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Reduced pain thresholds and signs of sensitization in women with persistent pelvic pain and suspected endometriosis

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ABSTRACT

Introduction: Endometriosis is a gynecological disorder that may cause considerable pelvic pain in women of fertile age. Determining pain mechanisms is necessary in order to optimize the treatment of the disease. The objective of the study was to evaluate pain thresholds in women with persistent pelvic pain with and without confirmed endometriosis, and healthy, unaffected controls, and analyze how pain thresholds in these cohorts related to duration of pelvic pain, quality of life, and symptoms of anxiety and depression. **Material and methods:** Pain thresholds for heat, cold, and pressure were assessed with quantitative sensory testing on six locations on a reference group of 55 healthy women and on 37 women with persistent pelvic pain who had been admitted for diagnostic laparoscopy on the suspicion of endometriosis. Validated instruments were applied to assess quality of life and symptoms of anxiety and depression. Data were analyzed by means of uni- and multivariate analysis of variance and Spearman's rank-order correlation. **Results:** The women with persistent pelvic pain had significantly lower pain thresholds compared with the reference women. No differences were observed in pain thresholds between the women with pain, with (13 women) and without (24 women) biopsy-proven endometriosis. The duration of pelvic pain correlated significantly positively to reduced pain thresholds i.e. the longer the duration, the more sensitization. In the persistent pelvic pain group, pain thresholds for heat correlated significantly with the Short Form Health Survey 36 (SF-36) dimension of bodily pain, while thresholds for cold correlated with SF-36 bodily pain and with symptoms of depression. **Conclusion:** Our results showed widespread alterations in pain thresholds in women with persistent pelvic pain that are indicative of central sensitization and a time-dependent correlation. Women with pelvic pain and suspicion of endometriosis should probably be treated more thoroughly in order to prevent or at least minimize the concomitant development of central sensitization.

Keywords

persistent pelvic pain, endometriosis, pain thresholds, quantitative sensory testing, sensitization, health-related quality of life, chronic pain

Abbreviations

CS	central sensitization
HADS	Hospital Anxiety and Depression Scale
PPP	persistent pelvic pain
QoL	quality of life
R	Spearman's rho
SF-36	Short Form Health Survey 36

Key Message

Women with persistent pelvic pain and symptoms indicating endometriosis show significantly reduced pain thresholds compared with healthy women, which is indicative of central sensitization.

INTRODUCTION

Endometriosis is an estrogen-dependent disease associated with persistent pelvic pain (PPP) [1,2]. The precise mechanisms of endometriosis-associated pelvic pain remain poorly understood but a combination of nociceptive, inflammatory, angiogenetic, neurovascular and neuropathic mechanisms seems to be involved [3]. The pain often reduces quality of life (QoL) and is associated with reduced physical and mental wellbeing [4–7].

Persons with persistent pain states often show widespread reduced pain thresholds, which are considered as proxies for central sensitization (CS). CS is defined in animal models as dorsal horn neurons that give hyperactive responses to various sensory inputs. The dorsal horns cannot be examined in the same way in humans. Therefore, widespread reduced pain thresholds to a given stimulus are used as a proxy [8]. A few studies have indicated that women with endometriosis-associated pain might have widespread reduced pain thresholds and CS [9–13], but more research on the subject is warranted to determine the pain mechanisms in order to optimize the treatment of the disease.

Previous studies of chronic pain have shown that the history and duration of pain are crucial factors for driving sensitization [8] but so far, this has not been addressed for patients with PPP.

The objective of this study was to evaluate pain thresholds in women with PPP with and without confirmed endometriosis, and healthy, unaffected women, and analyze how pain thresholds in these cohorts related to duration of pelvic pain, QoL, and symptoms of anxiety and depression.

MATERIAL AND METHODS

We conducted this cross-sectional observational comparative exploratory study between December 2013 and June 2016. Eligible for the study were women 18-40 years of age who had PPP and had been admitted to the Department of Obstetrics and Gynecology at a central hospital and a university hospital in southeast Sweden for diagnostic laparoscopy on suspicion of endometriosis. PPP was defined as self-reported moderate or severe pelvic pain for a period of four months or longer [14].

