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Physical activity and lower extremity lymphedema among endometrial cancer survivors: A population-based cross-sectional study

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HIGHLIGHTS

- Endometrial cancer survivors with higher levels of physical activity had a lower prevalence of lower extremity lymphedema.
- Meeting physical activity guidelines was associated with decreased odds of lower extremity lymphedema.
- Physical activity level was associated with odds of lower extremity lymphedema, but there was no dose-response association.
- Findings suggest that physical activity may prevent lower extremity lymphedema among endometrial cancer survivors.
- The causality of associations needs to be verified in a longitudinal setting.

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ABSTRACT

Objective. The aims of this cross-sectional study were to describe the prevalence of self-reported lower extremity lymphedema (LEL) by different physical activity (PA) levels and to examine if higher levels of PA are associated with lower odds of self-reported LEL among endometrial cancer survivors.

Methods. Women treated for assumed early-stage endometrial cancer between 2006 and 2021 were invited to complete the Lower Extremity Lymphedema Screening Questionnaire (LELSQ) and the Physical Activity Frequency, Intensity, and Duration (PAFID) questionnaire. Responses of PAFID were converted into metabolic equivalent of task minutes per week (MET-min/week), and participants were categorized into different PA levels: meeting (≥500 MET-min/week) versus *not* meeting PA guidelines; low active (<500 MET-min/week), active (500–1000 MET-min/week), and high active (>1000 MET-min/week); and PA quartiles.

Results. Among 1077 included, the prevalence of LEL was 48 %, 32 %, and 32 % among the low active, active, and high active survivors, respectively. Compared to the low active, the active survivors had 40 % lower odds of LEL (OR 0.60, 95 % CI 0.44–0.81), but no further reduction was observed among the high active survivors (OR 0.71, 95 % CI 0.47–1.06). According to PA quartiles, higher PA levels were associated with lower odds of LEL, but not in a linear dose-response way.

Abbreviations: BMI, body mass index; CI, confidence interval; DAG, Direct Acyclic Graph; LEL, lower extremity lymphedema; LELSQ, Lower Extremity Lymphedema Screening Questionnaire; LND, Lymph Node Dissection; MET, Metabolic Equivalent of Task; OR, odds ratio; PA, physical activity; PAFID, Physical Activity Frequency, Intensity and Duration; SLN, Sentinel Lymph Node; SD, standard deviation; WHO, World Health Organization.

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Conclusion. Findings suggest that regular PA according to the current PA guidelines is associated with decreased the odds of self-reported LEL among endometrial cancer survivors; however, causality of association needs to be verified in a longitudinal setting.

1. Introduction

Endometrial cancer is the most common gynecologic cancer in high-income countries, with a rising incidence rate mainly due to a more obese and aging population [1,2]. Despite a high five-year relative survival rate, endometrial cancer survivors face a risk of several cancer and treatment-related late effects, e.g., fatigue, sexual dysfunction, mental distress, reduced physical function, and lower extremity lymphedema (LEL) [3–6].

Lower extremity lymphedema is a result of dysfunction of the lymphatic system, causing swelling of the lower extremities and/or genitals [7]. Complete decongestive therapy or microsurgical procedures may help control swelling and prevent progression, but other treatment options are lacking [7]. This makes LEL generally considered incurable and might lead to lifelong morbidity such as recurrent skin infections, pain, physical functioning impairment, depression, and decreased quality of life [8–10].

The prevalence of LEL among endometrial cancer survivors varies widely, from three to 70 % [11–14]. Well-known risk factors are surgical removal of lymph nodes, chemo-radiation therapy, and a high body mass index (BMI) [11,12,14]. Physical activity (PA) has been identified as a potentially modifiable preventative factor for lymphedema among breast cancer survivors [15–17]. Today, only two non-European studies have investigated the association between PA and LEL in gynecologic cancer populations [18,19]. They found that being physically active according to the World Health Organization (WHO) PA guidelines or above this PA level was associated with decreased odds of LEL compared to inactive or low active women.

In order to increase knowledge about the association between different levels of PA and LEL among gynecologic cancer survivors, we used data from the large-scale cross-sectional Sensor study. We aimed to describe the prevalence of self-reported LEL by different PA levels and to examine if higher levels of PA are associated with lower odds of self-reported LEL among endometrial cancer survivors. We further investigated whether the association between PA and LEL differed by BMI categories and musculoskeletal complaints.

2. Material and methods

2.1. Design and participants

This cross-sectional questionnaire-based study is part of the Norwegian population-based multicenter Sensor study [20]. The recruitment process has been described in detail previously [6]. In short, women treated for assumed early-stage endometrial cancer at either the Oslo University Hospital from 2006 to 2021 or at St. Olavs Hospital from 2012 to 2021 were invited by mail to participate in an online survey in February 2022. Two reminders were sent non-responders by text messages in March and April 2022, followed by a paper version with a pre-paid envelope to non-responders after the final text message in May 2022. Patients could respond until November 2022, which was on average 5.5 years post-surgery (range 0.2–16.1 years). Women with LEL prior to the cancer treatment or invalid responses to PA or LEL questionnaires were excluded from the current analyses. The manuscript was written in accordance with the STROBE-guidelines [21].

