impact Questionnaire	PFIQ-7	It is a health-related quality of life questionnaire for women with pelvic floor conditions	1 (10)
European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30	EORTC QLQ-C30	Designed to measure cancer patients' physical, psychological and social functions. The questionnaire is composed of multi-item scales and single items	1 (10)
Urinary Distress Inventory-6	UDI-6	assess symptom distress and the impact on daily life of urinary incontinence	1 (10)
incontinence specific QoL using the Incontinence Impact Questionaire-7	IIQ-7	Refer to areas in your life that may have been influenced or changed by accidental urine loss	1 (10)
Incontinence Severity Index questionnaire	ISI	A questionnaire composed of a two-items which assess the frequency (4 levels) and amount (3 levels) of urine leakage	2 (20)
Questionnaire for Urinary Incontinence Diagnosis	QUID	A self-administered, 6-item questionnaire designed to distinguish between SUI and UUI	1 (10)
International Consultation on Incontinence Questionnaire Vaginal Symptoms Module	ICIQ-VS	A robust instrument for assessing a range of vaginal and sexual symptoms, in particular those of pelvic organ prolapse.	2 (20)
Pelvic Organ Prolapse/Urinary Incontinence Sexual questionnaire	PISQ-12	It is aimed at clinicians and other medical specialists that are interested to assess the sexual function in women with urinary incontinence or pelvic organ prolapse. The score consists of 12 items, all of which are questions pertaining to sexual life aspects.	1 (10)
International Consultation on Incontinence Questionnaire Anal Incontinence Symptoms and Quality of Life Module	ICIQ-B	A patient-completed questionnaire for evaluating symptoms of anal incontinence (including flatus incontinence) and impact on quality of life (QoL), provides a robust measure organized into three domains, bowel pattern, bowel control and impact on quality of life associated with anal incontinence symptoms.	1 (10)
Fecal Incontinence Severity Index	FISI	Quantify the impact of adult incontinence leakage on quality of life and describes the severity of different types of incontinence for bowel contents	1 (10)
Impact of Cancer version 2	IOCv2	Designed to assess the physical and psychosocial health experience of cancer survivors through its positive and negative impacts.	1 (10)

Table 3. Urinary incontinence evaluation before and after treatment of endometrial cancer.

	Study, Year	Pre-treatment				Post-treatment			
		n	SUI	OAB	UI	n	SUI	OAB	UI
1	Higgs *et al*., 2017 [13]	381	-	-	31/381 (8.1%)	207	-	-	18/207 (8.7%)
2	Lipetskaia *et al*., 2019 [14]	74	-	-	17/74 (23.0%)	74	-	-	22/74 (29.7%)
3	Zietek-Strobl *et al*., 2020 [15]	-	-	-	-	83	-	-	33/83 (39.7%)
4	Bernard *et al*., 2017 [16]	111	-	-	0/111 (0.0%)	111	-	-	11/111 (9.9%)
5	Nosti *et al*., 2012 [17]	-	-	-	-	25	-	-	19/25 (76.0%)
6	De Boer *et al*., 2015 [18]	-	-	-	-	202	-	-	83/202 (41.1%)
7	Segal *et al*., 2017 [19]	-	-	-	-	149	34/149 (22.8%)	31/149 (20.8%)	68/149 (45.6%)
8	De Boer *et al*., 2016 [20]	660	-	-	17/660 (2.6%)	660	-	-	19/660 (2.9%)
9	Erekson *et al*., 2009 [21]	-	-	-	-	70	52/70 (74.3%)	50/70 (71.4%)	56/70 (80.0%)
10	Bretschneider *et al*., 2016 [22]	94	27/94 (28.7%)	23/94 (24.5%)	35/94 (37.2%)	-	-	-	-
Total		1320	27/94 (28.7%)	23/94 (24.5%)	100/1320 (7.6%)	1581	86/219 (39.3%)	81/219 (37.0%)	329/1581 (20.8%)

Table 4. Pelvic organ prolapse evaluation before and after endometrial cancer treatment.

