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REVIEW

Efficacy of complete rings (MyoRing) in treatment of Keratoconus: a systematic review and meta-analysis

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Abstracts

Purpose We aimed to systematically review the existing evidence and determine the efficacy of MyoRing as a novel method for treatment of keratoconus using meta-analysis.

Methods Online electronic search of Medline, ISI Web of Science, Embase, Scopus, and Cochrane Library databases was performed with reference lists of relevant articles for pre–post trials published through August 2017. Uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), sphere, cylinder, spherical equivalent (SE), maximum, minimum, and mean keratometry were considered as the visual acuity outcomes. Weighted mean difference (WMD) with 95% confidence interval was used as pooled estimation of intervention efficacy using random-effects meta-analysis. Heterogeneity was measured with the Cochran Q statistic and quantified with the I^2 statistic using Stata software.

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Results Of the 47 potentially related studies, 21 eligible studies were included in the meta-analysis. The mean of uncorrected distance visual acuity (UDVA) based on LogMAR in patients with keratoconus had a significant change 3 months after implantation/embedding of the complete ring (WMD = − 0.73 (CI = − 0.88 to − 0.58), $I^2 = 79.9\%, p < 0.001$). Results support a statistically significance improvement in CDVA, SE, sphere, cylinder, and maximum keratometry after surgical intervention. Range of reported safety index, stability, and efficacy index by included studies was 1.7–2.7, 74–100%, and 0.9–1.96, respectively.

Conclusions MyoRing is an appropriate treatment option for keratoconus. Findings of this meta-analysis demonstrated that main visual outcomes have been improved 3, 6, and 12 months after the implantation of the complete ring (MyoRing).

Keywords Cornea · Keratoconus · MyoRing · Systematic review · Meta-analysis

Introduction

Keratoconus is an idiopathic, progressive, and non-inflammatory corneal disease in which the corneal stroma becomes thin and the cornea assumes the shape of a cone [1].This induces significant visual impairment and loss of vision. It occurs in 1 out of 2000 people (prevalence) with incidence rate ranging from 1 in 600 to 1 in 420 persons [2, 4]. Keratoconus induces mild-to-severe vision impairments by lengthening and thinning the cornea. This may be induced by irregular astigmatism, myopia, or repeated corneal scars [3, 5]. Although it is mostly bilateral disease, in some cases where the disease starts in one eye, it eventually spread to the other [6].

The disease progresses gradually such that it induces the loss of visual acuity particularly low contrast visual acuity even with the best vision correction devices, and over time, the corneal curvature becomes worse [7, 8]. The disease is usually detected by an optometrist when distortion in visual acuity is not correctable using glasses. This disease could develop in all races, and male preponderance have been demonstrated [9].

There are several treatment options for keratoconus, which are chosen based on the severity of the disease and the condition of the patient. At the initial stages, the use of corrective glasses is the best choice of treatment. However, in mild cases, the use of contact lenses can be helpful [10]. In more advanced or severe cases, and in cases where the cornea is deformed, keratoplasty is suggested as a treatment option. Although keratoplasty is an acceptable treatment option for keratoconus, research studies are currently being conducted to pursue less invasive treatment techniques such as cross-linking, laser methods (such as photorefractive keratectomy, phototherapeutic keratectomy, and LASIK), or a combination of these techniques. In recent decades, the alternative technique for the treatment of keratoconus involves the use of rings embedded in the cornea [11–14].

Two types of these rings are employed in the treatment of the cornea: segment rings and complete rings. The first is preferred because of its ability to strengthen the structure of the cornea in mild keratoconus; however, there are no proofs to demonstrate its effect on advanced cases of keratoconus [11, 15–17].

MyoRing is complete rings implanted into the cornea, and they have the advantage (compared to segment rings) of producing tremendous effect on advanced cases of keratoconus. They also have the ability to reduce the kerametric strength of the cornea [17, 18]. The use of complete rings as a refractive technique was proposed to minimize spherocylindrical error as well as balance the central curvature of the cornea and reduce high-order aberration by adjusting the surface of the cornea [17–19]. However, in 2008, the concept of a complete ring for correction of myopia was repeated employing an innovative embedding technique. This new technique called CISIS (system for embedding inside the corneal stroma) involves placing a complete and flexible ring in the corneal pocket [13, 20]. These rings are considered acceptable alternative treatment options for myopia, astigmatism, and corneal ectasia and may delay (and even eliminate) the need for a corneal transplant and ameliorate the patient's quality of life [19, 21].

Considering the novelty of this method, the limited trial studies published on the safety and efficacy of these rings with inconsistent findings, and the desire to provide powerful and applicable evidence for the clinical practice of this new healing technique, we

conducted a systematic review and meta-analysis of all published clinical trials to assess the efficacy and safety of complete rings (MyoRing) in the treatment of keratoconus. It seems this is the first study to combine the significant outcome measures from clinical trial studies on the treatment of keratoconus employing MyoRing procedure.

Methods

We reported this systematic review and meta-analysis using preferred reporting items for systematic reviews and meta-analysis (PRISMA) guidelines.

Search strategy

International databases (Medline, Embase, ISI Web of Science, Scopus, and Cochrane Library) were used as search engines to obtain scientific evidence relevant to MyoRing and keratoconus outcomes (uncorrected distance visual acuity (UDVA), corrected distance visual acuity (CDVA), sphere, and cylinder, spherical) throughout the month of August 2017. The following keywords were used to search for the related articles: keratoconus, keratocon, cornea, MyoRing, complete or continuous or full NEAR ring or implant, intrastromal near implant, or intracorneal near the implant. Moreover, the reference lists of any relevant original and reviewed articles were considered. No language restriction or publication date limitations were applied as criteria for the search, or criteria for inclusion in the study. Two authors (KT and FN) independently searched and screened the studies. Controversies were solved by L J.

Inclusion criteria and outcomes

We included all clinical trial studies (randomized and non-randomized) that grouped patients with moderate-to-advanced stage of keratoconus following MyoRing technique procedure, study intervention, use of complete rings or MyoRing, outcome considerations, and endpoints, as well as uncorrected distance visual acuity (UDVA, stated in LogMAR scale), and corrected distance visual acuity (CDVA, stated in LogMAR scale) as primary visual outcomes, and maximum keratometry value (Kmax), minimum keratometry value (Kmin), mean keratometry value (Kmean), sphere, cylinder, and spherical equivalent (SE) as the secondary outcomes. Efficacy was determined as the absolute differences among the mentioned outcomes from baseline (preoperative) to the postoperative endpoint.

Data extraction and quality assessment

Duplicate publications were removed, and two reviewers individually evaluated the studies identified by the search strategy in order to select those that fulfilled the eligibility criteria. Two independent reviewers (KT and FN) individually extracted the data, which included study design, country, and year of publication of the articles employed in the studies, population characteristics, participant inclusion and exclusion criteria, recruitment technique, participation and follow-up rates, intervention and outcome definitions, features of data collection, numbers of participants, effect sizes, and statistical significance tests. Where there was disagreement between the independent data extraction reviewers (KT and FN), the inconsistency was resolved in consultation with the predefined investigator (L J). In respect of cases of missing data, correspondence was sent to the first author of the articles by email request for the provision of the missing information (data).

