


Vaginal dilator use to promote sexual wellbeing after radiotherapy in gynecological cancer survivors

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Abstract

This study investigated the efficacy of a vaginal dilator (VD) for the treatment of radiation-induced vaginal stenosis (VS) and the effect of a VD on sexual quality of life.

Fifty three patients with endometrial or cervical cancers participated in this prospective observational study. All participants were treated with radical or adjuvant external beam radiotherapy and/or brachytherapy. They were routinely examined 4 times after radiotherapy (RT) and were also asked to complete a validated sexual function-vaginal changes questionnaire. SPSS version 20 and Minitab version 16 were used for the statistical analysis. The statistical significance was set at $P < .05$.

The VS grading score decreased and the comfortably insertable VD size gradually increased throughout a year of VD use; all patients with initial grade 3 showed a VS of grade 2 after 12 months of VD use and 65.8% of the patients with initial grade 2 demonstrated a final VS of grade 1, while 77.8% of the participants who started with the first size of VD reached the third size after 12 months. Starting VD therapy ≤ 3 months after the end of RT was associated with a significant decrease in VS. A total of 60.9% of participants reported that they did not feel their vaginas were too small during intercourse after 12 months of dilation, whereas only 11.5% gave the same answer before starting dilation. Furthermore, 47.17% rated their satisfaction with their sexual life 5 out of 7 and only 3.77% gave a score of 3 after 12 months of dilation.

Endometrial and cervical cancer survivors are encouraged to use VD to treat VS and for sexual rehabilitation after RT. This study recommends starting vaginal dilation no more than 3 months after treatment at least 2 to 3 times a week for 10 to 15 minutes over 12 months. However, larger, well-designed randomized clinical trials should be conducted to develop specific guidelines for VD use and efficacy in VS and sexual quality of life after RT.

Abbreviations: BT = brachytherapy, EBRT = external beam radiotherapy, QoL = quality of life, RT = radiotherapy, SVQ = sexual function-vaginal changes questionnaire, VD = vaginal dilators, VS = vaginal stenosis.

Keywords: cervical cancer, endometrial cancer, pelvic radiotherapy, sexual dysfunction, vaginal dilators, vaginal stenosis

1. Introduction

Over the past few decades, pelvic radiotherapy (RT) has become an essential tool to treat endometrial and cervical cancers. More advanced RT techniques can allow dose escalation and improve long-term tumor control rates.^[1]

Because the overall survival rates of endometrial and cervical cancer have increased, experts' attention has shifted to the acute and late toxicities of radiotherapy that could compromise cancer survivors' quality of life (QoL).^[2] The most frequent acute radiation toxicities after gynecological cancer involve vaginal stenosis (VS)^[3–5]; which is defined as the narrowing and/or

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This study was conducted in accordance with the 1964 Helsinki Declaration and its later amendments, as well as the local legal and regulatory requirements. Written informed consent was obtained from all the participants.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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shortening of the vaginal canal after external beam radiotherapy (EBRT) and/or intracavitary (IC) RT for adjuvant or definitive uterine, cervical, vaginal, and anorectal cancer treatment.^[6–10] There are 3 grades of VS depending on the severity of the disorder^[10,11] and the reported VS incidence varies from 1.25% to 88%.^[6,12–15] VS is the result of RT-induced inflammation of connective tissue and blood vessels, which leads to a reduced blood supply, hypoxia, loss of elastin, collagen deposition, fibrosis, and atrophy.^[6,16] The constriction of the vaginal canal can interfere with pelvic physical examination during follow-up visits and hamper the early detection of cancer recurrence.^[12,14,16–20] Additionally, VS after RT can cause uncomfortable sexual intercourse and impair sexual QoL.^[14,21]

The prevention and treatment options for VS include the use of vaginal dilators (VD), sexual intercourse, and topical therapies using lubricants, moisturizers, and estrogen agents.^[6,11,22,23–28] However, the evidence of the efficacy of topical therapies is poor and experts do not agree on the efficacy and conditions of VD use.^[22,23,25] Therefore, this study sought to evaluate VD use as a treatment for RT-induced VS and assess the effects of VD therapy on sexual QoL.

2. Methods

2.1. Study design

This study was designed as a prospective observational study following STROBE guidelines. Fifty three patients meeting the eligibility criteria were recruited and participated to the end of the study. All participants had endometrial or cervical cancer and were treated with EBRT and/or brachytherapy (BT) at the Radiotherapy Department of the University Hospital of Larissa in Greece from November 2017 to October 2019. Patients who received adjuvant therapy underwent surgery before RT at the Department of Obstetrics and Gynecology of the University Hospital of Larissa.

The inclusion criteria were

1. women aged 18 to 85 years at the time of treatment,
2. histologically proven endometrial or cervical cancer,
3. pelvic EBRT and/or intravaginal BT as definitive or adjuvant therapy \pm chemotherapy,
4. initial post-RT VS grading ≥ 2 according to the Common Terminology Criteria for Adverse Events (CTCAE version 5.0; see Table 1),^[10]
5. written informed consent, and
6. residing near the treatment site (Central Greece).

