CANCER DIAGNOSIS & PROGNOSIS
3: 320-326 (2023) doi: 10.21873/cdp.10218

Pre-treatment Emotional Distress in Patients Receiving Radiotherapy for Gynecologic Cancers

DIRK RADES[1], AHMED AL-SALOOL[1], NATHAN Y. YU[2] and TAMER SOROR[1]

[1]*Department of Radiation Oncology, University of Lübeck, Lübeck, Germany;*
[2]*Department of Radiation Oncology, Mayo Clinic, Phoenix, AZ, U.S.A.*

Abstract. *Background/Aim: Patients with gynecologic cancers selected for external-beam radiotherapy or brachytherapy may experience emotional distress. We aimed to identify patients who may benefit from early psycho-oncological intervention. Patients and Methods: We investigated 10 potential risk factors of emotional distress in a retrospective series of 122 patients planned for radiotherapy of gynecologic cancers. Factors included COVID-19 pandemic, number of physical problems, age, performance status, tumor site/stage, surgery, chemotherapy, brachytherapy, and history of another tumor. p-Values <0.005 indicated significance, and p-values <0.06 trends. Results: Frequencies of worry, fear, sadness, depression, nervousness, and loss of interest were 41%, 57%, 39%, 16%, 38%, and 20%, respectively. Significant associations with at least one of these symptoms were found for ≥5 physical problems and no upfront surgery. Trends were observed for chemoradiotherapy, history of another tumor, worse performance status, and younger age. Conclusion: The prevalence of pre-radiotherapy emotional distress was remarkable in patients with gynecologic cancers. Patients with risk factors may benefit from immediate psycho-oncological assistance.*

Correspondence to: Prof. Dirk Rades, MD, FASTRO, Department of Radiation Oncology, University of Lübeck, Ratzeburger Allee 160, 23562 Lübeck, Germany. Tel: +49 45150045401, Fax: +49 45150045404, e-mail: dirk.rades@uksh.de

Key Words: Gynecologic cancers, radiation therapy, emotional distress, risk factors.

A considerable number of patients with gynecologic cancers experience psychological and emotional distress (1-4). In an analysis of survey data from a cohort study, emotional problems such as fear, nervousness, sadness, and worry were reported by 30 to 50% of patients, respectively (3). The burden of emotional distress may be particularly present in patients assigned to or undergoing radiotherapy or chemoradiation due to patient concerns regarding exposure to radiation, dependence on high-tech machines, and radiotherapy-induced adverse events (5-11). In a study of 480 patients irradiated for cervical cancer, up to 69% of the patients reported worry as a significant emotional problem (4). For these patients, psycho-oncological assistance may be important for treatment completion and outcomes. Therefore, our study aimed to investigate risk factors of pre-treatment emotional distress in order to identify those who may benefit from early psycho-oncological support.

Patients and Methods

A total of 10 potential risk factors were evaluated for associations with the six symptoms of emotional distress included in the National Comprehensive Cancer Network Distress Thermometer (worry, fear, sadness, depression, nervousness, loss of interest in usual activities) (12). This retrospective study (Ethics Committee, University of Lübeck, Germany, number 2022-412) included 122 patients who were planned to receive external-beam radiotherapy (EBRT) and/or brachytherapy (BT) for gynecologic cancer, *i.e.*, uterine (n=62), cervical (n=46) or vaginal/vulvar (n=14) cancer. Investigated factors were COVID-19 pandemic (prior to *versus* after the start of the pandemic), number of physical problems (0-4 *versus* ≥5), age at radiotherapy (≤65 *versus* ≥66 years), Karnofsky performance score (KPS ≤80 *versus* ≥90), primary tumor site (cervix uteri *versus* uterus *versus* vagina/vulva), tumor stage according to the International Federation of Gynecology and Obstetrics (FIGO-stage I-II *versus* II-IV), surgery prior to radiotherapy (no *versus* yes), chemotherapy before and/or during radiotherapy (no *versus* yes), history of another malignant tumor (no *versus* yes), and family history of malignant tumors (no *versus* yes).

