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Changes in temporomandibular joint morphology in class II patients treated with fixed mandibular repositioning and evaluated through 3D imaging: a systematic review

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Al-Saleh M. A. Q., Alsufyani N., Flores-Mir C., Nebbe B., Major P. W. Changes in temporomandibular joint morphology in class II patients treated with fixed mandibular repositioning and evaluated through 3D imaging: a systematic review.

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Abstract To estimate the effects of skeletal class II malocclusion treatment using fixed mandibular repositioning appliances on the position and morphology of the temporomandibular joint (TMJ). Two independent reviewers performed comprehensive electronic searches of MEDLINE, EMBASE, EBM reviews and Scopus (until May 5, 2015). The references of the identified articles were also manually searched. All studies investigating morphological changes of the TMJ articular disc, condyle and glenoid fossa with 3D imaging following non-surgical fixed mandibular repositioning appliances in growing individuals with class II malocclusions were included in the analysis. Of the 269 articles initially reviewed, only 12 articles used magnetic resonance imaging and two articles used computed tomography (CT) or cone-beam CT images. Treatment effect on condyle and glenoid fossa was discussed in eight articles. Treatment effect on TMJ articular disc position and morphology was discussed in seven articles. All articles showed a high risk of bias due to deficient methodology: inadequate consideration of confounding variables, blinding of image assessment, selection or absence of control group and outcome measurement. Reported changes in osseous remodelling, condylar and disc position were contradictory. The selected articles failed to establish conclusive evidence of the exact nature of TMJ tissue response to fixed mandibular repositioning appliances.

Key words: class II malocclusion; functional appliance; orthodontic appliance; temporomandibular disc; temporomandibular joint

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Introduction

Mandibular retrusion is considered the most common characteristic of class II malocclusion in children and adolescents (1). Mandibular repositioning appliances have been reported to successfully correct class II malocclusions (2–6). However, it is uncertain whether these appliances have beneficial or harmful effect on the articular tissues of the temporomandibular joint (TMJ) (7, 8). It has been suggested that fixed repositioning appliances apply near constant forces to the TMJ and may cause remodelling of the articular condyle and glenoid fossa, repositioning of the condyle and rotation of the mandibular body (5), which may lead to permanent damage to the TMJ structure(s). However, one previous systematic review revealed weaknesses of the literature and lack of evidence for disc changes and/or condylar or glenoid fossa remodelling (9).

Many methods have been used in the literature to evaluate the TMJ tissues. Although magnetic resonance imaging (MRI) is a sensitive and valid tool to analyse the morphology of TMJ articular disc, joint effusions and synovitis (10, 11), the reported assessment of articular disc position has been of a subjective nature. Subjective assessment of stages of disc displacement has relatively poor interexaminer reliability (12). Moreover, MRI has limited value when it comes to accurately depicting TMJ osseous abnormalities (13). Computed tomography (CT) is the gold standard for imaging bone. Cone-beam CT (CBCT) has much lower radiation exposure than multidetector CT (14) and is now used widely in orthodontic practice for the assessment of TMJ bone remodelling (15, 16).

Although these different methods have been reviewed previously, an updated systematic review is necessary due to several reasons:

- The previous systematic review identified controversies that were not resolved.
- The previous systematic review is outdated, and several additional related articles have been published.
- The previous systematic review focused exclusively on one type of fixed functional appliance.

The purpose of this review was to evaluate the fixed mandibular reposition appliance's effects on TMJ morphology and position (condyle, glenoid fossa and articular disc) in skeletal class II malocclusion treatment.

Materials and methods

Search strategy

Four databases, (MEDLINE, EMBASE, All EBM Reviews and Scopus) were systematically searched in all languages (until 5 May 2015). Keywords used in the search were *orthodontic appliances, functional/activator appliances, Crossbow or Forsus or Jasper Jumper or Herbst or MARA or Functional Mandibular Advancer, temporomandibular joint, TMJ, temporomandibular joint disc, jaw joint, mandibular joint, computed tomography, cone-beam computed tomography, magnetic resonance imaging*. A librarian specializing in health sciences databases was sought to identify the best selection of both truncated and MESH terms. Specific words used and how they were combined per database can be found in Online Appendix S1. In addition, bibliographies of the identified articles were manually searched.

