



Endometriosis: Can diet help and if so, what kind?

Nicole Heinze, Iris Brandes

Abstract

Although approximately 10% of all women of reproductive age suffer from endometriosis and the pain and potential infertility associated with it, the etiology and pathogenesis of the disease are still largely unknown. It is believed that endometriosis symptoms, like those of other inflammatory diseases, can be positively influenced by dietary interventions. The present systematic literature review identified 20 publications confirming that diet has a fundamental influence on symptoms associated with endometriosis. However, no diet explicitly designed for endometriosis can be recommended based on this evidence. The only recommendation that can be derived from the findings is to maintain a balanced diet that is low in irritants, high in polyunsaturated fatty acids and includes sufficient amounts of fruits and vegetables, which should preferably be untreated and organically grown.

Keywords: dietary recommendations, inflammation, endometriosis, diet, women's health, gynecology

Introduction

The etiology and pathogenesis of endometriosis are still largely unknown [1]. Estimates of the prevalence of endometriosis among women of reproductive age vary from 1% [2, 3] to 10% [4]. Endometriosis has a significant societal impact because it decreases the work productivity and social functioning of a relatively young cohort of individuals. Impairment of various areas of life (school, education, work, partnership, sexuality, friends and family) and poor quality of life are common complaints [5]. As the available treatment options are limited and have numerous side-effects, the question of whether there is an endometriosis-specific diet is gaining increasing attention.

Chronic pelvic pain, the cardinal symptom

Endometriosis is, by definition, characterized by the presence of endometrial tissue outside the uterine cavity. The etiology and pathogenesis of the disease have not yet been conclusively established. Various explanatory models have been proposed in the literature, including the Coelomic metaplasia theory [6], the transplantation or implantation theory [7], and the archimetra concept [8]. However, none of the known theories alone can explain how and why endometriosis develops, so a multifactorial explanatory model seems to be required [1, 9].

In addition to infertility, the cardinal symptom of endometriosis is pelvic pain of various kinds. Dysmenorrhea is the most common type, followed by chronic recurrent cyclic and acyclic pelvic pain, dyspareunia (= pain during sex), dyschezia (= disturbance of defecation), and dysuria (difficult/painful emptying of the bladder). Endometriosis symptoms may occur in a wide range of different combinations. Pain genesis is presumably influenced by synthesized pain mediators (e.g., prostaglandins, interleukins, and kinins) and histamine released by endometriotic lesions themselves as well as by their number, activity, and

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depth of infiltration. Fundamentally, pelvic pain can occur as a result of inflammatory processes, strong contractions, nerve irritation, impaired organ function, lesions and/or scarring. Pain, the cardinal symptom of endometriosis, may be associated with a number of accompanying symptoms like headache, vomiting, diarrhea, constipation, fainting, depressive moods, listlessness, back pain, menorrhagia, hypermenorrhea, and intestinal bleeding [9]. These complaints are often associated with endometriosis pain.

Treatment

Endometriosis management is limited to controlling the symptoms. The goal of treatment is to maintain uterine and ovarian function, improve quality of life and prevent disease progression. Special emphasis is placed on reducing estrogen levels in order to suppress cyclic ovarian activity. Estrogen suppression usually results in the reduction of pain and other symptoms but is associated with relevant side effects. Furthermore, endometriotic lesions do not all respond equally to hormone therapy. Another important therapeutic option is surgery, which aims to remove all endometriotic lesions as completely as possible and prevent their recurrence. Non-steroidal anti-inflammatory drugs or analgesics are recommended purely for endometriosis pain relief and, under certain conditions, for pharmacologic treatment of endometriosis. A number of women are greatly interested in exploring alternative medicine and dietary approaches to endometriosis management as self-help options to improve their health and quality of life beyond the scope of conventional medicine treatments and their many side effects. Various complementary medicine interventions and concepts [10, 11] as well as endometriosis-oriented diet recommendations are currently the main focus of attention. However, the dietary recommendations put forward to date are few and sometimes contradictory.

The theory that diet might positively influence the clinical picture of endometriosis is based on the rationale that dietary recommendations exist for other diseases associated with pain and inflammation, such as rheumatoid arthritis, among other things [12] (■■■ „Chronisch-entzündliche Erkrankungen: Ansatzpunkte für die Ernährungstherapie“ und „Ernährung bei Erkrankungen des rheumatischen Formenkreises“ in ERNÄHRUNGS UMSCHAU Special Edition 4 Ernährungstherapie).