2.2. Variables and assessments

2.2.1. Outcome

Lower extremity lymphedema was assessed by the Norwegian version of the Lower Extremity Lymphedema Screening Questionnaire (LELSQ) [22,23]. The LELSQ contains 13 questions about symptoms of LEL experienced during the previous four weeks, with responses graded on a five-point scale (0 = not at all, 1 = a little bit, 2 = somewhat, 3 = quite a bit, and 4 = very much). Item scores are summed with a possible range of 0 to 52 points. A score of five points or higher indicates a positive screen for self-reported LEL. More than half (7/13) of the questions must be answered in order to give a valid result [22]. Missing items were replaced by non-missing items with a value of zero if a minimum of seven questions were answered.

2.2.2. Exposure

Level of PA was assessed by the Physical Activity Frequency, Intensity, and Duration (PAFID) questionnaire [24]. The PAFID questionnaire contains three items related to frequency, intensity, and duration of PA in an average week (Supplementary Table S1). All three items must be answered in order to give a valid result. Metabolic equivalents of task minutes per week (MET-min/week) were calculated by multiplying frequency (sessions per week), by intensity (assigned MET-value), and duration (average minutes per session) as described by Sagelv et al. [24] The total scores ranged from 0 to 2700 MET-min/week, i.e., 0 to 45 MET-hours/week.

To explore different nuances in the meaning of PA levels (PA exposure), PA was categorized in different ways;

1. Meeting (≥500 MET-min/week) versus *not* meeting the WHO PA guidelines for adults (at least 150 to 300 min of moderate-intensity activity or 75 to 150 min of vigorous-intensity activity or a combination of moderate- and vigorous-intensity throughout the week, equivalent to approximately 500 to 1000 MET-min/week) [25],
2. Low active (<500 MET-min/week), active (500–1000 MET-min/week), and high active (>1000 MET-min/week) according to the definitions of the Physical Activity Guidelines for Americans, 2nd edition [25], and
3. Quartiles of PA volume (Q1 ≤ 150 MET-min/week, Q2 150.01–337.5 MET-min/week, Q3 337.51–675 MET-min/week, Q4 > 675 MET-min/week) as recommended by Sagelv et al. [24]

2.2.3. Covariates

Socio-demographics, health, and lifestyle variables were self-reported and included age at survey, education level (low [≤13 years] versus high [>13 years]), marital status (living with a partner versus not living with a partner), BMI (kg/m^2) at survey (underweight or normal weight [<25], overweight [25–29.9], and obese [≥30]), smoking (never, sometimes, and daily), and comorbidities. Comorbidities were assessed by a modified version of the Self-Administered Comorbidity Questionnaire (SCQ) [26], adding "deep venous thrombosis (DVT)" and "pulmonary embolism" and categorized into cardiovascular disease (heart disease, DVT, and/or pulmonary embolism), hypertension, depression, and musculoskeletal complaints (osteoarthritis, degenerative arthritis, rheumatoid arthritis, and/or back pain).

Cancer-related variables were extracted from electronic medical records and included time since surgery (years), FIGO 2009 stage [27] (I or

II versus III or IV), adjuvant treatment ("yes, chemotherapy only", "yes, any radiotherapy with or without chemotherapy", and "no"), and nodal assessment (pelvic lymph node dissection (LND), sentinel lymph node algorithm (SLN), and no nodal assessment). Adjuvant treatment was later categorized into no versus yes in the regression analysis because of few participants who received radiotherapy.

2.3. Statistical analysis

Descriptive statistics were used to present background characteristics of the total study sample and for women meeting or not meeting the PA guidelines. Descriptive statistics were also used to present prevalence of LEL by PA exposures. Continuous variables were presented as means with standard deviation (SD) or median with minimum and maximum values, as appropriate, while categorical variables were presented as frequencies and percentages. Eligible survivors included and not included in the current study were compared using the independent-samples *t*-test or Mann-Whitney *U* Test for continuous variables and Chi-Square test for independence for categorical variables.

To explore the association between different PA levels (meeting versus *not* meeting PA guidelines; low active, active, and high active; and PA quartiles) and LEL, we conducted three logistic regression models for each type of exposure (Model 0: unadjusted logistic regression, Model 1: model 0 + adjusted for age, education, time since surgery, adjuvant treatment, nodal assessment, and Model 2: model 1 + adjusted for BMI). We also conducted a sensitivity analyses among survivors without lymph node dissection to explore if the association between different PA levels and LEL was the same in this subgroup. Results are presented as odds ratios (OR), 95 % confidence intervals (95 % CI), and *p* values (*p*). Responders with missing data in any of the covariates of model 2 ($n = 50$) were excluded from models 0, 1, and 2 (complete case analysis).

Covariates were selected based on a directed acyclic graph (DAG) created by a statistician and experts in lymphedema, exercise oncology, and gynecologic oncology (Supplementary Figs. S1 and S2). Additionally, a strong predictor of the outcome variable was included as covariate, i.e., nodal assessment, to increase the precision of the estimates. The causal relationship between BMI and PA may be bidirectional. This was represented by the two models, 1 and 2, with BMI as a hypothesized mediator (model 1) and BMI as a hypothesized confounder (model 2) [28]. We believe that high BMI is rather the cause of reduced PA than vice versa and hypothesized that DAG S2 (model 2) was the most "correct". Our primary results were therefore reported from logistic regression models 2.

To investigate whether the association between PA and LEL differed by BMI categories or musculoskeletal complaints, we added interaction terms to model 2 between the PA variables and BMI (≥30 versus <30) or musculoskeletal complaints (no versus yes), respectively.