	Study, Year	Pre-treatment			Post-treatment	
		n	n	POP	n	POP
1	Higgs *et al*., 2017 [13]	381	381	21/381 (5.5%)	207	4/207 (1.9%)
2	Zietek-Strobl *et al*., 2020 [15]	83	-	-	83	41/83 (49.4%)
3	Nosti *et al*., 2012 [17]	25	-	-	25	11/25 (44.0%)
4	Segal *et al*., 2017 [19]	149	-	-	149	7/149 (47.0%)
Total		638	381	23/381 (5.5%)	464	63/464 (13.6%)

3.1 Urinary incontinence

Urinary incontinence: Non-classified UI, SUI, and UUI were reported in all 10 studies. More specifically, all articles evaluated non-classified UI and only 3 assessed SUI and UUI. Pre-treatment UI rates ranged from 2.6 to 37.2%. According to the study results, the incidence of non-classified UI increased after EC therapy from 8.3% to 20.8% ($p < 0.001$). All studies indicate that the non-classified UI rates increase after EC therapy; the prevalence of non-classified UI increases from 2.6–37.2% before to 2.9–80.0% after EC treatment. However, the increase in the frequency of UI is not significant in all studies. Only in one study with 111 patients did the difference in UI significantly increase after EC treatment ($p < 0.001$) [16]; the other studies that included patients who had UI evaluation before and after EC treatment did not show a statistical difference (Table 3, Ref. [13–22]).

Stress and urge urinary incontinence: SUI and UUI were examined only in 3 studies, whereas there was no study to evaluate the prevalence of SUI or UUI both before and after EC therapy. According to data analysis from all 3 trials, the prevalence of SUI and UUI increased after EC treatment from 28.7% to 39.2% ($p = 0.07$) and from 24.5% to 37.0% ($p = 0.03$), respectively. There is a wide range of SUI and UUI incidence after oncological treatment in the included studies (SUI: 23.0–74.3%, UUI: 20.8–71.4%). However, these studies include a trial where SUI and UUI incidence of EC patients were recorded only before treatment ($n = 94$) [10], and two trials where SUI and UUI incidence of EC patients were recorded only after treatment ($n = 219$) [19,21] (Table 3).

3.2 Pelvic organ prolapse and Bowel dysfunction

Pelvic organ prolapse: The prevalence of POP in 638 survivors of EC was evaluated in 4 studies (Table 4, Ref. [13,15,17,19]) and a prolapse rate of 13.6% was found after EC therapy ($p < 0.001$) [13,15,17,19]. There was only one study that examined the POP before and after any oncology intervention, and a decrease in POP incidence after EC therapy from 6% to 2% was recorded ($p = 0.038$) [13].

Fecal incontinence: In three studies (732 patients) after EC therapy, the total rate of FI was 21%. The FI rates ranged from 6.0% to 47%, and there was a statistical increase in FI after EC treatment ($p < 0.001$) (Table 5) [13,18,19]. Higgs *et al*. (2017) found a baseline FI rate of 6% using the validated Pelvic Floor Distress Inventory (PFDI) and recorded a decrease of 1.2% after oncological therapy ($p = 0.54$) [13]. Segal *et al*. (2017) [19] found an incontinence of liquid stool rate of 47% (the highest rate reported) in EC survivors using the Fecal Incontinence Severity Index (FISI) with a follow-up of 84–96 months.

3.3 Surgery only treatment vs surgery plus radiotherapy with or without adjuvant chemotherapy

After being diagnosed with EC, the vast majority of women are subjected to hysterectomy, with adjuvant radiation therapy being recommended for roughly 45% of these

Table 5. Fecal incontinence evaluation before and after endometrial cancer treatment.

	Study, Year	Pre-treatment			Post-treatment	
		n	n	FI	n	FI
1	Higgs *et al*., 2017 [13]	381	381	23/381 (6.0%)	207	10/207 (4.8%)
2	De Boer *et al*., 2015 [18]	202	-	-	202	37/202 (18.3%)
3	Segal *et al*., 2017 [19]	149	-	-	149	70/149 (47.0%)
Total		732	381	23/381 (6.0%)	558	117/558 (21.0%)

patients based on pathologic findings [63]. External beam radiotherapy, chemotherapy, and brachytherapy may alter the structure and function of pelvic organs such as the bladder, colon, and vagina and may increase the chance of developing pelvic floor problems.