Exclusion criteria were a previously surgically verified diagnosis of endometriosis or by history any other diagnosed chronic pain syndrome such as fibromyalgia, chronic headache, arthritis or other joint problems, nerve damages or rhizopathia, mental illness with anti-depressive medication or mental disability, and on-going substance abuse. Pregnant or breast-feeding women were also excluded, as were women who did not speak or understand Swedish.

The administrative nurse in charge of the waiting list for surgery in the departments assessed all referral letters. Forty-six women fulfilled the criteria and were found eligible to participate. They were contacted by phone by the first author, who provided them with detailed verbal and written information about the study. Of these women, 40 agreed to participate, but three did not come to the scheduled appointment, leaving 37 participants. Written informed consent was obtained from all participants before inclusion. During and after the laparoscopy the women with PPP were treated surgically and/or pharmaceutically with hormonal therapies and/or analgesics in accordance with the clinical routines. The extent of the endometriosis was categorized according to the revised American Society for Reproductive Medicine score in minimal, mild, moderate and severe [15].

A group of 55 healthy women aged 18 – 40 years without a history of pelvic pain or other symptoms that might indicate endometriosis, or any other chronic pain syndrome served as a reference group. The women in the reference group were recruited through local advertisements at the hospitals and the university affiliated to the clinics. None of these women used any medication that could have any known effect on pain thresholds, but some of them used hormonal contraceptives. In an attempt to minimize the influence of menstrual cycle variability on the pain thresholds, the experimental sessions were conducted between days 1-7 of the cycle in women who were not using hormonal contraceptives [16,17].

Data concerning demographics and medical and surgical history, including current medication, were collected at inclusion in the study. Pain thresholds for cold, heat and pressure were measured within four weeks prior to the planned surgery. The participants were asked to refrain from analgesics before the pain threshold measurements on the day of assessment.

At the visit for the pain threshold measurements, all participants completed three questionnaires; two assessing QoL and one assessing symptoms of depression and anxiety. The perceived QoL was measured with two generic and widely used questionnaires, the Short Form-36 (SF-36) [18] and the EuroQoL-5 Dimension Questionnaire [19]. The Hospital Anxiety and Depression Scale (HADS) [20] was used to detect self-rated symptoms of anxiety and depression. Higher scores indicated better QoL or more symptoms of depression or anxiety. The three questionnaires have been validated in a Swedish context [21–23].

Sensitization was detected by quantitative sensory testing. This is a sensitive and formalized psychophysical test that quantifies the perception of pain by measuring the pain thresholds from many different body locations (in and outside painful areas). Thermal stimuli for heat and cold are usually combined with pressure stimuli [24].

The pain thresholds were measured on six locations on the body: a) the medial plane of the low back just below the fifth lumbar vertebra, b) the abdominal wall, seven cm lateral to the umbilicus on both sides, c) just above the symphysis pubis, five cm lateral to the midline on both sides, and d) on the dominant leg, four cm distally from the tuberositas tibiae (Figure 1). The sites a), b) and c) were assessed as the presumed referral areas of menstrual pain [16,25], and the site d) as the non-pain referral control area.

Pain thresholds for heat and cold were measured using quantitative sensory testing with a Medoc TSA II NeuroSensory Analyzer (Medoc Ltd., Ramat Yishai, Israel). From a baseline of 32°C a computer-controlled thermode with a surface area of 3x3 cm^2 was increased (maximum 50°C) or decreased (minimum 0°C) with a rate changing between 0.3°C/s and

4.0°C/s. On detection of the first painful stimulus, the participants mouse-clicked to stop the stimulation. The temperature of the thermode was registered by the computer as the threshold for heat or cold. The thermode then returned to the baseline temperature of 32°C. Three repeat measurements were performed on each location with an interval of 10 seconds. The average temperature of the three measurements of each stimuli was used in the calculations [24].