All statistical tests were two-sided, and a *p* value below 0.05 was considered statistically significant. All statistical analyses were performed using IBM SPSS version 27 (IBM Corp., Armonk, NY).

3. Results

Among the 2155 invited survivors, 1226 (57 %) responded to the questionnaire. A total of 149 women were excluded due to self-reported LEL prior to surgery or missing answers to PAFID or LELSQ, leaving 1077 participants for primary analysis (Fig. 1). Compared to eligible non-participants, participants were younger and had a lower BMI at surgery, had a shorter time since surgery, and were more likely operated with the sentinel lymph node algorithm (Supplementary Table S2).

3.1. Participant characteristics

Mean age at survey was 70.7 (SD 9.2) years and median time since surgery 5.5 years (range, 0–16) (Table 1). A total of 89 % had FIGO 2009 stages I or II, 65 % did not receive any adjuvant treatment, 35 % had undergone pelvic node dissection, and 35 % followed the sentinel lymph node algorithm. The majority of women (69 %) reported overweight or obesity, 17 % a cardiovascular disease, 44 % hypertension, 15 % depression, and 59 % musculoskeletal complaints (Table 1). Forty-five percent of the participants met the PA guidelines. Women who met the PA guidelines had higher education, lower BMI, and fewer comorbidities compared to women who did not. They did not differ regarding cancer-related variables (Table 1).

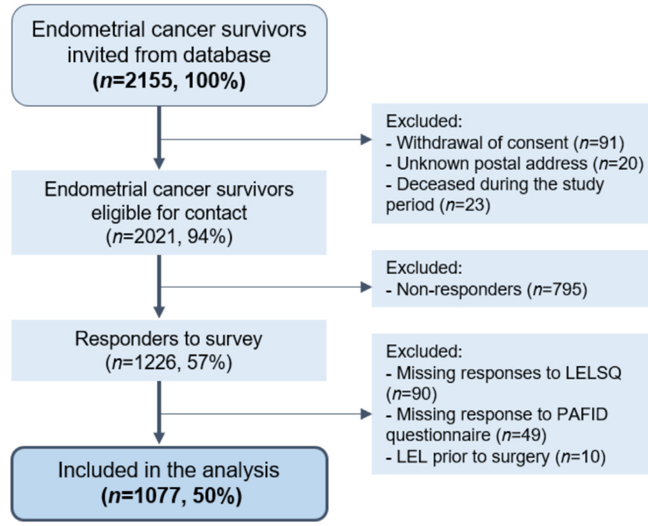

Fig. 1. Flowchart of inclusion.

3.2. Prevalence of LEL by PA exposures

Overall, 41 % reported LEL (Table 2). Women with LEL had a lower median level of PA compared to women without LEL (median 338 (range, 0–2025) MET-min/week versus 675 (range, 0–2700) MET-min/week) (Table 2). The prevalence of LEL was 32 % among women who met PA guidelines, compared to 48 % among those who did not. (Fig. 2). When participants were categorized into three groups, the prevalence of LEL was 48 %, 32 %, and 32 % among the low active, active, and high active survivors, respectively. Categorized into quartiles of PA volume, the prevalence of LEL decreased with higher PA volume up to quartile three (338–675 MET-min/week) (Fig. 2).

3.3. Association between level of PA and LEL

Unadjusted logistic regression analysis (model 0) showed that women who met the PA guidelines had 49 % lower odds of LEL (OR 0.51, 95 % CI 0.40–0.66) (global *p*-value <0.001) compared to those who did not (Table 3). Categorized into three groups, the active survivors had 50 % lower odds of LEL (OR 0.50, 95 % CI 0.38–0.67), and the high active survivors had 47 % lower odds of LEL (OR 0.53, 95 % CI 0.36–0.76) compared to the low active survivors (global p-value $p < 0.001$). Categorized into quartiles of PA volume, the odds of LEL were 57 % lower in quartile three (OR 0.43, 95 % CI 0.30–0.61) and 55 % lower in quartile four (OR 0.45, 95 % CI 0.31–0.65) compared to quartile one (global *p*-value <0.001). No differences were observed between PA volume quartile one and quartile two. Sensitivity analyses including survivors without lymph node dissection gave similar results (Supplementary Table S3).

Multivariable logistic regression analysis adjusted for age, education, time since surgery, adjuvant treatment, nodal assessment, and BMI (model 2) showed that women who met the PA guidelines had 37 % lower odds of LEL (OR 0.63, 95 % CI 0.48–0.83) compared to those who did not (global *p*-value <0.001). Categorized into three groups,

Table 1
Socio-demographic, cancer-related and health−/lifestyle characteristics, stratified by meeting physical activity guidelines.

