Journal of Optometry 16 (2023) 12—19

Journal of Optometry

www.journalofoptometry.org

REVIEW

Topical review of the relationship between contact lens wear and meibomian gland dysfunction

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KEYWORDS
Contact lens;
Meibomian Gland dysfunction;
Dry eye;
Meibomian glands;
Meibography

Abstract Contact lens (CL) wearers often suffer from ocular discomfort, which leads to cessation of CL wear. About 30% to 50% of CL wearers complain of dry eye (DE) symptoms. Meibomian gland dysfunction (MGD) is considered the most common cause of evaporative DE. Numerous studies have investigated whether CL wear might affect the meibomian glands. This manuscript reviews studies examining the relationship between CL use and MGD. A PubMed database search was conducted for studies published between 1980-2021 with one or a combination of search terms related to "meibomian gland", "meibomian gland dysfunction", "contact lens", and/or "dry eye". Of the 115 papers reviewed, 22 articles were identified that examined the association between CL and MGD. Fifteen showed that CL wear affects the morphology and function of meibomian glands (MGs), while seven reported no significant impact of CL wear on MGs. This review provides an overview of these studies, emphasizing the diagnostic tests of MGD and conclusions. The review highlights the need for longitudinal prospective large cohort studies with control non- CL wearers to clarify the ambiguous relationship between MGD and CL wear, with special attention to varying CL material and wear times in order to identify the long-term impact of CLs on MG.

Introduction

There are approximately 140—150 million contact lens (CL) wearers worldwide.[1,2] Approximately 30% to 50% of CL wearers report dry eye (DE) symptoms.[3,4] The Tear Film & Ocular Surface Society Dry Eye Workshop II (TFOS DEWS II) reported that CL wear increases the risk of developing DE by about 2—4 times.[5,6] CL induced ocular changes leading to DE disease include tear film instability,[3] increased tear evaporation rate and tear osmolarity[7] and decreased tear film meniscus volume.[8] DE and tear film changes in CL wearers are related to reduced visual acuity, decreased wear time,[9] and are a major causative factor for discontinuation of lens wear.[10]

In addition to DE, CL use may induce complications such as keratitis, giant papillary conjunctivitis, infections[3] and corneal disorders.[7,11—13] CL wear has also been shown to be correlated with changes in meibomian gland (MG) morphology and function.[2,4,10]

Meibomian gland dysfunction (MGD) has been defined by the subcommittee of The International Workshop on MGD as

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https://doi.org/10.1016/j.optom.2022.03.004

a chronic and diffuse disorder that occurs in MGs. MGD is characterized by glandular orifice obstruction and/or changes in the quality and/or quantity of meibum that is secreted by the MGs. It may affect the tear function, causing evaporative DE, and also evoke symptoms of ocular discomfort.[14] Furthermore, MGD has been associated with the cessation of CL wear.[15]

Key signs of MGD include plugged MG orifices and MG dropout.[16] Eyes with MGD exhibit altered MG secretion that is turbid or cloudy, and tears that are frothy or foamy.[17] Numerous structural changes occur, including thickening, rounding or irregularity of the lid, displacement of the mucocutaneous junction, vascular dilatation, telangiectasia,[18] madarosis or trichiasis,[19] and notching of the lower lid margin. [17]

MGD is one of the most common diseases observed in ophthalmic and optometric clinics.[20] Five pathophysiological mechanisms have been suggested: eyelid inflammation, conjunctival inflammation, corneal damage, microbiological changes and DE disease.[21]

In 2011, the International Workshop on MGD created a consensus of diagnostic criteria for the condition.[16] These criteria include a questionnaire based assessment of symptoms, along with functional and morphological measurements. Functional aspects include meibum expressibility and quality, and tear production (Schirmer test). A tear quality assessment should be performed, consisting of blink rate and interval, tear meniscus height, tear osmolarity, tear-film breakup time, and corneal and conjunctival fluorescein staining. Morphological aspects include quantification of specified lid features and meibography.[16] The Osmoprotection in Dry Eye Disease- Expert Opinion (OCEAN) group updated these diagnostic criteria in 2017[22] by adding functional diagnostic technologies such as interferometry, non- invasive tear film breakup time measurement, and a morphological assessment using *in vivo* confocal laser microscopy. Despite the international effort to create standardization in the diagnosis of MGD, the criteria are not often used in research, resulting in different definitions in various studies.[23]

