

RESEARCH

Open Access



Chronic cough in postmenopausal women and its associations to climacteric symptoms

Volker Ziller^{1,2*}, Thea Sophie Oppermann^{1,2}, Werner Cassel³, Olaf Hildebrandt³, Rolf F. Kroidl⁴ and Ulrich Koehler³

Abstract

Background Postmenopausal women often have chronic cough. Hormonal changes might be affecting lung function and the mucous membrane of the airways, causing hypersensitivity of the cough reflex. Therefore, postmenopausal hormonal changes could play a key role in the association between increased cough and menopause. The aim of this study is to evaluate the relation of chronic cough and postmenopausal symptoms.

Methods We performed a questionnaire-based cohort study in generally healthy postmenopausal women (age 45–65 years). Women with cough explained by a pre-existing diagnosis were excluded. Comorbidities, medication and baseline data were collected. The Menopause Rating Scale II (MRS II) was combined with the Leicester Cough Questionnaire. Groups were divided in chronic cough versus non-coughing participants, chronic cough was defined as symptoms over 8 weeks. We performed correlations and logistic regression for predicting cough based on postmenopausal symptoms.

Results Sixty-six of 200 women (33%) reported symptoms of chronic cough over 8 weeks. No significant differences in baseline data (age, BMI, onset of menopause, years since menopause, concomitant diseases, and medication) were found between coughing and non-coughing women. The MRS II showed higher menopausal symptoms in patients with cough, with significant differences in 2 of the 3 MRS-domains (urogenital ($p < 0.001$) and somato-vegetative ($p < 0.001$)). Climacteric symptoms correlated strongly with parameters of cough ($p < 0.001$). On the basis of the MRS total score ($p < 0.001$) and the somato-vegetative and urogenital domains ($p < 0.05$), the prediction for respiratory complaints could be shown.

Discussion Chronic cough was significantly associated with menopausal symptoms. Therefore chronic cough as a possible climacteric symptom and its underlying mechanisms should be further explored.

Keywords Chronic cough, Menopause, Menopause Rating Scale (MRS), Leicester Cough Questionnaire (LCQ)

*Correspondence:

Volker Ziller
vhz1974@gmail.com

¹ Clinic for Gynecology and Obstetrics, Department of Endocrinology, Reproductive Medicine and Osteology, University Hospital Gießen and Marburg, Philipps-University of Marburg, Baldingerstrasse 1, 35043 Marburg, Germany

² University Hospital Gießen and Marburg, 35043 Marburg, Germany

³ Clinic for Internal Medicine, SP Pneumology, Intensive Care and Sleep Medicine, University Hospital Gießen and Marburg, Philipps-University of Marburg, 35043 Marburg, Germany

⁴ Lung Center Stade, Frommholdstrasse 71, 21680 Stade, Germany

Background

Chronic cough in adults is defined by its persistence for at least 8 weeks [1–4]. Chronic cough is associated with a significant impairment of physical performance and quality of life [5–11]. In a relevant number of patients, etiology of chronic cough remains unclear despite extensive diagnostics. The cough receptors' hypersensitivity seem to be an underlying factor. Middle-aged women who complain of chronic cough are suspected



© The Author(s) 2023. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit <http://creativecommons.org/licenses/by/4.0/>. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

to have a causal relationship between coughing irritation and post-menopausal changes [2, 12–15].

Menopause is a complex phenomenon. The cessation of the ovarian activity and the subsequent lack of sex steroids, especially estrogen and progesterone, results in substantial changes in the female body that are generally summarized as "climacteric syndrome." Typically, among other symptoms, this includes hot flushes, sweats and vaginal atrophy, as well as muscle and joint complaints [16–19]. The changes in skin, connective tissue and mucous membranes from the lack of estrogen could also manifest in the respiratory tract. As estrogen deficiency leads to atrophy of vaginal epithelia, reduction or modification in mucus, ciliae or changes in sensitivity in respiratory tissue could cause a reduction in lung function and lead to chronic cough [20–26]. If postmenopausal estrogen deficiency plays a part in the development of cough the extend of climacteric symptoms should be correlated to symptoms of cough.

It was therefore the aim of this study to investigate the relationship between postmenopausal symptoms and chronic cough.

Methods

We performed a questionnaire-based cohort study in postmenopausal women recruited within the outpatient consultation at the University Hospital Marburg, Germany. The women visited the gynecological department for numerous medical reasons, but the majority took part in routine checkups or menopausal counseling including bone densitometry (in our hospital performed by the department of gynecological endocrinology). Participants between the ages of 45 and 65 were offered participation, although the last menstruation had to be at least one year ago.

We excluded women with irregular bleeding, smokers, history of any recent sex steroid treatment, including Menopause Hormone Therapy (MHT) or any differential diagnosis that might be connected to chronic cough (e.g. cancer, chronic bronchitis, gastro-esophageal reflux, chronic heart failure, therapy with ace-inhibitors).