For measuring pain pressure thresholds a hand-held electronic algometer (Sometic AB, Hornby, Sweden) with a probe area of 1 cm^2 was used. The pressure was applied at a constant rate of approximately 40 kPa/s. The women were instructed to verbally indicate when the perceived sensation changed from pressure to pain, by saying "stop". The measurement was repeated three times on each location with a 10-second pause between the measurements. The average of the three measurements was calculated and referred to as the pressure pain threshold [24]. Eventually, the mean value for each modality (heat, cold and pressure) was calculated as the average of all locations and used in the analyses.

The testing order of the three stimuli and the order of the locations on the body were altered randomly among the participants, but pain thresholds for cold were always determined before thresholds for heat, due to a pre-setting in the computer program. The measurements were performed by the first author and three female research nurses experienced in quantitative sensory testing.

Statistical analyses

Statistical analyses were conducted with the software Statistica v 13.1 (Dell Software, Aliso Viejo, CA, USA). Nominal data are presented as number and percentage. Continuous variables are described as mean, standard deviation and range.

Comparisons of demographic data between the groups were made by univariate ANOVA and Bonferroni post hoc test for continuous variables and with a Chi-square test or Fisher's exact test for categorical data. The level of statistical significance was set at $p < 0.05$.

Crude differences between pain thresholds in the different groups were measured with a univariate ANOVA and a Bonferroni post hoc test. In order to adjust for known or potential confounding factors, a multivariate ANOVA was conducted, with age and smoking habits simultaneously added to the model as confounders. The Bonferroni post hoc tests were used to analyze the pairwise associations between groups.

Spearman's rank-order correlation was used to measure the strength and direction of the assumed monotonic relationships between the means of pain thresholds for each stimulus (heat, cold and pressure), duration of pelvic pain, and the QoL regarding the specific subscales bodily pain and mental health in the SF-36, and level of anxiety and depression in the HADS, respectively. The Spearman's rho (R) and the *p*-value, are presented. A positive R indicates a positive correlation and a negative R indicates a negative correlation.

Ethical approval

The study was approved by the Regional Ethics Board of Linköping University (Dnr 2013/19-3).

RESULTS

A total of 92 women completed the study: 37 women with PPP and 55 healthy women in the reference group. Thirteen of the women with PPP were diagnosed (biopsy-proven) with endometriosis. The demographic and clinical characteristics of the participants are presented in Table 1. The women with PPP were significantly younger than the reference women were and had a lower parity but were more often smokers.

The outcomes of the measurements of the pain thresholds are shown in Table 2. The thresholds are depicted for each location. The mean thresholds of all locations are illustrated in Figure 2. The women with PPP had significantly lower pain thresholds on all anatomical locations including the reference location (TT4D, dominant leg) for the three stimuli compared to the reference group. The post hoc tests showed unanimously that all women with PPP had highly significantly deviating pain thresholds compared with those of the reference group. No significant differences were observed in pain thresholds between the women who received a biopsy-proven endometriosis diagnosis (13 women) and those without endometriosis (24 women) in any of the locations or stimuli modalities. These results remained even when adjustments were made for the confounders of age and smoking habits, as shown by the adjusted *p*-values (Table 2).

The correlations between the mean pain thresholds and the duration of pelvic pain were examined in the entire study group. The correlations were statistically significant for all three measured modalities of pain thresholds. ($R = -0.28$, $p = 0.006$ for heat, $R = 0.27$, $p = 0.009$ for cold, and $R = -0.34$, $p<0.001$ for pressure, respectively).

The women with PPP rated their QoL significantly lower than the reference women in all dimensions of SF-36 and EuroQoL-5 Dimension Questionnaire, and scored significantly higher than the reference women for symptoms of anxiety and depression according to HADS (Table 3). Generally, no significant differences were found in any of the scales between the two subgroups of women with PPP (Table 3).