Two reviewers (KT and LJ) independently evaluated the quality of the articles included in the study based on before–after quality assessment tool. This tool considers the methodological quality and risk of bias using 12 questions scale [22]; thereafter, the quality of each study was classified into poor, fair, and good.

Statistical analysis

In the present meta-analysis, we employed the weighted mean difference and a 95% confidence interval for the absolute difference of the concerned outcomes of uncorrected distance visual acuity (UDVA) and corrected distance visual acuity (CDVA) in the LogMAR scale. The pooled measure effect was estimated using the Der-Simonian and Laird technique.

Heterogeneity between studies was evaluated using the I^2 statistic ($I^2 = 0\%$ indicates low heterogeneity and $I^2 \geq 50\%$ indicates substantial heterogeneity) which represents the correct percentage of total

variation among the studies that exhibited heterogeneity. Cochran's Q statistic was also employed to analyze the statistical significance of the heterogeneity. In order to find out which study (if any) had the most impact on the heterogeneity test and assess the robustness of summary findings, we conducted sensitivity analysis by successively removing a particular study or group of studies. Additionally, we carried out subgroup analyses to assess the source of heterogeneity across studies and investigate whether the correlation differed depending on the type of surgical techniques (Femtosecond vs. PocketMaker).

Visual inspection of funnel plots was done in order to evaluate the publication bias [23]. Also, the publication bias was formally tested with Egger's regression asymmetry tests to determine the asymmetry of the funnel plots, where $p < 0.10$ was considered as evidence of bias. In addition, Begg's adjusted rank correlation test and the trim-and-fill method for simulation were employed. All statistical tests were two tailed, and the significance level was considered less than 0.05 ($p < 0.05$) for all tests except publication bias tests. Statistical analyses were performed using Stata software, version 11.2 (Stata Corp., College Station, TX, USA).

Results

Characteristics of studies

The process for selection of articles included in the study and articles excluded from the study is presented using the PRISMA flow diagram in Fig. 1. Characteristics of the pre–post studies included in the meta-analyses are presented in Table 1. Finally, this meta-analysis was conducted on the basis of 21 studies and involved 736 eyes of 694 patients in age groups 13–62 years. In 13 trials, keratoconus was treated employing PocketMaker surgical technique, but in other studies, Femtosecond technique was employed in the treatment of keratoconus. Five studies reported the safety index (postoperative CDVA/preoperative CDVA) in the range of 1.7–2.7. Stability of intervention (MyoRing) was reported only in three studies (minimum = 74% and maximum = 100%). The reported range of efficacy and efficacy index (postoperative UDVA/preoperative CDVA) in two of the studies examined was 22.5–97% and 0.9–1.96, respectively.

Outcomes

Visual acuity outcomes (UDVA, CDVA)

Visual acuity/insight was documented and investigated as the logarithm of the minimum angle of resolution (LogMAR) value. The uncorrected distance visual acuity (UDVA) was assessed as visual acuity outcome in three, six, and twelve and beyond twelve months after postoperative follow-up.

Pooled estimations related to UDVA are shown in Fig. 2. There was a significant change in UDVA (based on LogMAR) 3 months after embedding the complete ring (mean difference = − 0.73, CI = − 0.88 to − 0.58, $p < 0.001$, $I^2 = 78.3\%$) when compared with the preoperative time. There was no evidence of publication bias (Egger test $p = 0.11$).

There was a significant difference in UDVA 6 months after MyoRing implantation; however, due to high levels of heterogeneity, the results were not very reliable (mean difference = − 0.51, CI = − 0.72 to − 0.33), $p < 0.001$, $I^2 = 97.6\%$). Publication bias was not observed (Egger test $p = 0.49$).To assess the influence of every single study on pooled results, the positive effect of MyoRing was observed consistently in sensitivity analysis.

In order to find out the source of heterogeneity, subgroup meta-analysis was performed based on the surgical techniques (Femtosecond, PocketMaker), although this strategy showed no effect of surgical technique on heterogeneity. Subgroup analysis did not also contribute to the reduction of heterogeneity. The same procedure was repeated for a year after the surgical intervention. The visual acuity (CDVA) measured in 3 and 6 months after intervention (MyoRing) showed statistically significant changes compared to the baseline/preoperative values. However, heterogeneity was observed among the studies. In a sensitivity analysis, the significant positive effect of MyoRing was observed consistently.

The mean difference of CDVA in LogMAR scale was meaningfully inferior to the preoperative value in both follow-ups, after 12 months and beyond 12 months (Fig. 3). The quantity of heterogeneity at related weighted mean difference and a CI of 95% were − 0.22 (− 0.29 to − 0.14), $I^2 = 77.1\%$,