Variables	Total sample	Meeting physical activity guidelines[a]	
		Yes	No
	$n = 1077$	$n = 487$ (45)	$n = 590$ (55)
Socio-demographic variables			
Age at survey, mean (SD)	70.7 (9.2)	69.4 (8.8)	71.9 (9.4)
Education level, *n* (%)			
Low (≤13 years)	546 (51)	201 (42)	345 (59)
High (>13 years)	516 (49)	279 (58)	237 (41)
Missing	15	7	8
Marital status, *n* (%)			
Living with a partner[b]	668 (63)	319 (66)	349 (61)
Not living with a partner	391 (37)	163 (34)	228 (40)
Missing	18	5	13
Cancer-related variables			
Time since surgery (years), median (min.-max.)	5.5 (0.2–16.1)	5.4 (0.2–16.1)	5.5 (0.2–16.1)
Time since surgery (years), *n* (%)			
<3 years	305 (28)	137 (28)	168 (29)
3–5.9 years	285 (27)	126 (27)	159 (27)
6–8.9 years	196 (18)	99 (20)	97 (16)
≥9 years	291 (27)	125 (27)	166 (28)
FIGO 2009 stage, *n* (%)			
I and II	958 (89)	435 (89)	523 (89)
III and IV	119 (11)	52 (11)	67 (11)
Adjuvant treatment, *n* (%)			
Yes, chemotherapy only	368 (34)	170 (35)	198 (34)
Yes, radiotherapy with or without chemotherapy	8 (<1)	4 (<1)	4 (<1)
No	693 (65)	310 (64)	383 (66)
Missing	8	3	5
Nodal assessment, *n* (%)			
LND	380 (35)	167 (34)	213 (36)
SLN	372 (35)	167 (34)	205 (35)
No nodal assessment	323 (30)	152 (31)	171 (29)
Missing	2	1	1
Total number of lymph nodes removed[c], median (min.-max.)	3 (0–84)	3 (0–66)	3 (0–84)
Health−/lifestyle variables			
BMI at survey, mean (SD)	28.1 (5.7)	26.7 (4.9)	29.2 (6.0)
BMI at survey, *n* (%)			
Underweight or normal weight (BMI <25)	329 (31)	196 (41)	133 (23)
Overweight (BMI 25–29.9)	387 (37)	176 (37)	211 (37)
Obese (BMI ≥30)	334 (32)	109 (23)	225 (40)
Missing	27	6	21
Smoking, *n* (%)			
Never	963 (92)	452 (95)	511 (90)
Sometimes	29 (3)	10 (27)	19 (3)
Daily	53 (5)	15 (3)	38 (7)
Missing	32	10	22
Comorbidities at survey[d], *n* (%) yes			
Cardiovascular disease[e]	175 (17)	61 (13)	114 (21)
Hypertension	450 (44)	163 (35)	287 (51)
Depression	142 (15)	54 (12)	88 (17)
Musculoskeletal complaints[f]	608 (59)	263 (56)	345 (62)

BMI: body mass index (kg/m^2); LND: Pelvic lymph node dissection; Max.: maximum; Min.: minimum; SD: standard deviation; SLN: Sentinel lymph node algorithm. Percentages may not add up to 100 % because of rounding.
Missing in the continuous variables: BMI: $n = 26$, number of lymph nodes removed: 7.
[a] At least 150 to 300 min of moderate-intensity activity or 75 to 150 min of vigorous-activity equivalent to approximately 500 to 1000 MET-min/week.
[b] Married or cohabitant.
[c] Including pelvic- and paraaortic lymph nodes.
[d] The numbers add up to more than 100 % because a person could have more than one comorbidity.
[e] Heart disease, DVT or pulmonary embolism.
[f] Osteoarthritis or degenerative arthritis, back pain or rheumatoid arthritis.

Table 2
Prevalence of lower extremity lymphedema for different physical activity exposures ($n = 1077$).

Variables	Total sample[a]	Lower extremity lymphedema[b]	
		Yes	No
	$n = 1077$	$n = 436$ (41 %)	$n = 641$ (60 %)
MET-min/week, median (min.-max.)	338 (0–2700)	338 (0–2025)	675 (0–2700)
Meeting PA guidelines[c], *n* (%)			
No	590 (55)	281 (48)	309 (52)
Yes	487 (45)	155 (32)	332 (68)
PA level (MET-min/week), *n* (%)			
Low active (<500)	590 (55)	281 (48)	309 (52)
Active (500–1000)	335 (31)	107 (32)	228 (68)
High active (>1000)	152 (14)	48 (32)	104 (68)
Quartile of PA volume (MET-min/week), *n* (%)			
Q1 (≤150)	278 (27)	144 (52)	134 (48)
Q2 (150,01-337,5)	294 (27)	130 (44)	164 (56)
Q3 (337,51–675)	276 (27)	89 (32)	187 (68)
Q4 (>675)	229 (21)	73 (32)	156 (68)

Max.: maximum; MET: metabolic equivalent of tasks; Min.: minimum; PA: physical activity.
Percentages may not add up to 100 % because of rounding.
[a] Column percent.
[b] Row percent.
[c] 150 to 300 min of moderate-intensity activity or 75 to 150 min of vigorous-activity equivalent to approximately 500 to 1000 MET-min/week.

the active survivors had 40 % lower odds of LEL (OR 0.60, 95 % CI 0.44–0.81), while the high active survivors had no statistically significant reduced odds of LEL (OR 0.71, 95 % CI 0.47–1.06) compared to the low active survivors (global p-value $p = 0.003$). Categorized into quartiles of PA volume, the odds of LEL were 45 % lower in quartile three (OR 0.55, 95 % CI 0.38–0.80) and 38 % lower in quartile four (OR 0.62, 95 % CI 0.42–0.94) compared to quartile one (global p-value = 0.006). No differences were observed between PA volume quartile one and quartile two. Sensitivity analyses including survivors without lymph node dissection gave similar results (Supplementary Table S3).

No statistically significant interaction was found between any of the PA exposure variables and BMI (all $p_{interaction} > 0.2$) or musculoskeletal complaints (all $p_{interaction} > 0.7$).