Inclusion criteria

Study design

Clinical trials, cohort studies, case-control studies, cross-sectional studies, prospective and retrospective studies that investigated the TMJ morphologic and positional changes after non-surgical class II malocclusion treatment using fixed appliances were included. Case series/reports (unless consecutively treated), commentaries, editorials and letters were excluded.

Participants

Inclusion was restricted to children and adolescent patients with skeletal class II malocclusion treated with fixed mandibular anterior repositioning appliance.

Outcome measures

Any changes of the TMJ articular tissues, assessed by 3D imaging modalities (MRI, CT, CBCT), were included.

Selection process

All abstracts identified during the database search were screened thoroughly by two independent reviewers (M.A. and N.A.). Potentially relevant abstracts were then selected for full article independent evaluation by the same two reviewers. Any selection discrepancy was solved through discussion between the two reviewers.

Collected data

Study design, population, appliance type, treatment duration, imaging modality and measured outcomes for all included articles were summarized in Table 1. Outcomes that represent the change in condyle morphology/position, remodelling of glenoid fossa and disc morphology/position were reported and analysed.

Critical appraisal

To evaluate the articles for risk of bias, a recently developed quality assessment tool 'risk of bias assessment tool for non-randomized studies (RoBANS)' was used (17). Kim et al. (17) confirmed the inter-rater reliability, feasibility, concurrent, construct and face validities of this RoBANS tool. RoBANS was deemed suitable for the articles included in this review that assess before and after intervention outcomes.

The same reviewers independently evaluated the included articles for risk of bias.

Results

Database search

The electronic database search yielded a total of 269 articles. The primary review resulted in 30 potential articles that were further considered for inclusion. Based on a full-text review, 17 articles were selected (18–34). Two articles were identified by manual search as well (35, 36). The

article selection process is presented in Fig. 1. Finally, 14 papers fulfilled the inclusion criteria of our review (18–29, 35, 36). The remaining five articles from this final selection stage were excluded for the following reasons:

1. The MRI evaluation of the TMJ condition was performed after treatment. Data were compared with norms in the literature (30, 33).
2. The TMJ condition was evaluated using 2D imaging tools (such as transpharyngeal radiographs, conventional tomography, transcranial oblique radiographs or lateral cephalograms) (32, 34, 37).

Characteristics of the included articles

Included studies consisted of cohort groups of adolescent patients with class II malocclusions. Twelve articles reported the changes in TMJ articular tissues as demonstrated in MRI (18–24, 26–28, 35, 36). One article (25) used CT scan images to evaluate the volume of the condyle and glenoid fossa, while another (29) used co-registered serial CBCT images to assess TMJ osseous structure changes.

Synthesis of results

Results of the included studies were summarized in Table 2. Due to the heterogeneous nature of the finally selected studies, a meta-analysis was not attainable.

Quality assessment

The 14 included articles were assessed and scored according to guidelines of RoBANS (17). Assessments results are shown in Table 3. All included articles were considered to have high risk of bias. Multiple forms of bias were evident such as missing control group, ignoring gender effect as a co-factor, inadequate measurement tools and data analysis. Ten articles did not conduct blinding during image analysis (18–20, 25–29, 35). Four articles report descriptive analysis without proper statistical analysis (21–24). One article (17) reported results in graphics, which

Table 1. Characteristics of the included studies

	Study design	Population	Treatment type	Imaging	Measured outcome
Pancherz et al. (5)	Prospective cohort study	15 patients (11 M, 4 F) received treatments; mean age (13.5 years) No control	Herbst appliance; treatment duration (5–10 months)	MRI, 4 times (before, at start, during and after treatment)	Evaluated condyle and glenoid fossa remodelling following increased signal intensity in MR images. Evaluated condyle position using Joint Space Index (JSI)(38)
Ruf and Pancherz (20)	Prospective cohort study	39 patients (15 M, 22 F) received treatments; 25 adolescents (mean age 12.8 years), and 14 adults (mean age 16.5 years). No control	Herbst appliance; treatment duration (adolescents 7.1 months; adults 8.5)	MRI, 4 times (before, at start, during and after treatment). Lateral Ceph., 2 times (before and right before the end of treatment)	Evaluated condyle, glenoid fossa and ramus remodelling following increased signal intensity in MR images. Measured distances in lateral Ceph. to evaluate condyle and glenoid fossa remodelling
Pancherz et al. (18)	Prospective cohort study	15 patients (10 M, 5 F) received treatments; mean age (13.7 years). No control	Herbst appliance; treatment duration (6–11 months)	MRI [before, in 6 weeks, 13 weeks and right after treatment (7 month)]	Evaluated articular disc position and subjectively classified position using 'disc position index' (41). Three slices (medial, central and lateral) of closed and open-mouth MR image were analysed