Objective

This literature review (LR), originally performed in 2017 [13] and updated in 2020, aimed to evaluate the available data on the potential influence of diet on the symptoms of endometriosis and to thereby derive dietary recommendations suitable for everyday use (e.g., a recommended food list).

Methods

Based on a preliminary search for publications on the topic of nutrition and endometriosis, keywords for the SLR were identified and included in the search terms of the systematic search strategy. The search criteria were:

- scientific papers

- published in English or German
- from 2000 to 03/2020
- containing the results of in vivo clinical studies
- describing the effects of food or diet on the symptoms of endometriosis
- in women with endometriosis.

The search focused on the term “endometriosis” (“endometriosis”) in combination with “nutrition”, “food(s)” and their constituents as well as German and English keywords relating to “diet”, “food”, and “nutrition”, e.g., “zinc”, “vegan”, “vegetari*”, “caffeine”, “coffee”, “Kaffee”, “vitamin*”, “nutrient*”, “nutrition*”, “ernaehrung*”, “milk”, “food*”, “diet*”, „fat*”, “magnesium”, “heavy metal”, “iron”, “wheat”, “soy*”, “selenium”, and “antioxidants”. Formal reasons leading to exclusion of publications included lack of full-text availability and a rating of 5 or lower according to the Oxford Centre of Evidence Based Medicine (OCEBM) evidence rating system [14] (Letter to the Editor, conference paper, etc.). Results on the topics of cancer, genes/genetics, hormones, enzymes or epigenetics were classified as irrelevant and excluded from the review.

The search strategy developed in this manner was applied to the PubMed and ZBmed databases. The search results are presented in ♦ Figure 1.

Results

The search yielded 604 hits ($n_{\text{PubMed}} = 256$; $n_{\text{ZBmed}} = 348$), with duplicates assigned to the ZBmed database; these were supplemented by two additional publications from the hand search. After review of all titles by the lead author, 493 publications were excluded, after abstract screening further 65 publications, and on the basis of full text screening another 24 publications. Reasons for exclusion were publications that were not in English or German ($n = 4$), where no full text at all or no freely available full text ($n = 558$) was available, publications with insufficient quality (evidence level of the OCEBM 5 or lower) ($n = 8$), and studies describing animal experiments or in vitro studies ($n = 16$) (♦ Figure 1).

Description of the database

A total of 20 publications were included in the review, including one online survey of self-management strategies among women with endometriosis [15], three case-control