4. Discussion

In this large-scale population-based study, we found that the prevalence of LEL was lower with higher levels of PA among endometrial cancer survivors. Higher levels of PA were associated with lower odds of LEL, however, not in a linear dose-response way. A PA level according to the current PA guidelines seems to be sufficient to decrease the odds of LEL, and PA levels beyond that do not decrease the odds further.

Among survivors who met the PA guidelines, about a third reported LEL, compared to almost a half among survivors who did not meet the guidelines. These findings are in line with results from an American study among 213 endometrial cancer survivors, reporting a prevalence of LEL of 25 % among survivors who met the PA guidelines compared to 46 % among survivors who did not [18].

Our results also confirm previous studies demonstrating an association between higher levels of PA and lower odds of LEL among a gynecologic cancer population [18,19]. We observed a non-linear dose response association between PA and LEL, indicating that the intermediate PA level seems to be the most optimal PA level to reduce the odds of LEL in our sample. In contrast, Brown et al [18] observed lower odds of LEL among women with the highest level of PA, i.e., beyond PA guidelines, whereas non-significant results were found for all other PA levels.

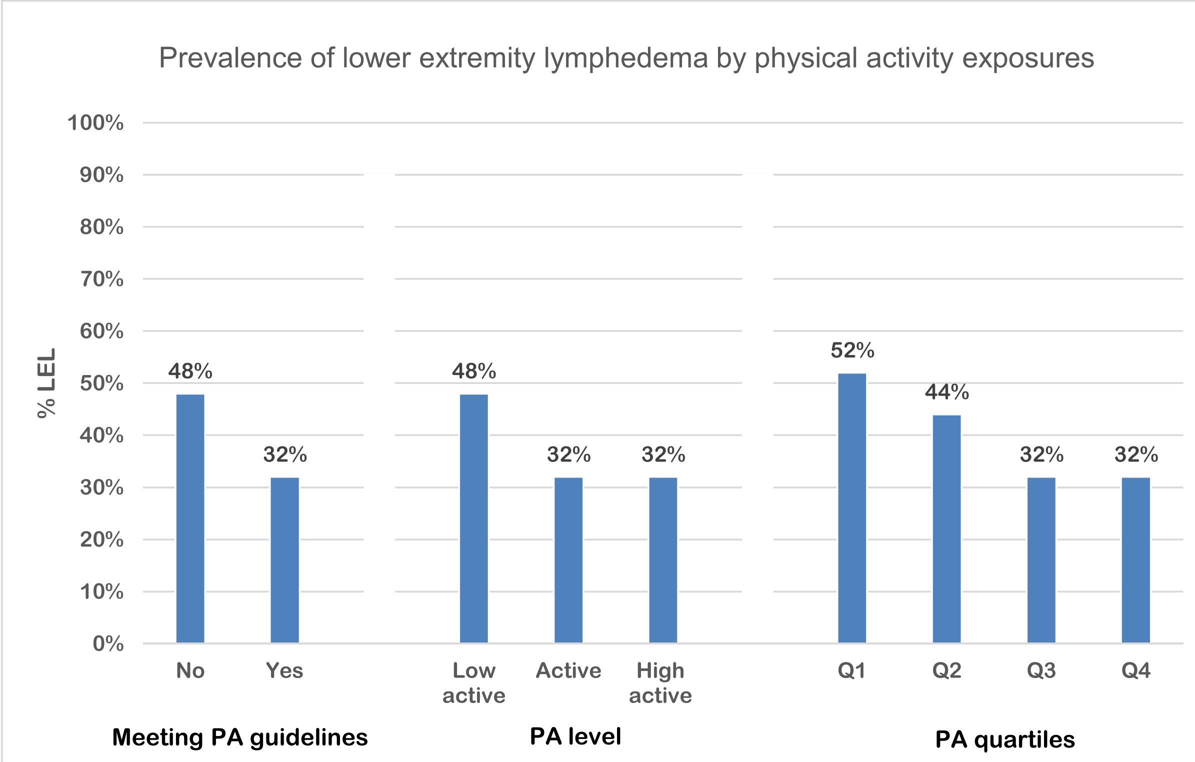

Fig. 2. Prevalence of lower extremity lymphedema by physical activity exposures. LEL: Lower extremity lymphedema; PA: physical activity.

We cannot rule out that the lack of a dose-response association in our study is caused by the small and potentially highly selected group of high active survivors in our study yielding a type II error or selection bias. However, one could speculate if there actually is no additional LEL risk reduction with a PA level beyond the PA guidelines of 150 to 300 min of moderate intensity PA per week. Worth nothing, a non-linear dose response pattern is also reported on other health outcomes from observational PA research generally [29]. Results from a meta-analysis showed that meeting the current PA guidelines showed the greatest risk reduction in all-cause mortality in the general population compared to a PA level above the target range of PA guidelines [30]. Considering that endometrial cancer survivors represent an older, typically overweight, or obese population with high levels of lifestyle-related comorbidities, we also believe that being highly active, beyond PA guidelines, is difficult for many of these women.

Our findings indicated that BMI was the only factor influencing the association between PA and LEL. When we adjusted for age, education, nodal assessment, adjuvant treatment, and time since surgery, there were minimal changes in the estimates compared to unadjusted estimates. However, when adjusting for BMI, the estimates became

Table 3
Logistic regression analysis of the association between physical activity exposures and lower extremity lymphedema, $n = 1027$.

