In patients treated for gynecologic cancer

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Gynecological cancer treatment

Affect daily functioning and HRQOL

- Low level of physical activity
- Physical and functional impairment
- Fatigue
- Psychological distress
- Pelvic floor symptoms

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Exercise in patients with lower limb lymphedema

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The importance of exercise

Physical activity on antitumorigenic potential

- Modulation of the inflammation, immune response, hormonal alterations
- Total decreased adiposity and weight loss
 - -> Lower estrogen production, decreased insulin resistance
- Decreased of obesity(low grade inflammation)
 - -> deceased chronic inflammation -> reduces cancer risk and mortality

Exercise interventions for patients with gynecologic cancer: a systemic review and meta analysis Lin (2016)

Author and year	Comparison: control group	Intervention programme	Exercise components	Supervision	Intensity
Ledderer 2013 [34]	Usual care	Psychosocial cancer rehabilitation intervention including supportive talks and a residential rehabilitation course	Education regarding exercise: physical activity (including walking, dancing and massage)	Unsupervised	NR
Yang 2012 [33]	Usual care	Pelvic floor muscle training programme comprising intensive pelvic floor muscle training incorporated with core exercise	Core exercise: strengthening exercises for the pelvic floor muscles and transverse abdominis muscles, stretching exercises for muscles attached to the pelvic girdle, and diaphragmatic breathing techniques	Supervised	NR
von Gruenigen 2012 [30], McCarroll 2014 [29] ^a	Usual care	Lifestyle intervention programme including nutrition, exercise and behavioural modification counselling	Education regarding exercise: physical activity goals were 150 minutes/week (five times per week for 30 minutes) for months 1 to 2, 225 minutes/week (five times per week for 45 minutes) for months 3 to 4 and 300 minutes/week (five times per week for 60 minutes) for months 5 to 6. Pedometers were given to provide immediate feedback and reinforcement. Three-pound hand and adjustable ankle weights were given for performing resistance exercises	Unsupervised	Moderate ^b

Donnelly 2011 [28]	Usual care	Moderate intensity, home-based physical activity intervention	Education regarding exercise: home-based physical activity intervention which included walking and strengthening exercises. The aim was to meet physical activity guidelines of 30 minutes of physical activity on at least 5 days per week. Participants were provided with exercise diary, pedometer and information booklet	Unsupervised	Moderate ^b	30 ^b
von Gruenigen 2009, 2008 [32,31] ^a	Usual care	Lifestyle intervention programme consisting of exercise and nutritional counselling with cognitive- behavioural modification	Education regarding exercise: physical activity. Intervention group was coached to gradually increase walking or other aerobic activity to 5 days per week for 45 minutes or more, if able. Pedometers were provided for patient feedback	Unsupervised	NR	45 ^b

(a) Self-reported physical activity levels

	Intervention Control			Mean Difference			Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% CI
von Gruenigen 2008	16.7	20.44	23	1.7	15.45	22	38.9%	15.00 [4.44, 25.56]	
von Gruenigen 2012	18	20.61	41	6.4	16.6	34	61.1%	11.60 [3.18, 20.02]	
Total (95% CI)			64			56	100.0%	12.92 [6.34, 19.51]	
Heterogeneity: Chi ² = 0.24, df = 1 (P = 0.62); I^2 = 0% -20 -10 0 10 20							-20 -10 0 10 20		
Test for overall effect: $Z = 3.85$ ($P = 0.0001$)									Favours control Favours intervention

(b) Health-related quality of life

	Inte	rventic	n	0	ontrol			Std. Mean Difference	Std. Mean	Difference	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% C	I IV, Fixed	d, 95% CI	
Donnelly 2011	10.25	16.31	16	5.65	17.28	17	22.7%	0.27 [-0.42, 0.95]		•	-
Ledderer 2013	0.3	24.6	19	8.7	24	21	27.3%	-0.34 [-0.96, 0.29]			
von Gruenigen 2009	1.8	13.69	23	2.3	13.15	22	31.2%	-0.04 [-0.62, 0.55]			
Yang 2012	1.8	15.76	14	-6.8	18.95	14	18.8%	0.48 [-0.27, 1.23]		•	
Total (95% CI)			72			74	100.0%	0.05 [-0.28, 0.37]	•	>	
Heterogeneity: Chi ² = 3	3.20, df :	= 3 (P =	0.36);	$I^2 = 6\%$					1 05 (0.5	
Test for overall effect:	Z = 0.28	(P = 0.	78)						-1 -0.5 (Favours intervention	0.5 Favours con	trol