Studies regarding the relationship between MGD and CL wear are inconclusive, some demonstrating a significant relationship between MGD and CLs,[2—4,10,24—34] and others concluding that there is no significant relationship between MGD and CLs.[7,35—40] This work aims to review the scientific literature regarding the effect of CL wear on MGD and to offer an objective approach to address the question in the future.

Methods

A Pubmed database search for research papers written in English between 1980 and 2021 was conducted. Primary search terms and their synonyms were used singly or in combination, including “meibomian gland,” “meibomian gland dysfunction,” “contact lens” and “dry eye", without Boolean operators. Studies whose purpose was to examine the structural and/or functional changes of the MGs in CL wearers were considered relevant and included. Searches were also performed for articles referenced in bibliographies that were not initially retrieved by the search.

Results

The database search resulted in 115 papers, of which 22 were pertinent to the topic of this review. Of these 22 studies, 15 showed an association between MGD and CLs[2—4,10,24—34] (Table 1) and seven did not (Table 2).[7,35—40]

Studies tabulated in Tables 1 and 2 used a wide variety of diagnostic criteria, making comparison of the results challenging. Some papers relied on functional assessments alone, while others also used morphological testing, which may better characterize the association of CL wear and MGD. Some papers did not include a control group, which could confound their observations. Thus, the following sections will focus on the studies that used both functional and morphological evaluations and included a control group.

Studies showing an association between MGD and CLs

Fifteen studies used functional assessment along with morphology [2—4,10,24—34] and of these, eight included a control group of non-CL wearers.[2—4,10,24,30,32,34] Ong and Larke[30] found that rigid, soft, and gas permeable CL wearers who wore their lenses for at least six months, had a higher prevalence of MGD (30%) than non-CL wearers (20%), as assessed by MG expression. There was no significant difference in MGD between the different types of CLs, or between male and female wearers. However, the ages of the participants were not specified. Similarly, a large cohort cross-sectional observational study[3] of rigid and soft CL wearers and non-CL wearers, found that CL wear was significantly associated with a reduced number of functional MGs, with a correlation between wear duration and the number of functional MGs. Furthermore, the average meiboscores of RGP and hydrogel CL wearers were not significantly different, suggesting that the loss of functional MGs does not depend on the CL material. In addition, the average difference between the meiboscores of CL wearers and non-CL wearers was significantly higher in the upper eyelids compared to the lower eyelids. However, they did not assess ocular surface symptoms or MG expressibility. Villani et al.[32] included *in vivo* laser scanning confocal microscopy to assess the morphology of the glands, alongside a subjective DE questionnaire. They observed significantly more morphological changes in MGs among asymptomatic soft hydrogel CL wearers, compared with non-CL wearers. These changes included lower acinar unit diameters, higher glandular orifice diameters, greater secretion reflectivity and greater inhomogeneity of the periglandular interstices. Moreover, the duration of CL wear was significantly correlated to the acinar unit diameters. Additionally, the CL wearers had significantly higher MG loss (dropout). However, the sample size was small and MGs were only evaluated in the lower eyelid, which may under-represent MGD as it affects the upper eyelid more than the lower eyelid.[3] Machalinska et al.[4] assessed MG function (meibum expressibility and quality), MG morphology and dropout (meibography), along with lid margin changes of daily soft CL wearers and non—CL wearer controls. CL use was significantly associated with abnormal meibum quality, lid margin telangiectasia, rounding, notching, hyperemia of the posterior lid margin, orifice plugging and retroplacement. Furthermore, lid margin abnormality and meibum quality scores were

Table 1 Studies showing an association between MGD and CLs. The Table summarizes research studies reporting an association between MGD and CL wear. Columns describe study authors (first column), subjects and controls including their age range (second column) and outcome parameters divided into morphological (columns 3-4), functional (columns 5-13), subjective (column 14), and other measures (last column).