The exclusion criteria were

1. patients previously treated for all stages (I–IV) of pelvic malignancy (except for treated non-melanoma skin cancer),

2. prior pelvic irradiation,
3. stage IV disease,
4. inability to fill out questionnaires due to language or cognitive barriers (e.g., dementia),
5. physical handicaps that would prohibit patients from full participation in the study (e.g., significant hearing deficit), and
6. refusal or inability to provide written informed consent.

All patients were instructed to use the VD regularly, at least twice per week, for the 12 months after completing RT or post-RT chemotherapy. The time between the end of RT and the onset of VD use ranged from 1 to 6 months, depending on whether or not chemotherapy was administered after RT. Patients were routinely examined 4 times: after the end of RT (when they were asked to start the use of VD) and at 3 months, 6 months, and 12 months after they started to use the VD. At the same times, the participants were asked to complete a validated sexual function-vaginal changes questionnaire (SVQ). Additionally, they reported the largest size of VD comfortably inserted at 3, 6, and 12 months after starting dilator use. The study ended after the 12-month follow-up with the last patient in November 2020.

2.2. Power analysis

Because this study was predefined to last 3 years starting in November 2017, the sample was restricted to this period. Although a priori power and sample size calculations were not feasible, we estimated the statistical power of our study based on the sample size (post hoc) from November 2017 to November 2020, with a specific duration of patient observation of 12 months. At a significance level of 5% ($\alpha = 5\%$) and sample size of 53 participants ($n = 53$), the estimated power (large effect) was 91% for alterations in the grade of VS and 74% for differences in VD size.

2.3. Radiotherapy techniques and planning

The 3-dimensional conformal radiation (3D-CRT) technique of EBRT has been generally applied with a 6 to 15 MV linear accelerator. All patients underwent computed tomography (CT) for treatment planning. A multi-field approach was used with all fields conformed to the pelvic anatomy. Pelvic EBRT was directed to the following target volumes:

1. gross disease (in inoperable cases) and parametrial/para-vaginal tissues and
2. the lower common, external, and internal iliac, obturator, and pre-sacral (in cases of cervical involvement) lymph nodes. An extended RT field was used to include the entirety of the common and para-aortic lymph nodal chains.

For microscopic disease, a total dose of 45 to 50.4 Gy in 1.8 Gy fractions was delivered daily (see Table 2). For gross primary or

Table 1
Common terminology criteria for adverse events v.5.0 grading for vaginal stenosis.

Adverse event	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5
Vaginal stricture (Definition)	Asymptomatic; Mild vaginal shortening or narrowing	Vaginal narrowing and/or shortening not interfering with physical examination shortening not interfering with physical examination	Vaginal narrowing and/or shortening, interfering with the use of tampons, sexual activity or physical examination.	Unspecified	Death
		A disorder characterized by a narrowing of the vaginal canal.			

Table 2**Patient demographic and clinical data.**

Demographic and clinical data		Number of patients	Percentage (%)	
Age (mean)		53	Mean (SD) 58 (9.53)	
BMI	normal weight (<25)	13	24.5	
	overweight (25–29)	20	37.7	
	obesity (30–39)	18	34.0	
	malignant obesity (>40)	2	3.8	
Education level	primary	13	24.5	
	secondary	29	54.8	
	higher education - university	9	17.0	
	master	2	3.8	
Smoking	yes	17	32.1	
	no	36	67.9	
Nulliparity	yes	6	11.3	
	no	47	88.7	
Menstrual cycle, prior to therapy	reproductive age	8	15.1	
	pre-menopause	3	5.7	
	post-menopause	42	79.2	
First symptom/clinical finding	vaginal bleeding (spotting metrorragia, menorrhagia)	40	75.5	
	abnormal Pap test	4	7.5	
	thick endometrium in TUS	3	5.7	
	other (dyspareunia, abdominal/pelvic pain, abnormal vaginal discharge)	6	11.3	
Diagnosis	Ca of the endometrium	41	77.4	
	Ca of the cervix	12	22.6	
Stage (FIGO)	I	36	67.9	
	II	10	18.9	
	III	7	13.2	
Grade of malignancy	grade 1	3	5.7	
	grade 2	30	56.6	
	grade 3	20	37.7	
Histological type	Endometrium	adenoCa endometrioid	30	56.6
		adenoCa clear cell/serous/other	7	13.2
		adenoCamixed	4	7.5
	Cervix	squamous cell Ca	11	20.8
		adenoCa	1	1.9
Therapy	1. THBSO + EBRT + BT	3	5.7	
	2. THBSO + BT	4	7.5	
	3. THBSO + LND + BT	4	7.5	
	4. THBSO + PLND + EBRT + BT	18	34.0	
	5. THBSO + PLND + EBRT	1	1.9	
	6. THBSO + LND + Omentectomy + EBRT + BT	11	20.8	
	7. RHPLND + EBRT + BT	8	15.1	
	8. EBRT + BT	4	7.5	
Chemotherapy	yes	31	58.5	
	no	22	41.5	
Dose (total) and EBRT sessions	45 Gy in 25 sessions	24	53.3	
	50.4 Gy in 28 sessions	21	46.7	
Dose (total) and BT fractions (after EBRT)	10 Gy in 2 fractions	6	13.6	
	14 or 15 Gy in 2 fractions	29	65.9	
	15 Gy in 3 fractions	5	11.4	
	20 Gy in 4 fractions	3	6.8	
	28 Gy in 4 fractions	1	2.3	
	18 Gy in 3 fractions (no EBRT)	4	7.7	
	21 or 22.5 Gy in 3 fractions (no EBRT)	5	7.7	
Initial grade of VS (before VD use)	grade 2 - moderate	38	71.7	
	grade 3 - severe	15	28.3	
Final grade of VS	grade 0 - absence of VS	12	22.6	
	grade 1 - mild	25	47.2	
	grade 2 - moderate	16	30.2	