(c) Body composition

Ot d O		erventio			Control	T-1-1	W-!-L-	Mean Difference	Mean Difference
Study or Subgroup	Mean	รบ	rotai	Mean	ŞD	lotai	Weight	IV, Fixed, 95% C	I IV, Fixed, 95% CI
2.3.1 Weight									
von Gruenigen 2008		29.21	23		25.93	22	0.2%	-2.50 [-18.62, 13.62]	
von Gruenigen 2012	-3.9	19.15	41	0.6	33.12	34	0.3%	-4.50 [-17.08, 8.08]	
Subtotal (95% CI)			64			56	0.6%	-3.74 [-13.66, 6.18]	
Heterogeneity: Chi ² =	-	•		$l^2 = 0\%$					
Test for overall effect:	Z = 0.74	(P = 0.	46)						
2.3.2 Waist circumfer	rence								
Donnelly 2011	-0.18	17.4	16	1.7	20.8	17	0.3%	-1.88 [-14.94, 11.18]	
von Gruenigen 2012	-2.54	12.45	41	-2.28	15.25	34	1.4%	-0.26 [-6.65, 6.13]	
Subtotal (95% CI)			57			51	1.7%	-0.57 [-6.31, 5.16]	
Heterogeneity: Chi2 =	0.05, df =	= 1 (P =	0.83);	$l^2 = 0\%$					
Test for overall effect:	Z = 0.20	(P = 0.	84)						
2.3.3 BMI									
Donnelly 2011	0.47	8.27	16	0.36	7.69	17	1.9%	0.11 [-5.35, 5.57]	
McCarroll 2014	-1.5	1.59	41	0.1	1.73	34	95.9%	-1.60 [-2.36, -0.84]	· ·
Subtotal (95% CI)			57			51	97.8%	-1.57 [-2.32, -0.82]	•
Heterogeneity: Chi2 =	0.37, df =	= 1 (P =	0.54);	$l^2 = 0\%$					
Test for overall effect:	Z = 4.09	(P < 0.	0001)						
Total (95% CI)			178			158	100.0%	-1.56 [-2.31, -0.82]	♦
Heterogeneity: Chi ² =	0.75. df =	= 5 (P =	0.98):	$l^2 = 0\%$				•	
Test for overall effect:		•	, .						-10 -5 0 5 10
. I I I I I I I I I I I I I I I I I I I	0	,							Favours intervention Favours control

- Positive effects: BMI, physical activity
- Limitation
 - Exercise training only one trial
 - Using self reported measures
 - No evaluation : muscle strength and functional exercise capacity
 - Limited number of RCTs, heterogeneous intervention programs and various time point, only obese endometrial cancer patients
 - Limited supervision exercise

Guideline of exercise prescription

Physical activity guidelines for adults and older adults

US Department of Health and Human Service's Physical Activity Guidelines for Adults and Older Adults⁵

Adults should move more and sit less throughout the day. Some physical activity is better than none. Adults who sit less and do any amount of moderate to vigorous physical activity gain some health benefits. Be as physically active as conditions and abilities allow.

- For substantial health benefits, adults should do at least 150 min (2 h and 30 min) to 300 min (5 h) a week of moderate-intensity, or 75 min (1 hour and 15 min) to 150 min (2 h and 30 min) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity. Preferably, aerobic activity should be spread throughout the week.
- Additional health benefits are gained by engaging in physical activity beyond the equivalent of 300 min (5 h) of moderate-intensity physical activity a week.
- Adults should also do muscle-strengthening activities of moderate or greater intensity and that involve all major muscle groups on ≥2 d a
 week, as these activities provide additional health benefits.