The correlations between pain thresholds and the outcomes of QoL and HADS forms used the mean value for each pain stimulus modality. Among all the women with PPP, both heat and cold pain thresholds but not pressure thresholds were significantly correlated with the SF-36 dimension covering bodily pain (R = 0.45, p = 0.011 for heat, R = -0.56, p = 0.001 for cold and R = 0.34, p = 0.059 for pressure, respectively). None of three pain stimuli modalities was significantly correlated with the SF-36 subscale mental health (data not shown). Only the cold pain threshold was also significantly correlated with the HADS subscale symptoms of depression (R=0.35, p=0.037).

In the reference group, no significant correlations were found between any of the three stimuli modalities and the SF-36 subscales bodily pain or mental health or HADS (data not shown).

DISCUSSION

This study showed widespread alterations in pain thresholds in the women with PPP and symptoms of endometriosis, which is indicative of CS. The women with PPP had significantly lower pain thresholds for heat, cold and pressure compared with the reference group of healthy women. However, there were no statistically significant differences in pain thresholds between the women with pain who had a confirmed diagnosis of endometriosis and those where no endometriosis was found, which highlights the effect of pain and not endometriosis *per se* in the development of this persistent pain state. The correlation analyses showed 1) that the duration of pelvic pain was associated with pain thresholds, and 2) the more pain the women experienced (SF-36 domain bodily pain), the more sensitive they were to cold and heat.

Prolonged noxious physical or pathological stimuli in animal models leads to CS in which the central nervous system amplifies the perception of pain [8]. Clinical signs as a proxy for CS can be measured by a general, widespread lowering of pain thresholds, as observed in the present study. Meanwhile, reduced pain thresholds in the painful area but not at the control site could also be due to peripheral sensitization. In endometriosis, the ectopic lesions

send noxious signals that are also consolidated by the inflammatory factors activated around the lesions [26]. Stratton et al. showed that women with any history of endometriosis (past or present) had a higher proportion of sensitization compared with women with PPP only, and pain-free controls [9]. Nonetheless, in accordance with Laursen et al. [13], our findings suggest that the reduced pain thresholds were not related to the presence of visible endometriosis lesions, but to the state of persistent pain. Thus, our findings support the "pain-focused" hypothesis where the persistent pain *per se* rather than the endometriosis contributes to the development of CS.

The study revealed statistically significant correlations between the duration of pelvic pain and the pain thresholds, and thereby confirmed previous studies on other groups of chronic pain patients [8]. To the best of our knowledge, this is the first study to show this correlation in women with pelvic pain. Our results thus support the previous suggestions that pain duration is a crucial factor in the development of sensitization [27].

There are some limitations to this study. The cross-sectional design prevented us from determining whether the reduced pain thresholds were a cause or a consequence of the pain experience. The duration of pelvic pain was a subjective variable and may have been inaccurately remembered by the women, which constitutes a risk for recall bias. Since the referred area related to pelvic pain involves both the lower back and the abdominal wall, the points were selected bilaterally for assessing referred pain somatic hyperalgesia. Only one point outside those regions was selected for assessing the generalized CS.

Four examiners conducted the quantitative sensory testing and might have informed the participants slightly differently or performed the pain pressure testing in different ways. The examiners were not blinded to group belonging (women with pelvic pain or controls), which might constitute a risk of expectation bias. Because of the equality in pain thresholds between the women with PPP and the relatively low number of individuals in the subgroups (endometriosis and no endometriosis), we decided to analyze them as one group in the correlation analyses.

Since the effect size in pain thresholds was unknown and the study has an exploratory character, we did not conduct an a priori power analysis but based our sample size on the scanty materials that have been presented in the literature for similar groups of patients [10,11,13]. The generalizability of the results may be limited due to the relatively small sample size. Interpretation should therefore be carried out with caution. Nevertheless, the results

contribute new information covering the combination of the three pain stimuli modalities and the unanimous outcomes in results of pain thresholds in women with PPP and suspicion of endometriosis.