Table 1. (continued)

	Study design	Population	Treatment type	Imaging	Measured outcome
Ruf and Pancherz (35)	Prospective cohort study	62 patients (27 M, 35 F) received treatments; mean age (14.4 years). No control	Herbst appliance; treatment duration (7.2 months)	MRI (before, right after treatment and one year after treatment)	Evaluated condyle and glenoid fossa remodelling following signal intensity in MR images. Evaluated condyle position using JSI. Evaluated articular disc position using [12 o'clock position (42), disc posterior band angle (43, 44) and intermediate zone position (41)]
Kinzinger et al. (26)	Prospective cohort study	20 patients (11 M, 9 F) received treatments; age (16–25 years). No control	Functional Mandibular Advancer (n = 17); Herbst (n = 3). Treatment duration (6–9 months)	MRI, 4 times (before, at start, during and after treatment)	Evaluated condyle position using JSI Evaluated articular disc position using 12 o'clock position and intermediate zone position. Three slices (medial, central and lateral) of closed and open-mouth MR image were analysed
Kinzinger et al. (27)			Functional Mandibular Advancer; treatment duration (6–9 months)		
Kinzinger et al. (36)		15 patients (8 M, 7 F) received treatments; age (12–16 years). No control	Functional Mandibular Advancer; treatment duration (6–9 months)		
Kinzinger et al. (28)		20 patients (10 M, 10 F) received treatments; age (6–16 years). No control			Evaluated condyle position using JSI. Evaluated condyle shape in axial, sagittal and coronal sections

Table 1. (continued)

	Study design	Population	Treatment type	Imaging	Measured outcome
Aidar et al. (21)	Prospective cohort study	20 patients (7 M, 13 F) received treatments; mean age (12 years). No control	Herbst appliance; treatment duration (12 months)	MRI, 3 times (before, during and after treatment)	Evaluated articular disc position using the angle between the disc posterior band, condyle and articular eminence. Three slices (medial, central and lateral) of closed and open-mouth MR image were analysed
Aidar et al. (22) Aidar et al. (23)		32 patients (16 M, 16 F) received treatments; mean age (12 years). No control		MRI, 4 times (before, during, after phase I, after phase II)	Evaluated articular disc position using 12 o'clock position and intermediate zone position. Three slices (medial, central and lateral) of closed and open-mouth MR image were analysed
Aidar et al. (24)					Evaluated the condylar morphology changes in the sagittal view and classified as normal (rounded with soft and intact cortex), remodelled (flattening) and degenerative (cavities, erosions, osteophytes or resorption)

Table 1. (continued)

	Study design	Population	Treatment type	Imaging	Measured outcome
Arici et al. (25)	Prospective clinical trial	30 patients (13 M, 17 F) received treatments; mean age (12 years). Control: 30 patients (9 M, 21 F) received no treatment; mean age (12 years)	Forsus nitinol flat spring (n = 30); treatment duration (6–9 months)	Computed tomography, 2 times (before and after treatment)	Evaluated the volume of the condyle and glenoid fossa. Evaluated the joint space using the circular space around the condyle in axial view
LeCornu et al. (29)	Case-control study	7 patients received treatments; mean age (13 years). Control: records of seven patients received class II elastics treatment; mean age (13.4 years)	Herbst appliance; treatment duration (13 months). Control group treatment duration (18.4 months)	CBCT, 2 times (before, after treatment)	Evaluated the condylar head, glenoid fossa remodelling using colour-mapped image super-imposition technique, scaled from –3 mm to +3 mm to represent bone remodelling