3D-CRT = 3-dimensional conformal radiotherapy, BMI = body mass index, BT = brachytherapy, Ca = carcinoma, EBRT = external beam radiotherapy, LND = lymph node dissection, PLND = pelvic lymph node dissection, RHPLND = radical hysterectomy with pelvic lymph node dissection, THBSO = total hysterectomy with bilateral salpingo-oophorectomy, TUS = transvaginal ultrasound, VD = vaginal dilator, VS = vaginal stenosis.

nodal disease, an additional boost of 60 to 64 Gy was delivered, respecting the constraints of the surrounding normal tissue.

For BT, high dose rate (HDR) IC brachytherapy was performed 7 to 10 days after completing EBRT in 2, 3, or 4 weekly fractions or without EBRT in 3 fractions applied once a week. Cylinders or ovoids were placed intravaginally and removed after each brachytherapy session. An iridium-192 (I^{192}) radiation source was used. The dose was prescribed to or at a depth of 0.5 cm from the vaginal surface and depended on the total EBRT-delivered dose (see Table 2).

Participants who received chemotherapy were treated with regimens including carboplatin, cisplatin, and paclitaxel, depending on the malignancy of their cancer.

2.4. Instruments

VS severity grading was evaluated via pelvic examination with a vaginal speculum according to the CTCAE version 5.0 criteria (see Table 1).^[10]

All patients were provided with a commercially available silicone dilator set containing 5 VDs in graduated sizes. A VD was used not only as a tool to treat VS but also as a measuring device. The size of the VD that could be comfortably inserted at 3, 6, and 12 months of VD use was used to assess vaginal stenosis. The participants were instructed to insert a VD in the vagina at least twice a week for a total of 10 minutes per session. VDs were used for 12 consecutive months after the end of RT, regardless of the frequency of sexual intercourse. Written instructions were given to all participants for gradual dilator insertion to stretch the length of the vagina and gentle rotation of the dilator to stretch the width of the vagina. Each patient was instructed to apply a water-based lubricant when using the VDs.

Sexual QoL was estimated with a SVQ.^[29] The SVQ was developed and validated by Jensen et al.^[29] It consisted of 20 core items assessing sexual interest, lubrication, orgasm, dyspareunia, vaginal dimensions, intimacy, sexual problems of the partner, sexual activity, sexual satisfaction, and body image. It was delivered before beginning VD use and at 3, 6, and 12 months of VD use.

2.5. Statistical analysis

All qualitative data are presented as percentages, while age, as quantitative data, is presented as the mean and standard deviation according to the normal distribution of the values. The analysis of the epidemiological data and the evaluation of the possible effect of VD use on VS was performed with Fisher exact test, a statistical procedure to determine whether a relationship between categorical variables exists. In particular, we tested the association between

1. the initial and final grades of VS and
2. the initial VD size (after 3 months of VD use) and final VD size (after 12 months of VD use).

Additionally, these associations were examined for the following control variables (intervening or confounding variables): diagnosis, chemotherapy, the total dose of BT, the total dose of EBRT, and the start time and frequency of dilation (Fisher exact test, Chi-Squared test).

Fisher exact test was also conducted to assess the effect of VD therapy on patients' sexual QoL in association with the duration of VD use (at 3, 6, and 12 months) and the overall effect of dilation on sexual well-being (before and 12 months after VD

use), and the questionnaire answers were analyzed to describe trends of vaginal symptoms and sexual function during the period of VD use after RT.

Statistical significance was set at $P < .05$. SPSS (version 20) and Minitab (version 16) software were used to statistically analyze the results.

