Incontinence, physical activity, and pelvic floor muscle training in female pelvic cancer survivors after radiotherapy

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To my dear family Robert, Livia and Edwin
and my parents Jonny and Margareta!

“Working hard for something we don’t care about is called stress; working
hard for something we love is called passion.” -Simon Sinek

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ABSTRACT

Background: Cancer treatment continues to improve, contributing to an ever-growing population of cancer survivors. Pelvic cancer survivors (PCS) constitute the second largest group of female cancer survivors after breast cancer. Many female PCS have been treated with radiotherapy as a part of their cancer treatment. Unfortunately, like all effective cancer treatments, pelvic radiotherapy is associated with a risk of subsequent, unwanted side effects. Some side effects remain or persist long after the end of treatment and some are even lifelong. A common and burdensome side effect after pelvic radiotherapy is urinary and/or fecal incontinence. Incontinence is known to negatively affect quality of life (QoL) and physical activity levels. Physical activity contributes to several positive health effects. In cancer survivors, it may reduce the risk of recurrence and even the mortality risk. Cancer survivors in general, and female PCS in particular, tend to be less physically active after cancer treatment than before treatment. When suffering from urinary and even fecal incontinence, pelvic floor muscle training (PFMT) is recommended as a first-line treatment for the general population. In addition to decreased incontinence levels, PFMT may contribute to increased physical activity and better QoL. However, little attention is given to PFMT as a potential treatment for incontinence in the Swedish national care program for pelvic cancer rehabilitation. Furthermore, there is as yet no evidence that PFMT is as effective in female PCS as in female non-cancer survivors. The effectiveness of PFMT cannot be taken for granted because female PCS survivors often have treatment-induced damage to structures in the pelvic floor that might affect its applicability. However, the problem of incontinence among female PCS remains, along with the fact that they tend to be less physically active than other cancer survivors. Indeed, this is an important research area and a necessary problem for health-care providers to resolve, not least for physiotherapists.

Aim: The overall aim of this thesis is to improve the understanding of female PCS' experiences of incontinence in relation to physical activity, QoL, and rehabilitative efforts, including PFMT. This includes gaining increased knowledge about the relation between incontinence and physical activity in the form of exercise and QoL, and whether PCS experience that physiotherapy contributes in a valuable way to reducing their incontinence. This could enable the development of meaningful physiotherapeutic interventions, that PCS can and are willing to engage in, to achieve a potential reduction in incontinence, as well as increased QoL and activity levels.

Methods: The thesis includes four different studies, using three different methods, all conducted with female PCS. Studies I (n=13) and IV (n=11) are qualitative individual interview studies, using semi-structured interview guides. Study II is a cohort-based cross-sectional observational study (n=578) and Study III is a prospective cohort-based observational study (n=260).

Results: Female PCS reported an absence of information regarding incontinence as a potential side effect of radiotherapy treatment. They experienced that incontinence prevented them from being as physically active as before treatment, and that incontinence of urine and feces impaired several aspects of QoL, including sexual health. They lacked potential rehabilitative options beyond conventional pelvic cancer rehabilitation. After practicing PFMT for three months, they found it a valuable rehabilitative measure for incontinence. They also experienced the physiotherapeutic support and guidance as valuable in teaching them how to contract the pelvic floor muscles correctly and providing individual guidance regarding dose, frequency, and progression of the training. In Study II, 67% of female PCS exercised at least once a week, while 33% exercised less than once a week. Women who reported leakage of large or all volume of feces ($p=0.01$, multivariable analysis) were statistically significantly more likely to exercise less than once a week. A similar co-variation was seen among women who reported leakage of moderate to large volumes of urine ($p=0.04$, univariate analysis). This, however, was not statistically significant in a multivariable analysis ($p=0.105$). When exercising on a weekly basis, they reported less frequently depressed mood ($p=0.044$) and better QoL ($p < 0.001$), compared to those who exercised less than once a week. Three months after an individually designed intervention program, in line with the conventional pelvic cancer rehabilitation offered within Swedish healthcare today, female PCS reported statistically significantly lower levels of urinary and fecal incontinence ($p=0.046$ and $p<0.001$). However, no statistically significant changes in frequency of exercise ($p=0.763$) were seen.

Conclusion: Incontinence was a barrier to physical activity and exercise, and it reduced QoL and impaired sexual health in female PCS. When experiencing incontinence, and in particular fecal incontinence, female PCS were less likely to exercise on a weekly basis. Female PCS who exercise at least once a week experienced better QoL and less frequently depressed mood than PCS who were not exercising every week. Female PCS did not exercise more often after conventional pelvic cancer rehabilitation, not even after incontinence levels were reduced.

Female PCS had a positive attitude towards PFMT. After at least three months' experience of practicing PFMT, they found it a valuable rehabilitative effort for incontinence. They also found physiotherapeutic support and guidance to be of great importance. Female PCS expressed a need for better information routines regarding side effects, such as incontinence, after cancer treatment. They also expressed a need for better information routines, including accessibility of additional rehabilitative efforts, beyond the conventional pelvic cancer rehabilitation offered today, when suffering from incontinence of urine and/or feces.

LIST OF PAPERS

- I. **Lindgren A**, Dunberger G, Enblom A. Experience of incontinence and pelvic floor muscle training after gynaecologic cancer treatment. *Support Care Cancer*. 2017;25(1):157-166
- II. **Lindgren A**, Dunberger G, Steineck G, Bergmark K, Enblom A. Identifying female pelvic cancer survivors with low levels of physical activity after radiotherapy: women with fecal and urinary leakage need additional support. *Support Care Cancer*. 2020;28(6):2669-81
- III. **Lindgren A**, Åkeflo L, Steineck G, Bergmark K, Skokic V, Dunberger G. Physical activity levels –follow up after individualized intervention among female pelvic cancer survivors with urinary and faecal incontinence. *Re-submitted to Acta Oncologica*.
- IV. **Lindgren A**, Börjeson S, Dunberger G. Female pelvic cancer survivors' experiences of pelvic floor muscle training. *In manuscript*

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Paper I

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ABBREVIATIONS

AIC	Akaike information criterion
CI	Confidence interval
FI	Fecal incontinence
HPV	Human papilloma virus
IQR	Interquartile range
MD	Median
NCU	Nordic Cancer Union
OR	Odds ratio
PCS	Pelvic cancer survivors
PFMT	Pelvic floor muscle training
QoL	Quality of life
RCT	Randomized controlled study
RR	Relative risk
SD	Standard deviation
UI	Urinary incontinence

INTRODUCTION

Cancer treatments continue to improve, resulting in an increasing number of cancer survivors. Pelvic cancer is common, with approximately 3000 women in Sweden being diagnosed annually with gynecological cancer and approximately 1000 with rectal or anal cancer (1). Many pelvic cancer survivors have been treated with radiotherapy, which, like all effective cancer therapies, is associated with the risk of subsequent unwanted side effects. Consequently, more and more PCS are living with treatment-induced cancer survivorship diseases, also commonly known as pelvic radiation diseases (2-6). Pelvic radiation diseases are defined as:

transient or longer term problems, ranging from mild to very severe, arising in non-cancerous tissues resulting from radiotherapy treatment to a tumor located in the pelvis (6, p. 391)

Among female PCS, urinary incontinence (UI) and fecal incontinence (FI) are commonly experienced after pelvic radiotherapy (7-10), which often have a negative effect on QoL (7, 8, 11, 12) and levels of physical activity (13-16). Among non-cancer female populations and male cancer populations, UI and FI can be a barrier to physical activity and physical exercise (13-17). Accordingly, it is plausible that incontinence may be a barrier for female PCS as well, keeping them from engaging in physical activity.

It is extremely important to achieve and maintain healthy activity levels among cancer survivors. Physical activity produces a variety of beneficial health effects in cancer survivors (18, 19), including a reduced risk of recurrence and lower mortality from cancer (20, 21).

Among women in general, pelvic floor muscle training (PFMT) is recommended as a first-line treatment for UI (22, 23) and is often also recommended for women with FI (24, 25). Besides reducing leakage, PFMT may also improve capacity in physical activity (13), QoL (22, 26) and sexual health (27, 28). However, no full-scale randomized controlled studies (RCT) have evaluated the effects of PFMT for female PCS after radiotherapy, either when this project was initiated or by the time of writing this thesis. Since pelvic radiotherapy may cause persistent damage to structures of the pelvic floor region, recommendations regarding PFMT as a treatment for urinary or FI cannot be generalized to PCS. Accordingly, knowledge is also lacking regarding whether PCS experience PFMT as a meaningful intervention when suffering from incontinence after radiotherapy. Furthermore, we ask: what support do female PCS need to achieve compliance with and benefits from PFMT?

BACKGROUND

Female pelvic cancer

In this thesis, PCS refers to female cancer survivors who have been treated with radiotherapy. Female pelvic cancers treated with radiotherapy include the diagnoses of endometrial, cervical, vaginal, vulvar, rectal, and anal cancer.

Endometrial cancer

Endometrial cancer is the most common gynecological cancer affecting women in Sweden and is the 6th most common cancer type among Swedish females, with an average incidence of 1373 annually (29). This is an older women's disease and used to be rare among women under 40 years of age. However, the incidence of endometrial cancer is increasing worldwide, and is now also being diagnosed in younger women. Endometrial cancer is the fastest growing gynecological cancer in the western world, due to growing obesity in the population. Globally, endometrial cancer is the 6th most common cancer type among females, but the incidence is highest in the western world and lowest in India and Africa (30).

Endometrial cancer can be divided into type I and type II, with differences in etiology, genetic changes, and prognosis. Most patients experience type I, which is associated with hyperestrogenism and has a good prognosis. Conditions involving high estrogen levels without a balance of progesterone, or with comorbidities of diabetes and hypertension, involve an increased risk of endometrial cancer. Tamoxifen treatment (hormone therapy for breast cancer) also carries an increased risk of endometrial cancer. For endometrial cancer type I, obesity is also a risk factor. In contrast, type II tumors are considered non hormone dependent and these patients have a poorer prognosis (31).

The treatment options depend on the type of tumor and stage of the disease. The most common treatment is surgery. Often, the entire uterus, fallopian tubes, and ovaries are removed. If affected, the pelvic lymph nodes are also removed. After surgery, additional radiation, including brachy therapy, or chemotherapy treatment can be obtained, or when surgery is not possible hormonal treatment is administered (31-33).

Cervical cancer

In Sweden, approximately 450 women are diagnosed with cervical cancer every year. This cancer affects pre-menopausal women and the median age for onset, in Sweden in 2016, was 45 years old (29). Thanks to gynecological cell sampling, only one-third as many women contract cervical cancer in Sweden as would have

done so if the screening did not exist. The disease is also detected at earlier stages, which means that more Swedish women survive (29). However, more than 85% of cervical cancer cases affect women in low-income countries. Globally, cervical cancer is the 4th most common, and in low and middle-income countries the 2nd most common cancer disease among women (30). The largest individual risk factor for cervical cancer is HPV (human papilloma virus). Almost 100% of cases are caused by persistent HPV infection and develop from dysplasia (cell changes) (34). Further known risk factors for developing cervical cancer are: a weakened immune system, smoking, previous genital infection, and long-term use of oral contraceptives (35). In Sweden, HPV vaccines are offered to girls within the general vaccination program for grades 5 or 6 at elementary school and supplemental vaccination should be offered to girls up to the age of 18. From the autumn of 2020, vaccination against HPV will be offered to both Swedish boys and girls in grade 5 of elementary school (36).

Cervical cancer is treated with surgery, radiotherapy, chemotherapy, or a combination of these, depending on the stage of the disease. Surgery in the forms of cervical conization, total simple hysterectomy, or radical hysterectomy, depending on the stage and spread of the cancer, is standard treatment for patients with early-stage cervical cancer. In more advanced stages, radical hysterectomy and removal of the pelvic lymph nodes is conducted, or chemotherapy in combination with radiotherapy. To combine surgery with radiotherapy should be avoided because it entails significant morbidity (34, 37).

Vaginal cancer

Vaginal cancer is a rare form of cancer (38). Approximately 40 women are diagnosed in Sweden annually (39). Vaginal cancer is also largely caused by persistent HPV infection, but here chronic inflammation also seems to be another background risk factor. Treatment principles follow those for cervical cancer, but radiotherapy or radio- and chemotherapy is recommended as a first treatment option. Surgery is considered in some cases at an early stage (38, 40).

Vulvar cancer

Vulvar cancer is most common among women over 65 years of age and approximately 160 women in Sweden are diagnosed annually (39). The causes of vulvar cancer are not fully understood, but infection with HPV is a risk factor. Some skin diseases, such as lichen sclerosis, carry an increased risk of developing vulvar cancer. Other risk factors are immunosuppression (decreased immune system), smoking, and history of cervical cancer. Vulvar cancer is treated individually by surgery, chemotherapy, radiation therapy, or a combination of these (41, 42).

Rectal cancer

Colorectal cancer is the 3rd most common form of cancer affecting women globally (30) and rectal cancer accounts for 30–35% of all colorectal cancers (43). Rectal cancer is the 9th most common cancer among Swedish women and approximately

800 are women are diagnosed with rectal cancer in Sweden annually. The median age at diagnosis is 71 years and only 5% are under 50 years of age (29). Most cases of rectal cancer arise from an adenoma (a neoplastic polyp). Both heredity and comorbidity, such as inflammatory bowel disease or diabetes, can increase the risk of developing rectal cancer (44). Lifestyle-related factors, such as a high BMI, meat consumption, alcohol consumption, and smoking are also risk factors for rectal cancer (30, 45).

Surgery is the first-choice treatment option and involves the intestinal part where the tumor is located being removed with broad margin (46). Sixty-one percent of all rectal cancer cases today are treated with proctectomy (surgical removal of all or part of the rectum) or proctocolectomy (surgical removal of the rectum and all or part of the colon) (4). More than half of rectal cancer patients are also treated with chemotherapy and/or radiotherapy preoperatively for better oncological results. If the tumor causes a stop in the bowel, surgery must be carried out without delay. Then, temporary relief with ostomy becomes necessary. In some cases, the patient receives chemotherapy treatment after surgery to reduce the risk of relapse (46). In recent years, for selected patients, if there is a significant response to neoadjuvant chemoradiation, organ-preserving strategies, such as the “Watch and Wait” strategy and local excision (surgical removal of a small part of the rectum) have become valid treatment options (47).

Anal cancer

Anal cancer is a relatively uncommon disease that accounts for approximately 1–2% of all tumors of the gastrointestinal tract (48). However, the incidence has increased over the last 30 years (49). Anal cancer is most common in the 65–70 age group (39) and only approximately 6% are under 50 years of age when anal cancer develops (50). In Sweden, approximately 160 women are diagnosed with anal cancer annually (39).