PA exposures	n	Model 0[a]				Model 1[b]				Model 2[c]				$p_{interaction}$ BMI[d]	$p_{interaction}$ musculoskeletal complaints[e]
		OR	95 % CI		p	OR	95 % CI		p	OR	95 % CI		p		
			Lower	Upper			Lower	Upper			Lower	Upper			
Meeting PA guidelines[f]					<0.001				<0.001				<0.001	0.204	0.840
No	557	1.0				1.0				1.0					
Yes	470	0.51	0.40	0.66		0.52	0.40	0.68		0.63	0.48	0.83			
PA level (MET-min/week)					<0.001				<0.001				0.003	0.405	0.740
Low active (<500)	557	1.0				1.0				1.0					
Active (500–1000)	324	0.50	0.38	0.67		0.51	0.38	0.69		0.60	0.44	0.81			
High active (>1000)	146	0.53	0.36	0.78		0.53	0.36	0.79		0.71	0.47	1.06			
Quartiles of PA volume					<0.001				<0.001				0.006	0.295	0.847
Q1	256	1.0				1.0				1.0					
Q2	284	0.74	0.53	1.03		0.78	0.55	1.11		0.86	0.60	1.22			
Q3	268	0.43	0.30	0.61		0.46	0.32	0.66		0.55	0.38	0.80			
Q4	219	0.45	0.31	0.65		0.46	0.31	0.68		0.62	0.42	0.94			

CI: 95 % confidence interval; MET: metabolic equivalent of tasks; OR: odds ratio; PA: physical activity.
[a] Model 0: Unadjusted logistic regression of LEL (0 = no, 1 = yes) and different PA exposures.
[b] Model 1: Model 0 + adjusted for age, education, time since surgery, adjuvant treatment, and nodal assessment.
[c] Model 2: Model 1 + adjusted for BMI.
[d] BMI ≥30 vs BMI <30.
[e] Musculoskeletal complaints vs no musculoskeletal complaints (42 missing cases, $n = 985$).
[f] At least 150 to 300 min of moderate-intensity activity or 75 to 150 min of vigorous-activity equivalent to approximately 500 to 1000 MET-min/week.

consistently weaker. In fact, BMI accounts for approximately 10 % of the relationship between PA and LEL. This could mean that BMI is either a confounder of the PA–LEL association or a mediator between them (i.e., increased PA in endometrial cancer survivors leads to reduced body weight, which then reduces the risk of LEL). Since this is a cross-sectional study, we cannot determine which of the two scenarios is more "true" and the associations might also be bidirectional over time.

The main strength of this study is the large population-based sample, including 1077 endometrial cancer survivors from two different hospitals. The Sensor study had a satisfying response rate to the survey and used validated assessment methods for self-reported LEL and PA. However, recall bias or social desirability could impact self-reported data [31]. A limitation of the PAFID is the lack of questions regarding sedentary time and resistance training. Both sedentary time and resistance training might have independent effects on LEL, but as we lack data it is therefore unknown whether these behaviors may have influenced the results. The use of MET-min/week may also lead to misclassification of PA level and categorization of "meeting PA guidelines" as it relies on total volume estimates rather than time spent in moderate- or vigorous PA. Additionally, Trent et al [6] hypothesized that musculoskeletal complaints could mimic LEL in the self-reported LEL assessment form, LELSQ, due to overlapping symptoms. This could potentially lead to an overestimation of LEL and or PA in our sample. Device-based measures of PA and objective LEL assessments would strengthen the results in future studies.

We acknowledge that half of the potential eligible participants responded to the survey, and these were younger, had a lower BMI, had a shorter time since surgery, and were more often operated with the sentinel lymph node algorithm compared to eligible non-participants. Our results are therefore mainly representative of endometrial cancer survivors with these characteristics. In the validation study by Yost et al. the sensitivity of the LELSQ in detecting LEL was excellent for patients with normal weight and those who were obese (≥30 kg/m2). However, they did note that the specificity was lower for obese study participants than for those with BMI <30. The authors do conclude that that the LELSQ is a sensitive and specific tool for detecting clinically relevant LEL among women, including those with a body mass index of ≥30 kg/m2. Furthermore, we found no significant interaction between any of the PA variables and BMI on the association with LEL. This also supports the assumption that LEL was not assessed or reported differently by normal and overweight women.

PA before diagnosis might influence LEL. We recognize that the lack of pre-diagnosis PA levels is a limitation of our study. The cross-sectional design of the study does not allow determination of causal associations. It remains unclear whether PA decreases LEL or vice versa. However, regardless of the unknown true causal association, we believe that the clinical implications remain the same. If PA decreases LEL, our findings could lead to fewer cases of LEL. Conversely, if LEL decreases PA, women may miss out on the numerous health benefits associated with PA. Therefore, clinicians and health workers should promote PA among endometrial cancer survivors because of its known health benefits and potential to prevent LEL.

5. Conclusion

Being physically active according to the WHO PA guidelines was associated with decreased odds of self-reported LEL among endometrial cancer survivors. Our study contributes to the growing body of evidence suggesting that PA is a potentially modifiable preventative factor for cancer-related lymphedema beyond breast cancer populations. Recommending and promoting regular PA according to the current PA guidelines may be warranted to decrease the odds of LEL for endometrial cancer survivors; however, the causality of association needs to be verified in a longitudinal setting. We are currently collecting data in a prospective study to further explore this question.

Ethics statement

The Sensor study [20] was approved by the South East Regional Committee for Medical Research Ethics (no. 149597, 2020) and the Data Protection Officer (no 18/05099) at Oslo University Hospital. Informed consent was obtained according to institutional guidelines. Data were handled in accordance with ethical regulations.