All but one of the 62 patients with uterine cancer received upfront surgery. Radiotherapy regimens included 4×5 Gy of BT alone (n=46), EBRT alone (n=5), or a combination of both

Table I. *Associations of the investigated characteristics and worry.*

Characteristic		Worry, n (%)		*p*-Value
		Yes	No	
COVID-19 pandemic	Before (n=69)	29 (42)	40 (58)	0.79
	During (n=53)	21 (40)	32 (60)	
Number of physical problems	0-4 (n=72)	18 (25)	54 (75)	**0.0002**
	≥5 (n=50)	32 (64)	18 (36)	
Age	≤65 Years (n=64)	28 (44)	36 (56)	0.51
	≥66 Years (n=58)	22 (42)	36 (62)	
Karnofsky performance score	≤80 (n=37)	18 (49)	19 (51)	0.26
	≥90 (n=85)	32 (38)	53 (62)	
Primary tumor site	Cervix uteri (n=46)	21 (46)	25 (54)	0.20
	Uterus (n=62)	21 (34)	41 (66)	
	Vagina/vulva (n=14)	8 (57)	6 (43)	
FIGO-stage	I-II (n=75)	32 (43)	43 (57)	0.63
	III-IV (n=47)	18 (38)	29 (62)	
Surgery prior to RT	No (n=20)	15 (75)	5 (25)	**0.0007**
	Yes (n=102)	35 (34)	67 (66)	
Chemotherapy before and/or during RT	No (n=69)	24 (35)	45 (65)	0.11
	Yes (n=53)	26 (49)	27 (51)	
Treatment volume of RT	Without LN (n=47)	18 (38)	29 (62)	0.63
	With LN (n=75)	32 (43)	43 (57)	
Brachytherapy	No (n=41)	19 (46)	22 (54)	0.39
	Yes (n=81)	31 (38)	50 (62)	
History of another malignant tumor	No (n=107)	41 (38)	66 (62)	0.11
	Yes (n=15)	9 (60)	6 (40)	
Family history of malignant tumors	No (n=62)	24 (39)	38 (61)	0.62
	Yes (n=58)	25 (43)	33 (57)	

COVID-19: Coronavirus Disease 2019; FIGO: International Federation of Gynecology and Obstetrics; RT: radiotherapy; LN: lymph nodes. After Bonferroni correction, *p*-values <0.0042 are significant and shown in bold.

techniques (n=11). The median EBRT dose was 50.4 Gy (5×1.8 Gy per week). One patient with uterine cancer received personalized concurrent chemotherapy with weekly carboplatin and paclitaxel. Of the 46 patients with cervical cancer, 33 patients received upfront surgery. Of this subgroup, 12 patients were treated with 50.4 Gy (5×1.8 Gy per week) of EBRT alone and 13 patients with 50.4 Gy of EBRT plus BT (2 to 5×5 Gy or 3×7 Gy). Of the 13 patients receiving definitive radiotherapy, 7 patients were treated with EBRT alone (median dose=59.4 Gy) and 6 patients with EBRT (median dose=50.4 Gy) plus BT (5×5 Gy, 4×6 Gy, or 3 to 4×7 Gy). Forty-two of the 46 patients with cervical cancer received concurrent chemotherapy with weekly cisplatin (n=34), weekly carboplatin (n=7), or two courses of mitomycin C (n=1). Upfront surgery was performed in 8 of the 14 patients with vaginal and/or vulvar cancer. Seven of these patients received postoperative EBRT alone (median dose=50.4 Gy), and one patient 50.4 Gy of EBRT plus 4×5 Gy of BT. Five of the six patients receiving definitive radiotherapy were treated with EBRT alone (median dose=50.4 Gy), and one patient with 45.0 Gy of EBRT plus 3×6 Gy of BT. Seven of the 14 patients with vaginal and/or vulvar cancer received concurrent chemotherapy with weekly cisplatin (n=3), weekly carboplatin (n=2), or two courses of mitomycin C and 5-fluorouracil (n=2).

Associations between the potential risk factors and the six symptoms of emotional distress according to the National Comprehensive Cancer Network Distress Thermometer (12) were evaluated with the Chi-square test (number of patients ≥5 in all cells) or the Fisher's exact test (number of patients <5 in at least one cell). The Bonferroni correction was used to account for multiple comparisons, and *p*-values <0.005 were considered significant (alpha level <0.05). Moreover, *p*-values <0.06 indicated trends for associations between a potential risk factor and a symptom of emotional distress.