3. Results

3.1. Participants

A total of 108 patients were evaluated for eligibility to participate in this study. Of these, 44 were excluded because they did not meet the inclusion criteria or refused to participate. Of the 64 remaining participants, 11 were lost to follow-up due to metastasis or other health problems, nonadherence to VD instructions, or family reasons. Ultimately, 53 patients were recruited according to the inclusion and exclusion criteria and participated through the end of the study (see Fig. 1).

3.2. Demographic and clinical data

The mean age at diagnosis was 58 years and the majority of patients were overweight and obese, 37.7% and 34%, respectively (see Table 2). About half of the participants had reached a secondary education level and 67.9% of the patients were nonsmokers. Only 6 of the 53 patients had no children and 79.2% were post-menopausal at the time of diagnosis. Vaginal bleeding was the most common symptom in the vast majority of patients (75.5%), followed by other symptoms and clinical findings such as dyspareunia, pelvic pain, vaginal discharge (11.3%), abnormal Pap test (7.5%), and thick endometrium on transvaginal ultrasound (5.7%). The majority were treated for endometrioid adenocarcinoma (56.6%), followed by those treated for squamous cell carcinoma of the cervix (20.8%). Thirty six patients were diagnosed with stage I cancer (67.9%) and 30 with stage II cancer (56.6%). About a third (34%) of the patients underwent total hysterectomies with bilateral salpingo-oophorectomy (THBSO) and pelvic lymph node dissection (PLND), EBRT, and BT, compared with the 7.5% of patients who received EBRT and BT as definitive therapy. Chemotherapy was administered to 58.5% of participants. The EBRT total dose was 45 Gy in 25 sessions for 53.3% of the patients and 50.4 Gy in 28 sessions for 46.7%. The majority (65.9%) received a total BT dose of 14 or 15 Gy in 2 fractions (see Table 2).

Before starting VD use, 71.7% of the participants showed a grade 2 VS and the remaining 28.3% of patients showed a grade 3 VS according to the CTCAE criteria. At the vaginal examination performed 12 months after starting VD use, 47.2% of patients showed grade 1 VS and 30.2% showed grade 2, while 12 patients (22.6%) showed no vaginal stenosis (see Tables 2 and 3).

At 3 months after beginning VD use, the largest comfortably insertable VD was the second in 28 patients (52.8%), while 25 participants (47.2%) could easily use the fourth VD after 12 months of VD use. Nearly two-thirds (64%) of the patients had used the VD 3 to 4 times per week and the vast majority (90.6%) were sexually active during the 12 months of VD use (see Tables 2 and 3).

3.3. Vaginal dilation and vaginal stenosis treatment

According to the clinical examination and the CTCAE criteria, VD use affected the VS grade, which significantly decreased after