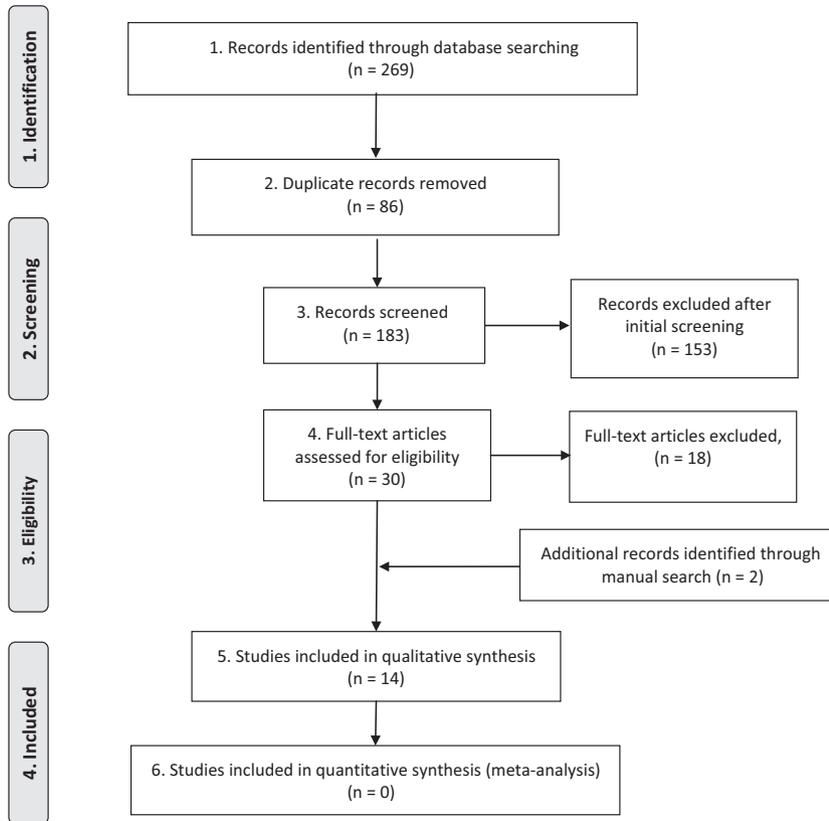


Fig. 1. PRISMA 2009 flow diagram.

led to missing or unclear data (18). One article (20) reported incomplete data (21). Scoring agreement between reviewers was 89% agreement, and kappa score of 0.8 both considered the substantial agreement (38).

Discussion

Since 2003, many articles have discussed the effect of different mandibular repositioning appliances on TMJ. The findings in these articles were critically analysed to shed the light on the evidence presented by the included articles. Popowich et al. (9) analysed the available evidence on the effect of Herbst appliance on TMJ in five articles. The included articles reported condylar and glenoid fossa remodelling and disc position using MRI, CT and tomography. Despite the methodological and assessment limitations of the reported articles, MRI data failed to provide conclusive evidence about condylar position relative to the glenoid fossa. This systematic review highlights the weaknesses of the reviewed

articles and the apparent lack of condylar and glenoid fossa remodelling, or disc position changes.

Osseous remodelling and condyle position

The articles published by Ruf and Panherz (19, 20) were based on subjective MRI assessment of remodelling of the glenoid fossa and condyle surface without evidence of blinding, report of calibration or reliability. The authors evaluated high signal intensity changes due to the hydrated subcortical layer in adolescents as an indicator to the bone remodelling, which has not been validated. Although MRI is considered as the most precise imaging technique to visualize the articular disc (39), it has poor identification of the osseous tissue margins and limited value when it comes to describing TMJ osseous abnormalities (13). Furthermore, these articles did not have an untreated control. Articles used a quantitative method to measure condyle position within the fossa. The condylar position was reported to be highly variable with a tendency of