Study procedures

After written informed consent, specified inclusion and exclusion criteria, as well as the differential diagnoses for chronic cough, were queried and documented. When all criteria for participation were met, the severity of menopausal symptoms and the severity of cough were measured using the Menopause Rating Scale II and the Leicester Cough Questionnaire LCQ [27, 28].

Definition of chronic cough

Chronic cough was defined as any cough that persisted for at least eight weeks [3, 29, 30]. The subjects had to give a time indication of the duration of their cough, if it was present.

If this duration was reported over 8 weeks or longer, we classified them as coughing subjects. There was no minimum level of symptoms, because minor complaints in the context of coughing should also be recorded.

Menopause Rating Scale II (MRS II)

The MRS II is a simple, flexible, and quickly implementable tool for evaluating postmenopausal symptoms [28, 31]. The 11 symptoms are given on a 5-point Likert scale (0=no complaints to 4=very severe complaints) [32]. The total score can range from 0 (asymptomatic) to 44 (highest level of complaints). A low scale value correlates with a higher quality of life.³¹ Within the MRS II, 3 subgroups can be distinguished. The "somato-vegetative" subgroup suffers increasingly from sleep disorders, heart problems, hot flushes and joint/muscle problems (items 1, 2, 3, and 11 with 0–16 possible points). The "uro-genital" type focuses on complaints of the urinary tract, vagina and sexuality (items 8, 9, and 10 with 0–12 possible points). The "mental" subgroup include exhaustion, irritability, anxiety and mood (items 4, 5, 6, and 7 with 0–16 possible points) [31]. To calculate the total score for the 3 subscales, the degrees of severity of the associated items are added. To calculate the total number of points, subscale values are combined.

Leicester Cough Questionnaire (LCQ)

The LCQ consists of 19 items that cover a physical (8 items), mental (7 items), and social (4 items) domains. The physical condition of the patient is inquired through items 1, 2, 3, 9, 10, 11, 14, and 15 and refers to symptoms that can be associated with cough, including abdominal/chest pain, the production of sputum, fatigue, sleep disorders, hoarseness and changed performance. In addition, certain situations that trigger the cough are recorded. Items 4, 5, 6, 12, 13, 16, and 17 deal with mental aspects: the ability to control the cough reflex and the emotions associated with the symptoms (fears, embarrassment, discouragement, frustration, and worry) play a role in the question selection. Social effects are covered by questions 7, 8, 18, and 19. In this case, the influence of cough symptoms on everyday situations, relationships with family members and on enjoyment of life is asked [27].

The 3 domains are evenly distributed across the entire questionnaire. Scores are calculated as a mean of each

domain and the total score is calculated by adding every domain score [27].

Statistics

To distinguish a correlation of $r \geq 0.2$ with sufficient test strength (0.8) from $r = 0$, an inclusion of $n = 200$ patients was planned. The statistical evaluation was carried out with IBM SPSS Statistics Version 22 (IBM GmbH). Due to the high number of cases of $n = 200$, parametric test methods were used for descriptive and inferential statistical analyzes. All variables were checked for normal distribution, skewness, and kurtosis. If there was a significant deviation from a normal distribution with very high skew values (> 2), then after visually inspecting the distribution, these parameters were either reverted to non-parametric evaluation methods or the variables were transformed, thus making an approximate normal distribution for the transformed variables. After defining two cohorts (cough versus non-cough) groups were analyzed by comparisons of means. Correlation analysis and logistic regression were applied to the whole cohort.

Ethics

The study was conducted in accordance to the guidelines and with approval of the local ethics committee of the Philipps-University of Marburg.

Results

There were 205 subjects interviewed and included after positive prescreening between July 6th, 2017 and October 18th, 2019. Five test subjects had to be excluded due to differential diagnoses afterwards. Finally, 200 women were included in the analysis.

Of the 200, 66 (33%) patients had symptoms of chronic cough over the last eight weeks. They were compared to the 134 (67%) that had none. There was no statistical difference between the two groups concerning their baseline datap (Table 1).

The mean age of the patients in both groups was 57.2 years. They did not differ significantly in terms of weight, height, time since menopause, number of previous illnesses and co-medication. The frequencies of the comorbidities hypothyroidism, osteoporosis, osteopenia and having a hysterectomy did not differ significantly according to the Fisher`s exact test ($p > 0.05$).

The age at the beginning of cough was estimated at 52.6 years on average. The coughing prevailed on average for 4.7 years. In comparison, the subjects entered menopause at 49.14 years on average and the cough started at 52.6 years on average (Table 2).