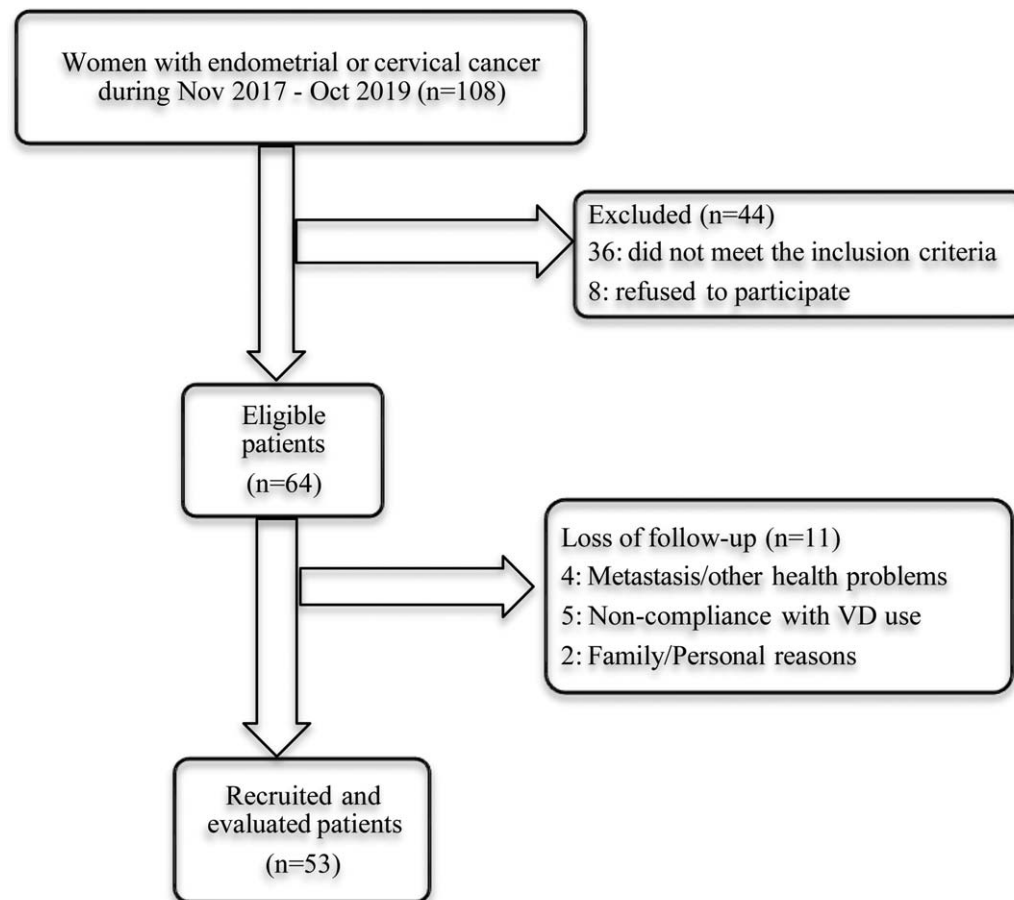


Figure 1. Study protocol flow diagram.

12 months of VD use compared with the initial grade. Specifically, 65.8% of the patients with initial grade 2 VS showed a final VS of grade 1, while all patients with initial grade 3 showed a final grade 2 VS after 12 months of VD use (see Table 4).

Clinical data about vaginal dilator use		Number of pts	Percentage (%)
Initial VD size (3 months after VD start)	1st	9	17.0
	2nd	28	52.8
	3rd	16	30.2
	4th	0	–
Final VD size (12 months after VD start)	1st	0	–
	2nd	2	3.8
	3rd	14	26.4
	4th	25	47.2
	5th	12	22.6
Frequency of VD use	2–3 times per wk	19	35.8
	3–4 times per wk	34	64.2
Sexually active	yes	48	90.6
	no	5	9.4

pts = patients, VD = vaginal dilator.

There was also a significant increase in the largest comfortable size of VD after 12 months of VD use; this result aligned with the above findings regarding the VS grade. Notably, 77.8% of the participants who started with the first VD size reached the third VD size after 12 months. Moreover, 21 of 28 (75%) and 7 of 28 (25%) participants starting with the second VD size had reached the fourth and third VD sizes, respectively, after 12 months. Similarly, 12 of 16 (75%) patients starting with the third VD size reached the fifth VD size (see Table 5).

Diagnosis, chemotherapy, the total dose of BT, the total dose of EBRT, and the frequency of VD use did not significantly alter the results. However, we noted the VD use start time did affect our findings; only the participants starting less than 3 months post-RT demonstrated a statistically significant decrease in VS after 12 months of VD use and those starting less than 2 months post-RT showed a considerable increase in final VD size (see Tables 6 and 7).

More specifically, all patients who started VD use from 2 to 3 months after RT and had grade 3 VS initially had grade 2 VS ultimately and 83.3% with VS grade 2 eventually showed VS grade 1 (Fisher exact test, $P < .001$), while 95.9% of those starting less than 2 months after RT with an initial VS grade 2 showed a final grade 0 or 1 (Chi-Squared test, $P = .000$; see Table 6).

In measuring the effect of the time interval between RT and the start of VD use on the final VD size, 92.3% of participants

Table 4**Grade of vaginal stenosis before the onset of vaginal dilator use (initial) and after 12 months of vaginal dilator use (final).**

			Final grade of vaginal stenosis			Total
			Grade 0	Grade 1	Grade 2	
Initial grade of vaginal stenosis	Grade 2	Count	12	25	1	38
		%	31.6%	65.8%	2.6%	100.0%
	Grade 3	Count	0	0	15	15
		%	0.0%	0.0%	100.0%	100.0%
Total		Count	12	25	16	53
		%	22.6%	47.2%	30.2%	100.0%
Fisher exact test						
P value			<.001			

Table 5**Size of vaginal dilator at 3 months of vaginal dilator use (initial) and at 12 months of vaginal dilator use (final).**

			Final vaginal dilator Size (12 mo of vaginal dilator use)				Total
			2nd	3rd	4th	5th	
Initial vaginal dilator size (3 months of vaginal dilator use)	1st	Count	2	7	0	0	9
		%	22.2%	77.8%	0.0%	0.0%	100.0%
	2nd	Count	0	7	21	0	28
		%	0.0%	25.0%	75.0%	0.0%	100.0%
	3rd	Count	0	0	4	12	16
		%	0.0%	0.0%	25.0%	75.0%	100.0%
Total		Count	2	14	25	12	53
		%	3.8%	26.4%	47.2%	22.6%	100.0%
Fisher's exact test							
P value			<.001				

starting less than 2 months post-RT with the second VD size reached the fourth size and 90.9% starting with the third size reached the fifth (Fisher exact test, $P < .001$). Similarly, 85.7% of patients starting from 2 to 3 months after RT with the first VD

size reached the third, 64.3% of those starting with the second size ended with the fourth, and 66.7% of patients starting with the third size reached the fifth (Fisher exact test, $P < .001$; see Table 7).