Table 2. Summary of the included articles results

Pancherz et al. (5)	<p><i>Osseous remodelling:</i></p> <p>Remodelling of post-glenoid process in 73% temporomandibular joints (TMJs) at 6–12 weeks.</p> <p>Remodelling of posterosuperior surface of the condyle in 96% TMJs at 6–12 weeks.</p> <p><i>Condyle position:</i></p> <p>Acceptable anterior and posterior joint spaces change that was not affected by Herbst treatment.</p>
Ruf and Pancherz (20)	<p><i>Osseous remodelling:</i></p> <p>Remodelling of posterosuperior surface of the condyle in adolescents and young adults in 92–96% TMJs at 6–12 weeks.</p> <p>Remodelling of posterior ramus in 7% TMJs at 6–12 weeks.</p> <p>Remodelling of glenoid fossa in 72–78% TMJs at 6–12 weeks.</p> <p>Higher signal intensity was noticed in adults after appliance replacement (~7 months)</p>
Pancherz et al. (18)	<p><i>Articular disc position:</i></p> <p>Before treatment, an average protrusive disc position was reported. During treatment, over 50% of TMJs showed retrusive disc position. After treatment, discs were at retrusive position in comparison with their initial position.</p> <p>There was large individual variation in disc position index scores</p>
Ruf and Pancherz (35)	<p><i>Osseous remodelling:</i></p> <p>Before treatment, osteoarthritic changes were noticed in 17 TMJs, with associated disc displacement in 10 TMJs.</p> <p>After treatment, osteoarthritic changes were seen in 7 TMJs.</p> <p>One year after treatment, osteoarthritic changes were seen in 4 joints with associated disc displacement.</p> <p><i>Condyle position:</i></p> <p>Condyles were at slightly anterior position in the fossa before and 1 year after treatment.</p>

Table 2. (continued)

	<p>Condyles were at more anterior position during the period of appliance treatment and returned to their original position after appliance removal.</p> <p><i>Articular disc position:</i></p> <p>General disagreement of the 3 systems to evaluate the disc position in the same individuals was reported in the study.</p> <p>Using 'disc posterior band angle', articular discs were at more retrusive position during treatment and returned to their original position after appliance removal.</p> <p>Using 'intermediate zone position', articular discs were at more retrusive position during treatment than its original position</p>
Kinzinger et al. (26)	<p><i>Condyle position:</i></p> <p>During early treatment, condyles were significantly anteriorly displaced and gradually reduced to a central position within the fossa after appliance removal.</p>
Kinzinger et al. (27)	<p><i>Articular disc position:</i></p> <p>Before treatment, 40% of TMJs had anterior disc displacement. Fifteen per cent of TMJs with displaced discs improved to the normal physiological position after treatment.</p> <p>The <i>posterior band angle</i> analysis, all normal joints remained at the same physiological position after treatment.</p> <p>Using the analysis of variance (ANOVA), joints with disc displacement were significantly improved ($p = 0.03$) from $28.5 \pm 12.7^\circ$ before treatment to $18.1 \pm 13.3^\circ$ towards physiological position after treatment.</p> <p>The <i>intermediate zone position</i> analysis revealed that mean values of disc anterior displacement were significantly improved ($p = 0.04$) from 1.47 ± 0.89 mm before treatment to 0.88 ± 0.76 mm towards physiological position after treatment</p>

Table 2. (continued)

Kinzingher et al. (36)	<p><i>Articular disc position:</i></p> <p>Before treatment, 37% of TMJs had anterior disc displacement.</p> <p>The <i>posterior band angle</i> analysis, all normal joints remained at the same physiological position after treatment. Using the analysis of variance (ANOVA), joints with disc displacement were significantly improved ($p = 0.01$) from $32.2 \pm 9.8^\circ$ before treatment to $19.1 \pm 11.2^\circ$ towards physiological position after treatment.</p> <p>The <i>intermediate zone position</i> analysis revealed that mean values of disc anterior displacement were significantly improved ($p = 0.01$) from 1.67 ± 0.67 mm before treatment to 0.86 ± 0.74 mm towards physiological position after treatment</p>
Kinzingher et al. (28)	<p><i>Condyle position:</i></p> <p>Neither anterior nor posterior joint spaces of all TMJs showed significant changes after treatment in comparison with the baseline findings.</p> <p><i>Condyle shape:</i></p> <p>The value of the dimension ratios indicated no changes in condyles morphology during or after treatment.</p>
Aidar et al. (21)	<p><i>Articular disc position:</i></p> <p>According to subjective assessment, all TMJs showed normal disc position before treatment, posteriorly displaced discs during treatment and normal disc position post-treatment.</p> <p>According to objective measurement, the central slice showed that discs were posteriorly positioned by a mean difference of 2.5° ($p > 0.01$) at the completion of treatment. No differences were detected in the medial or lateral slices.</p>
Aidar et al. (22)	<p><i>Articular disc position:</i></p> <p>65% of TMJs had normal position before and after treatment.</p>