Study	Subjects	Assessment												
		Morphology		Functional									Other	
		Meibography	Slit lamp - lid margin	MG expression	Fluorescein staining-cornea, conjunctiva	TBUT / NITBUT	Schirmer test	Tear meniscus height	Tear osmolarity	Tear evaporation rate	Lipid layer assessment	Blink rate	Questionnaire	Other
Ong and Larke[30]	CL wearers (N=70) non−CLs wearers (N=70) Age range not specified		✓	✓										Biochemical and physical examination of the MG secretion
Arita et al.[3]	CL wearers (N=121) non−CLs wearers (N=137) age: 16 − 46	✓	✓		✓	✓	✓							
Villani et al.[32]	CL wearers (N=40) non−CLs wearers (N=20) age: 25 − 28	✓	✓	✓	✓	✓	✓						✓	Examination of perigland-ular inflammation
Machalinska et al.[4]	CL wearers (N= 41) non−CLs wearers (N=31) mean age: 34	✓	✓	✓	✓	✓	✓					✓	✓	
Alghamdi et al.[10]	CL wearers (N=60) non−CLs wearers (N=20) age: 18 − 35	✓	✓	✓	✓	✓		✓	✓	✓	✓		✓	
Uçakhan and Arslanturk-Eren[2]	CL wearers (N=87) non−CLs wearers (N=55) age: 24- 36	✓	✓	✓	✓	✓	✓						✓	MG curling and thickening
Gu et al.[34]	CL wearers (N=85) non-CL wearers (N=63) mean age: CL wearers: 25.52 non-CL wearers: 23.35	✓			✓	✓		✓					✓	
Harbiyeli et al.[24]	CL wearers (N=65) non-CL wearers (N=26) mean age: 33.1	✓	✓	✓	✓	✓	✓						✓	
Korb and Henriquez[26]	CL wearers (N=78) (38 symptomatic vs. 40 asymptomatic) age: 16 − 82		✓	✓	✓			✓						Cytologic and bacteriologic examination of the lid margin and the MGs
Henriquez and Korb[25]	CL wearers (N=50) (38 symptomatic vs. 12 asymptomatic) Age range not specified			✓										Cytologic and bacteriologic examination of the MGs
Mathers and Billborough[28]	CL wearers (N= 42) (27 with giant papillary conjunctivitis vs. 15 without giant papillary conjunctivitis) age: 21- 50	✓	✓	✓			✓		✓					
Molinari and Stanek[29]	CL wearers (N=105) age: 14 − 58		✓	✓										

Table 1 (*Continued*)

Study	Subjects	Assessment														
		Morphology			Functional								Other			
		Meibography	Slit lamp - lid margin	MG expression	Fluorescein staining- cornea, conjunctiva	TBUT / NITBUT	Schirmer test	Tear meniscus height	Tear osmolarity	Tear evaporation rate	Lipid layer assessment	Blink rate	Questionnaire	Other
Siddireddy et al.[31]	CL wearers (N=30) (17 symptomatic vs. 13 asymptomatic) age: 18—41	✓	✓	✓	✓	✓		✓	✓	✓	✓		✓	Demodex colonization examination and eyelid sensitivity testing
Llorens-Quintana et al.[27]	CL wearers (N= 41) (33 experienced wearers vs. 8 unexperienced wearers) age: 19- 29	✓	✓		✓	✓		✓	✓				✓	
Young et al.[33]	CL wearers (N= 274) (226 symptomatic vs. 48 asymptomatic) mean age (symptomatic): 32.8 mean age (asymptomatic): 28.7			✓	✓	✓	✓	✓			✓	✓	✓	

significantly correlated with duration of CL wear. The study did not find significant morphological changes of MGs, and did not find a significant difference in tear film abnormalities between the groups, in contrast with previous studies.[3,32] Furthermore, a significant difference in subjective ocular symptoms between CL-wearers and controls was not found. This is in contrast to another study that did report a significant difference using the same questionnaire.[32]