Physical activity recommendation of cancer survivors

- The general physical activity guidelines or healthy adults were considered appropriate for cancer survivors
 - Flexibility with regards to chronic conditions and health status
 - Be modified based on individual fitness level, health status, type and stage of cancer, treatments received and their adverse effects, and anticipated disease course
 - Evaluate PPN, Osteoporosis, hormonal therapy use, bony metastasis, cardiac condition, obese

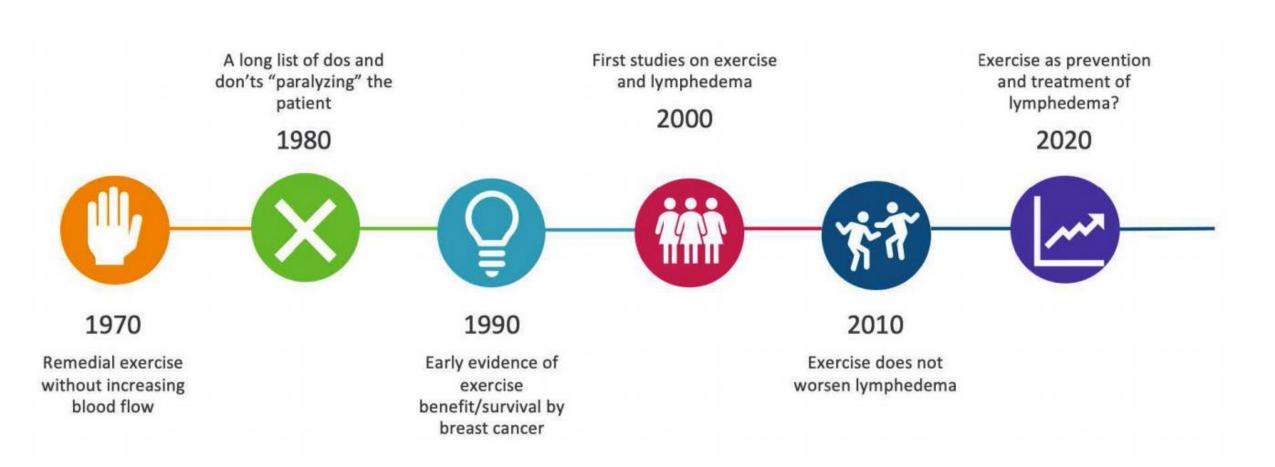
Symptom	Contraindications to and Considerations for Participation in Physical Activity (PA)
Treatment	
• Surgery	 May be up to 8 wk postsurgery prior to clearance to start PA program
	 Obtain clearance from physician, especially if abdominal, groin, or lower extremity edema/inflammation
 Intravenous chemotherapy (IV C) 	No PA on day of IV C or for 24 h after
	 Monitor closely for signs of infection, take extra infectious precautions at public fitness facilities
 Intraperitoneal chemotherapy (IP C) 	 No PA on day of IP C, avoid aquatic activities due to catheter
	 Monitor closely for signs of infection, take extra infectious precautions at public fitness facilities
 Radiation therapy 	 Aquatic activities may cause or increase the risk of skin irritation
	 Monitor closely for signs of infection, take extra infectious precautions at public fitness facilities

Fatigue	No PA if experiencing extreme fatigue
	PA may aide with mild-moderate fatigue
Anemia	• No PA if platelets <50,000 mcL, white blood cells <3000 mcL, hemoglobin <10 g/dL
Lymphedema	Wear well-fitting compression garments during PA
	 Often require medical evaluation if lower extremity edema prior to starting PA program
Acute infections	No PA if temperature >100°C
	 Asymptomatic for at least 48 h prior to PA
 Gastrointestinal symptoms (nausea, emesis, diarrhea) 	 No PA within 24–36 h of severe symptoms
	Ensure proper hydration
	Consider consultation with a dietician
Musculoskeletal symptoms	 No PA if recent bone pain, unusual muscle weakness, severe cachexia, or poor performance status
	 Consider altering PA if osteoporosis or bone metastases present, especially if receiving hormone replacement therapy
Neurologic symptoms	 No PA if experiencing significant cognitive decline, dizziness, light-headedness, ataxia, disorientation, or blurred vision
	 Given possible compromised balance, consider PA with body support (such as a stationary bike) if neuropathy present