The most common type of anal cancer is the squamous epithelium type, which is based on cells in the anal canal or immediately around the anus. The majority of anal cancers are caused by HPV (51). Further risk factors for anal cancer are human immunodeficiency virus (HIV), more than ten lifetime sexual partners, anoreceptive intercourse, chronic immunosuppression, smoking, and a history of gynecological or hematological malignancy (49). Treatments for anal cancer vary, depending on the spread of the disease. For one group of patients, surgery is the only treatment, for others surgery is combined with radiotherapy, and for a third group surgery is combined with both radiotherapy and chemotherapy. However, the primary treatment option is radiotherapy, in combination with chemotherapy (48, 51).

Pelvic cancer treatment

In pelvic cancers, the treatment options are surgery, external radiotherapy, brachytherapy, chemotherapy, and/or hormonal therapy, depending on the type of tumor. Immunotherapy is another treatment alternative for certain pelvic cancers, such as rectal cancer (52), but is currently only available in clinical trials.

Radiotherapy is an efficient lifesaving treatment commonly used when treating cancers in the pelvic region. By using high-energy beams, breaks in the DNA are produced which affect the malignant cells. Inevitably, nearby normal tissue will also be affected by the treatment. Besides direct tissue injuries, radiotherapy also induces an inflammatory process that can lead to fibrosis which reduces elasticity and activation of the muscles in the pelvic region. In addition, radiotherapy often induces nerve damage and reduces blood flow within the muscular tissues. This may further affect the structure of the pelvic floor muscles, causing atrophy, complicating muscular activation, and affecting the function of the pelvic floor muscles in a negative way (53-58). Radiation-induced fibrosis may also affect other structures in the irradiated area. Among others, treatment-related symptoms of the gastrointestinal and urinary tract system are common, due to decreased elasticity of the urethra, bladder wall, or bowel (56, 59, 60). Late side effects such as fibrosis, atrophy, vascular damage, and nerve damage tend to be irreversible and often progressive. Cancer survivors who have undergone pelvic radiotherapy for gynecological or other pelvic cancers, such as rectal or anal cancer, may have persistent symptoms for many years, possibly even lifelong, after cancer therapy (5, 56, 61).

Side-effects after pelvic radiotherapy

Radiation treatment will inevitably affect structures surrounding the tumor, such as the pelvic bones, pelvic floor muscles, urinary tract, bowel, and intestines. Thus, functional disorders, such as bowel and intestinal disorders, sexual dysfunction, urinary-tract dysfunction, lymphedema and pelvic pain due to, for example, pelvic micro fractures, are common consequences of radiotherapy for pelvic cancers in women (7-10, 57, 62-67). PCS treated with chemotherapy in addition to radiotherapy often experience even worse comorbidity than those treated with radiotherapy alone, because chemotherapy in combination with radiotherapy has toxic effects on the genitourinary and gastrointestinal tracts (68).

Incontinence

Incontinence is defined as a “complaint of involuntary loss of urine or feces” (69, 70). Bowel and intestinal disorders, urinary-tract dysfunction and pelvic floor muscle dysfunction can cause urinary incontinence (UI) or fecal incontinence (FI). Incontinence is a common and burdensome treatment-induced symptom and is defined as a pelvic radiation disease (5, 7-10).

The pelvic floor muscles play an important role in the maintenance of continence. This is why impaired pelvic floor muscle function, due to fibrosis and nerve damage, following radiotherapy treatment may contribute to UI and FI (57, 71). The external anal sphincter is part of the superficial layer of pelvic floor muscles (Fig. 1) and plays an important role in fecal continence. The intermediate layer of pelvic floor muscles consists of the compressor urethra muscle and the external urinary sphincter, which are important muscles for maintaining urinary continence. The levator ani muscles (pubococcygeus, iliococcygeus, ischiococcygeus, and puborectalis muscles) form the deep layer of pelvic floor muscles (Fig.2), which plays an important supporting role for pelvic organs and contributes to continence during increased abdominal pressure (72). Thus, if pelvic floor muscle function is impaired due to fibrotization after radiotherapy treatment, the ability to maintain continence is also affected.

Figure 1. Pelvic floor muscles, inferior view

(Picture by OpenStax - <https://cnx.org/contents/FPtK1znh@8.25:fEI3C8Ot@10/Preface>, CC BY 4.0, <https://commons.wikimedia.org/w/index.php?curid=30131690>)

Figure 2. Pelvic floor muscles, superior view

(Picture by OpenStax - <https://cnx.org/contents/FPTK1zmh@8.25:feI3C8Ot@10/Preface>, CC BY 4.0, https://commons.wikimedia.org/wiki/File:1116_Muscle_of_the_Female_Perineum.png)

Radiation therapy may also cause fibrotization of the bladder, the urethra, and/or the intestines (56, 71). A rigid and inelastic bladder results in reduced bladder capacity and poorer ability to store urine. This, in turn, may lead to impaired bladder compliance in PCS, in the form of frequency and urgency, which further contributes to UI (71). Fibrotization of the intestine and intestinal mucosa may lead to reduced elasticity and impaired functioning of the intestines (56). With the addition of chemotherapy, the cells of the gastrointestinal tract are even more damaged, which often gives rise to diarrhea (73). This contributes to a decreased ability to maintain fecal continence among PCS.

Urinary incontinence

Urinary incontinence is common among women in non-cancer female populations. The reported prevalence of UI varies widely between different studies, depending on outcome measures and definitions of UI. Aoki reports in an article from 2017

that studies converge on a prevalence of approximately 30% (range 5–72%) among adult women (74). However, UI is even more common among female PCS. One third of PCS in a cohort study reported UI, which made the risk of UI 75% higher, that is to say a relative risk of 1.75 for leakage, in PCS compared to the control group of women (non-cancer survivors) (7).

Urinary incontinence is usually divided into stress UI and urge UI (74). Stress incontinence is defined as a “complaint of involuntary loss of urine on effort or physical exertion, or on sneezing or coughing” (69). Urge incontinence is defined as a “complaint of involuntary loss of urine associated with urgency” (69), usually caused by involuntary contractions of the detrusor muscles of the bladder when not appropriate. These two conditions often co-exist and are then called mixed incontinence (74). Risk factors for UI in women, apart from pelvic radiotherapy, are surgeries such as hysterectomy, advancing age, vaginal delivery, number of deliveries, constipation, BMI greater than 30kg/m², generalized weakening of connective tissue, hormone deficiency, genital mutilation, and depression (74–76). According to a study by Bernard et al., pelvic floor muscle strength and endurance corresponds to the severity of UI in endometrial cancer survivors after hysterectomy and radiotherapy (58). This further supports the hypothesis that UI in female PCS, after radiotherapy treatment, can be partly explained by impaired pelvic floor muscle function.

Fecal incontinence

Fecal incontinence is defined as an “involuntary loss of solid or liquid feces” (70). The prevalence of FI in non-cancer populations varies widely in different studies, depending on definition and methodology. A review from 2016, including 30 studies, reports that FI prevalence varied from 1.4 to 19.5% (77). However, it has been reported that FI is more prevalent among female PCS than among women from the general population. In a study of more than 600 gynecological cancer survivors, 12% reported leakage of all feces without forewarning, compared to only 1% among the control population of women in the general population (78). In another, recently published, study, the prevalence of FI ranged from 10–15 % in gynecological cancer survivors, after curative radiotherapy treatment (10).

Risk factors associated with FI in women, in addition to pelvic radiotherapy, are advancing age, loose stools or diarrhea, fecal urgency, type 2 diabetes mellitus, inflammatory bowel disease, BMI greater than 30kg/m², vaginal delivery, number of deliveries, birthweight of the child, obstetric trauma such as anal sphincter trauma, multiple chronic medial illness, and UI (75, 79, 80). In addition, surgery in conjunction with pelvic cancer treatment, such as anterior resection in patients with rectal cancer, is associated with an increased risk of FI due to impaired functioning of the intestine. According to a review by Scheer et al., including 48 studies, the incidence of FI varied from 3. to 79.3% after anterior resection in patients with rectal cancer (81).

According to Smeenk et al., the prevalence of FI in prostate cancer survivors correlates with increased radiation dose to the muscles of the pelvic floor. The prevalence of FI was mainly associated with the doses of radiation to the external anal sphincter (82). Thus, since the external anal sphincter plays an important role in fecal continence (72), it is very likely that FI in female PCS can also be partly explained by impaired pelvic floor muscle function.

Secondary consequences of incontinence

Among women in general, as well as among PCS, UI and FI often reduce QoL (7, 8, 11-13, 74). The World health organization define QoL as:

individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the person's physical health, psychological state, level of independence, social relationships, personal beliefs and their relationship to salient features of their environment. (83, p. 28)

Among non-cancer survivors and male cancer populations, the level of physical activity may decrease when suffering from UI or FI (13-17). Among female PCS, a clear trend of covariation between severe FI and lower capacity in daily and sexual activities have also been found (78). Bernard et al. report that, among PCS who reported a new incidence of UI after hysterectomy and radiotherapy for endometrial cancer, 36.4 % of the 11 individuals answered that they avoided sexual activities, compared to none of those who did not report any UI after treatment (58). Incontinence is also frequently associated with stigma, a negative impact on social interactions, and toilet dependency (84-86).

Pelvic cancer rehabilitation

During the 2000s, cancer care and research has increasingly expanded to focus not only on curative care, but also on the rehabilitation of treatment-induced side effects. A commonly used definition of cancer rehabilitation in the Nordic countries was formulated by the Nordic Cancer Union (NCU) in 2004:

Cancer rehabilitation is a specific period of time during which the physical, psychological, social and existential consequences of cancer and the treatment are prevented and reduced. The rehabilitation initiatives are to have clear objectives and effects and provide each individual patient help and inspiration to have the best possible life. The individual rehabilitation plan is to be prepared in a close dialogue between the patient and the professionals. (87, p. 4)

According to the NCU, the purpose of rehabilitation is to provide the cancer patient/cancer survivor with knowledge and awareness of opportunities for action and support so that life can continue in the best possible way, while taking into account the limitations caused by the disease and its treatment, physically, mentally, socially, and existentially (87). On the initiative of the Swedish government, during the past 10 years, Regional Cancer Centers (RCC) have been established, one in each healthcare region. The purpose of these RCC is to increase the quality of cancer care and rehabilitation in order to improve the results of care, as well as to use health-care resources more efficiently (88). The RCC have subsequently collaborated to develop a national care program for cancer rehabilitation (89). In this care program, the NCU's definition of cancer rehabilitation has been updated as follows:

Cancer rehabilitation aims to prevent and reduce the physical, mental, social, and existential consequences of cancer disease and its treatment. The rehabilitation efforts must give the patient and relatives support and opportunities to live as good a life as possible. (89, p. 11)

On behalf of Sweden's municipalities and county councils, the RCCs in collaboration conducted a national project between 2016 and 2019, with the aims of improving care and coordinating the rehabilitation of patients with complications after pelvic cancer. As a guide for caregivers in Swedish health and medical care, a national care program for pelvic cancer rehabilitation was designed, and this was updated in 2020. The aim of the care program is to provide caregivers with support when dealing with symptoms and complaints that may occur during or after the treatment of pelvic cancer. The cancer rehabilitation offered within conventional pelvic cancer rehabilitation in Swedish health care today is largely based on this care program. The guide is divided into different sections covering different problem areas. Among these, there is one section for gastrointestinal side effects, including FI, and another for side effects of the urinary tract, including UI. Both sections include flow charts (algorithms) of recommended diagnostics and treatment as well as clarifying text sections describing recommended diagnostics and treatment. The recommended treatment for both UI and FI focuses on medical treatment as well as advice and lifestyle regimens, such as drinking, eating, and toilet habits. However, in the national care program for pelvic cancer rehabilitation, there is very little focus on the treatment alternative that is recommended as a first-line treatment for incontinence among women in general, namely PFMT. Pelvic floor muscle training is, admittedly, mentioned in passing, with the statement that written instructions can be given or that the patient can be referred to a physiotherapist. But no further clarification regarding PFMT as a treatment option is given (90).

Pelvic floor muscle training

Pelvic floor muscle training is one form of rehabilitation that aims to improve pelvic floor muscle function and reduce incontinence. This in turn may provide conditions for increased physical activity levels, and improved QoL and sexual health (13, 26, 28). In women generally, supervised PFMT for at least 12 weeks, preferably overseen by a therapist who specializes in pelvic floor muscle function, is recommended as an effective first-line treatment for UI and often even for FI (23-25, 91). The anal sphincter is linked to the puborectala muscles, and together they form the pelvic floor muscle plate, which theoretically is amenable to the same PFMT techniques used for UI (91).

When this project was initiated, large well-designed studies on PFMT in female PCS who have undergone radiotherapy were lacking. A small RCT (n=24) was found, reporting improved pelvic floor muscle strength, improved perceived sexual functioning, and better QoL after four weeks of PFMT in combination with transversus abdominus muscle training, after gynecological cancer treatment (92). Another small pilot study (n=40) reported that 12 weeks of PFMT, in combination with behavioral therapy, significantly reduced UI among gynecological cancer survivors (93). A third study reported that PFMT with biofeedback and electrical stimulation can be effective as a treatment for FI, improving QoL among patients after low rectal cancer surgery (intersphincteric resection) (94). However, none of these studies evaluated the effect of PFMT among female PCS, specifically only after radiotherapy treatment. Nor in rectal cancer were there any RCTs found that evaluate the effects of PFMT specifically after radiotherapy treatment when this project was initiated. However, a review reported that prospective and retrospective studies indicate positive effects of PFMT on bowel function and FI among patients experiencing FI after colorectal cancer surgery (95). At the time of writing this thesis, one recently published pilot study indicates that PFMT might have a protective effect to retain pelvic floor muscle strength and to prevent incontinence among female PCS after radiotherapy treatment, one month after radiotherapy (96). However, full-scale RCTs on the effects of PFMT on incontinence among female PCS, over the long term after radiotherapy, are still lacking. Thus, recommendations regarding PFMT as a treatment option for incontinence (22, 24, 25) cannot be generalized to female PCS with or FI who have undergone radiotherapy. It is not known whether tissue damage to structure and function of the pelvic floor muscles due to pelvic radiation (57, 82) affects the applicability or effect of PFMT. Thus, full-scale randomized controlled effect studies still need to be conducted on the effects of incontinence among PCS after pelvic radiotherapy.