In clinical praxis, alleviating pain is the major goal in the medical and surgical therapies of endometriosis for several reasons. The consequence of persistent pain in the development of CS emphasizes that endometriosis and symptoms indicating endometriosis might benefit from being treated actively and perhaps more aggressively from the beginning when the woman seek medical care. This might, in accordance with our findings of a time-dependent association between duration of pain and reduced pain thresholds, prevent or at least minimize the development of a state that may cause severe human suffering and reduced QoL. A comprehensive schedule for investigation and treatment with a multi-disciplinary approach should be followed. If the traditional treatment for suspected endometriosis does not soon alleviate the symptoms, the diagnosis should be re-considered, and invasive diagnostic tools should be employed to verify the diagnosis. The treatment should then be focused on both the specific disease and proper management of the pain condition. The "disease-focused" vs. the "pain-focused" mechanisms behind the consequences of endometriosis pain have been described previously but need further illumination [4,5,12].

CONCLUSION

Women with PPP, with or without proven endometriosis, showed similar widespread alterations in pain thresholds with significantly reduced pain thresholds compared with a reference group of healthy women. These findings suggest that CS may be a general feature in women with PPP and it seems unrelated to the presence of endometriosis *per se*, but the duration (although assessed in a cross-sectional design) of the pain state might be a driving force in the development of sensitization.

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Legends to Figures

Figure 1. The six locations on the body where the quantitative sensory testing was performed. a) the medial plane of the low back just below the fifth lumbar vertebra, b) the abdominal wall seven cm lateral to the umbilicus on both sides, c) just above the symphysis pubis, five cm lateral to the midline on both sides, and d) on the dominant leg, four cm distally from the tuberositas tibiae.

Figure 2. Mean heat, cold and pressure pain thresholds. A= PPP and endometriosis; B = PPP and no endometriosis; C= control. PPP = persistent pelvic pain. Plots indicate mean pain thresholds and bars present 95% confidence interval. * adjusted for age and smoking habits.

Table 1. Demographic and clinical characteristics of women with persistent pelvic pain with or without a biopsy-proven endometriosis diagnosis and of healthy reference women.

	Women with persistent pelvic pain and:		**Reference group of healthy women**		**Post hoc tests**		
Variable	biopsy-proven endometriosis (Group A; n=13)	no endometriosis (Group B; n=24)	(Group C; n=55)	*p*-value	A vs. B *p*-value	A vs. C *p*-value	B vs. C *p*-value
Age (years)	26.2±6.4;19-40	26.6±5.7;18-39	30.2±5.6;18-40	0.010[a]	>0.999[b]	0.073[b]	0.034[b]
Parity (no. of deliveries)	0.4±0.96;0-3	0.4±0.82;0-3	1.1±1.2;0-5	0.005[a]	>0.999[b]	0.074[b]	0.013[b]
BMI (kg/m^2)	25.1±5.8;17.8-33.4	24.2±4.2;19.0-31.9	24.2±3.8;18.4-34.6	0.844[a]			
Currently smoking (no. of women)	4 (30.8)	5 (20.8)	2 (3.6)	0.008[c]	0.691[d]	0.010[d]	0.024[d]
Current use of type of contraception (no. of women)							
None	8 (61.5)	9 (37.5)	21 (38.2)	0.164[c]			
Combined oestrogen/progestin	1 (7.7)	10 (41.6)	14 (25.5)				
Progestin only	4 (30.8)	5 (20.8)	20 (36.4)				
Current use of analgesics (no. of women)							
None	8 (61.5)	12 (50.0)					
Paracetamol	1 (7.7)	2 (8.3)					
NSAID and paracetamol	0 (0.0)	4 (16.7)					
NSAID	2 (15.4)	4 (16.7)					
Mild opioids and paracetamol	0 (0)	1 (4.2)					
Opioids	2 (15.4)	1 (4.2)					
rASRM classification of endometriosis (no. of women)							
Minimal	8 (61.5)						
Mild	1 (7.7)						