Exercise on Lower limb lymphedema

Avoidance of activities

Evolution of exercise advice for patients



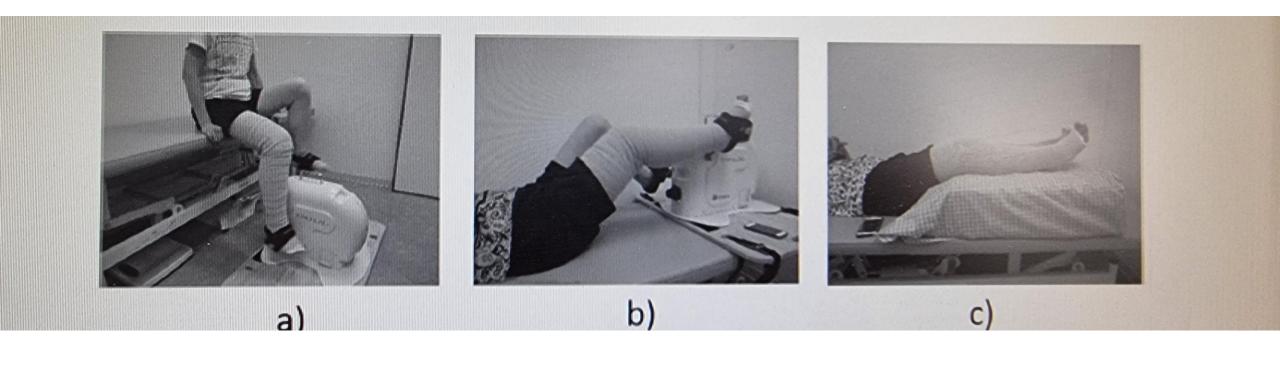
Low load vs high load exercise

Fukushima(2017)

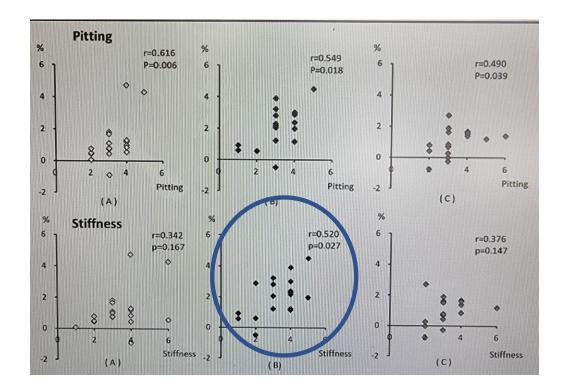
- 23 women with LLL (randomized controlled crossover trial)
- Bicycle ergometer with short stretch bandages
- Incenticity
 - High load AECT(active exercise with compression therapy)
 - Low load AECT
 - Compression only therapy(CT)
- Lower limb volume was significantly reduced after high-load AECT compared to that after CT
- General symptoms and skin symptoms were similar across the three interventions

Postural differences in the immediate effects of active exercise with compression therapy on LLL (kiriko 2021)

- Seated AECT(Active exercise compression therapy), supine AECT, compression only therapy (randomized, controlled, crossover trial)
- Bicycle ergometer with wearing elastic compression bandage for 15min



Outcomes	Mean percentage c	hange (95% CI)		P			
	Seated AECT	Supine AECT	СТ	P1	P2	P3	Overall P value
Lower-limb volume	1.19% ± 1.32% (0.62–1.76%)	$2.03\% \pm 1.24\%$ (1.46–2.60%)	0.99% ± 0.83% (0.42–1.56%)	1.00	0.01	0.06	0.01
Pain	27.9% ± 53.2% (8.95–46.87%)	$71.0\% \pm 22.4\%$ (52.08-89.99%)	45.4% ± 28.8% (26.44–64.35%)	0.41	0.10	0.02	0.03
Heaviness	27.5% ± 63.6% (6.34–48.69%)	$62.3\% \pm 26.2\%$ (41.16-83.51%)	57.6% ± 27.6% (36.47–78.82%)	0.07	1.00	0.03	0.02

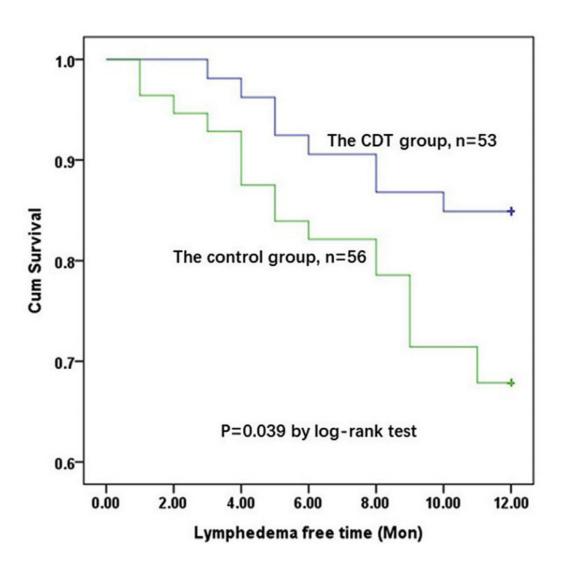


- More volume reduction on supine AECT
- Pre intervention pitting significantly correlation with change volume on all supine, seated, CT
- Pre intervention stiffness correlation with change volume on only supine AECT