The rationale for pelvic floor muscle training

Pelvic floor muscle training is primarily intended to improve the strength (i.e. the maximum force at a single muscle contraction), endurance (the ability to perform repeated muscle contractions over time), and/or ability to coordinate muscle activity to manage urgency. The characteristic of strength training is a low number of repetitions close to maximum contraction. Endurance training is characterized by

many repetitions with low to moderate intensity. The ability to coordinate muscular activity and prevent involuntary leakage during urgency often involves pelvic floor muscle contraction by maximum contraction (Fig. 3) during different situations, such as PFMC while coughing and PFMC when feeling a sense of urgency (22).

Figure 3. Relaxed and contracted pelvic floor muscles

(Picture freely drawn from figure in the leaflet “Bladder- and pelvic floor muscle training” by Astella Pharma 2014, p.4. Available from: https://blasen.se/wp-content/uploads/2019/11/URO_2019_0003_SE_K_WEB.pdf)

The explanations for why PFMT is an effective method in the treatment of UI are multiple. There are three proposed theories, based on current knowledge of the pelvic muscles’ functional anatomy, explaining how and why PFMT can reduce the severity of incontinence (22, 97, 98):

1. *Conscious contraction of the pelvic floor muscles during increased abdominal pressure*

When contracted, the pelvic floor muscles are lifted in an upward/forward direction, which supports the bladder neck and prevents the urethra and bladder from tilting forward, reducing the abdominal pressure. When the muscles are contracted, they might also squeeze around the urethra and increase the urethral

closure pressure. By deliberately contracting the pelvic floor muscles when a sudden increase in abdominal pressure occurs, such as coughing, sneezing, or straining, leakage can be prevented (22, 97, 98). However, according to Zubieta et al., the ability to affect the maximum urethral closure pressure by a voluntary contraction differs widely between women (98).

2. *Strength training*

Intense strength training of the pelvic floor muscles increases the muscle mass and muscle tone. This provides a permanent lift of the levator plate inside the pelvis, which in turn provides long-term structural support for the bladder neck.

3. *Indirect exercise of the pelvic floor muscles while exercising transversus abdominis (TRA).*

Studies have shown a co-contraction of the pelvic floor muscles during transversus abdominis muscle contractions in healthy women. This seems to be more common in women who do not suffer from incontinence with a co-activation of TRA and the pelvic floor muscles, but more research is needed in the area to confirm that assertion (22, 97).

There is as yet no clear consensus as to whether PFMT is an effective method in the treatment of FI. According to Norton et al., sphincter strength is not consistently reported as correlating with a reduction in FI among different studies, while improved rectal sensation is usually associated with improved ability to achieve fecal continence (25). Meanwhile, a review including 21 studies (n=1525) concluded that PFMT, in the form of sphincter exercises, may decrease FI but that larger, more well designed studies need to be conducted to confirm that assertion (24).

Physical activity for cancer survivors

Physical activity refers to “any bodily movement produced by skeletal muscle that requires energy expenditure”. The term physical activity thus encompasses physical movement during both working hours and leisure time and all the different forms of physical activity, gymnastics, exercise, and outdoor life. Physical exercise is described as “Physical activity that is planned, structured, repetitive and purposive, in the sense that the improvement or maintenance of one or more components of physical fitness is the objective” (99). Physical exercise is often included within the physiotherapeutic rehabilitation for cancer survivors. This physical exercise should follow the same established training principles as in healthy individuals. It is important for the outcome that the exercise and the training adaptation are both specific to the system/muscle that is supposed to be the target of the training (specificity). It is also important that the intensity of the workout is increased as the individual adapts to the training (progression) and that the exercise consists of more demanding physical activities than the individual is usually exposed to in terms of frequency, duration, and intensity (overload). Furthermore, it should also be considered that the greatest improvement in outcome measures will be registered among those individuals with the lowest values initially. If exercise is

stopped completely, the physical capacity will eventually return to the initial value (reversibility) and a smaller improvement in outcomes can be expected as the individual's physical ability improves (100).

In general, physical exercise is safe for individuals who have undergone cancer-related treatment (101, 102). Swedish Care Programs, the Canadian Society for Exercise Physiology, and the American Cancer Society, among others, recommend the following minimum level of physical activity as a general guideline for cancer survivors:

- At least 150 minutes / week of moderate intensity or 75 minutes of high intensity.
- Strength training 2–3 workouts per week, including large muscle groups, and large muscle groups should also be stretched after exercise.

According to existing guidelines for cancer survivors, cancer survivors should engage in exercise or be physically active, at least at a moderate intensity level, on a weekly basis (89, 103, 104). There are many negative consequences of physical inactivity, such as an increased risk of cardiovascular and musculoskeletal diseases, certain types of cancer, obesity, type 2 diabetes, osteoporosis, and mental illness. Conversely, regular physical activity has a positive effect on the functioning of the heart, blood vessels, skeletal muscles, immune system, brain, and other organs, among individuals in general as well as among cancer survivors (18, 105). Furthermore, physical activity can help in the management of cancer-treatment-induced side effects, prevent the recurrence of some types of cancer, prevent the development of new cancers (breast, prostate, and colorectal cancer) and even prevent premature death (18, 106)

Unfortunately, cancer survivors, in general, tend to decrease their physical activity levels compared to the level pre-cancer treatment. This is due to treatment-related side effects such as fatigue (lack of physical energy), nausea, and pain, as well as to a perceived lack of suitable exercise opportunities (107, 108). Cancer survivors after colorectal cancer have previously reported a low frequency of physical activity and high volume of sedentary time after cancer treatment (109). Another study found that colorectal cancer survivors report low levels of physical activity both before and after surgery (110). Also after gynecological cancer, 12% of 616 studied cancer survivors stated that they never practiced physical activity after their cancer treatment, compared to 6% among non-cancer-surviving control women (8). A recently published review, including six studies (n=1607), also supports the claim that gynecological cancer survivors report low physical activity levels compared to before treatment. Two years after treatment, 91% of the gynecological cancer survivors were not meeting physical activity guidelines, and three years after treatment 58% still reported that they were less physically active than before cancer treatment (111).

Rationale of the thesis

Female PCS tend to be less active than other cancers survivors and suffer from incontinence to a greater extent than women in general. This might be a further barrier to physical activity. They may also have greater difficulties in activating the pelvic floor muscles than other females due to radiation-induced damage to muscles and nerves in the pelvic region. Consequently, it is likely that PCS need even more support and guidance if encouraged to practice PFMT to reduce incontinence. Therefore, it is important to increase the knowledge of incontinence among PCS in relation to physical activity, QoL, and possible rehabilitative efforts, such as PFMT, in order to develop meaningful interventions, with the right form and level of support, in order to reduce incontinence and increase both QoL and physical activity levels among PCS.

AIMS OF THE THESIS

Overall aim

The overall aim of this thesis is to improve the understanding of female PCS' experiences of incontinence in relation to physical activity, QoL, and rehabilitative efforts, including PFMT. This includes gaining increased knowledge about the relation between incontinence and physical activity in the form of exercise and QoL, and whether PCS experience that physiotherapy contributes in a valuable way to reducing their incontinence. This could enable the development of meaningful physiotherapeutic interventions, that PCS can and are willing to engage in, to achieve a potential reduction in incontinence, as well as increased QoL and activity levels.

Specific aims

- To describe how PCS experience incontinence in relation to perceived QoL, opportunities for physical activity and exercise and how they perceive and experience PFMT.
- To investigate frequency of physical activity among female PCS after radiotherapy and whether PCS who practiced physical activity less than once a week differed from survivors practicing physical activity at least once a week with respect to urinary and fecal incontinence, clinical and sociodemographic characteristics, quality of life, and depressed and anxious mood.
- To investigate if incontinence of urine and feces could decrease, and low level of physical activity increase, among PCS after participating in an individual intervention at a nurse-led pelvic cancer rehabilitation unit. To analyze the relationship between PCS' characteristics and changes in urinary incontinence, fecal incontinence, and level of physical activity.
- To explore and describe female PCS, with urinary and/or fecal incontinence, experiences of a three-month PFMT period, with or without physiotherapy support.

MATERIALS AND METHODS

Table 1 Overview of the aims, designs, data collection, and participants in the four studies making up this thesis.

	Study I	Study II	Study III	Study IV
Aim	To describe how PCS ¹ experience incontinence in relation to perceived QoL ² , opportunities for physical activity and exercise and how they perceive and experience PFMT ³ .	To investigate frequency of physical activity among female PCS ¹ after radiotherapy and whether PCS who practiced physical activity less than once a week differed from survivors practicing physical activity at least once a week with respect to urinary and fecal incontinence, clinical and sociodemographic characteristics, QoL ² , and depressed and anxious mood.	To investigate if incontinence could decrease, and low level of physical activity increase, among PCS ¹ after participating in a nurse-led individual intervention. To analyze the relationship between PCS' characteristics and changes in urinary incontinence, fecal incontinence, and level of physical activity.	To explore and describe female PCS ¹ , with urinary and/or fecal incontinence, experiences of a three-month PFMT ³ period, with or without physiotherapy support.
Design	Qualitative individual interview study using a semi-structured interview guide	A cohort-based cross-sectional observational study	A prospective cohort-based observational study	Qualitative individual interview study using a semi structured interview guide
Participants	Female PCS ¹ (n=13) with urinary or fecal incontinence after radiotherapy and/or surgery for gynecological cancer, six months to 21 years previously.	Female PCS ¹ (n=578) who had received radiotherapy for gynecological, rectal, or anal cancer six months to four years previously and had answered the baseline questionnaire in 2011–2016.	Female PCS ¹ (n=260) who had received radiotherapy for gynecological, rectal, or anal cancer six months to four years previously, had answered the baseline questionnaire in 2011–2017 and agreed to and completed individual rehabilitation at a unit for rehabilitation of late side effects.	Female PCS ¹ (n=11) with urinary and/or fecal incontinence after radiotherapy, for gynecological, anal, or rectal cancer who had completed radiotherapy treatment 3–60 months previously. All participating women had also completed an ongoing randomized controlled intervention study during which they had practiced PFMT, with or without physiotherapy support, for three months.
Data analysis	Qualitative content analysis.	Descriptive statistics, univariable and multivariable comparisons.	Descriptive statistics, univariable and multivariable comparisons.	Qualitative content analysis.

¹Pelvic cancer survivors, ²Quality of life, ³Pelvic floor muscle training

Design and participants

Studies I and IV were qualitative descriptive interview studies. In Study I, 13 women who had undergone treatment for gynecological cancer and suffered from UI or FI were included. In Study IV, 11 women who had undergone radiotherapy treatment for gynecological, anal, or rectal cancer and suffered from UI or FI were included. They were interviewed after having practiced PFMT for three months, with or without physiotherapy support (the quantitative sections of the results are not included in this thesis). The physiotherapy support included four physiotherapist-led biofeedback sessions, i.e. monitored visual response to their pelvic floor muscle contraction and relaxation during PFMT. The physiotherapy support also included a physiotherapist-led group PFMT session, twice a week for ten weeks, in addition to a written home training program. The women practicing without physiotherapy support only received the written home training program by mail, with no further instructions. Data was collected through interviews using a semi-structured interview guide and was analyzed with content analysis [17].

Participants in Study I were recruited both from a patient association for gynecological cancer survivors (n=10) and through a Swedish oncology rehabilitation clinic for side effects (n=3). This was to ensure that some participants lived in a small city or in the countryside, some in a medium-sized city and some in a big city. Potential participants received an information letter about the study, and interested women were encouraged to send their contact details in order to receive further verbal information about the study. Women who met the study criteria and provided written informed consent were enrolled and interviewed until the content from the interviews was assessed as rich (n=13 study participants).

Inclusion criteria for Study I:

- women aged ≥ 18 years
- had received treatment for gynecological cancer
- had undergone subsequent verification after completion of treatment
- self-experienced involuntary leakage of urine or feces
- understood the Swedish language
- were able to move around indoors without aids.

Exclusion criteria for Study I were ongoing cancer or previously conducted or planned surgery against incontinence.

Participants in Study IV were recruited in connection with enrollment into an RCT, during which they were supposed to practice PFMT for three months, with or without physiotherapy support. In other words, the sample consisted of a convenience sample of female PCS who had practiced PFMT for three months. None of the women who agreed to join the RCT declined participation when asked if they were also willing to participate in the qualitative interview study.

Inclusion criteria for Study IV:

- women >18 years of age
- had completed curative radiation therapy for gynecological, anal, or rectal cancer, 3–60 months previously
- self-experienced involuntary leakage of urine or feces
- had agreed to participation in the ongoing RCT with the associated qualitative study. For further inclusion criteria in the RCT, see Appendix 1.

Study II was a cohort-based cross-sectional observational study and Study III was a prospective cohort-based observational study. Study participants were recruited from two different cohorts: A) a population-based study-cohort group including all female cancer patients who had been treated with curative intent between 2007 and 2017, identified from medical records at Sahlgrenska University Hospital in Gothenburg, Sweden, and B) a referred patient group including all female patients referred to the rehabilitation clinic from oncology health-care providers, general practitioners and private referrals (Fig. 4).

Inclusion criteria were:

- female PCS treated with radiotherapy, alone or as part of their oncological treatment, with curative intent at Sahlgrenska University Hospital.
- it was at least six months since completing oncological treatment
- > 18 years old

Exclusion criteria:

- recurrence of cancer
- physically or cognitively unable to understand and answer the questionnaire
- not understanding the Swedish language

An information letter to participants offered a follow-up visit to the clinic for individual rehabilitation for radiotherapy-induced consequences. To document potential consequences, they were asked to answer a study-specific questionnaire at baseline before the intervention. They were asked to do this even if they did not want to attend the clinic for support regarding radiotherapy-induced consequences. If they agreed to participate in individual rehabilitation, three months after the end of the rehabilitation, they were asked to answer a follow-up questionnaire.

Between 2011 and 2017, 868 female PCS received the baseline questionnaire. Of these, 605 completed and returned the form. The women who received ($n=677$), answered, and returned ($n=578$) the questionnaire before June 2016 were included in Study II (response rate 85%). All the women who answered the questionnaire between 2011 and 2017 ($n=605$), agreed to participate in individual rehabilitation ($n=379$), completed individual rehabilitation ($n=339$), and answered the follow-up questionnaire ($n=260$) were included in Study III (response rate 77%) (Fig. 4).

Figure 4 Flowchart depicting participants included in Studies II and III between January 2011 and June 2017.

Data collection

Qualitative studies

Background data

In Study I, the women were asked to answer a study-specific questionnaire with background data regarding sociodemographic data and type of cancer treatment, in connection with the interview (Table 4, background data). The same questionnaire was answered by the participating women in Study IV approximately three months before the interviews, close before they began their 3 months of PFMT. These questions have been used previously in the population gynecological cancer survivors with good validity and high response rate (85).