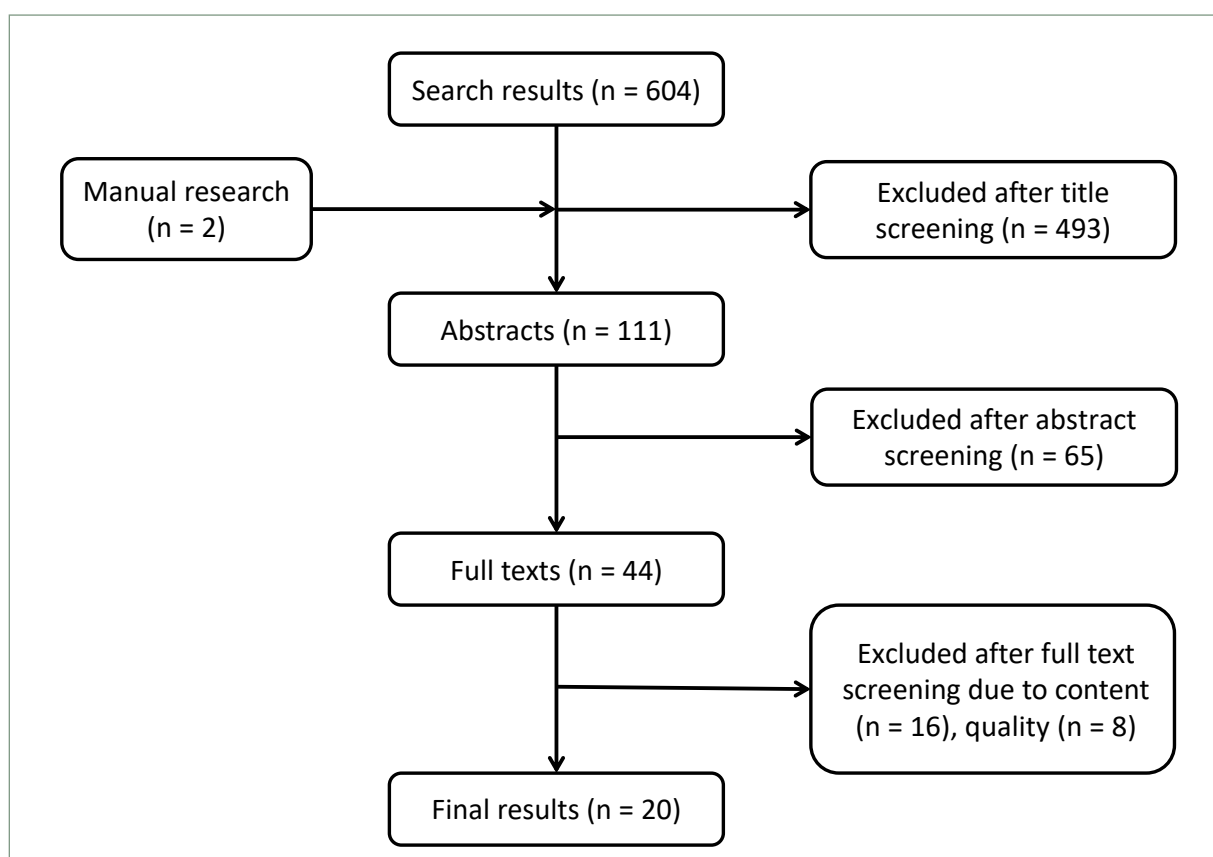


Fig. 1: Flow diagram depicting the study selection process

studies on diet or food consumption and endometriosis risk [16–18], five prospective long-term cohort studies (Nurses' Health Study II) on food consumption and endometriosis risk [19–23], one retrospective observational study on gluten-free diet and endometriosis risk [24], and two systematic reviews on selected food intake/diet and endometriosis risk [25, 26] as well as a paper on two matched case-control studies on selected food intake and endometriosis risk [27], a meta-analysis of coffee and caffeine intake and endometriosis risk [28], a prospective cross-sectional study on polyunsaturated fatty acids (PUFAs) and endometriosis [29], a retrospective analysis of prospectively collected data on the low-FODMAP diet and endometriosis [30], a retrospective study of fruit and vegetable intake and endometriosis [31], a retrospective study and review of the literature on the link between dietary intolerance, n3 fatty acids and endometriosis [32], and two reviews on dietary/nutritional aspects related to endometriosis [33, 34]. The sample sizes of the studies described in the papers ranged from $n = 57$ [32] to $n = 116,430$ [21, 22]. Eight of the studies were conducted in the USA [17–23, 29], four in Italy [24, 26–28], two in Australia [15, 30] two in Denmark [25, 34], and one each in Brazil [33], China [31], Iran [16] and Malta [32] (♦ Table 1 on p. 188).

Method discussion

The very open search yielded a number of hits, but only twenty publications met the predefined inclusion criteria. The selection

of publications was largely limited by the lack of availability of full texts (due to lack of funding) and/or the poor methodological quality of most studies. The validity of the results of this review is reduced, in particular, by small sample sizes and retrospective surveys with short evaluation periods. Hence, the results presented here must be interpreted against the background of the limited number of prospective long-term observational or case-control studies in representative study populations. The frequent use of case-control or cohort studies with a weaker strength of evidence compared with randomized trials partly contributes to reducing the validity of the findings. Overall, the quality of evidence of the identified publications, assessed based on the OCEBM rating scale [14], was classified as level three to four, corresponding to a low level of evidence (♦ Table 1).

Tab. 2: Studies with an evaluation of a possible connection between individual foods, food components, and diets and the symptomatology of endometriosis →