Results

Frequencies of the six symptoms of emotional distress, *i.e.*, worry, fear, sadness, depression, nervousness, and loss of interest in usual activities were 41%, 57%, 39%, 16%, 38%, and 20%, respectively. A greater number (≥5) of physical problems was significantly associated with worry (p=0.0002), fear (p=0.0041), sadness (p<0.0001), depression (p=0.0001), nervousness (p=0.0020), and loss of interest in usual activities (p<0.0001). In addition, no upfront surgery was significantly associated with worry (p=0.0007). Trends were found for associations between no upfront surgery and fear (p=0.026), nervousness (p=0.024) and loss of interest in usual activities (p=0.012), between additional chemotherapy and fear (p=0.026), between history of

Table II. *Associations of the investigated characteristics and fear.*

Characteristic		Fear, n (%)		*p*-Value
		Yes	No	
COVID-19 pandemic	Before (n=69)	40 (58)	29 (42)	0.72
	During (n=53)	29 (55)	24 (45)	
Number of physical problems	0-4 (n=72)	33 (46)	39 (54)	**0.0041**
	≥5 (n=50)	36 (72)	14 (28)	
Age	≤65 Years (n=64)	39 (61)	25 (39)	0.31
	≥66 Years (n=58)	30 (52)	28 (48)	
Karnofsky performance score	≤80 (n=37)	21 (57)	16 (43)	0.98
	≥90 (n=85)	48 (56)	37 (44)	
Primary tumor site	Cervix uteri (n=46)	30 (65)	16 (35)	0.29
	Uterus (n=62)	31 (50)	31 (50)	
	Vagina/vulva (n=14)	8 (57)	6 (43)	
FIGO-stage	I-II (n=75)	42 (56)	33 (44)	0.88
	III-IV (n=47)	27 (57)	20 (43)	
Surgery prior to RT	No (n=20)	16 (80)	4 (20)	0.026
	Yes (n=102)	53 (52)	49 (48)	
Chemotherapy before and/or during RT	No (n=69)	33 (48)	36 (52)	0.026
	Yes (n=53)	36 (68)	17 (32)	
Treatment volume of RT	Without LN (n=47)	22 (47)	25 (53)	0.085
	With LN (n=75)	47 (63)	28 (37)	
Brachytherapy	No (n=41)	28 (68)	13 (32)	0.063
	Yes (n=81)	41 (51)	40 (49)	
History of another malignant tumor	No (n=107)	57 (53)	50 (47)	0.057
	Yes (n=15)	12 (80)	3 (20)	
Family history of malignant tumors	No (n=62)	40 (65)	22 (35)	0.048
	Yes (n=58)	27 (47)	31 (53)	

COVID-19: Coronavirus Disease 2019; FIGO: International Federation of Gynecology and Obstetrics; RT: radiotherapy; LN: lymph nodes. After Bonferroni correction, *p*-values <0.0042 are significant and shown in bold.

another malignant tumor and fear ($p=0.057$) or nervousness ($p=0.057$), between KPS ≤80 and sadness ($p=0.055$), and between age ≤65 years and nervousness ($p=0.028$). Full results with respect to associations between potential risk factors and symptoms of emotional distress are given in Table I, Table II, Table III, Table IV, Table V, and Table VI.

Discussion

Gynecologic cancers are the second most common group of female malignancies (13). Many of these patients are treated with EBRT, BT or a combination of both techniques. A recommendation for radiotherapy may lead to considerable emotional distress requiring psycho-oncological assistance. There is a lack of studies focusing on the prevalence and risk factors of emotional distress prior to a course of radiotherapy for gynecologic cancer. This study investigated both aspects in a cohort of 122 patients irradiated for uterine, cervical, vaginal, or vulvar cancer. Emotional distress was characterized by the six symptoms of emotional distress included in the National Comprehensive Cancer Network Distress Thermometer, namely worry, fear, sadness, depression, nervousness, and loss of interest in usual activities (12). The frequencies of these symptoms ranged between 16% and 57%, and were not much different from those of previous studies in patients with gynecologic cancers in general (20% to 50%) or patients with cervical cancer during a course of radiotherapy (23% to 69%) (3, 4). These findings demonstrate consistency of the results of the present study.

In this study, significant associations with at least one of the six symptoms of the National Comprehensive Cancer Network Distress Thermometer (12) were found for ≥5 physical problems and no upfront surgery. A positive correlation between physical problems and emotional distress has been previously observed in other studies of patients with gynecologic cancers (10, 14). In the study by Cull *et al*. of women with early stage cervical cancer, psychological distress was significantly associated with physical complaints ($p<0.001$) and functional outcome ($p<0.02$) (10). In the study of Hazewinkle *et al*., better mental well-being was inversely correlated to the severity of urogenital and defecation symptoms (14). Moreover, in our previous study evaluating sleep disorders that can be a consequence of emotional distress, the prevalence of sleep