Interviews

The individual interviews took place at a location chosen by each respondent in Study I and at the clinic, in connection with the concluding measurements for the RCT, in Study IV. Study-specific semi-structured interview guides with basic open-ended questions were used in both studies (Appendices 1 and 2). The author of the thesis was the interviewer in Study I and the interviewing physiotherapist employed in the ongoing RCT study to conduct baseline and concluding measurements was the interviewer in Study IV. Prior to the start of the main interviews, two pilot interviews were conducted in each study. None of these pilot interviews were included in the analysis. In Study I, one pilot interview was conducted with a female non-cancer survivor, in the expected age range, and another with a woman with gynecological cancer and incontinence who had paused her ongoing treatment. In Study IV, the pilot interviews were conducted with two women with incontinence after pelvic radiotherapy who had practiced PFMT for three months but had received radiotherapy treatment more than 60 months previously. After these four pilot interviews, some minor alterations were made to the semi-structured interview guide to clarify the questions. All interviews were recorded with audio recording equipment and transcribed verbatim, in Study I by the author of this thesis and in Study IV by the physiotherapist who conducted the interviews. The interviews in Study I lasted for 25–54 minutes (median 37 minutes) and in Study IV for 20–45 minutes (median 30 minutes).

Quantitative studies

Study-specific questionnaires

The women answered a study-specific baseline questionnaire (Table 2) which consisted of 175 questions regarding background data, QoL and wellbeing, intestinal and defecation habits, micturition habits and urinary-tract symptoms (all questions referring to previous six months). The questionnaire also included a chapter of questions concerning self-reported needs, and an offer to visit the nurse-led clinic

for assessment, counselling and individual rehabilitation (Figure 3). The questionnaire was developed and satisfactorily validated according to clinometric methodology in ways of face-to-face validity (112) frequently applied to studies of cancer survivors (7, 8, 85, 113). Face-to-face validation with the target population ensured clear and understandable questions enabling the female PCS to acknowledge and answer the questions as intended (8).

Table 2 Summary of the study-specific baseline questionnaire, where sociodemographic data and variables included in the analyses in Studies II and III are highlighted in bold.

Section	Question areas
Sociodemographic	Gender Age Marital status Children Level of education Employment status
Quality of life and well-being	Quality of life Depression Worrying Anxiety Frequency of exercise
Body-perception and self-image	Femininity Self-esteem Fertility Childbirth Vaginal and perianal injury related to childbirth or physical trauma
Intestinal and defecation habits	Loose stool Fecal incontinence Urgency to defecation Excessive gas Abdominal pain Having stoma Medical treatments related to intestinal symptoms

Table 2 (continued). Summary of the study-specific baseline questionnaire, where sociodemographic data and variables included in the analyses in Studies II and III are highlighted in bold.

Micturition habits and urinary-tract symptoms	Urinary frequency
	Urinary incontinence
	Urgency to urinate
	Nocturia
	Having a urine catheter
	Medical treatment due to symptoms from the urinary tract
Sexual health	Menopause
	Use of systemic hormone replacement therapy
	Use of topical estrogen
	Impaired lubrication
	Vaginal shortness
	Vaginal inelasticity
	Dyspareunia
Sexual abuse	Experienced sexual abuse
	Experienced sexual harassment
	Age at sexual abuse or harassment
	To what extent the exposure affects sexual life
Lymphedema	Heaviness in legs, genitals, and abdomen
	If diagnosed with lymphedema, current lymphedema treatment
Concluding chapter	Self-reported needs
	An offer to visit the nurse-led clinic for assessment, counselling, and individual rehabilitation

Women who agreed to participate in individual rehabilitation for late side effects, such as incontinence, answered a follow-up questionnaire, three months after the end of their rehabilitation. The follow-up questionnaire contained the same questions regarding intestinal habits, defecation habits, micturition habits, urinary-tract symptoms, quality of life, and wellbeing as the baseline questionnaire, but the questions addressed the women's condition during the previous month.

Included primary variables:*Urinary and fecal incontinence*

The baseline questions regarding UI included in Study II were:

- “Have you been wetting yourself because you could not reach the toilet in time, within the past six months?” Optional answers: “Not applicable”, “No”, “Yes, occasionally”, “Yes, at least once a month”, “Yes, at least once a week”, “Yes, at least three times a week”, “Yes, at least once a day”.
- “Have you been wetting yourself while doing something strenuous (coughing, exercising, laughing), within the past six months?” Optional answers: “No”, “Yes, occasionally”, “Yes, at least once a month”, “Yes, at least once a week”, “Yes, at least three times a week”, “Yes, at least once a day”.

The baseline question regarding UI included in Studies II and III was:

- “How large a volume of urine do you leak on average?” Optional answers: “Not applicable”, “Small amount”, “Moderate amount”, “Large amount (Whole bladder volume)”.

The baseline questions regarding FI included in Study II were:

- “Have you leaked feces because you could not reach the toilet in time, within the past six months?” Optional answers: “No”, “Yes, occasionally”, “Yes, at least once a month”, “Yes, at least once a week”, “Yes, at least three times a week”, “Yes, at least once a day”.
- “Have you leaked feces without forewarning within the past six months?” Optional answers: “No”, “Yes, occasionally”, “Yes, at least once a month”, “Yes, at least once a week”, “Yes, at least three times a week”, “Yes, at least once a day”.
- “Have you leaked all feces without forewarning during the past six months?” Optional answers: “No”, “Yes, occasionally”, “Yes, at least once a month”, “Yes, at least once a week”, “Yes, at least three times a week”, “Yes, at least once a day”.

The baseline question regarding FI included in Studies II and III was:

- “How large a volume of stools do you leak on average?” Optional answers: “Not applicable, I do not leak stools”, “I only leak so little that it smudges the underwear (soiling)”, “I leak a small amount of feces when leaking”, “I leak a lot of feces when leaking”, “All volume of stools”

Physical activity

The baseline question regarding physical activity included in Studies II and III was:

- “Do you exercise?” Optional answers: “No”, “Yes, occasionally”, “Yes, at least once a month”, “Yes, at least once a week”, “Yes, at least three times a week”, “Yes, at least once a day”.

This question correlates satisfactorily with the Swedish National Board of Health and Welfare’s indicator question regarding moderate levels of physical activity (Spearman’s correlation coefficient, r_s , 0.556, $n=449$) (unpublished pilot data), which is valid when compared to objective activity measurements using an accelerometer (114).

Quality of life, depressed and anxious mood

The baseline question regarding QoL included in Study II was:

- “How has your quality of life been during the last six months?”
- Put a ring around the number that best describes you -
1-----2-----3-----4-----5-----6-----7
No quality of life at all *Best possible quality of life*
- Have you felt low or depressed in the last six months?
- Put a ring around the number that best describes you -
1-----2-----3-----4-----5-----6-----7
Never *All the time*
- Have you felt anxious within the past six months?
- Put a ring around the number that best describes you -
1-----2-----3-----4-----5-----6-----7
Never *All the time*

The three-month follow-up questions included in Study III to compare changes in UI, FI, and frequency of physical activity, between baseline and the three-month follow-up after intervention, were the same as the baseline questions for Study III. However, in the follow-up questionnaire, the questions referred to symptoms during the previous months.

An overview of the remaining variables included in Studies II and III is presented in Table 3.

Conventional pelvic cancer rehabilitation

The individual pelvic cancer rehabilitation that women were offered, after having answered the baseline questionnaire (Table 2), was in line with recommendations regarding radiotherapy-induced gastrointestinal side effects and side effects of the urinary tract in the Swedish national care program for pelvic cancer rehabilitation (90). The individual rehabilitation offered to female PCS in Study III was thus in line with conventional pelvic cancer rehabilitation offered to female PCS within Swedish healthcare today. The goal of these rehabilitation interventions is to restore or improve urinary tract health and intestinal health. Prior to the first visit to a nurse-led clinic, the female pelvic cancer survivor had filled in the baseline questionnaire, which addressed a wide range of symptoms, and graded the most troublesome symptoms. The clinical oncology nurses, specially trained in issues concerning cancer survivorship, offered face-to-face counseling and delivered education about treatment-induced late side effects, as well as basic anatomy and physiology. Together with the patient, the nurse discussed self-care strategies and interventions and took actions for supportive care through shared decision-making. The essential recommendation regarding self-care interventions comprised medication, nutrition, and coping with psychological and social challenges. To assess the cancer survivors' urinary-tract health, symptoms of urgency, nocturia, urinary retention, urinary tract infections, UI, and pelvic pain were measured. A 48-hour voiding diary, measuring the urine volume and fluid intake, served as a basis for the counseling. Interventions such as recommendations for topical estrogen, medical treatment, lifestyle modifications, and PFMT, were provided. However, only a written PFMT program was offered, with no further guidance or information regarding PFMT. In cases involving severe urinary tract symptoms, referrals were made to urology therapists, physiotherapists, or urologists (74, 115).

The assessment of intestinal health is based on the five intestinal syndromes described by Steineck et al. (5). Information on bowel habits, such as frequency of emptying and stool consistency, was collected, using validated instruments such as the Bristol scale. In addition, symptoms of abdominal bloating, leakage of mucus and blood, and signs of bacterial overgrowth were assessed. To support decision-making, the flow chart (algorithm) of recommended diagnostics and treatment for gastrointestinal side effects, included in the national care program for pelvic cancer rehabilitation, served as a guide for proposed treatments and interventions. When indicated, to diagnose specific intestinal diseases and states, blood tests were conducted, such as hemoglobin, thrombocyte, and thyroid tests. The interventions included specific and individualized self-care advice regarding medical treatment, and the provision of written instructions for PFMT (90).

Data analysis

In all four studies included in this thesis, descriptive data was calculated and presented as numbers (n) and proportions (%). Normally distributed continuous variables were presented as mean value with standard deviation ($+ 1$ SD). Not normally distributed continuous variables and ordinal variables were presented as median (md), with interquartile range (IQR).

The qualitative analyses were conducted using content analysis, as inspired by Krippendorff (116), taking an inductive approach because the knowledge about incontinence among female PCS in relation to exercise and physical activity, QoL, and PFMT was limited. The coding was conducted in the light of the purpose of the studies, but also with the intention of keeping an open mind, which meant including non-expected aspects that appeared to be important to the respondents, for further analysis. The steps of the analyses are summarized and exemplified in Table 3. To ensure the dependability of the results of the qualitative analyses, the second authors of each paper read the analyses and confirmed that the analyses the content of the transcripts. To further strengthen the trustworthiness of the analyses, the results were discussed in two different seminars with researchers from different research fields, including qualitative researchers.

Table 3 Content analysis in five steps.

	Example from Study I	Example from Study IV
1. Interviews were transcribed verbatim or listened to by all authors. Transcripts was read several times to <i>create a sense of the whole</i> .	Excerpt from note: <i>I was supposed to meet my former co-workers in town, but I did not dare to go there due to fear of leakage.</i>	Excerpt from note: <i>Then I have tried to establish a routine when it comes to this training at home myself.</i>
2. Phrases and sentences with information relevant to the purpose of the study, so-called <i>textual units</i> , were picked out by the first author. The intent was to select units that were not too long, as they might contain more than one phenomenon, or too short due to the risk that the material may become fragmented.	<i>Avoid going to town due to fear of leakage</i>	<i>Try to establish a training routine at home by myself</i>
3. The textual units were <i>condensed</i> by the first author to compress the text without losing its content. The first and the last author, independently of each other, placed the condensed textual units into groups representing different subcategories.	<i>Fear of leakage in public places</i>	<i>Establish a home training routine</i>
4. <i>Subcategories</i> were discussed, by the first and the last author until a consensus was reached that the categories reflected the central message of the interviews in light of the purpose of the study.	<i>Worry and fear of leakage</i>	<i>Impact and challenge of home training</i>
5. The subcategories were structured into <i>main categories</i> by the first and last authors.	<i>Emotional reactions, thoughts, and musings that incontinence contribute to</i>	<i>Facilitators and barriers to practicing pelvic floor muscle training</i>

Frequency of exercise was compared between subgroups of PCS with different characteristics regarding UI and FI, and different sociodemographic and clinical variables, first by univariate analysis then by multivariable analysis. In order to calculate the relative risk (RR) of “exercising less than once a week”, between different subgroups of PCS, the data regarding frequency of exercise was categorized into two groups based on guidelines that recommend weekly physical activity of moderate intensity (89, 103):

- “Exercised at least once a week” (i.e., “Yes, at least once a week”, “Yes, at least three times a week”, and “Yes, at least once a day”)

and

- “Exercised less than once a week” (“No”, “Yes, occasionally” and “Yes, at least once a month”)

An overview of the comparison between subgroups of PCS with different characteristics regarding UI and FI, and different sociodemographic and clinical variables, in terms of the RR of “exercising less than once a week” is presented in Table 4.

The two physical activity groups, “Exercised at least once a week” and “Exercised less than once a week”, were also compared using the Mann-Whitney U test regarding QoL, depressed mood, and anxious mood. The Mann-Whitney U test allows the comparison of ordinal data, such as QoL, between two unrelated groups.

Table 4 Overview of included variables and statistical methods comparing subgroups of PCS with different characteristics regarding urinary and fecal incontinence, and sociodemographic and clinical variables presented as RR for exercising less than once a week in Study II.

Univariate model			Multivariable model		
<i>Independent variable</i>	<i>Dependent variable</i>	<i>Statistical method</i>	<i>Independent variable</i> ²	<i>Dependent variable</i>	<i>Statistical method</i>
Frequency of urinary leakage Volume of urinary leakage Capacity to hold urine Frequency of fecal leakage Volume of fecal leakage Leakage of all stools Cancer type Years since radiotherapy Cancer treatment Marital status Education level Employment status Resident Smoking status Weight change Pain in the abdomen Lymphedema	Frequency of exercise	Generalized linear model ³	Volume of urinary leakage Volume of fecal leakage Cancer type Marital status Education level Smoking status Pain in the abdomen Lymphedema	Frequency of exercise ¹	Generalized linear model ³ , and generalized RR, (using binomial distribution and log link) to explain the variation in <i>frequency of exercise</i> ⁴

¹Frequency of exercise was categorized into “Exercised at least once a week” and “Exercised less than once a week”. ²Volume of fecal and urinary leakage and other possible sociodemographic and clinical variables (all independent variables in Table 2 resulting in a p-value of <0.10, according to the univariable analysis) were selected to explain the variation of frequency of exercise. ³ Log binomial regression. ⁴95% confidence interval.

To analyze changes in levels of FI and UI between baseline and follow up, three months after intervention, as well as to analyze changes in the frequency of exercise, between baseline and follow up, the Wilcoxon signed rank test was used. The Wilcoxon signed rank test allows the comparison of ordinal data, such as symptom severity and frequency of exercise, between two related groups.