Moderate	3 (23.1)				
Severe	1 (7.7)				
Duration of pelvic pain (months)	56.6.±48.2;6-144	47.4±43.1;4-162	--	0.556[a]	

Figures denote mean and ±SD; range, or number of women and (%). BMI – body mass index. NSAID – non-steroidal anti-inflammatory drugs. rASRM - revised American Society for Reproductive Medicine. [a]ANOVA; [b]Bonferroni, [c]χ^2 test for trends. [d]Fischers exact test

Table 2. Pain thresholds for heat (°C), cold (°C), and pressure (kPa) in women with persistent pelvic pain with or without a biopsy-proven endometriosis diagnosis and in healthy reference women.

HEAT (°C)	**Women with persistent pelvic pain and:**		**Reference group of healthy women**		**ANOVA**	**Bonferroni post hoc test**		
Location	biopsy-proven endometriosis (Group A; n=13)	no endometriosis (Group B; n=24)	(Group C; n=55)		*p*-value	A vs. B *p*-value	A vs. C *p*-value	B vs. C *p*-value
L5	43.6±4.2	43.6±4.5	47.2±2.7	Crude	<0.001	>0.999	0.003	<0.001
				Adjusted [a]	<0.001	>0.999	0.002	<0.001
Abd U7R	45.1±4.0	43.9±3.9	47.8±2.1	Crude	<0.001	0.803	0.012	<0.001
				Adjusted [a]	<0.001	0.814	0.013	<0.001
Abd U7L	44.0±4.6	43.5±4.2	47.6±2.3	Crude	<0.001	>0.999	0.002	<0.001
				Adjusted [a]	<0.001	>0.999	0.002	<0.001
ASP5R	44.6.0±4.1	43.6±3.9	47.5±2.4	Crude	<0.001	>0.999	0.009	<0.001
				Adjusted [a]	<0.001	>0.999	0.010	<0.001
ASP5L	43.9±4.7	43.3±4.3	47.5±2.4	Crude	<0.001	>0.999	0.002	<0.001
				Adjusted [a]	<0.001	>0.999	0.002	<0.001
TT4D	44.7±4.5	44.4±3.4	47.6±2.2	Crude	<0.001	>0.999	0.005	<0.001
				Adjusted [a]	<0.001	>0.999	0.005	<0.001

Table 2 *continued*.

COLD (°C)	Women with persistent pelvic pain and:		Reference group of healthy women		ANOVA	Bonferroni post hoc test		
Location	biopsy-proven endometriosis (Group A; n=13)	no endometriosis (Group B; n=24)	(Group C; n=55)		*p*-value	A vs. B *p*-value	A vs. C *p*-value	B vs. C *p*-value
L5	12.1±10.3	14.3±11.6	3.8±7.7	Crude	<0.001	>0.999	0.014	<0.001
				Adjusted [a]	<0.001	>0.999	0.013	<0.001
Abd U7R	12.3±9.9	10.5±9.4	3.0±6.3	Crude	<0.001	>0.999	0.001	<0.001
				Adjusted [a]	<0.001	>0.999	0.001	<0.001
Abd U7L	13.5±10.3	13.6±10.1	3.8±7.2	Crude	<0.001	>0.999	0.001	<0.001
				Adjusted [a]	<0.001	>0.999	0.001	<0.001
ASP5R	15.9±10.4	15.9±11.0	6.4±9.1	Crude	<0.001	>0.999	0.007	<0.001
				Adjusted [a]	<0.001	>0.999	0.007	<0.001
ASP5L	15.6±10.0	16.9±10.6	4.9±8.3	Crude	<0.001	>0.999	0.001	<0.001
				Adjusted [a]	<0.001	>0.999	0.001	<0.001
TT4D	6.8±9.6	8.4±9.6	1.4±4.1	Crude	<0.001	>0.999	0.035	<0.001
				Adjusted [a]	<0.001	>0.999	0.033	<0.001

Table 2 *continued*.