Table III. *Associations of the investigated characteristics and sadness.*

Characteristic		Sadness, n (%)		*p*-Value
		Yes	No	
COVID-19 pandemic	Before (n=69)	30 (43)	39 (57)	0.20
	During (n=53)	17 (32)	36 (68)	
Number of physical problems	0-4 (n=72)	15 (21)	57 (79)	**<0.0001**
	≥5 (n=50)	32 (64)	18 (36)	
Age	≤65 Years (n=64)	27 (42)	37 (58)	0.38
	≥66 Years (n=58)	20 (34)	38 (66)	
Karnofsky performance score	≤80 (n=37)	19 (51)	18 (49)	0.055
	≥90 (n=85)	28 (33)	57 (67)	
Primary tumor site	Cervix uteri (n=46)	12 (26)	34 (74)	0.061
	Uterus (n=62)	30 (48)	32 (52)	
	Vagina/vulva (n=14)	5 (36)	9 (64)	
FIGO-stage	I-II (n=75)	33 (44)	42 (56)	0.12
	III-IV (n=47)	14 (30)	33 (70)	
Surgery prior to RT	No (n=20)	11 (55)	9 (45)	0.098
	Yes (n=102)	36 (35)	66 (65)	
Chemotherapy before and/or during RT	No (n=69)	31 (45)	38 (55)	0.097
	Yes (n=53)	16 (30)	37 (70)	
Treatment volume of RT	Without LN (n=47)	24 (41)	23 (49)	0.024
	With LN (n=75)	23 (31)	52 (69)	
Brachytherapy	No (n=41)	15 (37)	26 (63)	0.75
	Yes (n=81)	32 (40)	49 (60)	
History of another malignant tumor	No (n=107)	39 (36)	68 (64)	0.21
	Yes (n=15)	8 (53)	7 (47)	
Family history of malignant tumors	No (n=62)	24 (39)	38 (61)	0.93
	Yes (n=58)	22 (38)	36 (62)	

COVID-19: Coronavirus Disease 2019; FIGO: International Federation of Gynecology and Obstetrics; RT: radiotherapy; LN: lymph nodes. After Bonferroni correction, *p*-values <0.0042 are significant and shown in bold.

Table IV. *Associations of the investigated characteristics and depression.*

Characteristic		Depression, n (%)		*p*-Value
		Yes	No	
COVID-19 pandemic	Before (n=69)	9 (13)	60 (87)	0.38
	During (n=53)	10 (19)	43 (81)	
Number of physical problems	0-4 (n=72)	3 (4)	69 (96)	**0.0001**
	≥5 (n=50)	16 (32)	34 (68)	
Age	≤65 Years (n=64)	10 (16)	54 (84)	0.99
	≥66 Years (n=58)	9 (16)	49 (84)	
Karnofsky performance score	≤80 (n=37)	8 (22)	29 (78)	0.22
	≥90 (n=85)	11 (13)	74 (87)	
Primary tumor site	Cervix uteri (n=46)	7 (15)	39 (85)	0.81
	Uterus (n=62)	9 (15)	53 (85)	
	Vagina/vulva (n=14)	3 (21)	11 (79)	
FIGO-stage	I-II (n=75)	12 (16)	63 (84)	0.87
	III-IV (n=47)	7 (15)	40 (85)	
Surgery prior to RT	No (n=20)	5 (25)	15 (75)	0.20
	Yes (n=102)	14 (14)	88 (85)	
Chemotherapy before and/or during RT	No (n=69)	8 (12)	61 (88)	0.17
	Yes (n=53)	11 (21)	42 (79)	
Treatment volume of RT	Without LN (n=47)	8 (17)	39 (83)	0.73
	With LN (n=75)	11 (15)	64 (85)	
Brachytherapy	No (n=41)	7 (17)	34 (83)	0.75
	Yes (n=81)	12 (15)	69 (85)	
History of another malignant tumor	No (n=107)	16 (15)	91 (85)	0.70
	Yes (n=15)	3 (20)	12 (80)	
Family history of malignant tumors	No (n=62)	9 (15)	53 (85)	0.88
	Yes (n=58)	9 (16)	49 (84)	

COVID-19: Coronavirus Disease 2019; FIGO: International Federation of Gynecology and Obstetrics; RT: radiotherapy; LN: lymph nodes. After Bonferroni correction, *p*-values <0.0042 are significant and shown in bold.