Alghamdi et al.[10] reported a relationship between MGD and the duration of soft CL wear. They divided CL wearers into short, medium, and long duration of wear, and compared them to previous CL wearers and non -CL wearers. They evaluated both functional and morphological parameters, in both eyelids. MG dropout was assessed with meibography and graded by a scale, while MG function was assessed by quality and quantity of MG expression. They found that all CL wearers had significantly higher rates of MG dropout compared to non-CL wearers. All CL wearers also demonstrated reduced MG expressibility, increased number of plugged orifices, shortening of non-invasive TBUT, and increased MG dropout. These measures did not resolve after a six-month cessation of CL wear, though they did not appear to worsen after two years of wear. Uçakhan and Arslanturk-Eren[2] divided CL wearers into three groups according to the duration of CL wear, comparing them to one another and to controls. MG expressibility was assessed and MG loss was evaluated by meibography. The authors reported that the mean meiboscores of the upper and lower eyelids, percentage of gland loss, and percentage of thickened and curled MGs in both lids were significantly higher in CL wearers compared with the non-CL wearers, while mean TBUT and mean MG expressibility were significantly lower in CL wearers. Silicone hydrogel lenses affected the upper lids mainly in the early years of CL wear. After three years, both lids appeared to be similarly affected. This was the first study to examine and rate MG thickening and curling on tarsal plate structures by meibography, finding that the earliest morphological change is MG thickening of the upper eyelids in CL wearers. Similarly to Villani et al.[32] they also reported that the OSDI score was significantly worse in CL wearers compared with non-CL wearers. This is in contrast to other studies[4,10] which found no significant differences in OSDI scores between the groups. Gu et al.[34] found significantly higher average total MG dropout and average total distorted MG count in soft CL wearers compared with non-CL wearers. In addition, the duration of CL wear was significantly correlated with MG dropout, and CL wearers had significantly more DE-related symptoms. MG expression and lid margin morphology were not evaluated. Harbiyeli et al.[24] assessed the condition of the MGs in soft and RGP CL wearers and a control group of non-CL wearers. MG evaluation included an assessment of meibum quality and expressibility. MG morphology was assessed and graded in both eyelids by meibography. Similarly to the results of three other studies,[3,4,32] they found that the duration of soft CL use correlated with MG loss in the upper eyelid compared with the control group. Furthermore, those who wore rigid CL materials also had a significantly greater tendency for MG loss. Of note, the rigid CL wearers in this study had keratoconus which can bias the results due to the abnormal ocular surface and different fitting characteristics in this cohort.[24] Moreover, subjects with keratoconus are more likely to suffer from DED and MGD.[41—43]

The majority of the studies that assessed the impact of CL wear duration on MGD found a significant association

Table 2 Studies reporting a lack of association between MGD and CLs. The Table summarizes research studies reporting a lack of relationship between CL wear and MGD. Columns describe study authors (first column), subjects and controls including their age range (second column), and outcome parameters divided into morphological (columns 3-4), functional (columns 5-13), subjective (column 14), and other measures (last column).

Study	Subjects	Assessment												
		Morphology		Functional									Other	
		Meibography	Slit lamp -lid margin	MG expression	Fluorescein staining-cornea, conjunctiva	TBUT / NITBUT	Schirmer test	Tear meniscus height	Tear osmolarity	Tear evaporation rate	Lipid layer assessment	Blink rate	Questionnaire	Other
Hom et al.[35]	CL wearers (N=162) non−CLs wearers (N=236) age: <10 - >60		✓	✓										
Marren[36]	CL wearers (N=20) non−CLs wearers (N=30) age: 22 − 35		✓	✓	✓									
Pucker et al.[39]	CL wearers (N=70) non−CLs wearers (N=70) age: 18 - 43	✓	✓	✓	✓	✓	✓	✓	✓				✓	
Ong[38]	CL wearers (N=81) non−CLs wearers (N=150) age: 15 - 40			✓										
Nichols and Sinnott[7]	CL wearers (N=360) Mean age: 31.1	✓	✓		✓			✓	✓		✓	✓	✓	
Na et al.[37]	CL wearers (N=58) age: 7- 18	✓	✓		✓	✓	✓		✓				✓	Evaluation of inflammation MG width
Pucker et al.[40]	CL wearers (N=112) (56 CL dropout vs. 56 successful CL wearers) age: 18-45	✓	✓	✓		✓							✓	MG width

between time and MGD severity,[3,4,24,32,34] for both soft and RGP CLs.[3] This strongly suggests that the length of time patients wear CLs is a significant factor in the development of MGD.