Erekson *et al*. conducted a cross-sectional study with a 51-month follow-up to assess SUI and UUI in 70 patients following surgery and radiotherapy using the UDI questionnaire. SUI occurred in 69% of patients following surgery alone, and in 84% following surgery and radiation. UUI occurred in 67% of patients following surgery alone and in 80% of individuals following surgery and radiation. The mean UDI-6 and IIQ-7 scores for women who had adjuvant radiation therapy were higher than those who did not receive adjuvant radiation therapy [47 (26.8) vs. 35.6 (21.7); $p = 0.05$)] and [24.4 (28.5) vs. 8.1 (16.4); $p = 0.004$)]. Adjuvant radiation therapy was related to worsening incontinence symptoms and a negative influence on QOL [21]. In the Saya Segal *et al*. (2017) study, 149 EC survivors were recruited, and radiation therapy was applied to 41% of these patients. The rates of UI in cancer survivors who were exposed and not exposed to radiation therapy were 48% and 58%, respectively ($p = 0.47$) and there was no difference in the prevalence of FI across groups [19]. de Boer *et al*. in their multicenter randomized trial enrolled 427 patients and established the efficacy of vaginal brachytherapy for local disease control with fewer side effects than external beam radiotherapy in patients with high-intermediate risk disease. It also evaluated bowel and urinary symptoms more than 7 years after treatment with surgery and brachytherapy or surgery and external beam radiotherapy using cancer-specific health-related QOL questionnaires. UI rates in the brachytherapy and external beam radiotherapy groups were 41% and 44%, respectively, among 196 survey respondents. Daytime frequency rates were 61% in both groups, but dysuria rates were slightly lower in the brachytherapy group than in the external beam radiotherapy group (6% and 9%, respectively). The FI and FU rates were higher in patients who got external beam radiotherapy (24% and 55%, respectively) than in those who received brachytherapy (15% and 32%, respectively) [18].

4. Discussion

The prevalence of PFD in survivors of EC after treatment is summarized in this review. Our findings show that all PFDs are very frequent in EC survivors. The incidence of UI ranges from 2.9–80.0% (range of SUI: 22.8–74.3%; range of UUI: 20.8–71.4%). The incidence of POP ranges from 1.9–49.0%. The incidence of FI ranges from 4.8–47.0%.

When comparing the findings of our study to the general population, the frequency of PFDs after treatment of EC appears to be increased. In the general population, the rate of UI ranges from 3.5% to 38.2%, while that of FI ranges from 2.6% to 21% [64]. The frequency of UI in the general population is almost half compared to that of UI in our study. The frequency of FI (is even lower compared to that of FI in our study. According to our study, there is a statistically significant increase in the incidence of UI ($p < 0.001$), OAB ($p = 0.03$), POP ($p < 0.001$), and FI ($p < 0.001$) in EC survivors after oncological treatment. However, due to (1) the methodology of this review, (2) the non-discrimination of the stage and the type of EC, and (3) the non-discrimination of the type of EC treatment, our results are not solid. Nevertheless, this data serves as indirect evidence of the increased PFD frequency in EC patients after treatment.

While research on the prevalence of PFD after therapy predominates in the literature, it is critical to evaluate the baseline prevalence before the initiation of any treatment. The lack of pre-treatment data across all these studies appears to be the main problem with the investigation of the frequency of PFD in EC patients after treatment. Thus, the calculation of any post-treatment changes in the frequency of PFD compared to the baseline symptoms is practically impossible. Our review confirms this lack of data, and for this reason we included the study of Bretschneider *et al*. (2016) [22] as a baseline for future comparisons of pre- and post-treatment.

It appears that the incidence of PFD in EC survivors varies widely due to the variations in the applied methodology (i.e., different PFD questionnaires) measurements, the variations in the type of treatment, and the variations in the length of the follow-up. Moreover, the absence of research where there is direct comparison related to the type and stage of EC precludes further discussion of the variations in PFD prevalence between EC survivors and the subtypes of EC. The long-term follow-up of the randomized controlled PORTEC studies has provided some information on the occurrence of PFD in EC survivors. In particular, in the follow-up study to PORTEC-2 [20], a comparative study in which patients underwent surgery followed by ei-

ther brachytherapy or radiotherapy, both treatment modalities were associated with high rates of urinary dysfunction, urinary frequency, and dyspareunia 84 months after treatment. Therefore, our data suggest that no conclusion about the relationship between the intensity of the PFDs and the type of EC can be elicited. As the kind of treatment method is determined by EC type and stage, many patients may receive numerous modalities of treatment, making it impossible to comment on the influence of individual treatment modalities on the development of PFDs. Moreover, there were many studies excluded from this review because the stated prevalence of PFD was not differentiated by gynecologic cancer type. Another important drawback is the absence of comparison research assessing the influence of various therapy modalities on PFDs.