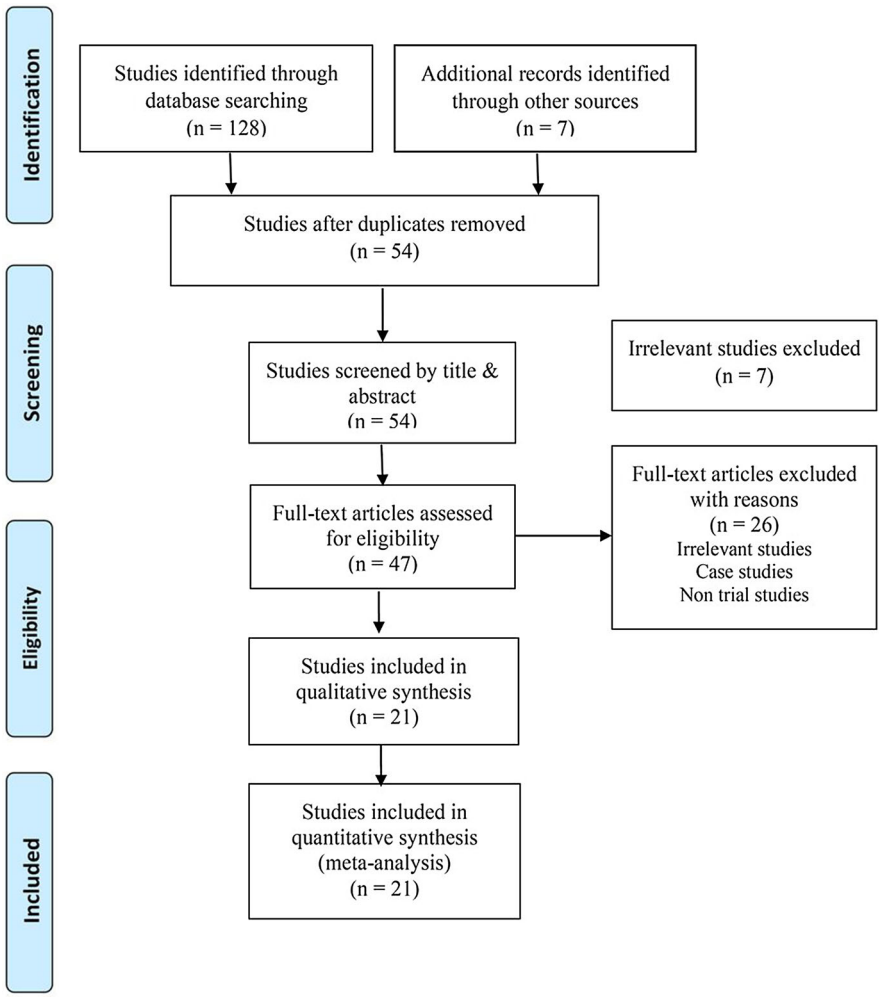


Fig. 1 PRISMA flowchart of included studies

$p < 0.001$, and -0.24 (-0.29 to -0.20), $I^2 = 24.8\%$ $p < 0.001$, respectively, with no evidence of publication bias in both cases.

Corneal topography outcomes (Kmax, Kmean, Kmin)

As seen in Table 2 and Fig. 4, Kmean was reduced 3 and 6 months after MyoRing implantation. Although the observed heterogeneity among the studies was significant in the sixth month after surgical intervention ($I^2 = 87.50\%$), no evidence of publication bias was found (Egger test $p = 0.58$). There was a significant change in Kmax during 3-, 6-, 12-, and > 12-month follow-up (Table 2).

Refractive Characteristics (Spherical Equivalent (SE), Sphere, and Cylinder)

Spherical equivalent was reported by studies following subsequent intervention in the third month. The SE refraction forest plots showed a considerable change after 3-, 6-, 12- and > 12-month follow-up, although the observed heterogeneity was significant at the 6-month follow-up (Table 2). The weighted mean difference of the sphere changed significantly during the 12-month follow-up (WMD = 3.5, 95% CI = 2.74, 4.25). The pooled summary result for cylindrical refraction at 12 months showed significant improvements after the 12-month follow-up (WMD = 2.68, 95% CI = 2.23, 3.12).

Table 1 Characteristics of studies included in the systematic review and meta-analysis

Author (Ref.)	Year	Patient's characteristics	Gender		Surgical technique	Diagnosis	Clinical outcome measures	Study quality
			Male *N* (%)	Female *N* (%)				
Alio et al. [24]	2011	12 eyes from 11 patients with ages ranging from 17 to 50 years were included. All cases presented with reduced best spectacle-corrected visual acuity, contact lens intolerance or discomfort, and central corneal thickness of more than 350 μm	7 (63.64)	4 (36.36)	Femtosecond	Corneal ectasia (A total of 11 keratoconus cases and 1 case of post-LASIK ectasia were included)	UDVA, CDVA, manifest refraction, keratometry, corneal asphericity, corneal higher-order aberrations, pachymetry, CH, CRF	Fair
Studeny et al. [25]	2014	22 eyes from 20 patients with mean age of 28.41 (from 18 to 50) years were included. Keratoconic eyes with no corneal scar, minimum corneal thickness 350 μm, and uncorrected distance visual acuity (UDVA) worse than 0.25 logMAR	14 (70)	6 (30.00)	Cross-linking & PocketMaker	Keratoconus	UDVA, CDVA, sphere, cylinder, mean k, corneal astigmatism	Fair
Studeny et al. [26]	2015	32 eyes from 30 patients with mean age of 30.08 (± 11.56) years were included. The classification of keratoconus was determined on the basis of a division according to Amsler Krumeich. In 4 patients 1st degree keratoconus, in 11 cases 2nd degree keratoconus, in 14 cases 3rd degree and in 3 cases 4th degree	23 (76.67)	7 (23.33)	PocketMaker	Keratoconus	UDVA, CDVA, the residual subjective refractive error, pachymetry, keratometry (Kmax, Kmean) and the size of corneal astigmatismus	Fair
Pashtayev et al. [27]	2014	30 eyes from 23 patients	Not reported	Not reported	Femtosecond	Keratoconus	keratometry (Kmean), CH (corneal hysteresis), CRF	Fair
Jabbarvand et al. [28]	2013	95 eyes from 95 patients with a mean age of 27.16 4.79 years and with moderate-to-advanced keratoconus were included. 56 eyes with stage II keratoconus, 18 eyes with stage III keratoconus, and 21 eyes with stage IV keratoconus	67 (70.50)	28 (29.50)	PocketMaker	Keratoconus	UDVA, CDVA, sphere, cylinder, SE, CCT, Km, HOA, coma-like, spherical-like	Good