MRS results

Table 3 and 4 list the individual results of the MRS II comparing the 2 cohorts. In in all three domains of the MRS there were statistically significant differences

Table 1 Baseline characteristics

n = 200	With cough (n = 66)		Without cough (n = 134)		t-test, p-value	95% CI
	Mean values	Standard deviation	Mean values	Standard deviation		
Age (years)	57.18	3.56	57.17	3.91	0.99	- 1.12; 1.14
Weight (kg)	70.38	13.83	67.82	12.23	0.19	- 1.08; 1.10
Height (cm)	165.5	6.10	165.74	6.19	0.80	- 2.07; 1.59
Bmi (kg/m ²)	25.63	4.44	24.65	4.03	0.12	- 0.26; 2.21
Years since menopause	8.05	5.60	8.15	6.27	0.91	- 1.90; 1.70
Number of diseases	1.23	0.97	1.01	1.00	0.16	- 0.08; 0.51
Number of medications	1.10	1.45	0.79	0.99	0.09	- 0.05; 0.65

Table 2 Ages and years since onset of menopause and cough symptoms (n = 66)

N = 66	Years since menopause	Years onset of cough	Age onset of menopause (years)	Age onset of cough (years)
Mean value	8.05	4.74	49.14	52.60
Standard deviation	5.60	4.50	4.85	5.17
Minimum	1	0.15	36	36
Maximum	24	20	57	61

in MRS scores between the subjects with versus without cough. A significant difference in mean MRS value among women in the cough group compared to women in the no-cough group was found in the following

symptoms: heart discomfort, sleep problems, physical/mental exhaustion, sexual problems, vaginal dryness and joint/muscle complaints (Table 3).

Table 3 comparison of mean values and t-test of single MRS items (n = 66 with cough, n = 134 without cough)

MRS items	Mean values with coughing (n = 66)	Mean values without coughing (n = 134)	Difference	t-test p-value
(1) Hot flushes, sweating	1.39	1.19	0.2	0.192
(2) Heart discomfort	0.88	0.51	0.37	0.007
(3) Sleep problems	1.92	1.34	0.58	0.001
(4) Depressive mood	0.85	0.66	0.19	0.164
(5) Irritability	0.86	0.80	0.06	0.640
(6) Anxiety	0.76	0.51	0.25	0.054
(7) Physical/mental exhaustion	1.30	0.91	0.39	0.007
(8) Sexual problems	1.32	0.82	0.5	0.002
(9) Bladder problems	0.70	0.46	0.24	0.053
(10) Vaginal dryness	1.58	1.13	0.45	0.009
(11) Joint/muscular discomfort	1.58	1.17	0.41	0.031

Table 4 Mean values and t-test of total score and MRS domains (n = 66 with cough, n = 134 without cough)

MRS	Mean values with cough (n = 66)	Mean values without cough (n = 134)	Difference	t-test p-value
MRS total score	13.14	9.51	3.63	<0.001
MRS somato-veg. (items 1, 2, 3, 11)	5.77	4.22	1.55	<0.001
MRS urogenital (items 8, 9, 10)	3.59	2.42	1.17	<0.001
MRS mental (items 4, 5, 6, 7)	3.77	2.87	0.9	0.036

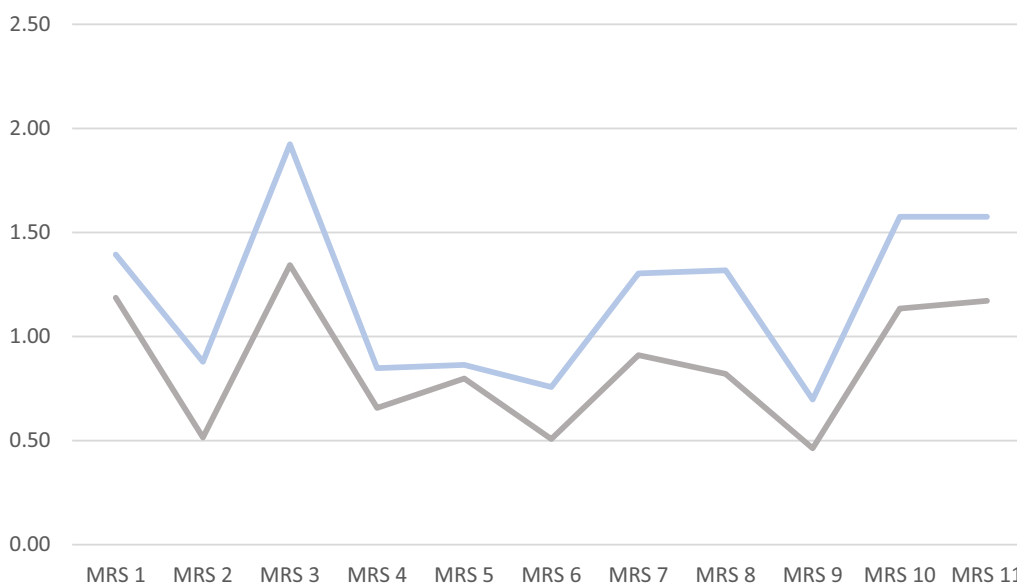


Fig. 1 comparison of mean values of single MRS items (n = 66 with cough (blue), n = 134 without cough (gray)) (graphic program: MS Office)

Figure 1 shows the mean value comparison of the individual MRS items in both groups.