	Negative correlation	Neutral/no results	Positive correlation
Fats			
fats in general	–	–	[17, 23]
monounsaturated fatty acids	–	[23, 25]	[17]
eicosapentaenoic acid (EPA)	–	–	[16]
fish oil	–	–	[25, 26, 34]
saturated fatty acids	–	[23]	–
polyunsaturated fatty acids	–	[29]	[26, 34]
n3 fatty acids	–	[29]	[23, 25, 26, 32, 34]
n6 fatty acids	–	[29]	[16]
oils	–	–	[16]
olive oil	–	[26]	–
oleic acid	–	–	[16]
palm oil	[23]	–	–
spreads and vegetable fats	–	[26]	[17]
animal fats	[23]	–	–
trans fatty acids	[17, 23, 26]	–	–
Vegetables			
vegetables in general	[31]	–	[16, 21, 26]
leaf lettuce and romaine lettuce	–	–	[21]
yellow vegetables	–	–	[16]
green vegetables	–	–	[27]
carrots	–	[26]	–
Brussels sprouts, red cabbage and cauliflower	[21]	–	–
Pulses			
pulses in general	–	–	[16]
corn, peas, and lima beans	[21]	–	–
soy	[18]	[26]	–
Carbohydrates (grains, potatoes)			
dietary fiber	–	[26]	[16]
gluten-free diet	–	–	[24]
potatoes	–	–	[16]
potatoes, deep-fried	[16]	–	–
whole grain products	–	[26]	–
Fruit			
fruit in general	[17, 31]	[26]	[16, 21, 27]
citrus fruits	–	–	[21]
Animal products			
eggs	–	[19]	–
fish	–	[19]	–
poultry	–	[19]	–
seafood	–	[19]	–
milk (dairy products)	–	[26]	[20, 22]
proteins	–	–	[16]
red meat	[19, 26, 27]	–	[16]
ham	[26, 27]	–	–
Miscellaneous			
low-FODMAP diet	–	–	[15, 30]
caffeine	[26]	[28]	–



Results and discussion

The published studies included in the analysis provide varied and partly contradictory evidence of a possible connection between nutrition and the symptomatology of endometriosis (♦ Table 2). The results are summarized and discussed below.

Fats and fatty acids

The results of three scientific reviews, a retrospective study and review ($n = 57$), and a prospective long-term cohort study ($n = 70,709$) suggest that a diet rich in $n3$ fatty acids contributes to the improvement of various endometriosis-associated symptoms [23, 25, 26, 32, 34]. This indicates that the consumption of fish oil, PUFAs and oils such as linseed oil can be beneficial.

Furthermore, spreadable fats such as butter and margarine and vegetable fats were generally recommended as well as monounsaturated fatty acids in a case-control study including $n = 944$ patients [17]. However, the higher consumption of fats overall was associated with an decreased risk of disease in the group of women diagnosed with endometriosis [17]. In addition, three publications (prospective long-term control study, systematic review, and population-based case-control study) [17, 23, 26] recommended reducing the consumption of trans fatty acids and palm fat in a population-based case-control study [23].

Dietary fats reported to be suboptimal for reducing endometriosis risk were trans-fatty acids in three papers [17, 23, 26] and palm fat in one paper [23].

The diet-related reduction of endometriosis-associated symptoms may be due to the reduction of inflammatory potential, according to research on other inflammatory diseases [35]. In particular, the anti-inflammatory mechanism of $n3$ fatty acids seems to have a beneficial effect on endometriosis symptoms and pain [33, 36]. Huis and Nap [37] derived concrete recommendations for the intake of fats on the basis of their current review. Their findings suggest that a diet that includes 1% energy intake from $n3$ fatty acids and 2% from $n6$ fatty acids is associated with a reduction in endometriosis symptoms. However, it should be considered that the consumption of $n3$ fatty acids from fish can impair fertility due to heavy metal contamination, for example, in older predatory fish [38]. Therefore, so-called non-predatory fish such as sardines, mackerel, herring or pollock as well as fish from farmed ponds or aquacultures such as carp or trout should be preferred [39]. If fatty acids from animal sources are not an option, high-quality vegetable oils such as rapeseed, linseed or walnut oil should be consumed [40].

Animal products

Unfortunately, it is less possible to draw unambiguous conclusions regarding the effects of animal products based on the papers included in this review. The literature distinguishes between foods produced by animals and meat products. The Nurses' Health Study II searched for an association between the intake of certain foods in adolescence and the occurrence of endometriosis in the following years (1991–2013) in three subpopulations. The study revealed an up to 30% lower risk of endometriosis associated with the regular consumption of milk and dairy products [20, 22], but no such statistical correlation for eggs [19]. Milk and dairy products are also inferred to have

a positive effect on endometriosis due to the calcium, vitamin D, vitamin A, and beneficial digestive lactobacilli they contain [37, 41]. Some lactobacilli strains have been associated with a reduction in pain, regulation of vaginal bacterial overgrowth, and a positive effect on the general colonization of the gut microbiota [42–44].

In contrast, most meat products except fish and seafood received a rather negative rating [19, 23, 26, 27]. Data from the Nurses' Health Study II ($n = 81,908$, $n = 70,709$), a case-control study ($n = 1,008$) and a systematic review show a statistical association between the regular intake of meat and meat products and an increased risk of endometriosis. One reason given was that a high fat content (e.g., in goose, duck, or pork) stresses the digestive tract and can thus lead to lower abdominal complaints [45].