The seven studies that did not include a control group of non-CL wearers [25—29,31,33] will not be described in detail but can be found in Table 1.

Studies showing no association between MGD and CLs

Seven studies that found no significant association between MGD and CL wear were identified (Table 2).[7,35—40] Six studies[7,35—37,39,40] used both functional and morphological assessments. Of these, three included a control group of non-CL wearers.[35,36,39]

Hom et al.[35] examined randomly selected participants, including both CL wearers and controls. They reported that MGD was significantly correlated with patient age. They found an overall prevalence of 38.9% of MGD, without a significant correlation between CL wear and poor MG expressibility. The study was conducted at several clinical sites which may have led to non-uniformity among the examiners in diagnosing impaired secretion from the glands. Marren[36] also did not find a significant relationship between MG blockage and CL wear, while investigating the relationship between CL wear, eye make-up use, eye rubbing and MGD. Their MGD evaluation included examination of the MG orifices and assessment of MG expression in CL-wearing participants compared to non-CL wearers. However, the cohorts were small and their examination included only the lower eyelid. Furthermore, neither study[35,36] considered CL type and duration of CL wear.

The third study that assessed both functional and morphological signs of MGD and that included a control group yielded equivocal results. This multicenter study[39] included non-CL wearers and CL wearers of all CL types and compared MG expressibility and meibum quality in both eyelids, as well as MG dropout, assessed by a meibography. Though higher meiboscores were found to be associated with CL wear, the mean difference of 0.2 was not clinically significant. When the authors controlled for CL wear and several clinical signs such as conjunctival staining and lid wiper epitheliopathy, they found an increased odds of a higher meiboscore in CL wearers. Conversely, OSDI score, TBUT, MG expressibility, meibum quality and tear osmolarity were not found to be associated with CL wear. Therefore, the authors concluded that there is an inconclusive association between CL wear and MG atrophy. However, as stated above, their findings cannot be interpreted as evidence for lack of effect of CL wear on MGs. In addition, the overnight CL wearers and CL dropouts, who are high risk for MG atrophy, were excluded[39] which may limit the conclusions that may be drawn from their study.

The three studies[7,37,40] that did not include a control group of non-CL wearers will not be described in detail but can be found in Table 2.

Discussion

The evidence for the effect of CL wear on the MGs is equivocal. Fifteen studies[2—4,10,24—34] (Table 1) reported functional and/or morphological changes in the MGs among CL wearers, with five studies showing significant correlations between the duration of CL wear and MG loss.[3,4,24,32,34]

Conversely, seven studies[7,35—40] (Table 2) did not report an association between CL wear and MGD suggesting that CL wear may not increase the risk of MGD. Of these, four found no correlation between CL wear and poor MG expressibility.[35,36,38,39] However, one did find a correlation between CL wear and a higher meiboscore.[39] Another examined overnight orthokeratology which differs greatly from other modalities of CLs, and may not be appropriate for assessing the effect of CL wear on MGs.[37] Finally, three other studies,[7,37,40] which found no effect of CL use on the MGs, did not include a control group of non-CL wearers, limiting these studies' conclusions.

Discrepancies between studies may be due to differences in the definition of MGD, specifically prior to the 2011 international workshop on MGD.[16] They may also stem from differences in the method of evaluation of MGD. For example, while some studies assess DE symptoms using the Contact Lens Dry Eye Questionnaire (CLDEQ),[7,10,31,33,40] others used the Dry Eye Questionnaire (DEQ-5),[10] or OSDI questionnaire.[2,4,10,24,27,32,34,37]

While some studies included a large pool of participants ($\geq$100)[2,3,7,10,29,30,34,35,38—40] others included small sample sizes[4,24—28,31,32,36,37] (Tables 1, 2). Furthermore, studies differ in the inclusion[2—4,10,24,30,32,34—36,38,39] vs. exclusion[7,25—29,31,33,37,40] of a control group of non-CL wearers.