PRESSURE (kPa)	Women with persistent pelvic pain and:		Reference group of healthy women		ANOVA	Bonferroni post hoc test		
Location	biopsy-proven endometriosis (Group A; n=13)	no endometriosis (Group B; n=24)	(Group C; n=55)		*p*-value	A vs. B *p*-value	A vs. C *p*-value	B vs. C *p*-value
L5	524.7±318.5.	498.1±318.5	815.0±334.2	Crude	<0.001	>0.999	0.014	<0.001
				Adjusted [a]	0.001	>0.999	0.016	<0.001
Abd U7R	237.4±85.6	255.2±167.1	435.8±179.5	Crude	<0.001	>0.999	0.001	<0.001
				Adjusted [a]	<0.001	>0.999	0.001	<0.001
Abd U7L	250.3±106.7	231.7±134.9	439.8±184.6	Crude	<0.001	>0.999	0.001	<0.001
				Adjusted [a]	<0.001	>0.999	0.001	<0.001
ASP5R	228.9±80.1	202.8±104.2	403.3±138.8	Crude	<0.001	>0.999	<0.001	<0.001
				Adjusted [a]	<0.001	>0.999	<0.001	<0.001
ASP5L	233.4±84.2	210.3±114.3	389.9±135.5	Crude	<0.001	>0.999	<0.001	<0.001
				Adjusted [a]	<0.001	>0.999	0.001	<0.001
TT4D	610.5±300.1	476.1±195.3	809.0±271.1	Crude	<0.001	0.402	0.043	<0.001
				Adjusted [a]	<0.001	0.409	0.045	<0.001

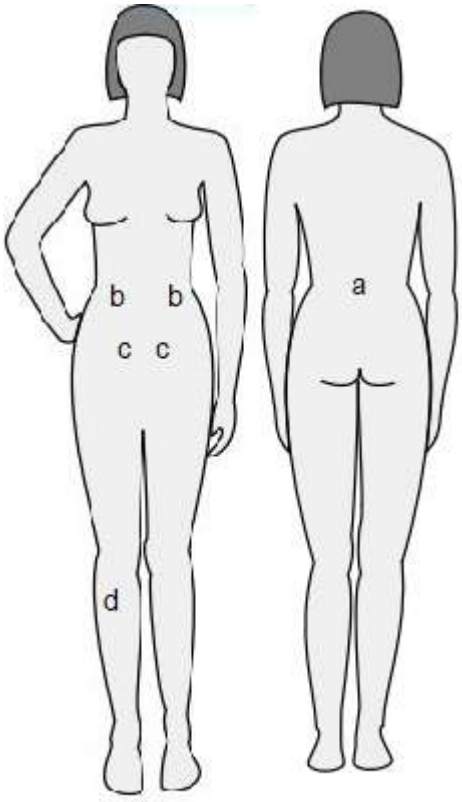
Figures denote means ± one standard deviation. [a] Adjusted for age and smoking.

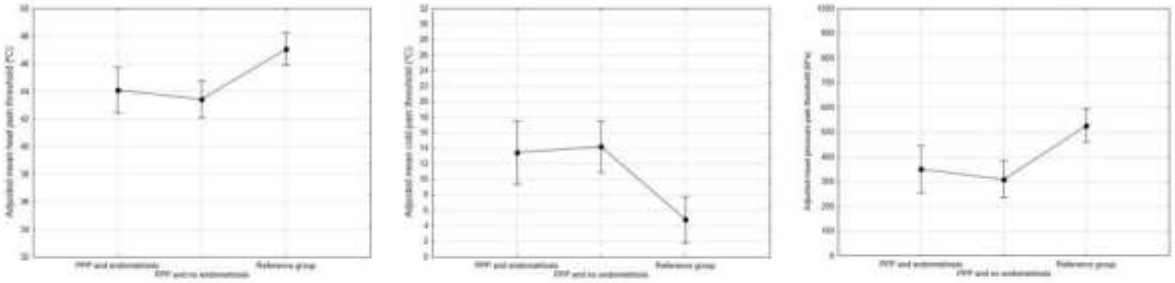
Location: L5 – back, over L5; Abd U7R – abdominal wall, 7 cm right of umbilicus; Abd U7L – abdominal wall, 7 cm left of umbilicus; ASP5R – above symphysis pubis, 5 cm right of midline; ASP5L – above symphysis pubis, 5 cm left of midline; TT4D – 4 cm distal of tuberositas tibiae of dominant leg.