LCQ results

The LCQ score was 17.81 in the subjects with a chronic cough and 20.79 in the subjects without cough ($p < 0.001$). We compared the mean values of the subscale values for the LCQ domains (physically, socially, and mentally). Comparing the subjects with cough versus no cough resulted in a score of 5.78 versus 6.80 ($p < 0.001$), 5.88 versus 6.99 ($p < 0.001$) and 6.16 versus 7.0 ($p < 0.001$), respectively (Table 5).

The results of the individual LCQ-items in comparison of the two groups are shown in Fig. 2 and Table 6 ($p < 0.001$).

Correlation MRS and LCQ

A correlation analysis of the MRS scale versus the LCQ scale was applied to the whole cohort. Results are presented in Table 7. There is a negative correlation of -0.428 between the total LCQ and MRS scores. After controlling for age, BMI and years since menopause, the result remains significant (-0.429). Correlating the overall MRS score with the three LCQ domains results in a negative correlation from -0.336 to -0.481. In particular, the LCQ domain for the physical symptoms of cough correlates negatively with the entire postmenopausal symptoms. As expected LCQ total score correlates very high with the mental, physical and social dimension of cough. A high correlation between the MRS total score and the three MRS-D domains could be shown.

Table 5 Mean values and t-test of total score and LCQ domains

LCQ	Mean values with coughing (SD) (n = 66)	Mean values without coughing (SD) (n = 134)	t-test p-value
LCQ total score	17.81 (2.35)	20.79 (0.24)	<0.001
LCQ physical	5.78 (0.22)	6.80 (0.79)	<0.001
LCQ mental	6.16 (0.80)	7.00 (0.00)	<0.001
LCQ social (items 7, 8, 18, 19)	5.88 (0.93)	6.99 (0.05)	<0.001

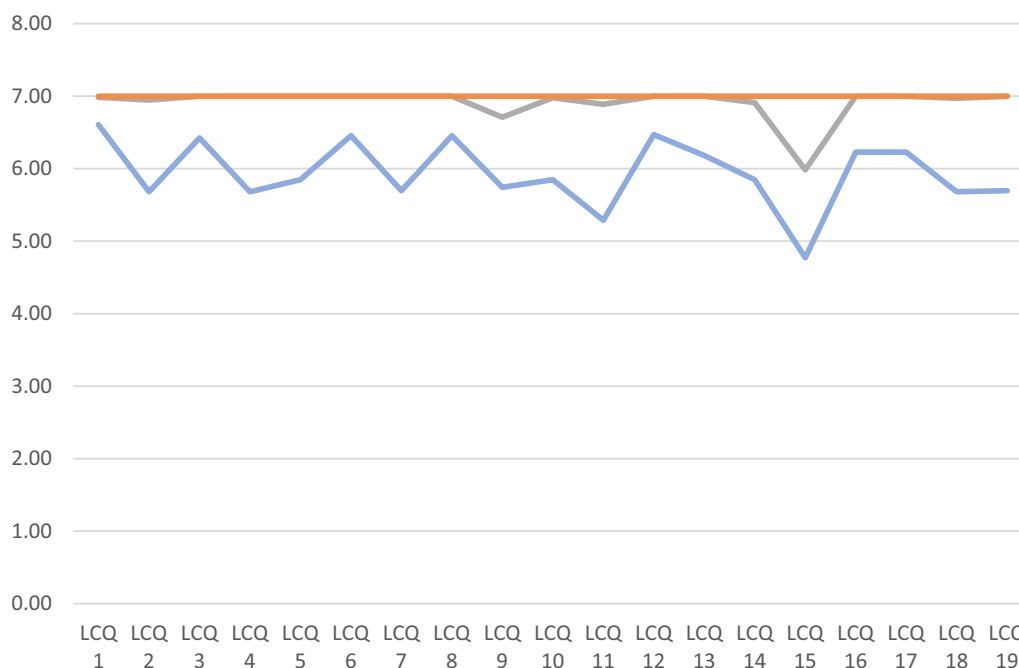


Fig. 2 comparison of mean values of single LCQ items. (n = 66 with cough (blue), n = 134 without cough (gray), possible points (orange)) (graphic program: MS Office)