Studies also vary in the assessment techniques. For example, MG morphological changes were assessed by transcutaneous infrared MG photography,[28] noncontact infrared meibography,[7,10,37] transillumination observation meibography,[32] BG-4M non-contact meibography system,[4] Oculus Keratograph 5M Meibo-Scan,[31,34,39,40] or scheimpflug imaging.[2,24] Some studies examined only the lower eyelid[4,7,25,26,28,32,35,36] or only the upper eyelid,[27] while others examined both eyelids.[2,3,10,24,31,34,39,40]

Arita et al.[3] reported that the total meiboscores of the upper eyelids were significantly higher compared to the lower eyelids in CL wearers. They suggested that the upper eyelid may experience more mechanical irritation since it completes larger movements during blinking. Therefore, there may be importance in the examination of both lids.

Another inconsistency between studies is the ages of participants which may influence the outcomes (see in Tables 1 and 2). Given that the number of MGs decreases with age,[44] studies that do not control for age, can be misleading.

A further source of discrepancy between studies is the CL materials used by participants of different studies. CL materials may affect the physiology of the MGs as a result of constant mechanical interaction between them.[27] Arita et al.[3] found no significant difference in gland atrophy area between rigid gas permeable and hydrogel CLs wearers, while Llorens-Quintana et al.[27] found significant changes in the area of gland atrophy and the number of glands of hydrogel CL wearers as opposed to silicone hydrogel CL wearers. Other studies[25,26,35] did not consider CL materials or duration of CL wear, parameters that may affect the results.

Studies conducted in different countries with different ethnic populations (Malaysia,[38] Los Angeles,[35] Spain,[27] Australia,[31] Turkey,[2] Japan[3]) may also account for differences in reported outcomes. For example, Asians have an absent or

lower crease and more fat in their upper eyelids,[45] and produce more secretion from the MGs upon expression compared to Caucasians.[38]

Additionally, some studies were multicenter clinical trials[24,33,39,40] which may be limited by inter-examiner variation in methodology, evaluation and rating of clinical findings.

The results of the studies in Table 1 suggest several pathophysiological mechanisms for loss of MGs in CL wearers. Korb and Henriquez[26] and Henriquez and Korb[25] suggested that mechanical obstruction in which epithelial cells accumulate into keratotic clusters, block the meibomian duct, thereby changing the oily secretion. In addition, their results suggest that the presence of bacteria and/or their toxins can damage the MGs. Ong and Larke[30] suggested that the permanent rubbing of the CLs at the lid margins during blinking may be a source of mechanical trauma to the lids. Arita et al.[3] noted that MG shortening in CL wearers began from the distal side, indicating that chronic irritation of the MGs by CLs through the conjunctiva is a major causal mechanism for changes in the glands. Uçakhan et al.[2] concluded that MG thickening may be due to friction, mechanical irritation, or as a result of primary or secondary inflammatory changes. Further research is required to elucidate the exact pathway and it may be a combination of mechanical obstruction, microbiological changes and mechanical abrasion by the CL that cause MGD.

Conclusions

Based on our review of the current literature, the effect of CL wear on the MGs is ambiguous and requires further elucidation. Prospective, longitudinal, large cohort, controlled, randomized studies are required to better understand the mechanisms of changes in MG morphology and function of CL wearers. Efforts should be made to include several CL materials, and CL wear-durations, with analysis taking these parameters into account. Furthermore, new studies should adopt the same criteria and techniques to diagnose MGD, such as those suggested by the international workshop on MGD[16] or OCEAN group[22] and include a control group. In so doing, these studies will efficiently and effectively identify the long-term impact of CLs on MG and MGD.

Declaration of Competing Interest

The authors have no conflicts to disclose.

Acknowledgments

We would like to thank Prof. Ariela Gordon Shaag, Dr. Jonathan Levine, Ms. Dinah Paritzky, and Prof. Desmond Fonn for their assistance with this review.

Funding statement

The authors have not received funding for this study.

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