Reductions in the amount of UI and FI were compared between subgroups of PCS with different sociodemographic and clinical characteristics, first by univariate analysis and then by multivariable analysis with stepwise variable selection. Changes in the frequency of exercise were compared between PCS who experienced “reduction of FI” and “no reduction of FI”, as well as between PCS who experienced “reduction of UI” and “no reduction of UI”, by univariate analysis.

In order to calculate relative risk (RR) and odds ratio (OR) for “reduction in incontinence”, between different subgroups of PCS, the data for changes in FI and the data for changes in UI were categorized into the following groups:

- “Reduction in urinary incontinence”:

If reporting at least one step of change in the direction of reduced amount of UI at three-month follow up, compared to baseline, when answering the question “How much urine did you leak in the event of leakage, on average, in the last month?” (Answers ranging from “Not applicable, I do not leak urine” to “Large amount (full bladder volume)”, four categories.)

- “No reduction in urinary incontinence”:

If not reporting at least one step of change in the direction of reduced amount of UI at three-month follow up, compared to baseline.

And

- “Reduction in fecal incontinence”:

If reporting at least one step of change in the direction of reduced amount of FI at three-month follow up, compared to baseline, when answering the question “How much stool did you leak in the event of leakage, on average, in the last month?” (Answers ranging from “Not applicable, I do not leak feces” to “I leak all the stool”, five categories.)

- “No reduction in fecal incontinence”:

If not reporting at least one step of change in the direction of reduced amount of FI at three-month follow up, compared to baseline.

The data for changes in frequency of exercise was categorized into the following two groups:

- “Increase in frequency of exercise”:

If reporting at least one step of change in the direction of increased frequency of exercise at three-month follow up, compared to baseline, when answering the question “Do you exercise?” (Answers ranging from “No” to “Yes, at least once a day”, seven categories.)

- “No increase in frequency of exercise”:

If not reporting at least one step of change in the direction of increased frequency of exercise at three-month follow up, compared to baseline.

An overview of the comparison of subgroups of PCS with different characteristics regarding sociodemographic and clinical variables, in the form of RR and OR for reductions in UI and FI is presented in Table 5. Also, the comparison of PCS with a decrease or no decrease in FI and UI, in the form of RR and OR for “increase in frequency of exercise” can be viewed in Table 5. Since the numerical algorithm for parameter and/or confidence interval estimates did not converge in all cases, corresponding estimates were included for both OR and RR. Furthermore, in order to be consistent and since RR is often considered easier to interpret, both OR and RR are presented consistently in the results tables in Paper III.

The analyses in Study II were performed in Statistical Package for the Social Science (SPSS) for Windows, version 24.0, and the analyses in Study III were performed in R versions 3.5 and 4.0.0 with a significance level of 5%.

Response analysis were made to ensure that loss, due to missing data, did not affect the results in the multivariable analyses. The Fisher exact test was applied to evaluate the level of association between the occurrence of missing data in the dependent and independent variables included in the final multivariable models. No such significant associations were found

Table 5 Included variables and statistical methods comparing subgroups of PCS with different characteristics regarding sociodemographic and clinical variables presented as RR and OR for changes in urinary and fecal incontinence and comparison between PCS with different characteristics regarding change in urinary and fecal incontinence presented as RR and OR for changes in frequency of exercise, as in Study III.

Univariate model		
<i>Independent variable</i>	<i>Dependent variable</i>	<i>Statistical method</i>
Age Type of cancer Years since radiotherapy Smoking status Parity Children with birthweight > 4 kg Number of different types of deliveries (fast-, slow-, vacuum-, forceps-, caesarean-, and breech deliveries) Vaginal or perineal injury	Change in volume of urinary leakage ¹	Generalized linear model ³ and Likelihood Ratio Test p-values.
All independent variables above and: Sphincter or rectal injury Change in defecation frequency Change in frequency of loose stools Change in frequency of sudden defecation urgency requiring lavatory Change in ability to hold stools at urgency Lactose intolerance Gluten intolerance	Change in volume of fecal leakage ¹	
Change in volume of urinary leakage Change in volume of fecal leakage	Change in frequency of exercise	

Table 5 (continued). Included variables and statistical methods comparing sub-groups of PCS with different characteristics regarding sociodemographic and clinical variables presented as RR and OR for changes in urinary and fecal incontinence and comparison between PCS with different characteristics regarding change in urinary and fecal incontinence presented as RR and OR for changes in frequency of exercise, as in Study III

Multivariable model after variable selection		
<i>Independent variable</i> ²	<i>Dependent variable</i>	<i>Statistical method</i>
Step 1: Age Sphincter or rectal injury Change in ability to hold stools at urgency Step 2: Age Change in ability to hold stools	Change in volume of fecal leakage ¹	Step 1: Multivariable generalized linear models ³ , taking all of the independent variables into account simultaneously, and generated RR and OR to explain the variation in <i>change in volume of fecal leakage</i> ⁴ Step 2: Further variable selection using backwards elimination with respect to AIC.

¹Change in urinary and fecal incontinence was categorized into “reduction in volume of urinary incontinence”, “no reduction in volume of urinary incontinence”, “reduction in amount of fecal incontinence” and “no reduction in amount of fecal incontinence”. ²Possible sociodemographic and clinical variables (all independent variables Table 5 resulting in a p value of < 0.10, according to the univariable analysis) were selected to explain the variation in changes in volume of fecal and urinary leakage ³ Log binomial regression and logistic regression. ⁴ 95% confidence interval.

Ethical considerations

The studies in this thesis were performed according to the Helsinki Declaration of Ethical Principles for Medical Research Involving Human Subjects (117) and was approved by The Regional Ethical Review Board. Permission to contact potential participants enrolled by a patient's association, in Study I, was obtained from the board of the selected patient's association. Permission to contact participants enrolled at a unit for pelvic cancer rehabilitation, in Study I, was obtained from the clinic manager for the selected clinic. The information letter received by the study participants in Studies I–IV clearly stated that it is voluntary to participate differently in the different studies, that all data is processed and stored securely so that it is not available to unauthorized persons, that the desire not to participate in the different studies will not affect future treatment, and that at any time during the course of the study they may choose to withdraw their participation or choose not to answer certain questions or fill in certain forms. All participants signed an informed consent form, after having read the study information in the written letters, before being included in the various studies. There was no position of dependence between researchers and study participants. The results of the studies are presented in such a way that the identities of the study participants cannot be determined. To increase knowledge about incontinence, physical activity, exercise, and potential rehabilitation alternatives for incontinence among female PCS is indeed important from an ethical perspective. Increased knowledge is a prerequisite for establishing improved rehabilitation measures for treatment-induced side effects, such as urinary and FI, as well as to enable the offering of appropriate support in achieving healthy physical activity levels among female PCS.

RESULTS

Participating women

Table 6 Sociodemographic data and clinical characteristics of the participating female pelvic cancer survivors in the thesis

	STUDY I n=13	STUDY II n=578	STUDY III n=260	STUDY IV n=11
<i>Cancer type, n (%)</i>				
Gynecological cancer	13 (100)	367 (63)	147 (57)	6 (55)
Rectal cancer	0	131 (23)	67 (26)	5 (45)
Anal cancer	0	77 (13)	44 (17)	0
Other	0	3 (1)	0	0
Age in years, ¹ mean $\pm$ SD or ² median (range)	66 (48-82) ²	n=577 64 $\pm$ 12.91 ¹	62.5 $\pm$ 11.71 ¹	69 (47-83) ²
Years since radiotherapy, mean $\pm$ SD		n=576 2.7 $\pm$ 3.4	2.9 $\pm$ 4.2	
<i>Cancer treatment, n (%)</i>		n=577		
External radiotherapy, only	2 (15)	131 (23)	61 (24)	3 (30)
Brachytherapy, only	0	1 (0.2)		0
External radiotherapy and brachytherapy	0	20 (3)	9 (4)	0
External radiotherapy, brachytherapy and surgery	0	178 (31)	67 (26)	0
External radiotherapy and surgery	6 (46)	243 (42)	123 (47)	8 (70)
Brachytherapy and surgery	0	4 (0.6)	0	0
Surgery only	5 (38)	0	0	0
<i>Marital status, n (%)</i>				
Married or living with a partner	5 (39)	386 (67)	186 (72)	6 (55)
Widow or lives alone, no partner	6 (46)	164 (28)	61 (23)	2 (18)
Has a partner but lives alone	2 (15)	28 (5)	13 (5)	3 (27)
<i>Education level, n (%)</i>		n=569	n=259	
Elementary school	3 (23)	171 (30)	55 (21.2)	2 (18)
Secondary school	5 (38)	211 (36)	111 (42.7)	6 (55)
College /University	5 (38)	187 (32)	93 (35.8)	3 (27)

Table 6 (continued). Sociodemographic data and clinical characteristics of the participating female pelvic cancer survivors in the thesis

	STUDY I n=13	STUDY II n=578	STUDY III n=260	STUDY IV n=11
<i>Employment status, n (%)</i>		n=573	n=259	
Student	0	4 (0.6)	2 (0.8)	0
Unemployed/job seeker	1 (8)	11 (2)	5 (1.9)	0
Employed, n (%)	2 (15)	161 (28)	96 (36.9)	2 (18)
Housewife	0	4 (0.6)	1(0.4)	0
On sick leave	0	48 (8)	20 (7.7)	1 (9)
Disability pension	0	31 (5)	17 (6.5)	0
Retired	10 (77)	314 (54)	118 (45.4)	8 (72)
<i>Resident, n (%)</i>		n=577		
In the countryside	3 (23)	108 (19)	52 (20.0)	3 (27)
Small or medium-sized city	7 (54)	297 (51)	123 (47.3)	8 (73)
Big city	3 (23)	172 (30)	85 (32.7)	0
<i>Smoking, n (%)</i>		n=555	n=235	
Yes		66 (11)	31 (11.9)	0
No		489 (85)	204 (78.5)	11 (100)
<i>Type of incontinence, n (%)</i>		n=544 ³	n=236 ³	
Only urinary	10 (77)	181 (33.8)	35 (13.5)	5 (45)
Only fecal	0	63 (11.6)	57 (21.9)	0
Urinary and fecal	3 (23)	96 (17.6)	93 (35.8)	6 (55)
No incontinence	0	204 (37.5)	51 (19.6)	0
<i>Practiced PFMT</i>				
Yes				11
No				0
<i>Practiced PFMT with support from physiotherapist</i>				
Yes				7
No				4

n (number) and proportion (%) of women is presented. n delivering data is presented in cases of missing data. SD = Standard Deviation. ³Type of incontinence is reported only for the female pelvic cancer survivors who provided data regarding both urinary and fecal incontinence.

Qualitative findings

The categories and subcategories determined for the qualitative content analyses are presented, together with examples of quotations, for Study I in Figure 5 and for Study IV in Figure 6.

Figure 5 Categories, subcategories and examples of quotations describing PCS' experiences of incontinence in relation to perceived QoL, opportunities for physical activity and exercise and their perceptions and experiences of pelvic floor muscle training in Study I.

Figure 6 Categories, subcategories and examples of quotations describing PCS' experiences of practicing PFMT with or without physiotherapy support in Study IV.

Quality of life and emotions

Incontinence reduced the women's QoL and contributed to negative emotions such as anxiety, fear, lack of freedom, and a sense of alienation. Fear of involuntary leakage in different contexts created anxiety about embarrassing themselves. For example, concerns about not being close enough to a toilet when outside their home. Incontinence could also lead to a sense of alienation and not fitting in due to feeling different from everyone else. The women described feelings of not being good enough and that people in their surroundings could be unaware of how much trouble they were going through. Realizing that they are not alone in suffering from incontinence was a relief. Incontinence felt like a handicap in their daily lives and caused feelings of limitation and lack of freedom. For example, they experienced not being able to be spontaneous in the same way as before. On the other hand, when experiencing less incontinence, after having practiced PFMT, they also experienced less fear of being ashamed due to involuntary leakage and less fear that the incontinence might worsen over time. No longer needing to have constant control over where the nearest toilet is located contributed to an increased sense of security and freedom in everyday life.

Physical activity and inactivity

Incontinence contributed to feelings of limitation in everyday activities like shopping, gardening, and running errands. The women did not dare to participate in social activities, such as dancing, travelling, or going out for dinner with friends. However, with good planning, they could be active in social settings to varying extents. Some could take daily walks, but often not as far as before. With the possibility of taking multiple breaks, others could perform physical exercises such as water aerobics. Also, no longer being able to engage in various forms of physical exercise, such as running, cycling, horse riding, gymnastics, and swimming was described. Some found it difficult to take part in physical exercise in a group, while others were still able to do so as long as a toilet was nearby. Inactivity caused by incontinence was said to cause weight gain and stiffness, as well as a decrease in energy, physical fitness, and desire to be physically active. Meanwhile, as they began to experience less incontinence, after having practiced PFMT, women dared to test physical activities that they had stopped doing because of incontinence. However, one woman described that increased pelvic pain sometimes made her avoid being physically active.

Pelvic floor function

After having practiced PFMT, the women experienced altered pelvic floor function in the forms of increased pelvic floor muscle strength and that it was easier to consciously contract their pelvic floor muscles in everyday life when necessary. PFMT also had an impact in the forms of less frequent urinary and fecal leakage, smaller volumes of urinary leakage and better ability to hold urine and feces in

case of urgency. One woman experienced that PFMT had led to slightly increased pelvic pain around the tailbone, which was a problem she had experienced even before entering the study.

Sexual health

The women described difficulties in being sexually active, which reduced after PFMT. One woman no longer experienced any pain during intercourse after having practiced PFMT, another experienced that it was easier to achieve orgasm and that intercourse was more pleasurable to her partner as well thanks to stronger pelvic floor muscles.

Pelvic floor muscle training

The women in Study I had little or no experience of PFMT. Those who had tried to practice it after cancer treatment had done so on their own initiative, not after being encouraged by any health-care professional. However, all the women had a positive attitude towards trying PFMT for rehabilitative purposes when experiencing incontinence after pelvic cancer treatment, and most of them thought that PFMT could reduce their incontinence problems. All participants in Study IV, in contrast, had experience of practicing PFMT for three months, with or without physiotherapy support. Having practiced PFMT according to a structured training program, they had had access to guidance regarding frequency, dose, and progression. For some, it was challenging to follow the training program when not given any further oral training information or practical training instructions beyond the written training program. Some experienced group training sessions as supportive, reassuring them about practicing PFMT on a regular basis, while others experienced it as less valuable and a bit problematic due to having to travel and adapt to scheduled training sessions. There were also diverse opinions regarding practicing at home, on their own. Being able to decide when to do the exercises was described as contributing to practicing regularly. However, some described home training as difficult and boring, primarily, without additional support from a physiotherapist. With only written instructions, without additional verbal or oral instructions, it was described as difficult to know whether they were contracting the pelvic floor muscle correctly, practicing at home by themselves. Integrating PFMT into daily activities, while doing other things, such as when brushing teeth or driving to work, was described as a good way to develop a daily training routine. In that way, practicing PFMT eventually became a daily habit, even though it took a couple of weeks to become established.