Table 6 Mean values and t-test of single LCQ items

n = 200	Mean values with cough (n = 66)	Mean values without cough (n = 134)	Diff	t-test p-value
(1) Chest/abdominal pain	6.61	6.99	0.38	< 0.001
(2) Sputum production	5.68	6.95	1.27	< 0.001
(3) Fatigue	6.42	7.00	0.58	< 0.001
(4) Cough control	5.68	7.00	1.32	< 0.001
(5) Inconvenience	5.85	7.00	1.15	< 0.001
(6) Anxiety	6.45	7.00	0.55	< 0.001
(7) Disturbing factor for oneself	5.70	7.00	1.30	< 0.001
(8) Mood impairment	6.45	7.00	0.55	< 0.001
(9) Trigger paint, fumes	5.74	6.71	0.97	< 0.001
(10) Sleep problems	5.85	6.98	1.13	< 0.001
(11) Coughing fits	5.29	6.89	1.60	< 0.001
(12) Discouragement	6.47	7.00	0.53	< 0.001
(13) Annoyance	6.18	7.00	0.82	< 0.001
(14) Hoarseness	5.86	6.91	1.05	< 0.001
(15) Energy, drive	4.77	5.99	1.22	< 0.001
(16) Worry about illness	6.23	7.00	0.77	< 0.001
(17) Fear of condemnation	6.23	7.00	0.77	< 0.001
(18) Interruption of conversation	5.68	6.97	1.29	< 0.001
(19) Disruptive factor for others	5.70	7.00	1.30	< 0.001

Table 7 Correlations of the results of MRS and LCQ (n = 200)

N = 200	LCQ total score	MRS total score	LCQ social	LCQ mental	LCQ physical	MRS somato-vegetative	MRS uro-genital	MRS mental
LCQ total score	1							
MRS total score	-0.428	1						
LCQ social	0.953	-0.336	1					
LCQ mental	0.959	-0.367	0.928	1				
LCQ physical	0.955	-0.481	0.848	0.846	1			
MRS somato-vegetative	-0.382	0.841	-0.296	-0.323	-0.436	1		
MRS urogenital	-0.365	0.734	-0.294	-0.322	-0.399	0.431	1	
MRS mental	-0.299	0.844	-0.233	-0.254	-0.339	0.558	0.449	1

Table 8 Coefficient table of the logistic regression to predict cough based on the MRS total score and the MRS domains (n = 200)

n = 200	rc	p-value	Odds ratio	95% CI
MRS total score	0.09	< 0.001	1.091	1.040–1.144
MRS somato-vegetative (items 1, 2, 3, 11)	0.15	0.024	1.164	1.020–1.328
MRS urogenital (items 8, 9, 10)	0.18	0.025	1.195	1.023–1.396
MRS mental (items 4, 5, 6, 7)	0.04	0.600	0.965	0.844–1.103

Rc Regression coefficient; CI Confidence interval

Logistic regression

A logistic regression to predict cough based on the presence of postmenopausal symptoms was performed. At the level of the individual items, no significant predictive value for chronic cough could be recorded. However, on the basis of the MRS total score and the individual domains, highly significant results with regard to the total score ($p < 0.001$) and significant results with regard to the somatovegetative and urogenital domains ($p < 0.05$) remained (Table 8).

Discussion

Although a variety of diseases can be linked to chronic cough, it is becoming increasingly clear that the majority of adult patients who have chronic cough as their main complaint present a common clinical picture [4, 33]. They often complain about a pronounced sensitivity when breathing in environmental irritants such as perfume, bleach or cold air that cause a tickling/irritable sensation in the skin, sore throat and coughing. Features that indicated increased sensitivity of neural pathways mediating the cough [34]. In addition, there is a unique epidemiology: two-thirds of patients are female and the highest prevalence in the fifties and sixties [35]. The main finding of this study is a strong association between cough and climacteric symptoms in postmenopausal women. The women in this study were a generally healthy cohort who mostly visited the outpatient department for preventive or prophylactic exams, as well as for menopausal complaints. Of the 200 postmenopausal women, 33% reported cough over at least 8 weeks, regarding LCQ-scores symptoms were rather mild but differed significantly from non-coughing women. When comparing these to 'women not presenting with chronic cough', they did not differ in baseline characteristics such as age, weight, number of diseases or years since onset of menopause (Table 1). In the affected women, the cough started an average of 3.5 years after entering menopause, in no case coughing preceded menopause.

Chronic cough was clearly associated with an increase of menopausal symptoms and especially in regard to the subscales of the MRS II that mirror urogenital and somato-vegetative symptoms (Table 3, Fig. 1, Table 4). In addition, the results of the MRS and LCQ correlated with one another (Table 7). Furthermore, a significant prediction for chronic cough based on two somatic MRS domains and the total score could be shown (Table 8). These results contribute well to the biologically plausible theory that changes in the skin and mucous membranes can also show up in the respiratory tract, can change the sensitivity of the cough receptors and thus lead to increased cough sensitivity. The skin and mucous membranes represent an organ that can be influenced by

hormonal changes. Decreasing estrogen level influence skin's glycosaminoglycan content and promote tendency to create wrinkles, dryness, atrophy and poor wound healing [30, 36]. The collagen content of the skin is significantly reduced by 1–2% per year after menopause [37]. Some of these changes might also affect the respiratory system. While some research was published these possible connections have not yet been in the clinical focus of either pulmonologists or gynecologists. Furthermore, lung function is strongly influenced by the female cycle and menopause [20, 26].