Table 2. (continued)

	<p>35% of TMJs had anterior disc displacement before treatment and improved to a normal position after treatment.</p> <p>14% of TMJs had partially reducing discs in open-mouth position before treatment, which became completely reducing after treatment.</p> <p>Disc morphology was improved in 14% of TMJs from no-biconcave to biconcave morphology in open-mouth position.</p>
Aidar et al. (23)	<p><i>Articular disc position:</i></p> <p>10% of TMJs that had normal disc position after appliance removal, suffered anterior disc displacement after phase II treatment.</p> <p>8% of TMJs had lost biconcavity shape of the articular disc after phase II treatment.</p>
Aidar et al. (24)	<p><i>Osseous remodelling:</i></p> <p>3% of TMJs changed from normal to remodelled.</p> <p>5% of TMJs changed from remodelled to normal.</p> <p>2% of TMJs changed from degenerative to remodelled.</p>
Arici et al. (25)	<p><i>Volume of articular tissues and condylar space:</i></p> <p>Volume of condyle and glenoid fossa continues to increase in the same rate in both test and control groups.</p> <p>Anterior joint space volume increased in the test group by 38% and in the control group by 20%.</p> <p>Posterior joint space volume decreased in the test group by 9% and increased in the control group by 2%</p>
LeCornu et al. (29)	<p><i>Osseous remodelling:</i></p> <p>Bone resorption was noticed at the anterior surface (1.4–1.7 mm) and bone deposition at the posterior surface (0.6–0.8 mm) of the glenoid fossa in the Herbst group.</p>

Table 2. (continued)

Class II elastics group showed bone deposition at the anterior surface (−1.3 to −1.5 mm) and bone resorption at the posterior surface (−1.2 to −1.4 mm) of the glenoid fossa. The condylar head was anteriorly displaced in the Herbst group by about 2.5–2.9 mm more than the comparison group.

anterior positioning in some cases. However due to ‘large individual variation’, the authors reported an acceptable joint space change that was not affected by Herbst treatment.

It appears that the Kinzinger et al. (26–28, 36) articles, which evaluated condyle position changes using MRI, were essentially the same treatment sample without a control group. Furthermore, there was no report of examiner blinding. The reproducibility study, which was based on an assessment of just four cases, carried out twice, showed significant method error. In addition, the plane orientation during imaging acquisition at multiple times produces an inevitable error that was not reported.

The 2013 Aidar et al. (24) article also used MRI to assess bone change. Again, there was no control group. Evaluator calibration process, blinding and interobserver agreement were reported: excellent (Kappa = 0.87). Accepting the limitation that there was no control group in this study, there was some evidence of insignificant condylar remodelling in some cases.

The CT images provide 3D reconstruction of the TMJ with high diagnostic quality, accurate and reliable linear measurements that allow evaluation of joint space changes (40–42). The volumetric approach used by Arici et al. (25) has not been validated and provides conflicting evidence with the more widely accepted approaches. The authors did not report standardization of joint or mouth positioning during the scan or adjustment of the head orientation of the volumetric data after image acquisition. The lack of standardization has a significant

impact on where the ‘central slice’ would be located and selected. Consequently, the three selected slices may not be reproducible nor do they adequately highlight or quantify the actual remoulding of the condyle and glenoid fossa or the change in joint space. A note is made of the relatively high radiation dose of helical CT used in their imaging protocol: CBCT would have been an alternative with less radiation dose. Despite including untreated control group, the authors also failed to address other methodological flaws such as randomization and blinding to avoid the significant risk of bias in the reported findings.

The LeCornu et al. study (29) provided the most appropriate method for assessing bone remodelling using CBCT superimposition of serial images. Unfortunately, they had a small sample size, and there was no randomization between the Herbst (test) and class II elastics (comparison) groups. CBCT imaging machines and time intervals were different between the two groups. The images were low resolution (0.5 mm voxel size), and reliability was not reported. There was some evidence of greater anterior positioning of the fossa with Herbst treatment compared to class II elastic wear. The Herbst patients showed resorption at the anterior wall of the glenoid fossa and deposition at its posterior wall by 3 and 2 mm, respectively, compared to control subjects.