Table V. *Associations of the investigated characteristics and nervousness.*

Characteristic		Nervousness, n (%)		*p*-Value
		Yes	No	
COVID-19 pandemic	Before (n=69)	27 (39)	42 (61)	0.71
	During (n=53)	19 (36)	34 (64)	
Number of physical problems	0-4 (n=72)	19 (26)	53 (74)	**0.0020**
	≥5 (n=50)	27 (54)	23 (46)	
Age	≤65 Years (n=64)	30 (47)	34 (53)	0.028
	≥66 Years (n=58)	16 (28)	42 (72)	
Karnofsky performance score	≤80 (n=37)	17 (46)	20 (54)	0.22
	≥90 (n=85)	29 (34)	56 (66)	
Primary tumor site	Cervix uteri (n=46)	21 (46)	25 (54)	0.36
	Uterus (n=62)	20 (32)	42 (68)	
	Vagina/vulva (n=14)	5 (36)	9 (64)	
FIGO-stage	I-II (n=75)	26 (35)	49 (65)	0.38
	III-IV (n=47)	20 (43)	27 (57)	
Surgery prior to RT	No (n=20)	12 (60)	8 (40)	0.024
	Yes (n=102)	34 (33)	68 (67)	
Chemotherapy before and/or during RT	No (n=69)	24 (35)	45 (65)	0.45
	Yes (n=53)	22 (42)	31 (58)	
Treatment volume of RT	Without LN (n=47)	15 (32)	32 (68)	0.30
	With LN (n=75)	31 (41)	44 (59)	
Brachytherapy	No (n=41)	17 (41)	24 (59)	0.54
	Yes (n=81)	29 (36)	52 (64)	
History of another malignant tumor	No (n=107)	37 (35)	70 (65)	0.057
	Yes (n=15)	9 (60)	6 (40)	
Family history of malignant tumors	No (n=62)	27 (44)	35 (56)	0.11
	Yes (n=58)	17 (29)	41 (71)	

COVID-19: Coronavirus Disease 2019; FIGO: International Federation of Gynecology and Obstetrics; RT: radiotherapy; LN: lymph nodes. After Bonferroni correction, *p*-values <0.0042 are significant and shown in bold.

Table VI. *Associations of the investigated characteristics and loss of interest in usual activities.*

Characteristic		Loss of interest in usual activities, n (%)		*p*-Value
		Yes	No	
COVID-19 pandemic	Before (n=69)	15 (22)	54 (78)	0.51
	During (n=53)	9 (17)	44 (83)	
Number of physical problems	0-4 (n=72)	4 (6)	68 (94)	**<0.0001**
	≥5 (n=50)	20 (40)	30 (60)	
Age	≤65 Years (n=64)	16 (25)	48 (75)	0.12
	≥66 Years (n=58)	8 (14)	50 (86)	
Karnofsky performance score	≤80 (n=37)	10 (27)	27 (73)	0.18
	≥90 (n=85)	14 (16)	71 (84)	
Primary tumor site	Cervix uteri (n=46)	12 (26)	34 (74)	0.38
	Uterus (n=62)	10 (16)	52 (84)	
	Vagina/vulva (n=14)	2 (14)	12 (86)	
FIGO-stage	I-II (n=75)	13 (17)	62 (83)	0.41
	III-IV (n=47)	11 (23)	36 (77)	
Surgery prior to RT	No (n=20)	8 (40)	12 (60)	0.012
	Yes (n=102)	16 (16)	86 (84)	
Chemotherapy before and/or during RT	No (n=69)	11 (16)	58 (84)	0.24
	Yes (n=53)	13 (25)	40 (75)	
Treatment volume of RT	Without LN (n=47)	8 (17)	39 (83)	0.56
	With LN (n=75)	16 (21)	59 (79)	
Brachytherapy	No (n=41)	9 (22)	32 (78)	0.65
	Yes (n=81)	15 (19)	66 (81)	
History of another malignant tumor	No (n=107)	22 (21)	85 (79)	0.73
	Yes (n=15)	2 (13)	13 (87)	
Family history of malignant tumors	No (n=62)	14 (23)	48 (77)	0.33
	Yes (n=58)	9 (16)	49 (84)	

COVID-19: Coronavirus Disease 2019; FIGO: International Federation of Gynecology and Obstetrics; RT: radiotherapy; LN: lymph nodes. After Bonferroni correction, *p*-values <0.0042 are significant and shown in bold.

problems was significantly associated with a greater number (≥4) of physical problems (p<0.0001) (15). The result that no upfront surgery was associated with increased emotional distress can be explained by the facts that the majority of these patients had advanced disease and that non-resectability is often associated with a worse prognosis. In a previous study in cervical cancer survivors, fear of disease progression was one of the three greatest fears reported by the patients (16).