Chronic refractory cough is a multifactorial symptom that can be the consequence of several pulmonary and extrapulmonary diseases including gastroesophageal reflux, upper airway cough syndrome, obstructive sleep apnea, and medications such as ACE inhibitors [7, 8, 10, 38, 39]. However, in a number of patients the genesis of chronic cough remains unclear, despite extensive diagnostics. Then it is defined as chronic cough of unclear etiology or a chronic idiopathic cough (CIC). The clinical complaints of CIC, sometimes persisting for years, are a dry and excruciating cough, the urge to clear the throat and dysphagia [1, 2]. To define chronic cough solely on duration falls probably too short in clinical practice. While recent guidelines still use an 8 week basis definition, as it was done in the present study, inclusion criteria for novel treatments would e.g. demand chronic treatment refractory cough for more than a year.

While some patients suffer from daily cough others show remittent and relapsing course. Using a time based definition was probably appropriate for this analysis as it served the purpose of separating symptomatic women from the healthy [40].

According to recent literature, idiopathic cough occurs in up to 20–42% of cases of chronic cough and can be triggered by weak subclinical triggers such as gastric acid, thermal stimuli, or passive smoking [41]. In most cases, chronic idiopathic cough is difficult to treat as it does not respond to classic therapeutic options. Most patients treated in a cough clinic are not only female, but also postmenopausal [1, 15]. Due to the reaction to subclinical triggers, the clinical picture of chronic idiopathic cough is causally associated with cough hypersensitivity syndrome, which defines a disturbance in the sensory nerve function. The concept of hypersensitivity is described as a valid and clinically useful concept and can be seen as a neuropathy of the cough reflex [29, 35]. Accordingly, the cough receptors' increased sensitivity and the changed central cough modulations lead to hyperreactivity of the cough reflex [30, 36, 42]. In postmenopausal women, the chronic cough stimulus may be due to the cough receptors' increased sensitivity and/or a changed central cough modulation as well as changes in gastroesophageal reflux

disease, laryngeal dysfunction or inflammation regulation [2, 12–15, 42]. However, according to the definition, no CIC can be assigned to the patients in this study, as they did not go through the necessary diagnostics.

The highly significant correlation of postmenopausal symptoms, especially the somato-vegetative subgroup and vaginal dryness and coughing, underline these assumptions and emphasize the need to further expand the complexity of the climacteric syndrome. MRS differences of 10–40% pre and post hormonal treatment on the score levels were described. Dinger and Heinemann suggested a statistical significant difference of at least 4 score points to be a reasonable goal for a direct head to head comparison of two medical treatments in menopause hormonal treatment. As not treatments but just coughing versus non coughing were compared in this study and subjects presented a difference of 3.63 ($p < 0.001$) between groups, this appears clinically relevant. Chronic (idiopathic) cough might be, in part, due to the lack of steroids in postmenopausal women and could be diagnosed and treated differently in the future. Further studies are needed to clarify the connections, the underlying pathomechanisms, and the effects of hormonal replacement therapy on the bronchopulmonary symptoms [35].

A limitation of this study is that it is a simple interview and questionnaire-based study with no additional information on individual findings such as mucus parameters, X-rays etc. On the other hand, a strength is that a reasonable and well-selected representative number of patients were involved. Also, the groups appeared to be well-balanced to baseline characteristics, the effects shown are statistically substantiated and the questionnaires that were used are validated and established tools to measure the aimed effects. At first glance a rate of 33% of rather healthy postmenopausal women that report coughing might seem high and was a surprising finding. On the other hand, existing cough was mainly defined by the time aspect of 8 weeks and majority of women reported rather mild symptoms. The LCQ values are lower in patients with COPD and chronically productive cough [43].

Therefore postmenopausal women might not be aware of their symptoms or connect them to their postmenopausal changes.

In addition, there is disagreement about the exact prevalence of chronic cough [44, 45].

Conclusion

In conclusion, the results of our study demonstrate a clinically relevant, statistically significant relationship between climacteric symptoms and postmenopausal cough, along with a significantly reduced quality of life in women with postmenopausal chronic cough. These

associations should raise awareness, regarding this previously unknown climacteric symptom serve as basis for further evaluation and should add another facet to the climacteric syndrome.

Abbreviations

BMI	Body mass index
MRS	Menopause Rating Scale
LCQ	Leicester Cough Questionnaire
CIC	Chronic idiopathic cough
COPD	Chronic obstructive pulmonary disease

Acknowledgements

We would like to thank all subjects who agreed to take part in this study.

Author contributions

VZ: project development, data collection and management, Data analysis, Manuscript writing/editing. TSO: project development, data collection and management, Data analysis, Manuscript writing/editing. WC: project development, Data analysis, Manuscript editing. OH: project development Manuscript editing. RK: project development Manuscript editing. UK: project development, Manuscript writing/editing. All authors read and approved the final manuscript.

Funding

Open Access funding enabled and organized by Projekt DEAL.