The role of the physiotherapist

Women who did not have any experience of PFMT believed that it would be valuable to be instructed by someone who was familiar with it regarding how best to practice the training. To regularly participate in a PFMT group, to receive a written home training program, and to get initial PFMT instructions from a physiotherapist was described as probably a good way to practice PFMT. However, the women in

Study I said that they had never been offered any physical therapy after their cancer treatment. Women who had experience of PFMT with the support of a physiotherapist confirmed the idea that such support was an important element when practicing PFMT. They experienced guidance on how to contract the pelvic floor muscles, with the help of biofeedback, as supportive, in order to learn how to contract the pelvic floor muscles without contracting other, surrounding muscles. It was more fun and motivating to practice PFMT when they received feedback from the physiotherapist that they were doing it correctly. Support from a physiotherapist was also described as contributing to motivation to increase the difficulty of the PFMT in terms of frequency, intensity, and duration. To be able to ask questions of the physiotherapist regarding, for example, training techniques and progression, and to get tips and advice on how to integrate training into everyday life, such as how to use your pelvic floor muscles when lifting heavy objects was described as valuable. If the opportunity was given to ask questions regarding incontinence in privacy, alone with the physiotherapist, that was also described as a valuable part of the physiotherapy support.

Information and future considerations

The women felt that they had not received any information about incontinence as a possible side effect after radiotherapy treatment, and that no one had mentioned PFMT during or after their pelvic cancer treatment. Lack of information contributed to the belief that they were alone in their situation and to unrealistic expectations of treatment because they were unaware of potential side effects. They stressed the importance of better information, both before and after treatment, regarding incontinence as a possible side effect of pelvic cancer treatment and requested more information regarding possible rehabilitative efforts beyond the existing rehabilitation alternatives in conventional female pelvic cancer rehabilitation. Women who had experience of PFMT expressed the desire that PFMT, with the support of a physiotherapist, should become a mandatory part of conventional pelvic cancer rehabilitation, and preferably that it should be introduced even before the start of cancer treatment to learn what a correct pelvic floor muscle contraction feels like before any potential injury is induced to the pelvic floor muscle by the treatment. All the women who had practiced PFMT for three months, with or without physiotherapy support, intended to continue practicing PFMT and to try to integrate it into their everyday activities.

Quantitative findings

Incontinence

Of the 260 women who participated in individual rehabilitation and answered the follow-up questionnaire in Study III, 57% (n=147) reported UI and 55% (n=144) reported FI. After the individually-designed intervention program, 27% of those who had reported UI at baseline reported lower levels of UI ($p=0.046$) and 53% of those who had reported FI at baseline reported lower levels of FI ($p<0.001$). When comparing RR and OR for “reduction in urinary and fecal leakage” between subgroups with different sociodemographic and clinical characteristics, no statistical difference was found for “reduction in urinary leakage” (Table 5). However, according to the multivariable model (Table 5), “age” and “change in ability to hold stools at urgency” were found to explain the variations in change in volume of leakage. Women with a “Decrease in ability to hold stools at urgency” were less likely to experience a “reduction in amount of feces leaked” compared to women without this symptom (RR 0.43, $p=0.034$).

Quality of life

In study II, female PCS who exercised at least once a week reported better QoL (md 5, IQR 4–6) and less frequent depressed mood (md 3, IQR 2–5) compared to those who exercised less than once a week (QoL: md 4, IQR 3–5, $p < 0.001$, depressed mood: md 3, IQR 2–5, $p = 0.044$).

Physically activity and exercise

Overall, 12% of the female PCS in Study II never exercised, 18% did so on single occasions, 3% at least once a month, 28% at least once a week, 23% at least three times a week, and 16% exercised at least once a day. In other words, 67% exercised at least once a week while 33% exercised less than once a week.

Of the 310 women who reported no urinary leakage, 29% exercised less than once a week. Meanwhile, a statistically significant larger percentage of women who reported urinary leakage exercised less than once a week according to the multivariate model (Table 4). Of the women who reported “daily urinary leakage in case of urgency” (n=27), 52% exercised less than once a week, of the women who “could keep urine less than a minute in case of urgency” (n=74) 55% exercised less than once a week and of the women who reported “a moderate to all volume of leakage” (n=74), 32% exercised less than once a week. When adding other independent variables into the analysis (Table 4, multivariable model), such as volume of fecal leakage, the relationship between urinary leakage and the dependent variable “frequency of exercising” was no longer significant. This is possibly because fecal leakage had a greater explanatory value for “decrease in frequency of exercise” than urinary leakage.

Of the 223 women who reported no fecal leakage, 30% exercised less than once a week. As with the women reporting urinary leakage, a statistically significant larger percentage of women who reported fecal leakage exercised less than once a week according to the univariate model (Table 4). Of the women who reported “daily fecal leakage in case of urgency” (n=13), 62% exercised less than once a week, of the women who reported “fecal leakage without forewarning anytime within the preceding six months” (n=98), 50% exercised less than once a week and of the women who reported “a large or all volume of fecal leakage” (n=54), 50% exercised less than once a week. When adding the other independent variables into the analysis (see Table 4, multivariable model), such as volume of urinary leakage, the relationship between fecal leakage and the dependent variable “frequency of exercise” was still significant.

In Study III, after three months of individually designed rehabilitation for UI and/or FI, female PCS reported no significant change in “frequency of exercise” compared to before rehabilitation. In addition, when comparing “change in frequency of exercise” with “decrease” and “no decrease in fecal and urinary incontinence” after individual rehabilitation (see Table 5, univariate model), no statistically significant difference was found (“no decrease” vs “decrease in urinary leakage” $p=0.586$ “no decrease” vs “decrease in fecal leakage” $p=0.830$). In other words, not even women who reported decreased levels of FI and UI, after intervention, reported any statistically significant change in “frequency of exercise” after the intervention compared with before.

DISCUSSION

Summary and discussion of main findings

This thesis contributes with new knowledge regarding female PCS' experiences of incontinence, physical activity, and PFMT as well as a new understanding of the relation between incontinence, physical activity level, and quality of life among female PCS. Furthermore, the thesis contributes to increased knowledge about how physiotherapists might contribute, in a valuable way, to incontinence rehabilitation for PCS. The main findings of the thesis are that female PCS experience incontinence as a barrier to exercise and physical activity, that incontinence affects all aspects of QoL that WHO names as physical, psychological, social and existential QoL, including sexual health, and that PCS who exercise on a weekly basis report less frequent depressed mood and better QoL than PCS who do not exercise on a weekly basis. Pelvic cancer survivors, unfortunately, do not exercise more frequently after conventional pelvic cancer rehabilitation, even though the rehabilitation contributes to increased incontinence levels. PCS with three months' experience of practicing PFMT experience it as a valuable rehabilitative effort for incontinence. They also experience physiotherapeutic support and guidance as important when practicing PFMT in order to learn how to contract the pelvic floor muscles correctly and to receive individual guidance regarding dose, frequency, and progression of the training. PCS experience an absence of information regarding incontinence as a potential side effect of radiotherapy treatment, and also about potential rehabilitative options beyond conventional pelvic cancer rehabilitation.

Physical activity

The studied female PCS reported that incontinence was a barrier to practicing physical activity, compared to their activity levels before cancer treatment. If experiencing a large amount of fecal leakage, they were even less likely to be physically active. Also, women who had UI reported the same experience, that they were also less physically active. Incontinence as a barrier to physical activity among female PCS has not previously been studied. It is known that FI hinders female gynecological cancer survivors from being active and a co-variation between severe FI and decreased levels of physical activity has been reported (85). However, there are studies among male cancer survivors and non-cancer populations who also reported urinary and FI as barriers to physical activity (13-17). In a study of 9487 women with incontinence, in 14 European countries, more than 45% of the women were moderately to totally limited by incontinence from practicing physical activity (14). Loprinzi and Satish also reported that FI was a barrier to practicing moderate-to-vigorous physical activity among a non-cancer population (16). In a recently published review, the authors Fox et al. concluded that incontinence was a barrier to physical activity among male PCS (17).

When analyzing physical activity among women with incontinence, a covariation was found between low frequency of exercise and high incontinence levels. However, the analysis does not reveal the direction of the covariation. It could be hypothesized that physical activity causes stronger pelvic floor muscles and in turn decreases incontinence, and vice versa. However, Carvalhais et al. report that, among non-cancer women ($n = 58$), no such association between physical activity level and pelvic floor muscle strength or endurance exists. They reported a higher physical activity level among the 20 women with incontinence compared to the 38 continent women (118). It is, admittedly, known from previous studies that, among non-cancer survivors, mild to moderate physical activity, such as brisk walks, can decrease the risk of experiencing urinary and FI. But it is also known that female athletes and women who engage in high-intensity sports are more likely to have urinary and FI compared to controls who are only engaging in mild to moderate physical activity (119, 120). Based on previous research (13, 14, 16, 17, 85, 118-120), and PCS' experiences of incontinence as a barrier to physical activity, it is most likely that the direction of the measured covariation is that a larger amount of leakage causes a lower frequency of exercise and not vice versa. Furthermore, it is most likely that individuals with a smaller degree of incontinence tolerate higher physical activity levels than individuals with a greater degree of incontinence. However, future studies on incontinence as a barrier to physical activity among PCS is a prerequisite to confirm this assertion. From planning this project up to the time of writing this thesis, to the knowledge of the author, no other studies have evaluated FI or UI as a barrier to physical activity among female PCS, or among women in general.

Even if incontinence is most likely to be a barrier to physical activity among female PCS, we could not see any significant changes in physical activity levels among PCS three months after individual rehabilitation, not even after reporting decreased levels of urinary or FI. The fact that these women reported decreased levels of FI and UI, but did not report any statistically significant "change in frequency of physical activity" after individual pelvic rehabilitation, reveals a need for additional rehabilitative interventions in order to help these cancer survivors to reduce incontinence even further. It is likely that the conventional pelvic cancer rehabilitation offered today is not enough to achieve a sufficient reduction in incontinence for PCS. To feel safe enough to be physically more active, the survivors probably need targeted intervention support to help them reduce incontinence of feces and urine. For prostate cancer survivors, in contrast, there is an organized focus on support and education to help patients with UI in order to maintain QoL and increase physical activity levels (121, 122). However, an organized focus on support and education, such as that seen in prostate cancer rehabilitation, is lacking for many female PCS. This is the case even though studies have reported that female cancer survivors are even less active than prostate cancer survivors. Stevison et al. report in a study from 2014 that prostate cancer survivors were those who best met the recommendations for physical activity (30%), while gynecological cancer survivors reported the lowest levels of physical activity, at only 12% of the 26 indi-

viduals studied (123). Furthermore, a recent review concludes not only that gynecological cancer survivors report lower levels of physical activity than before treatment, but also that most gynecological cancer survivors did not even meet the physical activity guidelines two years after treatment (111). The finding that decreased incontinence after pelvic cancer rehabilitation did not facilitate PCS to exercise more frequently further indicates that incontinence is not the only barrier to physical activity after pelvic cancer treatment. It is most likely that PCS, as well as other cancer survivors, also experience other barriers to being physically active. In addition to incontinence, radiation therapy, surgery, chemotherapy, and hormonal treatment often induce a variety of side effects that in turn impair aerobic and muscular fitness and physical functioning (104). However, many of these side effects, such as lymphedema, decreased range of motion, pain, fatigue, and decreased aerobic and muscular fitness, which might constitute a barrier to practicing physical activity, can be minimized or prevented with exercise (18, 103, 104, 124). Furthermore, anxiety, depression, self-esteem, and various components of QoL (125), such as physical, functional, and emotional QoL (ref), that also might affect the ability to adhere to physical activity guidelines, can be improved by exercise in cancer survivors (104, 124). According to recently updated exercise guidelines for cancer survivors, health-related QoL can be even further improved in cancer survivors if the exercise is mainly supervised, compared to home-based exercise or exercise mainly without supervision (124). Heston et al. also point out the value of supervised exercise for cancer survivors. For those suffering from side effects that constitute a barrier to physical activity, the authors state that the greatest benefits from exercise might be achieved if support is given by a physiotherapist (126). An important research question for further studies, to give PCS the best possible support in resuming a healthy activity level, is what kind of support they need beyond further incontinence rehabilitation. It is probable that female PCS, just like other cancer survivors, need additional support in the rehabilitation of other treatment-induced side effects that can pose a barrier to physical activity. Furthermore, as seen among other cancer survivors (125), PCS probably achieve better reduction of side effects by exercising, if supervised by a physiotherapist. However, it is very likely that PCS with incontinence need even more support in achieving healthy activity levels since incontinence is associated with stigma, low self-esteem, and a sense of not being able to trust your body (84, 86, 127). According to Dibley et al., if clinicians identify patients who associate their incontinence with high stigma, and offer them support in achieving emotional control, social support, and mastery over their disease, then disease tolerance will be achieved more easily, which can decrease the sense of stigma (127). If the stigma surrounding incontinence decreases, incontinence as a barrier to physical activity ought to be reduced even more than from improved continence only. In accordance with all these recommendations, we need to ensure that future female PCS are offered sufficient support to resume a healthy physical activity level in conjunction with cancer treatment and cancer rehabilitation. This is an important mission for all healthcare providers, not least for physiotherapists.