Temporomandibular disc position

Pancherz et al. (18) used subjective analysis to determine the disc position using the ‘*disc position index*’. The study concluded that Herbst appliance treatment placed the articular disc in a normal functional position even when it was initially anteriorly displaced. Data were reported using line charts that made exact data extraction impossible. Also, it was not clear whether the disc position index was a reliable tool to quantify disc displacement, especially with the significant variation in disc morphology between subjects. Although error of measurements was reported, the error margin of the assessment tool itself was not reported. Ruf and Pancherz (35)

Table 3. The risk of bias assessment tool for non-randomized studies (RoBANS) for the included articles

	Pancherz et al. (5)	Ruf & Pancherz (20)	Pancherz et al. (18)	Ruf & Pancherz 2000 (35)	Kinzinger et al. (26)	Kinzinger et al. (27)	Kinzinger et al. (36)	Kinzinger et al. (28)	Aidar et al. (21)	Aidar et al. (22)	Aidar et al. (23)	Aidar et al. (24)	Arici et al. (25)	LeCornu et al. (29)
The selection of Participants: Selection Biases caused by the inadequate selection of participants	High	High	High	High	High	High	High	High	High	High	High	High	Low	High
Confounding variables: Selection Biases caused by the inadequate confirmation and consideration of confounding variables	High	High	High	High	High	High	High	High	High	High	High	High	High	High
Measurement of exposure: Performance biases caused by the inadequate measurement of exposure	High	High	High	High	High	High	High	High	High	High	High	High	High	Low

Table 3. (continued)

Blinding of outcome assessments:	High	Ruf & Pancherz et al. (5)	High	Ruf & Pancherz et al. (18)	High	Ruf & Pancherz 2000 (35)	High	Kinzinger et al. (26)	High	Kinzinger et al. (27)	High	Kinzinger et al. (36)	High	Kinzinger et al. (28)	High	Aidar et al. (21)	Low	Aidar et al. (22)	Low	Aidar et al. (23)	Low	Aidar et al. (24)	Low	Arici et al. (25)	High	LeCornu et al. (29)	Unclear
Detection biases caused by the inadequate blinding of outcome assessments	Low		Low	High	High	Low	High	High	High	Low	Low	Low	Low	Low	Low	High	Low	Low	Low								
Incomplete outcome data: Attrition biases caused by the inadequate handling of incomplete outcome data	Low		Low	High	High	Low	High	High	High	Low	Low	Low	Low	Low	Low	High	Low	Low	Low								
Selective outcome reporting: Reporting biases caused by selective reporting outcome	Low		Low	High	High	Low	High	High	High	Low	Low	Low	Low	Low	Low	High	Low	Low	Low								
Overall risk of bias	High		High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High	High

reported results of 62 patients that were included in the previous article (18). The authors analysed the disc position using three assessment tools that were not proven to be valid or reliable. The authors categorized the disc to have 'displacement tendency' if indicated by one tool only and 'completely displaced' if indicated by two assessment tools. There was a lack of agreement between the tools resulting in variations in categorizing disc position. Moreover, disc position was found to 'vary largely in different image slices and at different times of examination'. In one assessment tool (*intermediate zone assessment*), the disc position was in a retrusive position post-treatment compared to its initial position by 0.3 mm. However, the reported method error was larger than the detected difference (0.2–0.6 mm). In addition to the lack of control/comparison group and blinding, and failing to rule out gender differences at baseline, the authors applied multiple *t*-tests to analyse multiple variables and outcomes thus increasing type I error. In our opinion, the studies designed by Pancherz et al. (18, 35). were unnecessarily complicated with several methodological flaws that warrant caution when interpreting their results.

Kinzinger et al. (27, 36) objectively assessed the disc position in one central slice image using two assessments tools. Findings were in agreement with the ones reported by Ruf and Pancherz (18, 35). It was not clear whether the same subjects were used in the two studies. Taking into consideration the method error and the fact that one central slice does not reflect the disc position change, a significant bias in the findings can be implied. Ideally, disc position should be considered in all image slices or in 3D to account for possible mediolateral rotation/displacement. The method error of the tools was reported. However, it is unclear whether these tools were valid or reliable. The findings showed that the disc was retruded to more physiologically correct position compared to its initial position by a mean difference of 0.6 mm in the first article (27) and 0.8 mm in the second article (36). These differences were even smaller than what was reported as an error

of the assessment tool itself, which was 0.98 mm. The study did not consider the gender of participants, blinding of image assessment and the different appliance types as a confounder. The findings of these two articles should be interpreted with caution.