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CRediT authorship contribution statement

Anette Engh: Conceptualization, Methodology, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Corina Silvia Rueegg:** Formal analysis, Methodology, Visualization, Writing – review & editing. **Pernille K. Bjerre Trent:** Data curation, Investigation, Resources, Writing – review & editing. **Linn Ø. Opheim:** Data curation, Writing – review & editing. **Ida Engeskaug:** Data curation, Writing – review & editing. **Nina Jebens Nordskar:** Data curation, Investigation, Resources, Writing – review & editing. **Arnhild Bakken:** Supervision, Writing – review & editing. **Jostein Steene-Johannessen:** Methodology, Writing – review & editing. **Ane Gerda Z. Eriksson:** Conceptualization, Investigation, Methodology, Project administration, Resources, Supervision, Writing – review & editing. **Lene Thorsen:** Conceptualization, Methodology, Supervision, Visualization, Writing – review & editing.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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During the preparation of this work the first author used ChatGPT and QuillBot in order to improve language and readability when preparing the manuscript. After using these tools, the first author reviewed and edited the content as needed and take full responsibility for the content of the publication.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ygyno.2025.03.009.

Data availability

The dataset analysed in the current study are from the Sensor study. The data are available upon reasonable request to the corresponding author.

References

[1] T.L. Sollberger, O. Gavrilyuk, C. Rylander, Excess body weight and incidence of type 1 and type 2 endometrial cancer: the Norwegian women and cancer study, Clin. Epidemiol. 12 (2020) 815–824, https://doi.org/10.2147/clep.S253866.

[2] E.J. Crosbie, S.J. Kitson, J.N. McAlpine, A. Mukhopadhyay, M.E. Powell, N. Singh, Endometrial cancer, Lancet 399 (10333) (Apr 9 2022) 1412–1428, https://doi.org/10.1016/s0140-6736(22)00323-3.

[3] H. Poort, B.H. de Rooij, H. Uno, et al., Patterns and predictors of cancer-related fatigue in ovarian and endometrial cancers: 1-year longitudinal study, Cancer 126 (15) (Aug 1 2020) 3526–3533, https://doi.org/10.1002/cncr.32927.

[4] H. Gao, M. Xiao, H. Bai, Z. Zhang, Sexual function and quality of life among patients with endometrial cancer after surgery, Int. J. Gynecol. Cancer 27 (3) (Mar 2017) 608–612, https://doi.org/10.1097/igc.0000000000000905.

[5] S. Sanjida, D. Kissane, S.M. McPhail, A. Obermair, M. Janda, Anxiety and depression in patients with early stage endometrial cancer: a longitudinal analysis from before surgery to 6-month post-surgery, J. Psychosoc. Oncol. Res. Pract. 1 (3) (2019), e13, https://doi.org/10.1097/or9.0000000000000013.

[6] P.K. Bjerre Trent, N.J. Nordskar, K.R. Wangen, et al., Self-reported lower extremity lymphedema and quality of life after surgical staging of endometrial carcinoma: a population based cross-sectional study, Gynecol. Oncol. 175 (2023) 72–80, https://doi.org/10.1016/j.ygyno.2023.05.070.

[7] The diagnosis and treatment of peripheral lymphedema: 2020 consensus document of the International Society of Lymphology, Lymphology 53 (1) (2020) 3–19.

[8] M.R. Fu, S.H. Ridner, S.H. Hu, B.R. Stewart, J.N. Cormier, J.M. Armer, Psychosocial impact of lymphedema: a systematic review of literature from 2004 to 2011, Psycho-Oncol. 22 (7) (2013) 1466–1484, https://doi.org/10.1002/pon.3201.

[9] S.G. Rockson, V. Keeley, S. Kilbreath, A. Szuba, A. Towers, Cancer-associated secondary lymphoedema, Nat. Rev. Dis. Primers 5 (1) (2019), https://doi.org/10.1038/s41572-019-0072-5.

[10] J.N. Cormier, R.L. Askew, K.S. Mungovan, Y. Xing, M.I. Ross, J.M. Armer, Lymphedema beyond breast cancer, Cancer 116 (22) (2010) 5138–5149, https://doi.org/10.1002/cncr.25458.

[11] A. Pigott, A. Obermair, M. Janda, et al., Incidence and risk factors for lower limb lymphedema associated with endometrial cancer: results from a prospective, longitudinal cohort study, Gynecol. Oncol. 158 (2) (2020) 375–381, https://doi.org/10.1016/j.ygyno.2020.04.702.

[12] V.L. Beesley, I.J. Rowlands, S.C. Hayes, et al., Incidence, risk factors and estimates of a woman's risk of developing secondary lower limb lymphedema and lymphedema-specific supportive care needs in women treated for endometrial cancer, Gynecol. Oncol. 136 (1) (2015) 87–93, https://doi.org/10.1016/j.ygyno.2014.11.006.

[13] M. Wedin, K. Stålberg, J. Marcickiewicz, et al., Incidence of lymphedema in the lower limbs and lymphocyst formation within one year of surgery for endometrial cancer: a prospective longitudinal multicenter study, Gynecol. Oncol. 159 (1) (2020) 201–208, https://doi.org/10.1016/j.ygyno.2020.07.014.