Table 1 continued

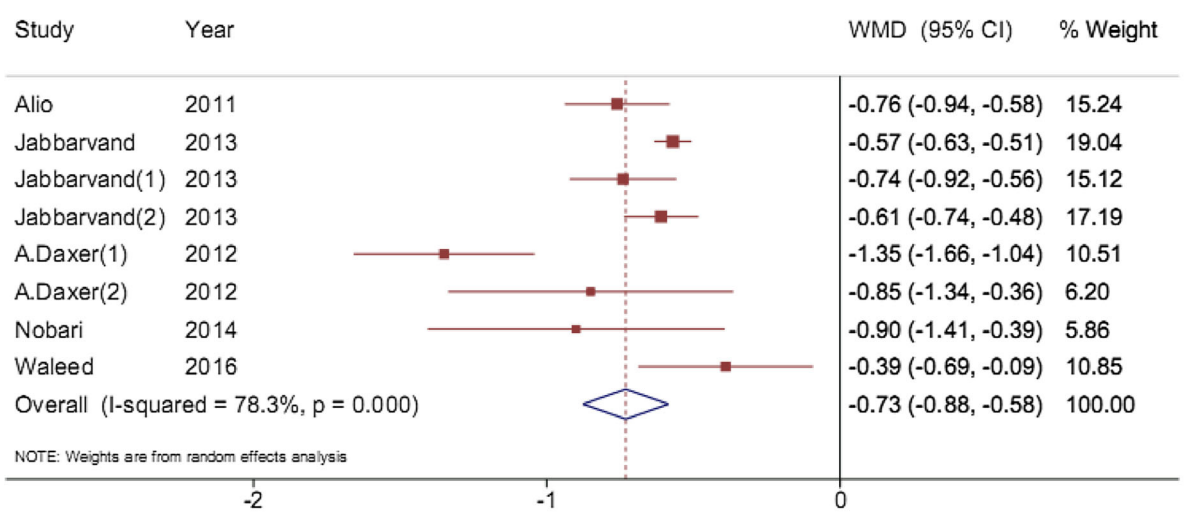
Author (Ref.)	Year	Patient's characteristics	Gender		Surgical technique	Diagnosis	Clinical outcome measures	Study quality
			Male *N* (%)	Female *N* (%)				
Jabbarvand et al. [21]	2013	98 keratoconic eyes of 98 patients with a mean age of 30.7 years ± 9.01 (SD) with moderate and advanced keratoconus, all patients presented with reduced visual acuity, contact lens intolerance, and a central corneal thickness of more than 360 mm	43 (43.87)	55 (56.13)	Femtosecond	Keratoconus	UDVA, CDVA, manifest refraction, keratometry, corneal higher-order aberrations (HOAs), pachymetry, corneal hysteresis (CH), and corneal resistance factor (CRF)	Good
Saeed et al. [29]	2014	23 eyes from 23 patients with KC and mean age of 21.7 ± 10.9 years (range 13–48 years) and with moderate-to-advanced keratoconus were included.	12 (52.17)	11 (47.82)	PocketMaker	Keratoconus	UCVA, BCVA, Kmin, Kmax, Kmean, corneal astigmatism, corneal thickness, slit-lamp examination	Fair
Hosny et al. [30]	2015	15 eyes, mean age of patients was 22.4 year. Substantial number of keratoconus grade IV cases were included. Inclusion criteria were reduced spectacle correction or contact lens intolerance, and a Kmax of between 42 and 65 D	Not reported	Not reported	Femtosecond	Keratoconus	UCVA, BCVA, mean K (Km), sphere, topographic cylinder, and corneal asphericity value	Poor
Jabbarvand et al. [18]	2014	21 eyes from 21 patients, patients were > 20 years with moderate-to-advanced keratoconus and intolerant to contact lenses or glasses	Not reported	Not reported	Femtosecond	Keratoconus [depth 250] Keratoconus [depth 300]	UDVA, CDVA, sphere, cylinder, keratometry, corneal biomechanical characteristics	Fair
Daxer et al. [31]	2010	15 eyes from 11 patients, with a mean age of 35 years ± 12 (SD) (range 22 to 60 years). Patients with no corneal scar, no history of corneal surgery, a minimum corneal thickness 350 mm, an uncorrected distance visual acuity (UDVA) not better than 0.25, and a keratometry (K) reading greater than 42.00 diopters were included	8 (72.72)	3 (27.28)	PocketMaker	Keratoconus	UDVA, CDVA, sphere, cylinder, spherical equivalent, keratometry	Poor
Bikbov and Bikbova [32]	2012	26 eyes from 22 patients with progressive keratoconus of the I-II disease degree according to the Amsler classification	Not reported	Not reported	PocketMaker	Keratoconus	UDVA, CDVA, keratometry, corneal astigmatism	Poor

Table 1 continued

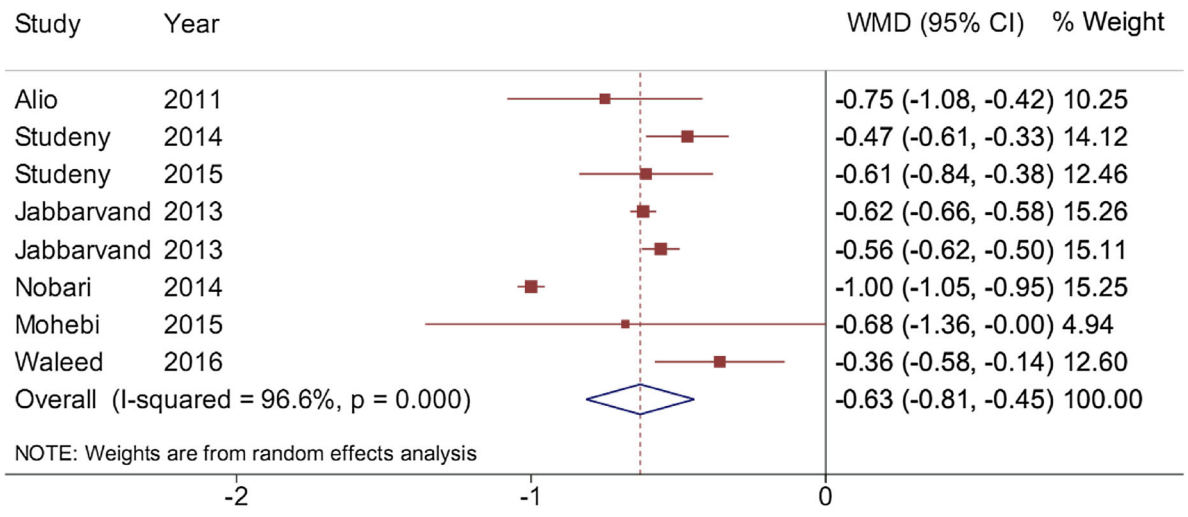
Author (Ref.)	Year	Patient's characteristics	Gender		Surgical technique	Diagnosis	Clinical outcome measures	Study quality
			Male *N* (%)	Female *N* (%)				
Zhadan et al. [33]	2014	22 eyes from 22 patients	Not reported	Not reported	PocketMaker	Keratoconus	keratometry (Kmin, Kmax), Corneal thickness (the thinnest point)	Poor
Daxer et al. [34]	2016	17 eyes from 13 patients with the age at the time of surgery ranged from 21 to 50 years (median 35 years). Of the 17 eyes 3 had grade I, 4 had grade II, 5 had grade III, 3 had grade IV and 2 had grade V. A minimum of 3 eyes experienced progression Of the disease in the year prior to surgery	11 (84.61)	2 (15.39)	PocketMaker	Keratoconus	UDVA, CDVA, keratometry, sphere, cylinder, corneal thickness	Fair
Daxer [35]	2012	5 eyes suffering from keratoconus with central cones and 5 eyes suffering from keratoconus with non-central cones were compared Both groups consisted of advanced cases with preoperative central K-reading ranging from 58.4 diopters (D) to 68.8 D in the central cone group and 55.75 to 65.8 D in the non-central cone group. Both groups have also comparable age structure	4 (40.00)	6 (60.00)	PocketMaker	Keratoconus	UDVA, CDVA, sphere, cylinder	Poor
Janani et al. [36]	2016	40 eyes from 37 patients with moderate and severe keratoconus aged 18 and 45 years	19 (51.30)	18 (48.70)	PocketMaker	Keratoconus	UDVA, CDVA, sphere, cylinder, spherical equivalent, keratometry (Kmin, Kmax, Kmean)	Fair
Daxer et al. [37]	2012	Ziemer (7 eyes) and Dioptex (7 eyes) with comparable age structure and sex distribution. All patients consisted of moderate and advanced keratoconus with comparable severity of the disease	Not reported	Not reported	PocketMaker	Keratoconus	UDVA, CDVA, sphere, cylinder	Poor
Nobari et al. [38]	2014	54 eyes from 50 patients with mean age of 28.48 ± 6.3, patients with moderate and severe (stage II and III) keratoconus	27 (54.00)	23 (46.00)	PocketMaker	Keratoconus	UDVA, CDVA, sphere, cylinder, spherical equivalent, keratometry (Kmin, Kmax, Kmean)	Good