Table 3. Outcome of quality of life (SF-36, EQ-5D-3L) and anxiety and depression (HADS) in women with persistent pelvic pain with or without a biopsy-proven endometriosis diagnosis and in healthy reference women.

		Women with persistent pelvic pain and:		Reference group of healthy women	ANOVA	Bonferroni post hoc test		
Form/subscale		biopsy-proven endometriosis (Group A; n=13)	no endometriosis (Group B; n=24)	(Group C; n=55)	*p*-value	A vs. B *p*-value	A vs. C *p*-value	B vs. C *p*-value
SF-36	Physical functioning	78.1±26.8	78.3±21.0	98.9±3.5	<0.001	>0.999	<0.001	<0.001
	Role limitation physical	28.9±26.7	25.0±35.4	98.6±5.7	<0.001	>0.999	<0.001	<0.001
	Bodily pain	33.1±13.6	41.4±20.9	85.3±18.6	<0.001	0.651	<0.001	<0.001
	General health	42.5±25.5	42.1±20.0	83.7±14.7	<0.001	>0.999	<0.001	<0.001
	Vitality	28.5±22.1	33.1±23.7	65.7±17.6	<0.001	>0.999	<0.001	<0.001
	Social functioning	52.9±22.3	40.3±20.4	92.6±13.7	<0.001	0.135	<0.001	<0.001
	Role limitation emotional	35.9±44.0	42.0±44.0	93.8±19.5	<0.001	>0.999	<0.001	<0.001
	Mental health	45.5±22.1	40.9±18.4	81.0±13.9	<0.001	>0.999	<0.001	<0.001
	Physical component summary	39.4±7.7	41.2±9.3	55.5±3.6	<0.001	>0.999	<0.001	<0.001
	Mental component summary	29.4±13.1	26.3±11.4	48.8±8.7	<0.001	>0.999	<0.001	<0.001
EQ-5D-3L	Health state index	0.49±0.32	0.46±0.32	0.95±0.11	<0.001	>0.999	<0.001	<0.001
HADS	Anxiety	9.4±5.4	10.1±3.7	4.6±3.4	<0.001	>0.999	<0.001	<0.001
	Depression	8.1±4.6	7.7±4.2	2.3±2.4	<0.001	>0.999	<0.001	<0.001

Figures denote means ± one standard deviation.
SF-36, Short Form Health Survey 36; EQ-5D-3L, EuroQoL-5 Dimension Questionnaire; HADS – Hospital Anxiety and Depression Scale.





		ANOVA	Bonferroni post hoc test		
			A vs. B	A vs. C	B vs. C
		p-value	*p*-value	*p*-value	*p*-value
Mean heat (°C)	Crude	<0.001	>0.999	0.001	<0.001
	Adjusted*	<0.001	>0.999	0.001	<0.001
Mean cold (°C)	Crude	<0.001	>0.999	<0.001	<0.001
	Adjusted*	<0.001	>0.999	<0.001	<0.001
Mean pressure (kPa)	Crude	<0.001	>0.999	<0.001	<0.001
	Adjusted*	<0.001	>0.999	<0.001	<0.001

Figure 2. Mean heat, cold and pressure pain thresholds. A= PPP and endometriosis; B = PPP and no endometriosis; C= control. PPP = persistent pelvic pain. Plots indicate mean pain thresholds and bars present 95% confidence interval. * adjusted for age and smoking habits.