In addition, trends were observed for associations between emotional distress and additional chemotherapy, history of another tumor, worse performance status, or younger age. The trend regarding additional chemotherapy can be explained by the increased toxicity of chemoradiation when compared to radiotherapy alone that was found in previous studies, reviews and meta-analyses (17-24). For example, in the randomized trial of Teng *et al*. in patients with cervical cancer, rates of treatment-related toxicities were 37% in the chemoradiation group and 18% in the radiotherapy alone group, respectively (p=0.02) (17). In a more recent randomized trial of patients with endometrial cancer, adverse events grade ≥2 and grade ≥3 were significantly (p<0.0001) more common in patients treated with chemoradiation than in patients receiving radiotherapy alone (18). Moreover, neuropathy persisted significantly more often after chemoradiation (19, 20). Another tumor in a patient's history may increase the level of emotional distress, as previously reported in a study of breast cancer patients receiving adjuvant radiotherapy (25). Moreover, fear of disease progression often means significant distress for many patients (16). Associations between worse performance score and high levels of distress were previously found in a large retrospective study of patients with breast and gynecologic cancers (26). An inverse correlation between age and distress was also found in previous studies of patients with gynecologic cancers and breast cancer (11, 25-28).

In summary, a considerable proportion of patients with gynecologic cancers experience emotional distress prior to the start of radiotherapy. Patients with risk factors including ≥5 physical problems, unresectable tumors, additional chemotherapy, history of another tumor, worse performance status, and younger age likely benefit from immediate psycho-oncological assistance.

Conflicts of Interest

The Authors report no conflicts of interest in relation to this study.

Authors' Contributions

All Authors participated in the study design. A. A.-S. and D.R. collected the data, which were analyzed by D.R. The article, which was drafted by D.R. and N.Y.Y., was reviewed and approved by all Authors.

References

1 Wilford J, Osann K, Hsieh S, Monk B, Nelson E and Wenzel L: Validation of PROMIS emotional distress short form scales for cervical cancer. Gynecol Oncol *151(1)*: 111-116, 2018. PMID: 30078504. DOI: 10.1016/j.ygyno.2018.07.022

2 Tahseen S and Reid PC: Psychological distress associated with colposcopy: patients' perception. Eur J Obstet Gynecol Reprod Biol *139(1)*: 90-94, 2008. PMID: 17980478. DOI: 10.1016/j.ejogrb.2007.09.001

3 Jewett PI, Teoh D, Petzel S, Lee H, Messelt A, Kendall J, Hatsukami D, Everson-Rose SA, Blaes AH and Vogel RI: Cancer-related distress: Revisiting the utility of the National Comprehensive Cancer Network distress thermometer problem list in women with gynecologic cancers. JCO Oncol Pract *16(8)*: e649-e659, 2020. PMID: 32091952. DOI: 10.1200/JOP.19.00471

4 Li LR, Lin MG, Liang J, Hu QY, Chen D, Lan MY, Liang WQ, Zeng YT, Wang T and Fu GF: Effects of intrinsic and extrinsic factors on the level of hope and psychological health status of patients with cervical cancer during radiotherapy. Med Sci Monit *23*: 3508-3517, 2017. PMID: 28720749. DOI: 10.12659/msm.901430

5 Kise S, Arakaki Y, Kudaka W, Ariga T, Kinjo N, Kohatu H and Aoki Y: Sarcopenia is an independent prognostic factor for squamous cell carcinoma of the cervix treated with concurrent chemoradiotherapy. Anticancer Res *42(10)*: 4887-4893, 2022. PMID: 36191992. DOI: 10.21873/anticanres.15994

6 Meyer HJ, Wienke A and Surov A: Pre-treatment apparent diffusion coefficient does not predict therapy response to radiochemotherapy in cervical cancer: a systematic review and meta-analysis. Anticancer Res *41(3)*: 1163-1170, 2021. PMID: 33788707. DOI: 10.21873/anticanres.14873

7 Chang YL, Chuang CM, Chien CH, Huang XY, Liang SY and Liu CY: Factors related to changes in resilience and distress in women with endometrial cancer. Arch Womens Ment Health *24(3)*: 413-421, 2021. PMID: 33161489. DOI: 10.1007/s00737-020-01090-4

8 Ahlberg K, Ekman T and Gaston-Johansson F: Fatigue, psychological distress, coping resources, and functional status during radiotherapy for uterine cancer. Oncol Nurs Forum *32(3)*: 633-640, 2005. PMID: 15897938. DOI: 10.1188/05.ONF.633-640