[14] M.M. Leitao, Q.C. Zhou, N.R. Gomez-Hidalgo, et al., Patient-reported outcomes after surgery for endometrial carcinoma: prevalence of lower-extremity lymphedema after sentinel lymph node mapping versus lymphadenectomy, Gynecol. Oncol. 156 (1) (2020) 147–153, https://doi.org/10.1016/j.ygyno.2019.11.003.

[15] Y.-f. Liu, J.-E. Liu, Y.W. Mak, et al., Prevalence and predictors of breast cancer-related arm lymphedema over a 10-year period in postoperative breast cancer patients: a cross-sectional study, Eur. J. Oncol. Nurs. 51 (2021), 101909, https://doi.org/10.1016/j.ejon.2021.101909.

[16] S.C. Hayes, B. Singh, H. Reul-Hirche, et al., The effect of exercise for the prevention and treatment of cancer-related lymphedema: a systematic review with meta-analysis, Med. Sci. Sports Exerc. 54 (8) (Aug 1 2022) 1389–1399, https://doi.org/10.1249/MSS.0000000000002918.

[17] F.T. Baumann, A. Reike, M. Hallek, J. Wiskemann, V. Reimer, Does exercise have a preventive effect on secondary lymphedema in breast cancer patients following local treatment - a systematic review, Breast Care 13 (5) (2018) 380–385, https://doi.org/10.1159/000487428.

[18] J.C. Brown, G.M. John, S. Segal, C.S. Chu, K.H. Schmitz, Physical activity and lower limb lymphedema among uterine cancer survivors, Med. Sci. Sports Exerc. 45 (11) (2013) 2091–2097, https://doi.org/10.1249/mss.0b013e318299afd4.

[19] S.C. Hayes, M. Janda, L.C. Ward, et al., Lymphedema following gynecological cancer: results from a prospective, longitudinal cohort study on prevalence, incidence and risk factors, Gynecol. Oncol. 146 (3) (Sep 2017) 623–629, https://doi.org/10.1016/j.ygyno.2017.06.004.

[20] The SENSOR Study. Oslo university Hospital, 2024 , Accessed 14.08.2024 https://www.ous-research.no/home/dgo/Studies/24654.

[21] EQUATOR-Network, Enhancing the Quality and Transparency of Health Research, the Centre for Statistics in Medicine (CSM), NDORMS, University of Oxford, 2024, https://www.equator-network.org/.

[22] K.J. Yost, A.L. Cheville, A.L. Weaver, M. Al Hilli, S.C. Dowdy, Development and validation of a self-report lower-extremity lymphedema screening questionnaire in women, Phys. Ther. 93 (5) (May 2013) 694–703, https://doi.org/10.2522/ptj.20120088.

[23] P. Bjerre Trent, R.S. Falk, A.C. Staff, D. Jorde, A.G. Eriksson, Translation and cross-cultural adaptation of the gynecologic cancer lymphedema questionnaire and the lower extremity lymphedema screening questionnaire, Int. J. Gynecol. Cancer 33 (2) (2023) 231–235, https://doi.org/10.1136/ijgc-2022-003979.

[24] E.H. Sagelv, L.A. Hopstock, J. Johansson, et al., Criterion validity of two physical activity and one sedentary time questionnaire against accelerometry in a large cohort of adults and older adults, BMJ Open Sport Exerc. Med. 6 (1) (2020), e000661, https://doi.org/10.1136/bmjsem-2019-000661.

[25] U.S. Department of Health and Human Services, Physical Activity Guidelines for Americans, 2nd edition, 2024. https://health.gov/paguidelines/second-edition/pdf/Physical_Activity_Guidelines_2nd_edition.pdf.

[26] O. Sangha, G. Stucki, M.H. Liang, A.H. Fossel, J.N. Katz, The self-administered comorbidity questionnaire: a new method to assess comorbidity for clinical and health services research, Arthritis Rheum. 49 (2) (Apr 15 2003) 156–163, https://doi.org/10.1002/art.10993.

[27] S. Pecorelli, Revised FIGO staging for carcinoma of the vulva, cervix, and endometrium, Int. J. Gynecol. Obstet. 105 (2) (2009) 103–104, https://doi.org/10.1016/j.ijgo.2009.02.012.

[28] C.S. Rueegg, Directed acyclic graphs to foster transparency and scientific dialogue, Lancet Oncol. 25 (6) (Jun 2024) 693–694, https://doi.org/10.1016/S1470-2045(24)00271-7.

[29] U. Ekelund, M.A. Sanchez-Lastra, K.E. Dalene, J. Tarp, Dose-response associations, physical activity intensity and mortality risk: a narrative review, J. Sport Health Sci. 13 (1) (Jan 2024) 24–29, https://doi.org/10.1016/j.jshs.2023.09.006.

[30] L. Garcia, M. Pearce, A. Abbas, et al., Non-occupational physical activity and risk of cardiovascular disease, cancer and mortality outcomes: a dose-response meta-analysis of large prospective studies, Br. J. Sports Med. 57 (15) (Aug 2023) 979–989, https://doi.org/10.1136/bjsports-2022-105669.

[31] J.M. Warren, U. Ekelund, H. Besson, A. Mezzani, N. Geladas, L. Vanhees, Assessment of physical activity – a review of methodologies with reference to epidemiological research: a report of the exercise physiology section of the European Association of Cardiovascular Prevention and Rehabilitation, Eur. J. Cardiovasc. Prev. Rehabil. 17 (2) (2010) 127–139, https://doi.org/10.1097/hjr.0b013e32832ed875.