Ham, red meat, and deep-fried foods were also associated with an increased risk of worsening endometriosis [16, 19, 26, 27]. The stress on the digestive tract caused by fatty foods plays a role here, too, because of their unfavorable fatty acid patterns. For example, a connection has been established between the consumption of trans fatty acids produced by deep-frying and the occurrence of endometriosis [34]. For this reason, some authors recommend that endometriosis patients should avoid these products or preparations [16, 19, 26, 27]. Huis and Nap [37], on the other hand, emphasize the nutritional value of meat products. In particular, meat products contain relatively large quantities of B vitamins, iron, selenium, and zinc, which are associated with milder endometriosis symptoms.

Fruit and vegetables

The consumption of vegetables is generally recommended in several studies [16, 21, 26]. Leaf and romaine lettuce (Nurses' Health Study II, $n = 116,430$) [21] as well as green and yellow vegetables were explicitly mentioned in this context (two case-control studies, $n = 156$, $n = 1,008$) [16, 27]. Only Brussels sprouts, red cabbage and cauliflower were found to cause problems in women with endometriosis, as determined in a prospective cohort study [21]. Although the results for fruit were similar, the overall picture is more heterogeneous [16, 21, 27]: two further publications – a population-based case-control study ($n = 944$) and a retrospective study with interviews ($n = 234$) – recommend that endometriosis patients keep fruit consumption at relatively low level [17, 31].



Fruits and vegetables are generally considered to have a protective health effect, as they are important suppliers of vitamins, minerals and antioxidants. They contain substances like carotenoids, vitamin B₆, vitamin C and vitamin E, calcium, magnesium, selenium, indole-3-carbinol and polyphenols, which can help to alleviate symptoms associated with endometriosis [37, 46]. This protective effect is related to the fact that, for example, antioxidant food components inhibit oxidative stress, which plays an important regulatory role in the menstrual cycle and, thus, in reproduction [47]. This recommendation applies to all women, particularly endometriosis patients, whose existing health problems can thus be mitigated. However, in these and all cases, it should be stressed that basically all foods, especially fruits and vegetables, should be thoroughly washed or peeled before consumption because dust particles, which may contain heavy metals, pesticides and/or fungicides, can adhere to the surface [39] and thus counteract the protective effects of the antioxidants, minerals, vitamins and so forth contained in the foods. The reason for the negative effect of pesticides on endometriosis symptoms is that these chemicals can mimic estrogen; hence, they have the potential to influence the menstrual cycle and increase the risk of endometriosis [48]. Investigators like Trabert et al. [17] and Dai et al. [31] identified an unfavorable effect of increased fruit-related pesticide exposure on endometriosis symptoms [17] and concluded that endometriosis patients should be advised to consume organic food [31].

The problems associated with cruciferous vegetables (e.g., Brussels and cauliflower) and certain legumes (e.g., peas) may be due to their low digestibility and high content of fermentable oligosaccharides, disaccharides, monosaccharides and polyols, Harris et al. suggest [21]. These foods can cause indigestion in women with endometriosis, who often have bowel symptoms. The severity of which can be potentiated when they occur in combination with the lower abdominal pain frequently associated with endometriosis. Armour et al. and Moore et al. confirmed this hypothesis in a cross-sectional online survey (n = 484) and a retrospective analysis of a prospective intervention study (n = 160), respectively [15, 30]. Therefore, endometriosis patients should be individually tested for tolerance to different foods. Individual sensitivity thresholds to be tested include cruciferous vegetables, as the

phytochemical indole-3-carbinol has been shown to be effective against hormone-related cancers and may thus have regulatory effects on the estrogen metabolism [49–51].

Legumes

The findings regarding the effects of legumes are inconsistent. In a retrospective survey of the typical dietary behavior of two comparable groups of patients (n = 156), Samaneh et al. observed that the group without endometriosis consumed more legumes [16] and inferred from this that legumes have a generally preventive effect. In contrast, the prospective cohort study (1991–2013) with 116,430 participants by Harris et al. [21] suggested that corn, peas, and lima beans were associated with an increased risk of endometriosis. In a population-based case-control study (n=1,037), researchers from the USA demonstrated that soy and soy products are associated with a more than twofold increased risk of endometriosis [18].

Soy and soy products are especially widely discussed in the literature due to their estrogen-like effects. A recent systematic review by Huijs and Nap [37] revealed that a reduction of soy intake may be associated with improvement of endometriosis symptoms. Since many endometriosis patients suffer from allergies [52], they should be individually tested for intolerance or allergy to soy-based foods.