Table 1 continued

Author (Ref.)	Year	Patient's characteristics	Gender		Surgical technique	Diagnosis	Clinical outcome measures	Study quality
			Male *N* (%)	Female *N* (%)				
Mohebbi et al. [39]	2015	47 eyes from 46 patients age between 15 and 35 years (mean age of 26.08 ± 6.21 years) with keratoconus grade 1 to 3 according to the Amsler–Krumeich grading system	(55.30)	(44.70)	Femtosecond	Keratoconus	UDVA, CDVA, sphere, cylinder, spherical equivalent, keratometry (Kmin, Kmax, Kmean), CCT, minimal corneal thickness, ACD, PD	Good
Al-Tuwairqi et al. [40]	2016	18 eyes from 18 patients aged between 18 and 50 years (mean age of 28.85 ± 6.08). Substantial number of cases were had moderate-to-advanced keratoconus	12 (66.67)	6 (33.33)	Femtosecond	Keratoconus	UDVA, CDVA, sphere, cylinder, spherical equivalent, keratometry (Kmin, Kmax, Kmean), central corneal thickness (CCT), root mean square (RMS)	Fair
Bikbova et al. [41]	2018	Myoring (41 eyes) myoring + CXL (39 eyes) patients aged older than 18 years with keratoconus II–III Amsler classification. Inclusion criteria: diagnosis of keratoconus, intolerance of contact lenses or glasses, and documented progression of a disease	54 (70.00)	24 (30.00)	PocketMaker	Keratoconus	UDVA, CDVA, sphere, cylinder, spherical equivalent, keratometry (Kmin, Kmax, Kmean), pachymetry thinnest point, CCT, corneal astigmatism	Fair
Pashtaev et al. [42]	2017	Grade 2 (29 eyes from 28 patients) Grade 3 (41 eyes from 37 patients)	Not reported	Not reported	Femtosecond	Keratoconus	CDVA, keratometry (Kmean), higher-order aberrations (HOAs)	Poor



Pre-and 3-months Post-operative UDVA results

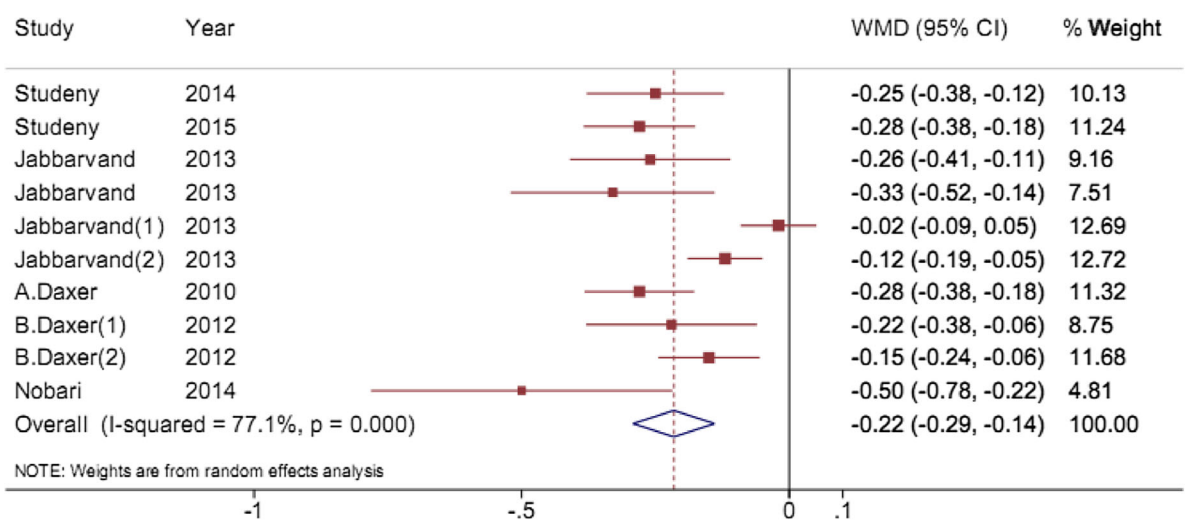


Pre-and 6-months Post-operative UDVA results

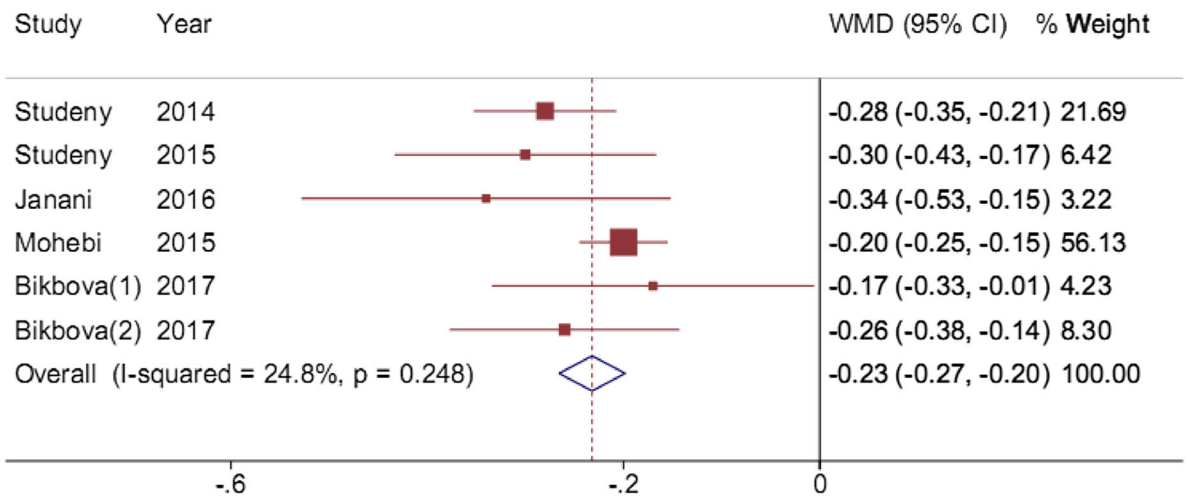
Fig. 2 Forest plot of weighted mean difference in visual acuity (UDVA) after MyoRing technique, separated by length of the follow-up. Diamond represents the weighted mean difference estimate, and its width shows corresponding 95% CI with random-effects model. The size of the square and its central point reflect the study-specific statistical weight (inverse of variance) and point estimate of the mean difference, and horizontal line reflects corresponding 95% CI of the study. I^2 test is used to assess the statistical heterogeneity ($p < 0.10$) across studies

A few studies were conducted on the COMA index after the operation. Individual study effects and the overall summary effects at 12 months after embedding the complete ring are presented in Fig. 5. Publication bias was observed (Egger test, $p = 0.01$); however, no omitted study was explored by the trim-and-fill technique.