Early prevention of CDT and rehabilitation exercise for prevention of LLL after operation of gynecologic cancer

(Xiaoli 2021)

- N=109 female
- CDT with exercise group (n=56) vs education control group (n=57)
- Within 24 h after the surgery
- CDT : massage + elastic band (for 40 days)
- Exercise : supine position
 - ankle flexion, dorsiflexion, varus and valgus
 - knee joint, straight leg raising
 - hip exercise
 - repeated for 15-20 times once, twice one day, for 40 days



Quality of life and cancer related fatigue.

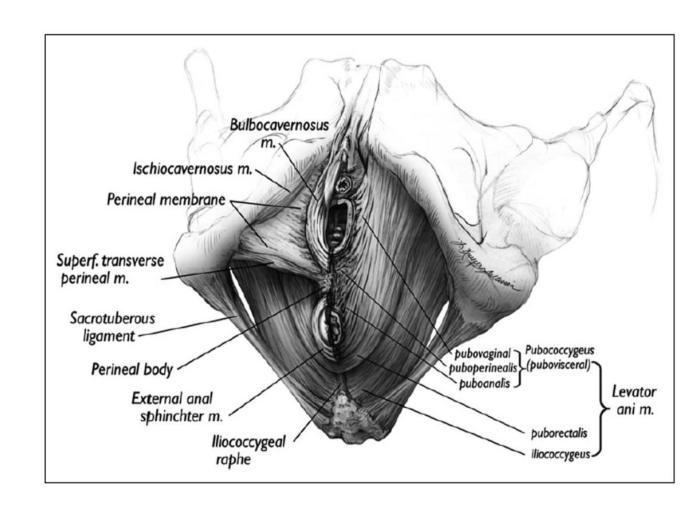
Variables	CDT group, $n = 53$	$Control\ group,\ n=56$	P							
EORTC QLQ-C30-GHS										
3 mon	69.71 ± 7.79	66.82 ± 6.70	0.022							
1 y	69.24 ± 7.30	66.0 ± 6.46	0.016							
ORTC QLQ-C30-	-FS									
3 mon	19.22 ± 5.05	21.83 ± 4.96	0.008							
1 y	19.58 ± 4.49	23.67 ± 3.50	0.000							
EORTC QLQ-C30	O-SS									
3 mon	64.18 ± 6.41	61.19 ± 6.27	0.015							
1 y	65.43 ± 6.8	61.58 ± 5.82	0.002							
BFI										
3 mon	2.33 ± 1.09	2.80 ± 1.18	0.036							
1 y	2.18 ± 1.07	2.87 ± 1.16	0.002							

Pelvic floor exercise

Pelvic floor dysfunction

- Pelvic organ prolapse
- Urinary incontinence
- Fecal incontinence

Sexual dysfunction



Treatment for cancer affect the pelvic floor

- Surgical procedures
 - Scar tissue restriction and swelling
 - Hormonal changes associated with removal of ovaries
- Adjuvant therapy (chemotherapy, radiation)
 - Radiotherapy -> fibrosis -> narrowing and shortening in the vaginal canal
 - Fibrosis in the vaginal wall and pelvic floor
 - Incontinence and urgency of bowel and bladder, pelvic pain, and sexual dysfunction
- Lower libido, altered sexual response, change in body image, distress related to changes in sexual health
- Genitalia lymphedema
 - Impact bladder function

Pelvic floor disorders and sexual function

Rutledge(2017)

- Control(n=150) : general gynecologic clinic who were >30 ys
- Study(n=100): survivors of gynecologic cancer

Pelvic floor disorder statistics

Variable	Gynecologic patients (n = 108), n (%)	Survivors of gynecologic cancer (n = 260), n (%)	P value ^a
Any urinary incontinence: Incontinence Severity Index Score > 0	56 (56)	176 (70)	NS
Moderate/ Severity urinary incontinence	26 (26)	105 (42)	NS
Prolapse	14 (13)	20 (8)	NS
Fecal incontinence	34 (32)	106 (43)	.02
Mean fecal incontinence severity score	1.0	2.8	.003
Mean Pelvic Organ Prolapse/Urinary Incontinence Sexual questionnaire total score	37 ± 6	32 ± 7	<.001