Availability of data and material

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

Declarations

Ethics approval and consent to participate

The study was conducted in accordance to the guidelines and with approval of the local ethics committee of the Philipps-University of Marburg. This confirms that all methods were carried out in accordance with the relevant guidelines and regulations. It is hereby confirmed that all test protocols have been confirmed by the named ethics committee. After detailed explanation of the purpose of the study, informed consent to participate in the study was obtained from all subjects. The declaration of consent was obtained in writing.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 30 October 2021 Accepted: 13 February 2023

Published online: 08 March 2023

References

- Kardos P, Berck H, Fuchs KH, et al. Guidelines of the German Respiratory Society for diagnosis and treatment of adults suffering from acute or chronic cough. *Pneumologie*. 2010;64:701–11.
- Kardos P. Chronic idiopathic cough. *Dtsch Med Wochenschr*. 2017;142:197–200.
- Koehler U, Hildebrandt O, Walliczek U, et al. Chronic cough: New diagnostic options? *Dtsch Med Wochenschr*. 2017;142:47–53.
- Morice AH, Jakes AD, Faruqi S, et al. A worldwide survey of chronic cough: a manifestation of enhanced somatosensory response. *Eur Respir J*. 2014;44:1149–55.
- Brignall K, Jayaraman B, Birring SS. Quality of life and psychosocial aspects of cough. *Lung*. 2008;186:55–8.