Higher-order aberration (HOA) as corneal parameter was reported in only one of the studies 3 months after surgical intervention, but this parameter



Pre-and 12-months Post-operative CDVA results



Pre-and more than 12-months Post-operative CDVA results

Fig. 3 Forest plot of weighted mean difference in visual acuity (CDVA) after MyoRing technique, separated by length of the follow-up. Diamond represents the weighted mean difference estimate, and its width shows corresponding 95% CI with random-effects model. The size of the square and its central point reflect the study-specific statistical weight (inverse of variance) and point estimate of the mean difference, and horizontal line reflects corresponding 95% CI of the study. I^2 test is used to assess the statistical heterogeneity ($p < 0.10$) across studies

improved dramatically in both the 6- and 12-month follow-up (Fig. 6). No evidence of publication bias was observed in both cases (Egger test $p = 0.09$, and $p = 0.26$, respectively).

Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis conducted to investigate the efficacy of complete rings (MyoRing)

Table 2 Corneal topography outcomes before and after MyoRing at 3, 6, 12, and > 12 months

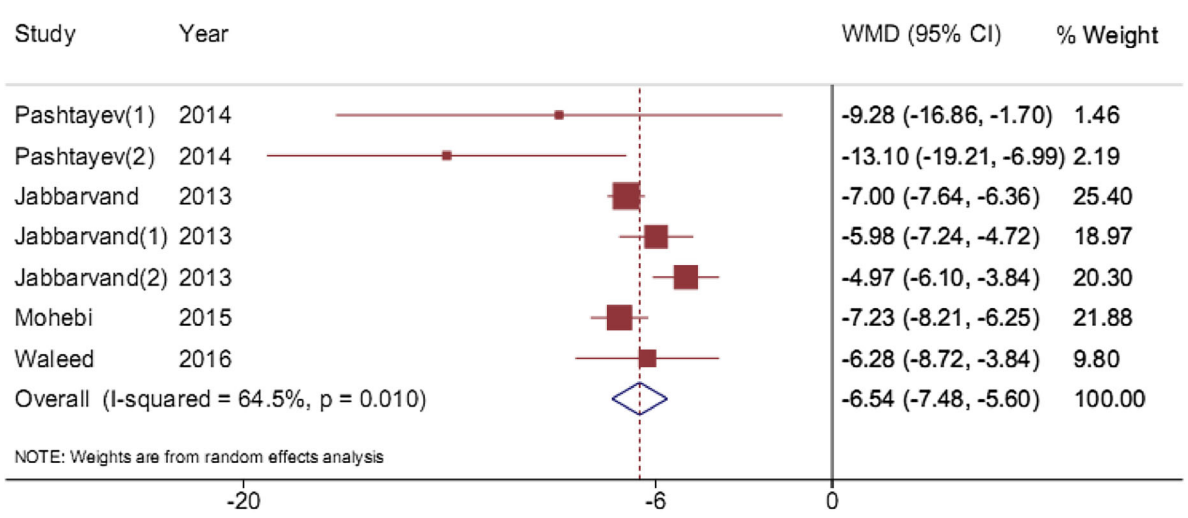
Outcome	WMD[a]	95% CI	*p* value	Heterogeneity (I^2 %)
Kmean				
3 month	− 6.54	− 7.48, − 6.50	< 0.001	64.50
6 month	− 6.86	− 8.30, − 5.42	< 0.001	87.50
12 month	No study was reported			
> 12 month	No study was reported			
Kmax				
3 month	− 7.18	− 8.23, − 6.13	< 0.001	13.39
6 month	− 6.29	− 7.09, − 5.50	< 0.001	0.00
12 month	− 5.9	− 7.25, − 4.55	< 0.001	0.00
> 12 month	− 5.18	− 5.97, − 4.39	< 0.001	47.70
Kmin				
3 month	One study was reported			
6 month	− 4.98	− 6.37, − 3.59	< 0.001	47.70
12 month	− 3.29	− 5.08, − 1.51	< 0.001	51.00
> 12 month	− 3.31	− 5.78, − 0.84	0.009	66.08
SE[b] *refraction*				
3 month	6.24	4.26, 8.23	< 0.001	0.00
6 month	6.09	4.78, 7.39	< 0.001	78.20
12 month	4.68	3.63, 5.73	< 0.001	0.00
> 12 month	5.15	4.07, 6.23	< 0.001	0.00
Sphere				
3 month	No study was reported			
6 month	No study was reported			
12 month	3.50	2.74, 4.25	< 0.001	65.50
> 12 month	No study was reported			
Cylidrical Refraction				
3 month	No study was reported			
6 month	No study was reported			
12 month	2.68	2.23, 3.12	< 0.001	69.50
> 12 month	No study was reported			

[a]Weighted mean difference
[b]Spherical equivalent

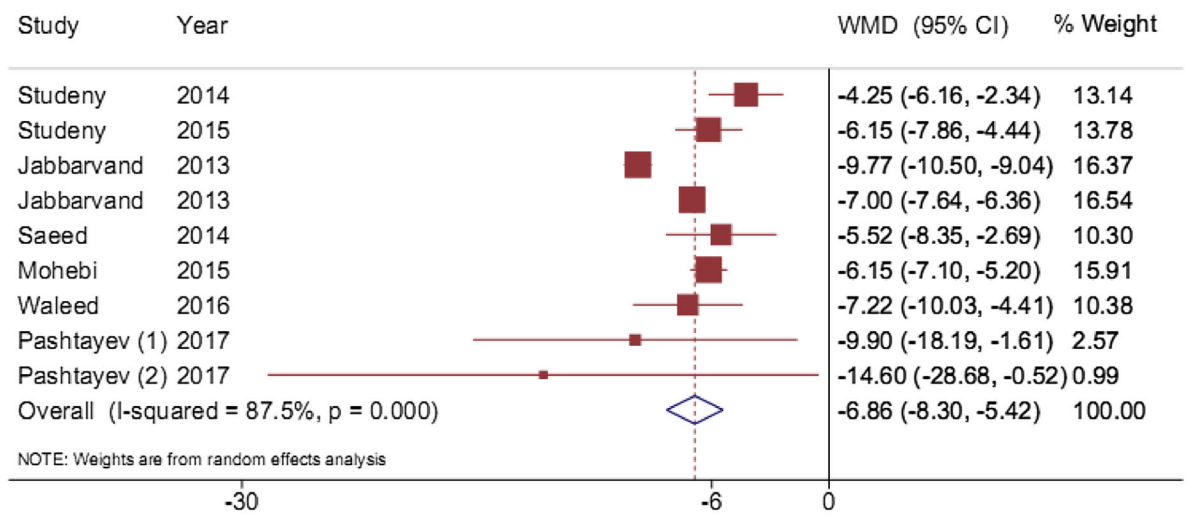
in the treatment of keratoconus. MyoRing (Dioptex GmbH, Austria) is a 360° continuous full-ring implant available in diameters ranging from 5 to 6 mm and thickness ranging from 200 to 400 μm in 20 μm increments. The anterior surface is convex, and the posterior surface is concave, with a radius of curvature of 8.00 mm [43].