Table 6**Impact of start time of vaginal dilator use on final grade of vaginal stenosis.**

Start time of vaginal dilator Use			Final grade of vaginal stenosis			Total	
			Grade 0	Grade 1	Grade 2		
<2	Initial grade of vaginal stenosis	Grade 2	Count	10	13	1	24
			%	41.7%	54.2%	4.2%	
	Total		Count	10	13	1	24
Chi-Squared goodness of fit test P value = .000							
[2–3]	Initial grade of vaginal stenosis	grade 2	Count	2	10	0	12
			%	16.7%	83.3%	0.0%	100.0%
	grade 3	Count	0	0	12	12	
		%	0.0%	0.0%	100.0%	100.0%	
Total		Count	2	10	12	24	
Fisher exact test P value <.001							
≥4	Initial grade of vaginal stenosis	Grade 2	Count	8.3%	41.7%	50.0%	100.0%
			%	100.0%	0.0%	100.0%	
	Grade 3	Count	0	3	3	3	
		%	0.0%	100.0%	100.0%		
	Total		Count	2	3	5	5
Fisher exact test P value = 1.000							

Start time of vaginal dilator use			Final vaginal dilator size (after 12 months of vaginal dilator use)					
			2nd	3rd	4th	5th		
<2	Initial vaginal dilator size (after 3 mo of vaginal dilator use)	2nd	Count		1	12	0	Fisher exact test P value <.001
			%		7.7%	92.3%	0.0%	
	3rd	Count		0	1	10		
		%		0.0%	9.1%	90.9%		
	Total	Count		1	13	10		
	%		4.2%	54.2%	41.7%			
[2-3]	Initial vaginal dilator size (after 3 mo of vaginal dilator use)	1st	Count	1	6	0	0	Fisher exact test P value <.001
			%	14.3%	85.7%	0.0%	0.0%	
	2nd	Count	0	5	9	0		
		%	0.0%	35.7%	64.3%	0.0%		
	3rd	Count	0	0	1	2		
%		0.0%	0.0%	33.3%	66.7%			
Total	Count	1	11	10	2			
	%	4.2%	45.8%	41.7%	8.3%			
>=4	Initial vaginal dilator size (after 3 mo of vaginal dilator use)	1st	Count	1	1	0		P value = .067
			%	50.0%	50.0%	0.0%		
	2nd	Count	0	1	0			
		%	0.0%	100.0%	0.0%			
	3rd	Count	0	0	2			
%		0.0%	0.0%	100.0%				
Total	Count	1	2	2				
	%	20.0%	40.0%	40.0%				

3.4. Vaginal dilation and sexual life

The patients’ answers from the SVQ before and 12 months after the start of VD use indicated a reduction in the feeling of vaginal dryness, pain, and bleeding during intercourse and in the feeling that the vagina was too small (see Figs. 2-5).

More specifically, during the 12 months of dilation the answer “not at all” for vaginal dryness trended upwards from 3.8% to 19.6%, 72.3%, and 95.7% before the start of VD use and at 3, 6, and 12 months of VD use, respectively (P value = .000), while the answer “quite a bit” fell from 61.5% before starting dilation to 17.4% at 3 months of dilation and 0% at 6 and 12 months (P = .000; see Fig. 2). Similarly, 89.1% of patients did not experience pain during intercourse after 12 months of VD use compared with 11.5% before starting dilation (P = .000). “A little” pain was felt by 61.5% of participants before dilation

while only 10.9% reported the same at 12 months of dilation (P = .000; see Fig. 3). No patient had bleeding during intercourse at 12 months, with 84.6% having answered no bleeding before starting dilation (P = .015; see Fig. 4). It is noteworthy that 60.9% of patients did not feel at all that their vaginas were too small during intercourse after 12 months of dilation, whereas only 11.5% gave this answer before starting dilation (Fisher exact test; see Fig. 5).

Furthermore, 47.17% described their satisfaction with their sexual life with a score of 5 out of 7 and only 3.77% gave a score of 3 out of 7 after 12 months of VD use (see Fig. 6).

4. Discussion

In this prospective study, we examined the efficacy of VD use for VS and sexual QoL after RT for endometrial or cervical cancer.

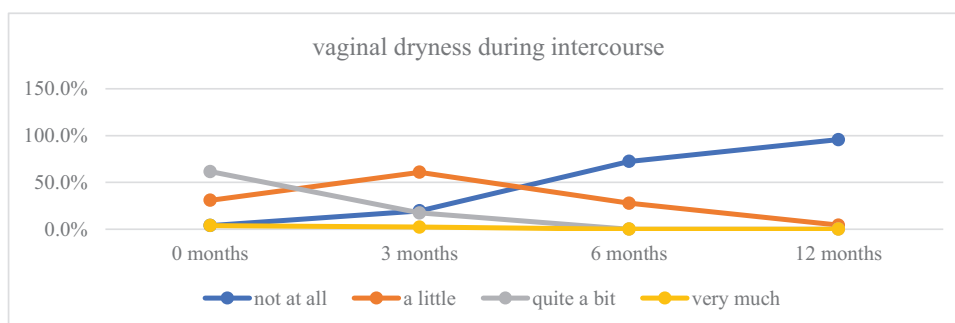


Figure 2. Graph of vaginal dryness during intercourse.