6. Dicipinigaitis PV, Tso R, Banauch G. Prevalence of depressive symptoms among patients with chronic cough. *Chest*. 2006;130:1839–43.
7. Chan KKY, Ing AJ, Laks L, et al. Chronic cough in patients with sleep-disordered breathing. *Eur Respir J*. 2010;35:368–72.
8. Decalmer S, Stovold R, Houghton LA, et al. Chronic cough: relationship between microaspiration, gastroesophageal reflux, and cough frequency. *Chest*. 2012;142:958–64.
9. Dicipinigaitis PV. Angiotensin-converting enzyme inhibitor-induced cough: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129:169–73.
10. Emilsson ÖI, Bengtsson A, Franklin KA, et al. Nocturnal gastroesophageal reflux, asthma and symptoms of OSA: a longitudinal, general population study. *Eur Respir J*. 2013;41:1347–54.
11. Palombini BC, Villanova CAC, Araujo E, et al. A pathogenetic triad in chronic cough: asthma, postnasal drip syndrome, and gastroesophageal reflux disease. *Chest*. 1999;116:279–84.
12. Dicipinigaitis PV, Rauf K. The influence of gender on cough reflex sensitivity. *Chest*. 1998;113:1319–21.
13. Fujimura M, Kasahara K, Kamio Y, et al. Female gender as a determinant of cough threshold to inhaled capsaicin. *Eur Respir J*. 1996;9:1624–6.
14. Kelsall A, Decalmer S, McGuinness K, et al. Sex differences and predictors of objective cough frequency in chronic cough. *Thorax*. 2009;64:393–8.
15. Plevkova J, Buday T, Kavalcikova-Bogdanova N, et al. Sex differences in cough reflex. *Respir Physiol Neurobiol*. 2017;245:122–9.
16. Lugo, Tania; Tetrokashvili, Maggie (2021): StatPearls. Hot Flashes. Treasure Island (FL)
17. Mili N, Paschou SA, Armeni A, Georgopoulos N, Goulis DG, Lambrinou I. Genitourinary syndrome of menopause: a systematic review on prevalence and treatment. *Menopause*. 2021;28(6):706–16.
18. Makwana N, Shah M, Chaudhary M. Vaginal pH as a diagnostic tool for menopause: a preliminary analysis. *J Mid-Life Health*. 2020;11(3):133–6. https://doi.org/10.4103/jmh.JMH_1_20.
19. Khatoun A, Husain S, Husain S, Hussain S. An overview of menopausal symptoms using the menopause rating scale in a tertiary care center. *J Mid-Life Health*. 2018;9(3):150–4.
20. Behan M, Zabka AG, Thomas CF, Mitchell GS. Sex steroid hormones and the neural control of breathing. *Respir Physiol Neurobiol*. 2003;136(2–3):249–63.
21. Memoalia J, Anjum B, Singh N, Gupta M. Decline in pulmonary function tests after menopause. *J Menopausal Med*. 2018;24(1):34–40.
22. Hayatbakhsh MR, Najman JM, O'Callaghan MJ, Williams GM, Paydar A, Clavarino A. Association between smoking and respiratory function before and after menopause. *Lung*. 2011;189(1):65–71.
23. Soylu Özler G, Akbay E, Akkoca AN, Karapınar OS, Şimşek GÖ. Does menopause effect nasal mucociliary clearance time? *Eur Arch Otorhinolaryngol*. 2015;272(2):363–6.
24. Topozada H. The human nasal mucosa in the menopause (a histochemical and electron microscopic study). *J Laryngol Otol*. 1988;102(4):314–8.
25. Beule AG. Physiology and pathophysiology of respiratory mucosa of the nose and the paranasal sinuses. *GMS Curr Top Otorhinolaryngol Head Neck Surg*. 2010;9:Doc07.
26. Nappi C, Spiezio Sardo AD, Guerra G, Di Carlo C, Bifulco G, Acunzo G, et al. Comparison of intranasal and transdermal estradiol on nasal mucosa in postmenopausal women. *Menopause*. 2004;11(4):447–55.
27. Birring SS, Prudon B, Carr AJ, et al. Development of a symptomatic specific health status measure for patients with chronic cough: Leicester Cough Questionnaire (LCQ). *Thorax*. 2003;58:339–43.
28. Hauser GA, Huber IC, Keller PJ, et al. Evaluation der klimakterischen beschwerden (Menopause Rating Scale MRS). *Zentralbl Gynakol*. 1994;116:16–23.
29. Birring SS, Matos S, Patel RB, et al. Cough frequency, cough sensitivity and health status in patients with chronic cough. *Respir Med*. 2006;100:1105–9.
30. Faruqi S, Murdoch RD, Allum F, Morice AH. On the definition of chronic cough and current treatment pathways: an international qualitative study. *Cough*. 2014;10:5. <https://doi.org/10.1186/1745-9974-10-5>.
31. Hauser GA, Potthoff P, Rosemeier PJ, Schneider HPG die selbstbeurteilungs-skala für klimakterische beschwerden (Menopause Rating Scale II)
32. Potthoff P, Heinemann LA, Schneider HP, et al. Menopause-Rating-Skala (MRS II): methodische standardisierung in der deutschen bevölkerung. *Zentralbl Gynakol*. 2000;122:280–6.
33. Morice AH, Millqvist E, Bieksiene K, et al. ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. *Eur Respir J*. 2020;55:1901136 (**The European respiratory journal**, 56(5)).
34. Millqvist E. The airway sensory hyperreactivity syndrome. *Pulm Pharmacol Ther*. 2011;24:263–6.
35. Morice AH, Millqvist E, Belvisi MG, et al. Expert opinion on the cough hypersensitivity syndrome in respiratory medicine. *Eur Respir J*. 2014;44:1132–48.
36. Hall G, Phillips TJ. Estrogen and skin: the effects of estrogen, menopause, and hormone replacement therapy on the skin. *J Am Acad of Dermatol*. 2005;53:555–68.
37. Brinca M, Kabalan S, Studd JW, et al. A study of the decrease of skin collagen content, skin thickness, and bone mass in the postmenopausal woman. *Obstet and Gynecol*. 1987;70:840–5.
38. Dicipinigaitis PV. Angiotensin-converting enzyme inhibitor-induced cough – ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129:169–73.
39. Palombini BC, Villanova CAC, Araujo E, et al. A pathogenetic triad in chronic cough – asthma, postnasal drip syndrome, and gastroesophageal reflux disease. *Chest*. 1999;116:279–84.
40. XXXX.
41. Chung KF. Approach to chronic cough: the neuropathic basis for cough hypersensitivity syndrome. *J Thorac Dis*. 2014;6:699–707.
42. Bai H, Sha B, Xu X, Yu L. Gender difference in chronic cough: Are women more likely to cough? *Front Physiol*. 2021;12:654797. <https://doi.org/10.3389/fphys.2021.654797>.
43. Berkhof FF, Boom LN, ten Hertog NE, Uil SM, Kerstjens HA, van den Berg JW. The validity and precision of the Leicester Cough Questionnaire in COPD patients with chronic cough. *Health Qual Life Outcomes*. 2012;10:4. <https://doi.org/10.1186/1477-7525-10-4>.
44. Morice AH, Jakes AD, Faruqi S, Birring SS, McGarvey L, Canning B, et al. A worldwide survey of chronic cough: a manifestation of enhanced somatosensory response. *Eur Respir J*. 2014;44(5):1149–55.
45. Song W-J, Chang Y-S, Faruqi S, Kim J-Y, Kang M-G, Kim S, et al. The global epidemiology of chronic cough in adults: a systematic review and meta-analysis. *Eur Respir J*. 2015;45(5):1479–81.
46. Shah MG, Maibach HI. Estrogen and skin: an overview. *Am J Clin Dermatol*. 2001;2:143–50.
47. Chung KF. Chronic cough hypersensitivity syndrome: a more precise label for chronic cough. *Pulm Pharmacol Ther*. 2011;24:267–71.
48. Chung KF, Mc Garvey L, Mazzone SB. Chronic cough as a neuropathic disorder. *Lancet Respir Med*. 2013;1:414–22.

Publisher's Note

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Ready to submit your research? Choose BMC and benefit from:

- fast, convenient online submission
- thorough peer review by experienced researchers in your field
- rapid publication on acceptance
- support for research data, including large and complex data types
- gold Open Access which fosters wider collaboration and increased citations
- maximum visibility for your research: over 100M website views per year

At BMC, research is always in progress.

Learn more biomedcentral.com/submissions