The results showed considerable improvement in visual acuity outcomes (UDVA, CDVA), and almost, the same conclusion can be attributed to the secondary outcomes (minimum, maximum, and mean of keratometry values as corneal topography outcomes, refractive characteristics, spherical equivalent (SE), sphere, cylindrical refraction, and higher-order aberration).

The findings revealed significant improvement 3 months after the operation, which is clinically important; and after this period (3 months), consistency of



Pre-and 3-months Post-operative Mean Keratometry results



Pre-and 6-months Post-operative Mean Keratometry results

Fig. 4 Forest plot of change in corneal topography features (Kmean) after MyoRing technique, separated by length of the follow-up. Diamond represents the weighted mean difference estimate, and its width shows corresponding 95% CI with random-effects model. The size of the square and its central point reflect the study-specific statistical weight (inverse of variance) and point estimate of the mean difference, and horizontal line reflects corresponding 95% CI of the study. I^2 test is used to assess the statistical heterogeneity ($p < 0.10$) across studies

visual indicators was discussed. The findings of the study showed the consistency or steadiness of the main consequences (UCVA and BCVA) after 6 months and 1 year of subsequent surgical procedure. Typically, the complete ring is inserted into an intrastromal pocket, which is created by femtosecond laser [21, 24] or a PocketMaker microkeratome (Dioptex GmbH, Austria) [44]. Daxer et al. [37] have shown that visual outcomes of MyoRing implantation for keratoconus do not depend on whether the corneal pocket is created by the femtosecond laser or mechanical dissection using the PocketMaker microkeratome.

According to the results of this study, there was sufficient evidence that the full-ring implantation was

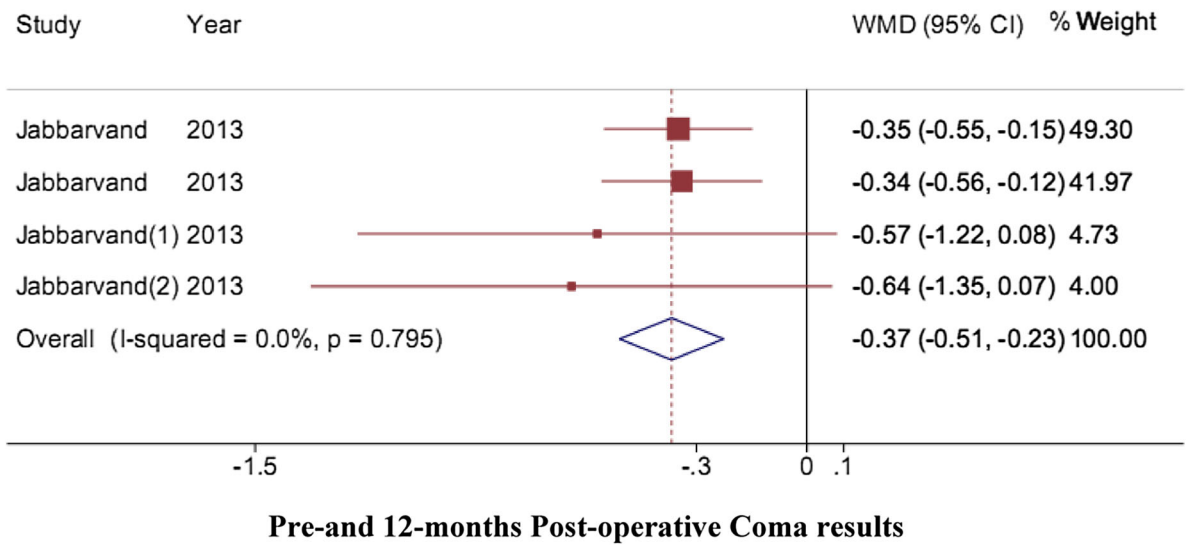


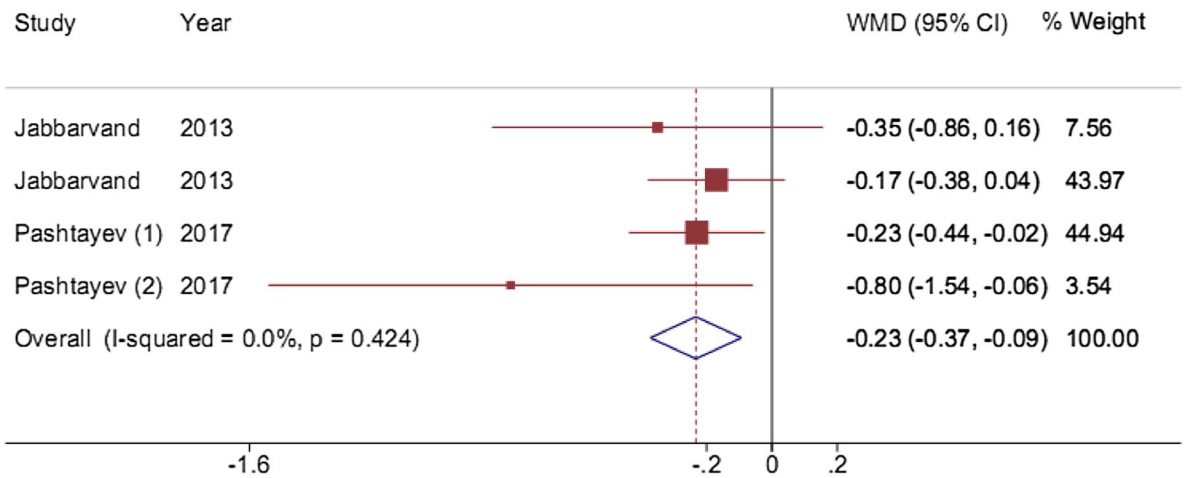
Fig. 5 Forest plot of change in COMA parameter after MyoRing technique, Diamond represents the weighted mean difference estimate, and its width shows corresponding 95% CI with random-effects model. The size of the square and its central point reflect the study-specific statistical weight (inverse of variance) and point estimate of the mean difference, and horizontal line reflects corresponding 95% CI of the study. I^2 test is used to assess the statistical heterogeneity ($p < 0.10$) across studies

efficacious in the treatment of keratoconus as well as improvement in visual indicators employing the PocketMaker technique. However, regarding the Femtosecond technique, the results cannot be relied upon and should be interpreted with caution owing to the heterogeneity of studies in some of the outcomes such as the BCVA.