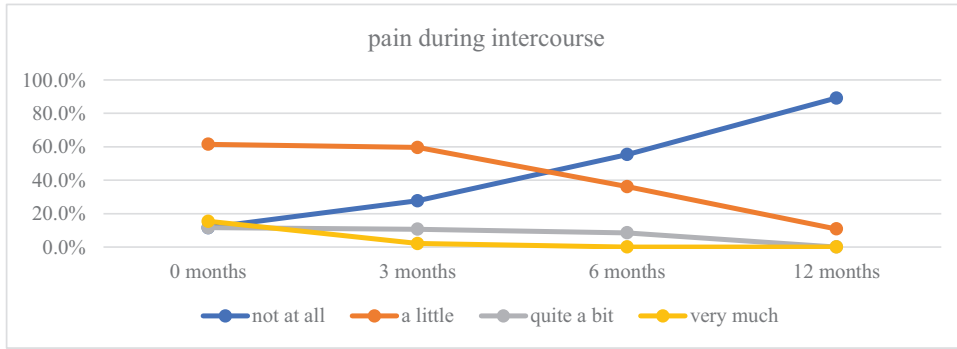


Figure 3. Graph of pain during intercourse.

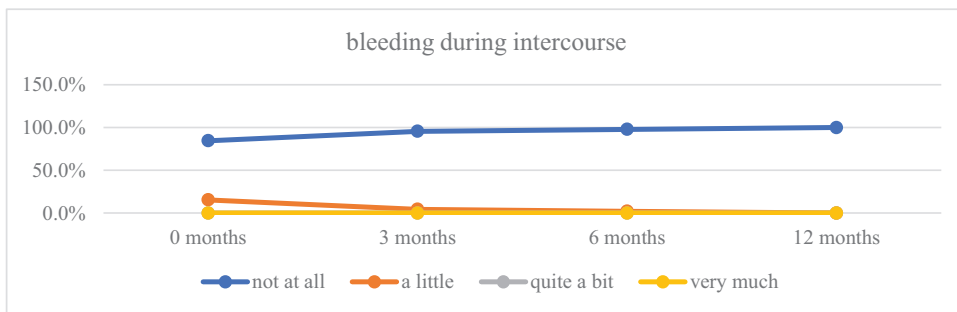


Figure 4. Graph of bleeding during intercourse.

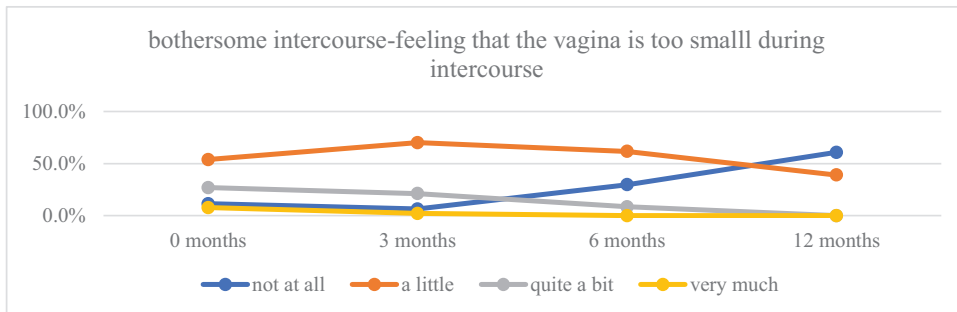


Figure 5. Graph of the feeling that the vagina is too small during intercourse.

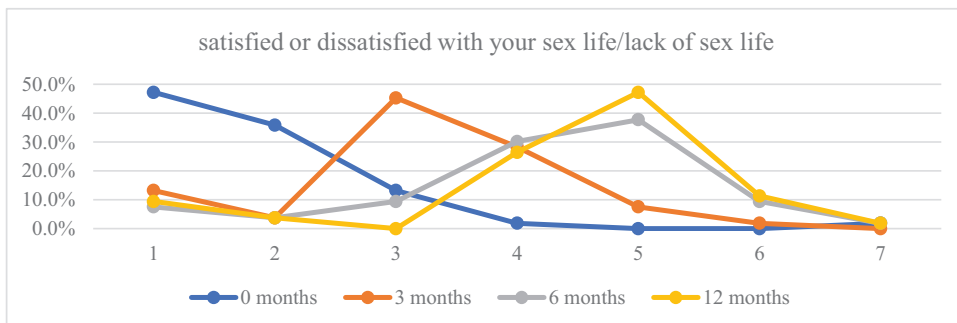


Figure 6. Graph of patient satisfaction or dissatisfaction with their sex life/lack of sex life.