- Survivors: less sexual desire, less ability to climax, less intensity of the climaxes achieved, less sexual excitement and satisfaction with the variety of sexual activities, more negative emotional reactions to sexual activity
- No difference: dyspareunia(radical surgery or radiation), impact of pelvic floor disorders, partner functioning
- Multifactorial causes: Physical, social, psychological factors
 - Body image, hormone function
- Asked about urinary/fecal incontinence or sexual function by their oncologist
 - Only 40% of survivors
 - 23% of the women

Factors that affect rates of PFD

Timing

- Highest in the early post operative period
- UI rate: 55% (1mo after surgery) (Ceccaroni et al), 48% (1.5 mo) and 17%(12 mo) (Naik et al)

Treatment modality

- Nerve sparing surgical technique : lower rates
- Radiation alone or combination : higher rates
- Radical surgical intervention : immediate symptom
- Radiation : late effects over many months

Systematic review (2018) Ramaseshan(2020)

Effect of a pelvic floor muscle training program on gynecologic cancer survivors with pelvic floor dysfunction: Ynag EJ (2012)

- PFRP (pelvic floor rehabilitation program) and QOL, prospective, randomized, controlled trial
- PFRP group (n=17), non PFRP group (n=17) in 4weeks
 - Pelvic floor strength (perineometer, 2 channel EMG)
 - Pelvic floor dysfunction questionnaire
 - MEP of sacral nerve
 - HRQOL

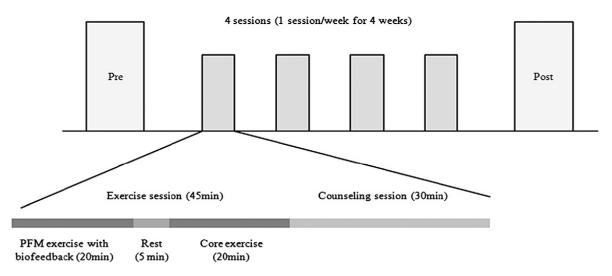


Fig. 3. Flow chart of participants through the randomized controlled trial of the exercise program and analysis.

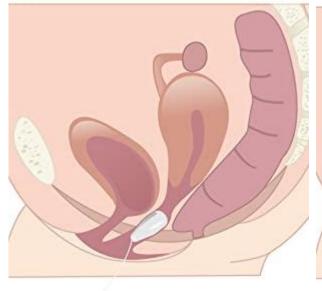
Effects of PFRP within-group and between-group differences.

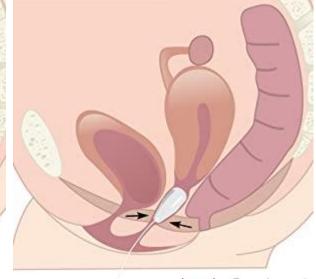
Variables	Within group (T1-T0)		Between group (i	ntervention vs. control)				
				Mean difference Regression statistics				
	PFRP group $(n=12)$	Non-PFRP group $(n=12)$	P-value	between groups	β coefficient (95% CI)	t-Value	df	P-values
Pelvic floor questionnaire								
Bladder function score ^b	-0.83 ± 1.08	-0.83 ± 1.25	0.710	0.00	0.15(-0.57-1.23)	0.771	17	0.452
Bowel function score ^b	-0.67 + 0.65	-0.51 + 1.47	0.412	-0.16	-0.15(-0.66-1.31)	0.69	17	0.497
Sexual function score ^b	-5.62 ± 2.27	-2.42 ± 3.47	0.047	-0.38	-0.55(-0.860.01)	-2.292	9	0.048
Pelvic floor muscle strength (cm/H ₂ O)	21.78 ± 7.64	7.56 ± 8.65	0.004	14.22	2.15 (1.17-3.57)	2.389	9	0.036
Motor evoked potential								
Sacral stimulation								
Latency	-0.41 ± 0.88	-0.03 ± 0.27	0.283	1.90	0.19 (-4.19-6.79)	0.610	5	0.569
Amplitude	0.30 ± 0.27	0.05 ± 0.27 0.05 ± 0.20	0.142	0.25	0.38 (-0.21-0.65)	1.166	9	0.273
Threshold	-32.00 ± 9.75	-11.71 ± 14.24	0.010	-20.29	-0.49(-1.080.15)	-2.835	13	0.014
Cranial stimulation at rest								
Latency	-0.15 ± 0.02	3.93 ± 1.72	0.731	-4.08	-0.27(-3.40-1.43)	-0.908	10	0.385
Amplitude	-0.08 ± 0.20	0.00 ± 0.29	0.295	-0.08	-0.05(-0.17-0.15)	-0.155	10	0.880
Threshold	-19.40 ± 14.29	-9.40 ± 19.67	0.548	-10.00	-0.43(-34.48-10.04)	1.206	7	0.235
Cranial stimulation with facilitation								
Latency	0.15 ± 1.58	-1.06 ± 4.57	0.731	1.21	-0.10(-3.36-2.47)	-0.341	10	0.740
Amplitude	-0.20 ± 0.42	-0.22 ± 0.83	0.445	0.02	-0.05(-0.33-0.28)	-0.175	10	0.865
Threshold	-12.50 ± 21.79	-9.67 ± 11.69	0.914	-2.83	-0.14 (-26.70 - 19.30)	-0.380	7	0.715