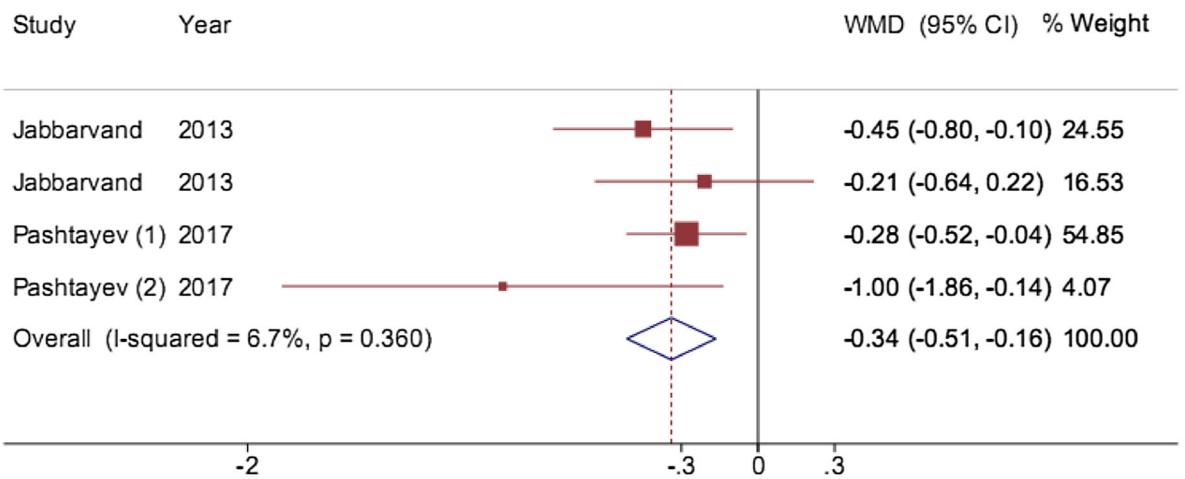
Findings of this meta-analysis were consistent with previous studies and buttressed the fact that MyoRing implantation alone could have satisfactory effect in preventing the progression of keratoconus and significantly flatten and normalize the cornea [4, 24, 34, 38, 45]. MyoRing implantation in patients with keratoconus leads to visual rehabilitation and by forming a new biomechanical balance could stop the development of the disease [46]. MyoRing implantation into a corneal pocket changes the shape of the cornea and therefore, the distribution of forces acting within the tissue. Since Myoring is a closed, complete ring, and located in a pocket (through a small incision) that has larger implant diameter, the cornea can find a new biomechanical equilibrium around the implant and rest biomechanically neutral in the postoperative corneal shape [46]. MyoRing is a safe treatment with uncommon complications. Extrusions, infections, or perforations are potential and rare complications. Merely one infection, two perforations, and seven extrusions have been observed on the more than 1500 MyoRing treatments in recent years in the world's leading keratoconus center in Austria (Dr. Daxer International Keratoconus Centre). Of course, these rare complications could be handled without any deadly results [47].

Al-Tuwairqi et al. [40] have compared two types of intracorneal rings, Keraring as an intrastromal corneal ring segment (ICRS) and MyoRing as an intrastromal corneal continuous ring (ICCR). Keraring 355° (ICR; Mediphacos, Minas Gerais, Brazil) is a new intracorneal ring design made of polymethyl methacrylate (PMMA) and is specially developed for a nipple-type keratoconus. It is available in a diameter of 5.7 mm and a thickness range of 200 and 300 µm [48]. Their study showed that Keraring and MyoRing corneal implants both performed well in improving visual outcomes and stabilizing the cornea. The stromal lenticule addition keratoplasty procedure as recent innovation is another new technique for the treatment of advanced keratoconus that is clinically effective in improving the corneal shape and vision of patients [49]

Implantation of the MyoRing caused greater improvement in the coma and better patient



Pre-and 6-months Post-operative HOA results



Pre-and 12-months Post-operative HOA results

Fig. 6 Forest plot of change in corneal parameters (HOA) after MyoRing technique, separated by length of the follow-up. Diamond represents the weighted mean difference estimate, and its width shows corresponding 95% CI with random-effects model. The size of the square and its central point reflect the study-specific statistical weight (inverse of variance) and point estimate of the mean difference, and horizontal line reflects corresponding 95% CI of the study. I^2 test is used to assess the statistical heterogeneity ($p < 0.10$) across studies

satisfaction, but BCVA improved only in the Keraring group, at the final follow-up visit.

A study by Sammour et al. [50] has compared Feraring as an intrastromal corneal ring segment (ICRS) and MyoRing, and also their study showed that there were no differences in different parameters except that the Ferrara ring showed more improvement in BCVA and spherical component.

Considering all the aforementioned, further large well-designed studies are required to clarify and ascertain the potential role and mechanism of MyoRing.

It should be noted that most of the studies included in the study reported no intra-operative complications during the MyoRing procedure [4, 5, 10, 19, 28]. This claim also applies to serious complications following

MyoRing surgery. However, few studies have reported that a very small number of patients complained of seeing a residual halo and glare [5, 8, 18, 36]. These side effects were more frequent in the early postoperative period than the late postoperative period.

Publication bias is of utmost concern in any systematic review and meta-analysis. However, visual assessment of the funnel plots, as well as corresponding appropriate statistical tests, showed no evidence of bias in this meta-analysis (data not shown). No missing study was identified by the trim-and-fill method in all independent analysis.

Findings of this meta-analysis should be interpreted with caution in the context of limitations related to the availability of data. Weakness in the reporting of results of studies conducted in some of the clinical disciplines, such as ophthalmology, was a limitation we encountered during the study. All of the articles included in this meta-analysis were non-randomized pre–post trials with no control group; thus, escalating the risk of bias and reduction in reliability is inevitable. It is important to consider the role of confounding factors (characteristics of the participants) which would most likely induce bias. It can be stated that residual confounding could exist in published studies. Furthermore, the relatively low power of the model should be considered because of the small number of articles involved in the study, which could be separated by study outcomes in some meta-analysis. Nonetheless, the argument for MyoRing implantation as a technique in the treatment of keratoconus seems logical considering its efficacy.

Conclusion

The embedding of complete rings including MyoRing is an appropriate treatment option for keratoconus. Findings of this meta-analysis demonstrated that visual outcomes (UDVA and CDVA) improved 3 months after the implantation of the complete ring (MyoRing); this trend was maintained for 6 months and 1 year after the operation. Summary estimates for studied secondary outcomes also confirmed this discovery. In order to confirm these findings, further prospective comparative clinical trials with large sample size and longer follow-up time are necessary.

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Authors' contributions LJ, KJ, and FN conceived the idea and designed the study. KT, LJ, and FN collected data, reviewed literature, and extracted data. KT, LJ, and MS, and MD participated in the analysis of data and interpreted the results. LJ, MD, and MS conceived the study aims and design, provide the data and measures, and designed the analysis. KJ, FN, and SJH reanalyzed data, made substantial contribution to interpretation of data, drafting the manuscript and revising it critically for important intellectual content and final approval of the version to be submitted and any revised version. All authors reviewed, discussed, provided critical comments, and approved the final manuscript. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Compliance with ethical standards

Conflict of interest The authors declared that they have no conflict of interest.

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