Pelvic floor muscle training

Pelvic cancer survivors had varying experiences of rehabilitation efforts beyond the conventional pelvic cancer rehabilitation offered at pelvic cancer units and did little, if any, PFMT. However, despite little or no experience, they had a positive attitude towards trying PFMT, preferably with physiotherapy support. After having practiced PFMT for three months, with or without physiotherapy support, the PCS described experiences of increased pelvic floor strength, decreased urinary and FI, and better ability to hold urine and feces. One woman described increased pelvic floor pain and another decreased pelvic floor pain, due to PFMT. Two small pilot studies, already published when this project was initiated, report an effect of PFMT among female PCS after cancer treatment, however, not specifically only after radiotherapy (92, 93). One of them reports that PFMT can increase pelvic floor muscle strength, and improve physical and sexual functioning (92), the other that PFMT in combination with behavioral therapy can reduce UI (93). Some effects of PFMT on bowel function and incontinence after colorectal cancer surgery (but not specifically among women) have also been reported (95). Additionally, a recently published pilot study reports that PFMT before radiotherapy treatment may have a preservative effect on muscle strength and continence for women when undergoing cervical cancer treatment (96). Nevertheless, RCT evaluations of the effect of PFMT in women with incontinence after radiotherapy is still lacking. Since the tissue in the pelvic area often becomes fibrotic and rigid due to radiotherapy (53-56, 128), the possibility cannot be ruled out that PCS might have even greater difficulties in activating the pelvic floor muscles and experience less benefit from PFMT than females in non-cancer populations. Thus, it is a valuable insight that PCS experienced PFMT as a meaningful intervention. They also described how improved pelvic floor muscle function and decreased urinary and fecal leakage facilitated increased physical activity levels. This gives courage and real hope that further support may result in greater reductions in incontinence, and that further support can also prevent incontinence becoming an obstacle to physical activity among female PCS after radiotherapy treatment.

A structured training program, individual support, and guidance from a physiotherapist, including biofeedback, and finding a daily routine at home for the training were described by the PCS as important factors for facilitating PFMT progress. The PCS stated that PFMT guidance and support ought to be offered to all PCS. The finding that therapeutic support and guidance is a valuable component for successful PFMT is in line with previous research. Research among non-cancer populations highlights the importance of guidance on how to practice PFMT, in terms of intensity, dose, and progression as well as guidance about how to contract the pelvic floor muscles correctly to attain increased strength and endurance in order to achieve decreased incontinence (22, 24). Some previous research supports the experiences of the PCS, suggesting that biofeedback may be beneficial in addition to PFMT (24, 129). According to Norton et al., there is some evidence that biofeedback in addition to PFMT, in the form of sphincter exercises, have a better effect on FI than PFMT alone (24). Meanwhile, according to the results of a recently published review, biofeedback added to other interventions, such as PFMT,

was no more effective than PFMT alone for the treatment of female stress UI (130). Still, previous studies have suggested that it can be difficult for females to activate the pelvic floor muscles without any guidance (22, 24). Furthermore, Uechi et al. report in a recent study that most women in a non-cancer population believe that they can do a voluntarily pelvic floor muscle contraction, but that most of them do not have a correct self-perception regarding whether they actually contract the muscles or not. Only 33% of the 82 women, considering the examiner as a reference, were able to evaluate their pelvic floor muscle contraction correctly (131). Since PCS, due to their rigid tissue, might have even more difficulty in activating the pelvic floor muscles than non-cancer survivors (57), it is likely that PCS will benefit even more than non-cancer populations from guidance and support when practicing PFMT. PCS-described experiences, together with previous research (22, 24, 129-131), highlight the importance of therapeutic guidance and support, not least for PCS, in order to achieve a positive effect from PFMT on incontinence. In other words, physiotherapeutic support would probably be valuable in pelvic cancer rehabilitation, not only for support in the rehabilitation of side effects that can be relieved by exercise, but also for support in pelvic floor muscle rehabilitation. However, it is important to focus further research on the type and level of guidance and support in PFMT that is needed to achieve a possible positive effect among PCS with incontinence. Pressing research questions for further studies, based on existing research from others and the results of the studies included in this thesis, are, tentatively: Should therapeutic guidance in how to contract the pelvic floor muscles in combination with PFMT be preferred over biofeedback in combination with PFMT? Should support in PFMT also be offered before initiating cancer treatment, including radiotherapy, for female PCS in order to achieve the optimal effect from PFMT?

Group training, on the other hand, was described as both facilitating and sometimes complicated due to the frequency of scheduled appointments and difficulties in sharing experiences of incontinence-related matters with strangers. This is especially true of FI, which is surrounded by stigma, and it can be embarrassing and shameful to share experiences of incontinence with strangers (84, 86, 127). For this reason, group training is probably not a suitable option for all PCS. However, some PCS described group training sessions as contributing to training progress by, for example, getting inspiration from other participants. In a recently published review, Bø states similar pros and cons of group PFMT as those expressed by the PCS in Study IV. Inspiration from other group participants is highlighted as an advantage, and that women might feel too embarrassed about incontinence to appreciate the context of being in a group is a disadvantage. Further advantages pointed out in the review regarding group PFMT are the cost-effectiveness compared to individual training. It is also less time-consuming, and more individuals can be reached simultaneously. Examples of possible disadvantages of group PFMT stated in the review were: possible loss of individual patient contact, difficulties in knowing whether pelvic floor muscle contractions were being performed properly without therapist assessment during contractions, that time needed to be set aside for group PFMT might affect the adherence, and that certain women

might need individual support in terms of follow-up and manual therapy (23). Our studies and previous research thus indicate the value of optional group training sessions, but only in addition to individual support from a physiotherapist, if implementing PFMT in conventional pelvic cancer rehabilitation. However, since the women's experiences of group training varied, it would be interesting to study the value of group training in addition to individual support compared to only individual support in PFMT in a full-scale randomized controlled effect study.

Quality of life and emotions

Fecal and urinary incontinence affect QoL in a negative way due to worry and fear of leakage, but problem-focused coping strategies could help PCS to maintain their QoL to some extent. Coping strategies include always bringing a change of clothes, locating available toilets before going anywhere, and trying to accept the situation. It is well known that FI or UI affect QoL negatively among female PCS (7, 85). Monz et al. reported that UI also hindered social activities due to the fear of not being able to reach a toilet in time (14). PCS who practiced physical activity at least weekly experienced better QoL and less frequent depressed mood than PCS practicing physical activity less than once a week. This is indeed a valuable finding because level of physical activity is a modifiable factor. This result is in line with a recently published study reporting a positive association between increasing physical activity levels and improved QoL among endometrial cancer survivors (n=100). Increased physical activity level was associated with better QoL regarding three different aspects of QoL among the female PCS; namely, improvements in general health, role limitation due to physical health, and somatic distress. Thus, supporting PCS to increase their physical activity levels could possibly also improve their QoL.

Experiences of increased pelvic floor strength and endurance and decreased urinary and FI after having practiced PFMT were described as contributing to feeling less concerned about incontinence, increased security, and a greater sense of freedom in everyday life among participants. These findings are supported by those from a recently published review of 24 studies (n=2394) of females with UI from a non-cancer population. The review reports significantly better QoL, due to a reduction in incontinence symptoms, among the women after having practiced PFMT for at least six weeks (26). The experiences of female PCS together with previous research by others, thus indicates that PFMT might possibly contribute not only to reduced incontinence but also to less anxiety, increased security to trust their bodies, and improved QoL for PCS.

Sexual health

Incontinence also affected the women's sexual health and sometimes prevented them from being sexually active. However, PCS stated that perceived improved pelvic floor muscle function after having practiced PFMT improved their sexual health. They described less concern about experiencing leakage or pain during intercourse. Others have previously reported that PCS experience impaired sexual health after cancer treatment, due to incontinence (58, 132-134), as well as pain

during intercourse (135). Of 11 PCS who reported new incidence of UI after hysterectomy and radiotherapy for endometrial cancer, 36.4% stated that they avoided sexual activities compared to none of those who did not report any UI after treatment (58). Among female, postmenopausal, non-cancer survivors, a correlation between sexual dysfunction and lower pelvic floor muscle strength has also been reported (27). According to a review by Ferreira, which included eight RCTs (n=1341), most studies reported significantly improved sexual function among female non-cancer survivors with pelvic floor dysfunction, after having practiced PFMT (28). Thus, PCS experiences, together with previous research by others, indicates that PFMT might have a positive effect not only on incontinence and QoL in general but also on sexual health among PCS. According to the WHO:

Sexual health is a state of physical, emotional, mental, and social well-being in relation to sexuality; it is not merely the absence of disease, dysfunction, or infirmity. Sexual health requires a positive and respectful approach to sexuality and sexual relationships, as well as the possibility of having pleasurable and safe sexual experiences, free of coercion, discrimination, and violence. (136, p.9)

This also highlights the importance of further research into the effects of PFMT as a rehabilitative effort among PCS to retain sexual health. An interesting extended research question when evaluating the effects of PFMT on incontinence among PCS would be: Does PFMT also have an effect on sexual dysfunction after radiotherapy treatment, such as pain during intercourse?

Information/knowledge

The PCS pointed out the importance of improved information routines regarding potential side effects and available rehabilitative measures after radiotherapy. They highlighted the importance of receiving better information regarding incontinence as a potential side effect of cancer treatment and PFMT as a potential way to reduce incontinence, and stated that the absence of such information had severely affected their ability to cope with their situation. Sadly, no one had received sufficient information regarding potential side effects of radiation therapy, such as incontinence, or about potential rehabilitation options for incontinence, such as PFMT. This does not necessarily mean that they had not received any information. However, if they did receive such information, they were not receptive to it as it was delivered. This indicates a need to reconsider information routines regarding potential treatment-induced side effects and available rehabilitation within conventional female pelvic cancer treatment and rehabilitation. Participation and consultation, as formulated in the Patient Act, presupposes that the patient is given the opportunity to discuss all disease information and that it is as comprehensible as possible. It must be designed based on the patient's conditions and constitute an important aspect of enabling and strengthening the patient's participation. The person who provides information from the healthcare system must design it in such a way that it is clear that the patient understands. Anyone who has the task of ensuring the patient's participation in care should know the content of the Patient Act. It states, for example, that the patient should receive information about side effects

(137). Previous research also describes the importance of sufficient information being provided in cancer care in order for the patient to achieve good QoL and health benefits from treatment and rehabilitation (138-140). Male PCS who received comprehensive information regarding potential side effects from radiotherapy treatment for prostate cancer reported significantly fewer side effects, such as fatigue and sleep problems, compared to controls who did not get any information regarding side effects (140).

So, why is sufficient support and information regarding incontinence as a possible side effect of radiotherapy not offered to female PCS when there is an organized focus on support and education among prostate cancer survivors who experienced incontinence after cancer treatment? Are women in general expected to have greater knowledge regarding incontinence due to pre- and postnatal regimes and information about incontinence, PFMT, and pelvic floor muscle function? Or is incontinence more accepted among women because it is more prevalent than among men due to pregnancy and giving birth? These questions will not be answered in this thesis, but the findings highlight the need and importance of establishing a similar organized focus on support and education to reduce UI in order to maintain QoL and increase physical activity levels among female PCS. It is not ethically defensible that the support given for treatment-induced incontinence rehabilitation and support in achieving healthy activity levels varies so widely between two different, both very extensive, patient groups: prostate cancer survivors and female PCS.

Methodological considerations

The fact that this thesis includes two qualitative studies is considered a strength. Thus, the results are highly permeated by the women's individual perspectives on incontinence, physical activity, and PFMT, ensuring that light is shed on which aspects are most likely to be perceived as meaningful to female PCS. The content of the interviews was considered to be rich, and the results of the analyses were considered to reflect the experiences of the PCS in respect to the aims of the studies. The analysis was validated by triangulation, whereby two of the researchers/authors conducted the analysis and a third researcher/author confirmed its trustworthiness. The third authors (in study I and IV; GD and SB) listened to all the interviews, read the transcripts and the categories, and confirmed that the categories reflected the experiences of the PCS. In both studies, the women in the final interviews were describing experiences similar to those in the previous interviews and therefore these final interviews did not contribute any new information. Thus, some form of redundancy is considered to have been achieved in the interviews in both studies and it is thus likely that the aspects most meaningful to the PCS, in light of the purposes of the two studies, have been captured in the categories presented in the results.

The preunderstanding of the researchers involved in the qualitative studies is considered to have had a positive impact on the results. The broad experience in the research group contributed to selecting relevant questions for the interview guides in both studies. Two of the researchers are nurses (SB and GD), one of them a specialist oncology nurse (GD), and the third is a physiotherapist (AE). All three researchers have PhDs in medicine and long experience of clinical cancer rehabilitation and both qualitative and quantitative research in the field of cancer rehabilitation. The fourth researcher is the author of this thesis, a physiotherapist, and a PhD student (AL), with four years' experience of clinical rehabilitation in women's health, especially regarding pelvic floor dysfunction. In the first qualitative study, AL was the interviewer. In the other qualitative study (Study IV), the interviewer was a physiotherapist with more than ten years' experience of clinical rehabilitation in women's health and pelvic floor dysfunction, but with limited experience of qualitative research (SR). However, the researchers' broad experience overall (SB, GD, and AL) contributed to giving relevant guidance regarding asking follow-up questions to the interviewer (SR) in order to achieve rich interviews. It could have been an issue that the researchers might have excluded certain questions of significance to the patient from the interview guides, since their pre-understanding may have led to preconceived notions about what is meaningful to the patient. However, this is not considered an issue since the researchers have different pre-understandings and were able to complement each other, by means of broader thinking, when the interview guide was developed. Both interviewers have experience of clinical rehabilitation in women's health, with a comprehensive pre-understanding regarding incontinence rehabilitation. This was not considered an issue in terms of preconceived notions about what is meaningful to the patient because the content of the interviews was assessed as being rich. Since incontinence, and especially FI, is surrounded by stigma (84, 86, 127), and may be perceived as embarrassing and shameful to talk about, the interviewers' experience of incontinence rehabilitation, which the PCS were all aware of, was considered to contribute to a sense of security so that PCS had the courage to share their experiences of incontinence and PFMT in depth.