After the 12-month follow-up, the degree of VS was reduced and the largest VD size that could comfortably be inserted into the vagina had increased. Notably starting VD use more than 3 months after the end of RT was not associated with a significant effect on VS. Furthermore, sexual well-being gradually improved over 12 months of VD therapy. Vaginal and sexual signs and symptoms such as dryness, pain, blood, and the feeling that the vagina is small during intercourse decreased significantly and patients' satisfaction with their sex lives increased.

Several studies have reported similar results regarding the effect of VD on VS.^[9,20,30–32] Velaskar et al^[33] observed a significant increase in vaginal canal length after 4 months of VD therapy. In a prospective cohort study by Law et al,^[8] VD minimized VS in rectal and gynecological cancer survivors. Vaginal size was evaluated similarly to our study: by the largest vaginal dilator that could be comfortably inserted and maintained for 10 minutes without pain or bleeding. However, they demonstrated that adherence to VD use after 12 months decreased.^[8] Son et al^[34] observed reduced VS in patients with rectal cancer who adhered to VD use.

Bahng et al^[31] showed an increase in vaginal length after VD use at least 2 to 3 times per week after BT. Likewise, Gondi et al^[30] observed that high compliance with VD therapy was associated with less severe VS after RT in patients with locally advanced cervical cancer. In contrast, other authors did not find any effect of VD use on VS after RT.^[3,23,32,35,36]

Despite mixed evidence of the possible benefit of VD use for VS after RT, the American Cancer Society recommends VD therapy or sexual intercourse 3 times per week against VS.^[11,28]

There is no evidence to support starting VD use during or after RT.^[11] However, to our knowledge this study is the first to show that starting vaginal dilation more than 3 months after RT is not associated with a significant decrease in VS. Several studies' results align with our finding that VD therapy correlates well with improving patients' sexual health; Carter et al^[37] found a reduction of vaginal symptoms by applying moisturizing agents and using VDs.^[3,37] Similarly, Bakker et al reported that VD therapy and interventions targeting sexual recovery led to improved sexual QoL.^[7]

However, van Leeuwen et al^[38] did not find that VD use affected patients' QoL; that study showed an improvement in QoL with decreased vaginal symptoms 1 year after RT.^[3,38] Although Akbaba et al^[32] demonstrated that sexual QoL is considerably diminished after surgery and radiotherapy due to vaginal toxicity, they found no association between VD use and improved sexual function. Similarly, Jeffries et al^[18] and Robinson et al^[20] showed no increase in the sexual function scores of patients using VDs with guidance and patients with no psychoeducational intervention.^[18,20,39] Despite inconclusive studies concerning the correlation between VD therapy and improvement of sexual function, experienced practitioners support the use of VDs along with vaginal moisturizing, lubricating, and estrogen agents to improve sexual QoL after RT in gynecological cancer survivors.^[6,39,40]

Notably, VD therapy in this study is high compared with the previously published studies.^[8,19,41,42] Our educational interventions for high adherence were the provision of consistent written instructions for VD, detailed demonstration of the equipment, and strong motivation that VD therapy will prevent VS, which is important for sexually active patients and follow-up examinations to rule out disease recurrence. Additionally, participants were provided with written and illustrated instruc-

tions on how to perform Kegel exercises to relax their pelvic muscles before using VDs. In addition to the 4 follow-ups after RT, there was phone contact once a month for the physician to advise each participant on any emotional or technical difficulties in VD use and strengthen their motivation to continue dilation.

Our study's limitations include that the measuring devices for the assessment of VS and sexual function after RT were mainly subjective

1. vaginal examination at 4 times to determine the grade of VS according to the CTCAE version 5.0 criteria,
2. the largest VD size easily insertable in the vagina with no pain or bleeding,
3. a SVQ answered by each participant at 4 times.

In addition, there was no pre-RT measurement of vaginal dimensions and, considering the psychological impact of cancer diagnosis and pre-RT treatment with surgery, we did not measure vaginal dimensions to avoid causing more emotional distress. The study design lacks a control group which reduces the statistical power of our findings; these are also compromised by the small sample size. Furthermore, a follow-up after more than 12 months is needed to draw more reliable conclusions and determine the optimal duration of VD use.

5. Conclusions

This study reveals that VD therapy after RT could decrease VS and enhance sexual QoL, which is substantially compromised by irradiation toxicity. Despite the limitations of this study, we suggest VD use for endometrial and cervical cancer survivors, starting no more than 3 months after the end of RT and performed at least 2 to 3 times per week for 10 to 15 minutes. Nevertheless, psycho-educational interventions, including counseling, motivation, and guidance on VD use, are vital to improving patient compliance. Multi-centered, well-designed randomized clinical trials with high statistical power and longer follow-up times should be conducted to confirm the efficacy of VD use in managing VS and low sexual QoL after RT in gynecological cancer patients. Moreover, further evidence is needed to develop a uniformly recognized method regarding the time between the end of RT and the onset of use, technique, frequency, duration, time of use, and VD size.

Data access statement: All relevant data are within the paper and its supporting information files.

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