9 Im CM, Cho IJ, Yu HJ, Han B, Oh HH, Seo YJ, Kim KH, Myung DS, Cho SB, Lee WS, Nam TK and Joo YE: Clinical outcome and risk factors of chronic radiation proctitis following pelvic radiation therapy. Anticancer Res *42(12)*: 5951-5959, 2022. PMID: 36456158. DOI: 10.21873/anticanres.16105

10 Cull A, Cowie VJ, Farquharson DI, Livingstone JR, Smart GE and Elton RA: Early stage cervical cancer: psychosocial and sexual outcomes of treatment. Br J Cancer *68(6)*: 1216-1220, 1993. PMID: 8260376. DOI: 10.1038/bjc.1993.507

11 Uno A, Yamamoto S, Iihara H, Fujii H, Makita C, Hayasaki Y, Ueda Y, Ito M, Takenaka M, Kumano T, Mori M, Yasue M, Kato-Hayashi H, Kobayashi R, Morishige KI, Matsuo M, Hayashi H and Suzuki A: Control and risk factors of nausea and vomiting in patients with cervical cancer receiving radiotherapy. Anticancer Res *42(6)*: 3117-3123, 2022. PMID: 35641271. DOI: 10.21873/anticanres.15800

12 Holland JC, Andersen B, Breitbart WS, Buchmann LO, Compas B, Deshields TL, Dudley MM, Fleishman S, Fulcher CD, Greenberg DB, Greiner CB, Handzo GF, Hoofring L, Hoover C,

Jacobsen PB, Kvale E, Levy MH, Loscalzo MJ, McAllister-Black R, Mechanic KY, Palesh O, Pazar JP, Riba MB, Roper K, Valentine AD, Wagner LI, Zevon MA, McMillian NR and Freedman-Cass DA: Distress management. J Natl Compr Canc Netw *11(2)*: 190-209, 2013. PMID: 23411386. DOI: 10.6004/jnccn.2013.0027

13 Siegel RL, Miller KD, Fuchs HE and Jemal A: Cancer statistics, 2022. CA Cancer J Clin *72(1)*: 7-33, 2022. PMID: 35020204. DOI: 10.3322/caac.21708

14 Hazewinkel MH, Sprangers MA, Velden Jv, Burger MP and Roovers JP: Severe pelvic floor symptoms after cervical cancer treatment are predominantly associated with mental and physical well-being and body image: a cross-sectional study. Int J Gynecol Cancer *22(1)*: 154-160, 2012. PMID: 22080883. DOI: 10.1097/IGC.0b013e3182332df8

15 Rades D, Kopelke S, Soror T, Schild SE, Tvilsted S, Kjaer TW and Bartscht T: Sleep disorders prior to adjuvant radiation therapy for gynecological malignancies. Anticancer Res *41(9)*: 4407-4410, 2021. PMID: 34475061. DOI: 10.21873/anticanres.15246

16 Hanprasertpong J, Geater A, Jiamset I, Padungkul L, Hirunkajonpan P and Songhong N: Fear of cancer recurrence and its predictors among cervical cancer survivors. J Gynecol Oncol *28(6)*: e72, 2017. PMID: 28758378. DOI: 10.3802/jgo.2017.28.e72

17 Tseng CJ, Chang CT, Lai CH, Soong YK, Hong JH, Tang SG and Hsueh S: A randomized trial of concurrent chemoradiotherapy *versus* radiotherapy in advanced carcinoma of the uterine cervix. Gynecol Oncol *66(1)*: 52-58, 1997. PMID: 9234921. DOI: 10.1006/gyno.1997.4721

18 de Boer SM, Powell ME, Mileshkin L, Katsaros D, Bessette P, Haie-Meder C, Ottevanger PB, Ledermann JA, Khaw P, Colombo A, Fyles A, Baron MH, Kitchener HC, Nijman HW, Kruitwagen RF, Nout RA, Verhoeven-Adema KW, Smit VT, Putter H, Creutzberg CL and PORTEC study group: Toxicity and quality of life after adjuvant chemoradiotherapy *versus* radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): an open-label, multicentre, randomised, phase 3 trial. Lancet Oncol *17(8)*: 1114-1126, 2016. PMID: 27397040. DOI: 10.1016/S1470-2045(16)30120-6