Aidar et al. (21) evaluated the disc position in 20 patients using coronal and parasagittal MRIs at three times. It was noted that findings of coronal images were not reported in the article. Authors performed nonparametric Wilcoxon signed-rank test to analyse the data of each slice at different times. Another robust statistical test should have been performed instead of multiple Wilcoxon signed-rank tests, to avoid type I error. The images were assessed three times by double-blinded calibrated evaluators. However, too many unnecessary variables were considered with limited sample size to support adequate statistical analyses. Also, the central slice evaluation revealed a difference in disc position after treatment by 2.5°. Considering the 1.5° method error reported in the study, the small difference in the central slice should not be considered clinically significant. In 2009 (22), it was not clear whether the authors had included patients from their previous study. The study was further complicated by introducing more variables pertaining to disc position categories (12 categories based on the displacement severity in mouth-closed position and to five categories based on reduction during mouth opening) and two new categories of disc morphology. Further weakening the study, the authors provided descriptive data only, likely because multiple variables existed with a small sample size that failed to support any robust statistical test. In 2010 (23), further MR imaging was carried out to evaluate the disc position after full orthodontic treatment was completed. The article provided similar descriptive data that were not statistically analysed and resulted in inconclusive results.

This systematic review followed a thorough procedure to screen the available literature in four common databases and critically analysed the included articles. PRISMA reporting guidelines (check list and Flowchart) were followed to ensure detailed appraisal for the reviewed

articles. The level of evidence regarding the change in disc position and disc morphology with mandibular anterior positioning appliances is low. Using a validated tool to objectively evaluate the disc position change is essential. Nebbe et al. (43). described a valid technique to measure changes in disc location relative to the functional load-bearing intermediate zone of the articular disc. The mid-point of the intermediate zone was measured relative to two anatomical reference lines (Frankfort horizontal line and articular eminence plane).

Limitations of the included articles

Significant methodological limitations were identified in all the included articles. The high risk of bias in considering gender as confounding variable, blinding, untreated control and incomplete outcome reporting deemed the findings questionable.

Future directions

A well-designed study is required to establish articular tissue reactions to the mandibular anterior appliances to treat class II malocclusion in the adolescent population. Suggestions for future research design are as follows:

1. Although ethically questionable if not properly planned, a randomized clinical trial with untreated control is the ideal design to detect the causal effect on TMJ accurately.
2. A larger sample size to empower the collected data analysis and support the clinical significance of the reported findings.
3. Use 3D volumetric CBCT images before and after treatment with a standardized imaging protocol to overcome the shortcomings of the 2D images in evaluating the osseous changes of the TMJ. A valid and reliable superimposition technique should be conducted to quantify the osseous remoulding (44).
4. Despite the MRI implicit soft tissue contrast and high resolution, it is paramount to

adequately evaluate the disc position in relation to the condyle and glenoid fossa using a valid and reliable tool adequately. Ideally, the articular disc should be segmented to avoid losing critical data and enhance the accuracy of the assessment process.

5. A double-blinded experienced examiner should conduct the image analysis to reduce method error and improve the assessment reliability.
6. Appropriate data analysis that considers age and gender should be performed to assess the evidence of the collected findings.

Conclusions

Current literature that investigated the short-term effect of fixed functional appliances on actively growing patients showed critical design problems and analytical flaws that prevented drawing any definite conclusions about conducted treatments.

The articles failed to establish evidence of the TMJ tissue reaction to the forces applied by the mandibular anterior positioning appliances.

Clinical significance

Fixed repositioning appliances are commonly used in class II correction treatment. Several related articles have been published in the past 10 years, and it is obvious that controversy in the published literature is remaining. A thorough understanding of the fixed functional appliances' effect on TMJ is required. This systematic review has shed light on the research progress in this area, highlighted the limitations and weaknesses of the published studies and provides recommendations for future areas of research.

Conflict of interest

The authors declare that they have no conflict of interest.

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Effect of functional appliances treatment on temporomandibular joint morphology: a systematic review.