Pelvic floor exercise

- Restore normal pelvic muscle strength, endurance, power, resting tone, reverse damage to the muscles and connective tissue
 - Electrical stimulation
 - Biofeedback
 - Vaginal weighted cone
- Regimens
 - 4-8 hour long sessions/week
 - Depending on the severity and complexity of symptoms, some women may need to continue exercise for several months









How to exercise?

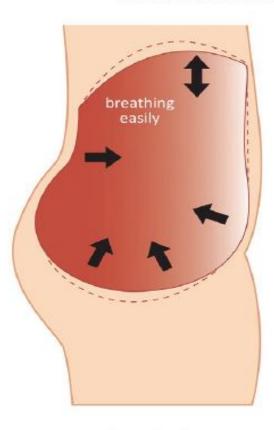
- Identify the correct muscle
 - Stop or slow the flow of urine midway thorough emptying the bladder
 - Stopping the flow of urine repeatedly on the toilet is not an exercise

Kegel

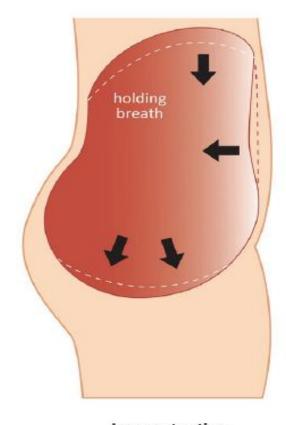
- Sit in a comfortable position
- Tighten these muscles as much as possible.
- Hold this position for 3–5 seconds. It should feel as though the muscles are lifting up as a result of the squeezing.
- Release the muscles and rest for several seconds.
- Repeat this up to 10 times.
- People can vary this exercise by doing it while standing, lying down, or crouching on all fours.

PELVIC FLOOR MUSCLE CONTRACTION

- In ideal situation
 - Increased abdomen pressure(during exercise)
 - Pelvic floor muscle lift, abdominal and back muscles draw in to support the spine and breathing is easy
- In weakened of core musc
 - During exercise
 - Potential to overload the pelfloor, causing downward pressure



Correct action
The pelvic floor lifts, the deep
abdominals draw in and
there is no change in breathing



Incorrect action
Bracing the abdominals strongly
without focusing on lifting the
pelvic floor first, can result in
downwards pressure on the
pelvic floor

- No strong abdominal exercise
- Avoid breath holding by exhaling with effort
- Lift your pelvic floor first and hold it during the exercise, then relax after
- Reduced repetition before pelvic floor muscle fitness improves

Pelvic floor safe core exercises

Lower intensity abdominal challenge

- Single leg extension with one leg supported by a hand on stationary knee or moving foot on ball
- Knees side to side with feet on ball
- Modified plank on hands or knees with a slight bend at the hips
- Wall push ups
- Ball bridge (feet on ball or back on ball, +/single leg lift)
- Arm and leg lift on all fours
- Leg lift sitting on the ball
- Shoulder rotations with back on the ball
- Standing balance work on the bosu or balance disc

Core exercises to avoid

Higher intensity abdominal exercises

- Sit ups, curl ups, crunches
- Abdominal exercises with medicine ball
- V-sit
- Hundreds
- Double-leg lowers
- Plank position on hands and feet (e.g. hovers, full push ups)

pelvic floor first

The pelvic floor and core exercises

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