Further diets

Dietary fiber, a gluten-free diet and potatoes prepared by all methods except deep-frying were also found to be beneficial to the health of endometriosis patients in several studies, as reported in a case-control study (n = 156) and a retrospective observational study (n = 207) [16, 24].

Parazzini et al. [26] furthermore recommended keeping caffeine and coffee consumption to a minimum as they could potentially increase the risk of endometriosis.

Two publications explicitly highlight the benefits of a diet low in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (low-FODMAP diet) for endometriosis patients [15, 30]. In the review by Huis and Nap [37] and the qualitative study by Vennberg Karlsson et al. [53], in which women were interviewed about their diet, patients confirmed the positive effect of such specific diets on their endometriosis-related complaints.

Conclusion

In summary, this systematic review of the literature confirmed that diet has an influence on endometriosis-associated symptoms, but no recommendations for any specific endometriosis-specific diet could be derived due to the limited and partly inconclusive nature of the available data.

The validity of the recommendation to eat a balanced diet low in potential irritants (e.g., allergens), rich in PUFAs, and containing sufficient quantities of fruits and vegetables, which should ideally be untreated and organically produced, is indisputable. Any dietary modifications in endometriosis patients should be made in consultation with a doctor and a nutritionist in order to ensure



Authors	Year	Place	Number of cases n	Methodology	Level of evidence [14]
Armour et al. [15]	2019	Australia	484	cross-sectional online survey	4
Baron [32]	2014	Malta	57	retrospective study + review	3
Chiapparino et al. [28]	2014	Italy	0	meta-analysis	3
Dai et al. [31]	2018	China	234	retrospective study + interviews	3
Fjerbaek & Knudsen [25]	2007	Denmark	0	systematic review	3
Halpern, Schor & Kopelman [33]	2015	Brazil	0	review	3
Hansen & Knudsen [34]	2013	Denmark	0	systematic review	3
Harris et al. [21]	2018	USA	116,430	prospective cohort study	3
Harris et al. [22]	2013	USA	116,430	prospective long-term cohort study	3
Hopeman et al. [29]	2015	USA	205	prospective cross-sectional study	3
Marziali et al. [24]	2012	Italy	207	retrospective observational study	3
Missmer et al. [23]	2010	USA	70,709	prospective long-term cohort study	3
Moore et al. [30]	2017	Australia	160	retrospective analysis of data prospectively collected from an interventional study	3
Nodler et al. [20]	2020	USA	32,868	prospective long-term cohort study	2
Parazzini et al. [27]	2004	Italy	1,008	mixed case-control study	3
Parazzini et al. [26]	2013	Italy	0	systematic review	3
Samaneh et al. [16]	2019	Iran	156	case-control study	4
Trabert et al. [17]	2011	USA	944	population-based case-control study	4
Upton et al. [18]	2015	USA	1,037	population-based case-control study	4
Yamamoto et al. [19]	2018	USA	81,908	prospective long-term cohort study	3

Tab. 1: Characteristics of the studies included in this review

a sufficient supply of all important nutrients, while taking hormone therapy, planned surgeries and other patient-related factors into account.

A diet low in potential irritants generally appears to be beneficial for some endometriosis patients. In this context, a low irritation and low inflammation diet should be designed to include a selection of appropriate foods while taking into account the individual irritation level of the patients with regard to their tolerance of such foods. Based on the available data in the literature, food intolerance and allergies must be considered, endometriosis patients must be individually tested for their tolerance of possibly bloating foods, and highly processed and fatty foods may have to be eliminated from the diet.

It is crucial to adapt dietary changes to the patient's individual needs and conditions, such as allergies, intolerances, and comorbidities like bowel and bladder diseases. Training endometriosis patients to have healthy body awareness and to closely observe how their body reacts to individual foods can facilitate the development of a customized endometriosis-specific diet for each individual patient. Like the present review, another recent study showed that an individually adapted, balanced diet plan can help to alleviate the symptoms of endometriosis [53]. As a rule, food is a key element of quality of life and should be enjoyed.

The results of this review demonstrate that further study of the relationship between nutrition and endometriosis is greatly needed for two reasons: first, to close the existing gaps in knowledge on factors like individual food groups or specific symptoms and,

second, to validate the current findings and/or evaluate their transferability to other countries in a larger number of cases.

Conflict of Interest

The authors declare no conflict of interest.

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