19 de Boer SM, Powell ME, Mileshkin L, Katsaros D, Bessette P, Haie-Meder C, Ottevanger PB, Ledermann JA, Khaw P, Colombo A, Fyles A, Baron MH, Jürgenliemk-Schulz IM, Kitchener HC, Nijman HW, Wilson G, Brooks S, Carinelli S, Provencher D, Hanzen C, Lutgens LCHW, Smit VTHBM, Singh N, Do V, D'Amico R, Nout RA, Feeney A, Verhoeven-Adema KW, Putter H, Creutzberg CL and PORTEC study group: Adjuvant chemoradiotherapy *versus* radiotherapy alone for women with high-risk endometrial cancer (PORTEC-3): final results of an international, open-label, multicentre, randomised, phase 3 trial. Lancet Oncol *19(3)*: 295-309, 2018. PMID: 29449189. DOI: 10.1016/S1470-2045(18)30079-2

20 Post CCB, de Boer SM, Powell ME, Mileshkin L, Katsaros D, Bessette P, Haie-Meder C, Ottevanger NPB, Ledermann JA, Khaw P, D'Amico R, Fyles A, Baron MH, Kitchener HC, Nijman HW, Lutgens LCHW, Brooks S, Jürgenliemk-Schulz IM, Feeney A, Goss G, Fossati R, Ghatage P, Leary A, Do V, Lissoni AA, McCormack M, Nout RA, Verhoeven-Adema KW, Smit VTHBM, Putter H and Creutzberg CL: Long-term toxicity and health-related quality of life after adjuvant chemoradiation therapy or radiation therapy alone for high-risk endometrial cancer in the randomized PORTEC-3 trial. Int J Radiat Oncol Biol Phys *109(4)*: 975-986, 2021. PMID: 33129910. DOI: 10.1016/j.ijrobp.2020.10.030

21 Maduro JH, Pras E, Willemse PH and de Vries EG: Acute and long-term toxicity following radiotherapy alone or in combination with chemotherapy for locally advanced cervical cancer. Cancer Treat Rev *29(6)*: 471-488, 2003. PMID: 14585258. DOI: 10.1016/s0305-7372(03)00117-8

22 Falcetta FS, Medeiros LR, Edelweiss MI, Pohlmann PR, Stein AT and Rosa DD: Adjuvant platinum-based chemotherapy for early stage cervical cancer. Cochrane Database Syst Rev *11(11)*: CD005342, 2016. PMID: 27873308. DOI: 10.1002/14651858.CD005342.pub4

23 Yi L, Zhang H, Zou J, Luo P and Zhang J: Adjuvant chemoradiotherapy *versus* radiotherapy alone in high-risk endometrial cancer: A systematic review and meta-analysis. Gynecol Oncol *149(3)*: 612-619, 2018. PMID: 29530332. DOI: 10.1016/j.ygyno.2018.03.004

24 Li M, Hu M, Wang Y and Yang X: Adjuvant chemoradiotherapy *versus* radiotherapy in cervical cancer patients with intermediate-risk factors: A systematic review and meta-analysis. Eur J Obstet Gynecol Reprod Biol *238*: 1-6, 2019. PMID: 31082737. DOI: 10.1016/j.ejogrb.2019.04.039

25 Rades D, Narvaez CA, Dziggel L, Tvilsted S, Kjaer TW, Schild SE and Bartscht T: Emotional problems prior to adjuvant radiation therapy for breast cancer. In Vivo *35(5)*: 2763-2770, 2021. PMID: 34410966. DOI: 10.21873/invivo.12561

26 Lim SY, Ke Y, Mok NK, Tan YY, Neo PSH, Chan A and Yang GM: Factors associated with distress and the impact of distress on acute health-care service utilization among patients diagnosed with breast and gynecological cancers. Palliat Support Care: 1-8, 2023. PMID: 36622079. DOI: 10.1017/S1478951522001444

27 Kornblith AB, Powell M, Regan MM, Bennett S, Krasner C, Moy B, Younger J, Goodman A, Berkowitz R and Winer E: Long-term psychosocial adjustment of older *vs* younger survivors of breast and endometrial cancer. Psychooncology *16(10)*: 895-903, 2007. PMID: 17245695. DOI: 10.1002/pon.1146

28 Tsatsou I, Parpa E, Tsilika E, Katsaragakis S, Batistaki C, Dimitriadou E and Mystakidou K: A systematic review of sexuality and depression of cervical cancer patients. J Sex Marital Ther *45(8)*: 739-754, 2019. PMID: 31018789. DOI: 10.1080/0092623X.2019.1610125

Received March 2, 2023
Revised March 10, 2023
Accepted March 13, 2023