To identify sources of bias and avoid the possibility that confounding factors might hide an association between variables, the hierarchical step-model for causation of bias was used in Studies II and III (141). If confounding factors are neither measured nor considered, results may be biased. To be defined as a confounding factor, a phenomenon must be both associated with the exposure (volume of leakage in Study II, and change in volume of leakage and change in frequency of physical activity in Study III) and an independent risk factor for the outcome (frequency of exercise in Study II and change in frequency of exercise and change in frequency of incontinence in Study III). When confounding factors are not considered, this may lead to an over- or under-estimation of the association between exposure and outcome. In these studies, detailed preventive procedures were carried out during the preparatory phase in order to avoid systematic errors due to confounding factors. As much information as possible was collected about possible confounding factors, through either the study questionnaire or medical records. Information

taken from the female cancer survivors in the studies included age, education, smoking, weight gain, information regarding vaginal birth, and a variety of comorbidities. From medical records, data was collected on previous cancer diagnoses, diagnosed stage of the cancer disease, and treatment modality. Known or suspected relevant factors were considered in the analyses of the relation between leakage/change in leakage and frequency of physical activity/change in frequency of physical activity. For example, female PCS who were diagnosed with lymphedema but were not receiving any treatment for this were found to be more likely to practice physical activity less than once a week than other PCS, and female pelvic cancer patients reporting “decreased ability to hold stools in case of urgency” were less likely to report “increased FI levels” after individual rehabilitation compared to PCS who did not report “decreased ability to hold stools in case of urgency”. Non-participation may bring about bias as well as selection-induced bias, i.e. misrepresentation. However, the response rate was high in both studies (85% compared to 77%). The studies were well grounded during the preparatory qualitative phase with validation of the study questionnaire. When 1068 cancer survivors answered a study-specific questionnaire regarding their health condition, including the same questions used in our study, 95% found their study participation valuable and 54% stated that answering the questionnaire *per se* had had a positive impact (142). Based on the preparatory phase, previous studies using the same questions (7, 8, 85), and previous evaluations of the reasonable patient burden, there were good conditions for achieving high response rates. Information on the excluded women’s health or physical activity and the reasons for their deaths is not known; it can only be hypothesized that women who had died prior to data collection belonged to the group of women in poorest health and thus with the lowest frequency of exercise and lowest frequency in change of exercise. Since only female PCS were studied, the observations cannot be generalized to male PCS. In the hierarchical step-model for causation of bias, bias due to incorrect data is handled in the third step. An important aspect was the validity of data-collection methods. The baseline study questionnaire and the three-month follow-up questionnaire were developed and satisfactorily validated, according to established (7, 8, 85), previously described methodology (112). When developing the study questionnaire for use in semi-structured qualitative individual interviews within the target population, we gave the women the opportunity to express their personal experiences. The interviews proceeded with additional cancer survivors until the material was rich and the interviewer was no longer gathering any new data, so-called saturation in other qualitative methodologies. An important task was to make all the questions clear and understandable. By developing questions in cooperation with the target population in a face-to-face situation, the likelihood of the female PCS acknowledging and answering the questions as intended increased, thus decreasing the risk of misclassification. There is, however, a disadvantage in not using evaluation instruments that are well established to evaluate, for example, incontinence among patient groups other than female PCS, in that comparison of the results with other studies involving other patient groups becomes more complicated.

Physical activity is a complex behavior and, thus, complex to measure. Under free-living conditions, self-report questionnaires are preferable because they are easy to administrate for large samples (143). It is important, however, to take into account the risk of recall bias as well as under- and over-estimation of physical activity. Accelerometry, on the other hand, has been shown to be reliable and valid for measuring free-living physical activity and sedentary time and to provide detailed information on intensity, frequency, and duration of activity, but their administration can be too complex and costly for use in regular health-care practice (143, 144). Therefore, during our preparatory studies, methodology testing was performed for the self-assessed physical activity study question. The physical activity question previously satisfactorily correlated to the Swedish National Board of Health and Welfare's indicator question (145) regarding a moderate level of physical activity (Spearman's correlation coefficient, r_s , 0.556, $n=449$) (unpublished pilot data), which is valid compared to objective activity measurements using an accelerometer (114). The physical activity question in the study questionnaire also showed satisfactory test-retest reliability (r_s 0.694, $n=46$) when cancer survivors answered the question twice, at an interval of one week. The cut-off when categorizing the physical activity data was chosen based on the fact that physical activity guidelines for cancer survivors propose weekly activity at a moderate level. A limitation of the physical activity question is that the duration and intensity of physical activity are not registered. Thus, it is not possible to state whether the physical activity levels of the women who exercised at least once a week were in line with activity guidelines for cancer survivors (89, 103). However, we can with great certainty draw the conclusion that the women who exercised less than once a week were not adhering to the physical activity guidelines for cancer survivors, which advocate weekly physical activity at a moderate level. The questionnaires were posted by mail and the women answered them in privacy in an attempt to avoid therapist-induced bias (146).

CONCLUSIONS

Female PCS experienced incontinence as a barrier to exercise and stated that incontinence reduced QoL and impaired sexual health. PCS with incontinence, primarily fecal incontinence, but also urinary incontinence, were less likely to exercise on a weekly basis than those without. PCS who exercised on a weekly basis experienced better QoL and less frequent depressed mood compared to PCS who exercised less than once a week. PCS did not exercise more often after conventional pelvic cancer rehabilitation, even when the rehabilitation reduced incontinence levels. PCS had a positive attitude towards trying PFMT and PCS who had at least three months' experience of practicing PFMT on a regular basis found it to be a valuable rehabilitative tool for relieving incontinence. PCS experienced that physiotherapeutic support and guidance were of great importance when practicing PFMT to be able to contract the pelvic floor muscles correctly and to receive individual guidance regarding dose, frequency, and progression. PCS expressed a need for better information routines regarding incontinence as a potential side effect after radiotherapy treatment, as well as better information routines for additional rehabilitative efforts for incontinence, and greater accessibility of these, beyond those offered in conventional pelvic cancer rehabilitation today.

CLINICAL IMPLICATIONS

This thesis argues that better information routines regarding urinary and fecal incontinence as a potential side effects after pelvic cancer treatment, along with information about additional rehabilitative efforts that could reduce incontinence, such as PFMT, ought to be implemented in conventional pelvic cancer care. Furthermore, this thesis argues that additional rehabilitative measures need to be implemented within conventional cancer rehabilitation care in order to increase the currently low physical activity levels among PCS suffering from incontinence after radiotherapy treatment. This is in order to achieve a sufficient reduction in incontinence levels to eliminate it as a barrier to physical activity. Such rehabilitation could also help to eliminate further possible barriers to physical activity, such as other treatment-induced side effects and the stigma surrounding incontinence, in order to improve QoL and improve sexual health. Since PCS experience PFMT as a meaningful intervention for incontinence, it is justifiable to encourage female PCS with incontinence to practice PFMT, even though radiotherapy and surgery for pelvic cancer might have caused damage to the pelvic floor.

FUTURE RESEARCH

The effects of PFMT on incontinence among female PCS, and the level and type of support needed to achieve the best effect, needs to be further studied before it is fully implemented as routine in existing pelvic cancer rehabilitation guidelines or in pelvic cancer rehabilitation clinics. Also, the most effective time for PFMT to be implemented in female pelvic cancer care, in order to reduce or even potentially prevent incontinence as a side effect after pelvic cancer treatment, needs to be studied. PFMT can then be implemented with the best possible results, perhaps even preventing incontinence among PCS. Further studies on incontinence as a barrier to achieving healthy physical activity levels and good QoL are needed to further highlight the importance of improved incontinence rehabilitation for PCS.

SVENSK SAMMANFATTNING

Bakgrund: Behandlingen av cancersjukdomar förbättras ständigt vilket bidrar till en växande population av canceröverlevare. Bäckencanceröverlevare utgör den näst vanligaste gruppen kvinnliga canceröverlevare efter bröstcanceröverlevare. Många av kvinnorna behandlas med strålterapi som är associerad med en risk för önskade sidoeffekter. Vissa sidoeffekter kvarstår eller uppstår långt efter behandlingen och andra medför ett livslångt rehabiliteringsbehov. En vanlig, belastande sen sidoeffekt av strålterapi mot bäckenet är urin- och eller avföringsinkontinens. Inkontinens påverkar ofta såväl livskvalitet som fysisk aktivitetsnivå negativt. Fysisk aktivitet kan bidra till ett flertal positiva hälsoeffekter som att minska risken för återfall i sjukdomen. Det kan sannolikt också bidra till ökad överlevnad. Canceröverlevare i allmänhet, och kvinnliga bäckencanceröverlevare i synnerhet, har ofta en lägre fysisk aktivitetsnivå efter cancerbehandlingen jämfört med innan. Vid urin- och även vid avföringsinkontinens rekommenderas bäckenbottenmuskelträning (BMT) som ett förstahandsval av behandling till kvinnor i allmänhet. Bäckebottenmuskelträning kan, förutom att bidra till att minska inkontinens, även bidra till ökad fysisk aktivitetsnivå och förbättrad livskvalitet. Bäckebottenmuskelträning har emellertid fått obetydligt utrymme som potentiell behandlingsmetod för inkontinens i det svenska nationella vårdprogrammet för bäckencancerrehabilitering. Än så länge saknas evidens för att BMT är lika effektivt hos kvinnliga bäckencanceröverlevare som hos kvinnor som inte genomgått cancerbehandling. Att BMT skulle vara lika effektivt hos dessa kvinnor är inte självklart då de ofta har behandlingsinducerade skador i strukturer i bäckenbotten som kan påverka träningens resultat. Problemet att kvinnliga bäckencanceröverlevare ofta besväras av inkontinens och ofta är mindre fysiskt aktiva än andra canceröverlevare kvarstår. Det är således ett viktigt område för vidare forskning och ett problem som behöver lösas av hälso- och sjukvårdspersonal, inte minst av fysioterapeuter.

Syfte: Det övergripande syftet med avhandlingen är att förbättra förståelsen för kvinnliga bäckencanceröverlevares upplevelser av inkontinens i relation till fysisk aktivitet, livskvalitet och rehabiliteringsinsatser, inklusive BMT. Detta inkluderar förbättrad kunskap om relationen mellan motion och livskvalitet och huruvida bäckencanceröverlevare upplever att fysioterapi kan bidra på ett värdefullt sätt till att reducera inkontinensbesvär. Detta för att möjliggöra utformande av meningsfulla fysioterapeutiska interventioner, som bäckencanceröverlevare kan och är villiga att delta i, för att uppnå en potentiell minskning av inkontinens såväl som ökad livskvalitet och ökad fysisk aktivitetsnivå.

Metod: Avhandlingen innehåller fyra studier, med tre olika metoder, där alla studiedeltagare utgörs av kvinnliga bäckencanceröverlevare. Studie I (n=13) och IV (n=11) är kvalitativa studier där individuella intervjuer genomfördes med semi-strukturerade intervjuguider. Studie II är en kohortbaserad tvärsnittsstudie (n=578) och Studie III är en prospektiv, kohortbaserad observationsstudie (n=260).

Resultat: Kvinnorna uttryckte avsaknad av information om inkontinens som en potentiell bieffekt av strålterapi. De upplevde att inkontinens hindrade dem från att vara fysiskt aktiva i samma utsträckning som innan behandlingen och att urin- och avföringsinkontinens försämrade flera aspekter av deras livskvalitet, inklusive sexuell hälsa. Det uttryckte avsaknad av rehabiliteringsalternativ utöver det som erbjuds inom konventionell bäckencancerrehabilitering i svensk hälso- och sjukvård. Efter att ha tränat BMT under tre månader upplevde de BMT som en meningsfull rehabiliteringsåtgärd för urin- och avföringsinkontinens. De upplevde även att stöd och guidning från en fysioterapeut var värdefullt för att lära sig att kontrahera bäckenbottenmuskulaturen korrekt och för att få individuell guidning avseende dos, frekvens och progression av träningen.

I Studie II, rapporterade 67% av 568 kvinnor att de motionerade minst en gång i veckan medan 33% rapporterade att de motionerade mindre än en gång i veckan. Kvinnor som rapporterade stor mängd avföringsläckage, ($p=0.01$, multivariabel analys) var statistiskt signifikant mer benägna att motionera mindre än en gång i veckan. En liknande samvariation sågs hos kvinnor som rapporterade stor mängd av urinläckage ($p=0.04$, univariat analys). Samvariationen var inte statistiskt signifikant i en multivariabel analys ($p=0.105$). Kvinnliga bäckencanceröverlevare som motionerade minst en gång i veckan rapporterade mer sällan nedstämdhet ($p=0.044$) och bättre livskvalitet ($p < 0.001$) jämfört med de som motionerade mindre än en gång i veckan. Tre månader efter individuell sedvanlig bäckencancerrehabilitering rapporterade kvinnorna statistiskt signifikant lägre nivåer av urin- och avföringsinkontinens ($p=0.046$ and $p < 0.001$). Däremot, rapporterade inte kvinnorna någon statistiskt signifikant förändring i hur ofta de motionerade ($p=0.763$).

Konklusion:

Inkontinens utgjorde ett hinder för att utöva fysisk aktivitet och för att motionera bland kvinnliga bäckencanceröverlevare. Inkontinens försämrade dessutom livskvalitet och sexuell hälsa. De som upplevde inkontinens, i synnerhet avföringsinkontinens, var mindre benägna att motionera veckovis. Kvinnliga bäckencanceröverlevare som motionerade varje vecka upplevde bättre livskvalitet och mer sällan nedstämdhet än de kvinnor som inte motionerade veckovis. Kvinnliga bäckencanceröverlevare motionerade inte oftare efter konventionell bäckencancerrehabilitering även om inkontinensbesvären minskade. Kvinnliga bäckencanceröverlevare hade en positiv attityd till BMT. Efter tre månaders erfarenhet av BMT, upplevde de att det var en meningsfull rehabiliteringsåtgärd för inkontinens. De ansåg även att stöd och guidning från en fysioterapeut var av stor vikt. Kvinnliga bäckencanceröverlevare efterfrågade bättre informationsrutiner avseende potentiella biverkningar efter cancerbehandling, så som urin- och avföringsinkontinens. De efterfrågade även bättre informationsrutiner och tillgänglighet vad gäller rehabilitering av inkontinens utöver det som erbjuds inom sedvanlig bäckencancerrehabilitering idag.

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APPENDIX 1

Interview guide in Study I

1. Can you tell us about how incontinence affects your life in general, for example, in what is usually called quality of life?
 - (a) How would it affect your quality of life if the incontinence decreased or you became completely recovered from incontinence?
2. How do you see your opportunities to be active in daily life in general in view of the incontinence?
 - (a) Daily chores
 - (b) Socialising
 - (c) Recreational activities
 - (d) Physical training
 - (e) If incontinence decreased or you became completely restored from incontinence, how would that affect the extent to which you are physically active?
3. Can you tell us about your experience to train the pelvic floor muscles after your illness (if you have any experience of it)?
4. Can you tell us about your perceptions about pelvic floor muscle training?

The following are suggestions for follow-up questions to get the respondent to talk more:

1. Can you expand on this a bit more?
2. In what way?
3. What do/did you feel?
4. What do you mean?

The interviewer finally summarizes all the questions and asks the respondent if she wants to add anything.

APPENDIX 2

Interview guide in Study IV

Preliminary overall question:

” How has it been for you to practice pelvic floor muscle (PFMT) training now during the study period?”

Further questions:

1. How have you been able to practice according to the current training plan?
2. What has been good and what has been less good about exercising the way you have done?
3. What effects do you think the PFMT has had?
4. In what way have the effects of the PFMT affected your everyday life?
5. How do you think about PFMT training in the future?

The following are suggestions for follow-up questions to get the respondent to talk more:

Can you expand on this a bit more?

In what way?

What do/did you feel?

What do you mean?

The interviewer finally summarizes all the questions and asks the respondent if she wants to add anything.

Papers

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