Furthermore, there was little uniformity in the types of validated instruments utilized for objective PFD evaluation. Many of the excluded research utilized no validated questionnaires, raising concerns about the data's reliability and repeatability. The use of 14 different questionnaires in PFD research hinders the capacity to directly compare studies and findings. The ICIQ-FLUTS was the most frequently used questionnaire in the literature we evaluated. This instrument evaluates and quantifies lower urinary tract symptoms (LUTS) and their influence on quality of life. It comprises 12 LUTS-related questions split into three categories: filling (4 questions), voiding (3 questions), and incontinence (5 questions). The responses are based on LUTS experiences during the past four weeks. Furthermore, no included publication utilized clinical examination or urodynamic studies (UDS) to evaluate the PFD symptoms; the complete absence of clinical evaluation in all evaluated articles reduces the validity of the data gathered.

EC treatments seem to deteriorate pre-existing PFD or elicit new symptoms. The most common surgery performed on EC patients is abdominal hysterectomy with bilateral salpingo-ophorectomy. It is expanded, when necessary, by pelvic lymphadenectomy, paracolpium removal, or debulking surgery. This more invasive and severe surgery causes immediate intra-operative and early post-operative problems, as well as damage to surrounding tissues, and contributes to an increase in the likelihood of PFDs. The goal of radical pelvic surgery is to limit the recurrence of the cancer, but it may also harm urogenital nerves and blood vessels. Tissue hypoxia, scarring, and local ischemia can all raise the likelihood of PFD. Furthermore, the combination treatment (surgery plus radiation and chemoradiation) has a detrimental impact on the lower urinary tract and pelvic floor organs. The danger of problems following pelvic radiation is obvious, affecting not only the genitourinary system but also the gastrointestinal tract. Urgency, stress urine incontinence, interstitial cystitis, urinary bladder fibrosis, vaginal fibrosis, and vesico/urethro-vaginal fistulas are among the side effects that might affect patients immediately or for a long period following therapy [15].

This review's key strengths include an overall rigorous methodology, defined inclusion criteria, a thorough search of numerous databases, and duplicate assessments of titles/abstracts, full-text, and data to guarantee accuracy before qualitative analysis. Furthermore, the absence of reviews, and more specifically, better organized ones, that correlate EC treatment with PFD enhances the dynamics of this review. The main drawback, as with most evaluations, was the inadequacies of the examined literature. The research demographics, evaluation methods, and timing of survey administration all differed significantly. Moreover, the heterogeneity and the methodological discrepancies among the studies indicate that in the future only well-designed studies should be conclusive. Finally, a potential problem with this type of research is the lack of clear clinical value of PFDs in the management of EC patients. It is true that PFDs do not change the EC treatment at all, and should be considered as a nearly separate entity, either induced by EC treatment or not. PFDs should be treated in the same manner as in healthy patients when the clinical status of EC survivors enables that. However, the possible increase in PFDs rates in EC patients may indicate that there may be treatments that induce the clinical burden of PFDs and that potential research could highlight the pathways for minimizing such influence.

In conclusion, PFDs are common in EC survivors and should be discussed with patients. The results of this review highlight a few suggestions for the forthcoming studies. The use of validated questionnaires is mandatory in order to determine baseline prevalence and the influence of particular oncologic therapy methods on PFD. Additional comparisons between EC survivors and the general population regarding PFDs are important in order to calculate the relevant PFD rates. Future research should focus on improving quality of life in EC survivors by using oncologic therapies that produce less pelvic floor injury and lead to a reduced incidence of PFD. Gynecology oncologists should consider screening for PFD at the time of EC diagnosis before starting therapy, and they should continue to evaluate PFD during treatment to identify the best time for intervention for control of the symptoms if clinically required. Early detection and identification of PFD in EC survivors would allow for comprehensive management, which might reduce morbidity from therapy and enhance quality of life.

Author contributions

IT, TM, DT and GFG designed the protocol. IT, TM, LZ, and GFG participate in project development. IT and TM performed the data collection. IT, TM, LZ, and DT analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable.

Acknowledgment

We would like to acknowledge all those who helped me during the writing of this manuscript. Thanks to all the peer reviewers for their opinions and suggestions.

Funding

This research received no external funding.

Conflict of interest

The authors declare no conflict of interest.

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