



An updated systematic review on the effectivity of clear aligner therapy: A review

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ABSTRACT

Introduction: Several studies have evaluated the strengths and weaknesses of orthodontic aligners however, the results are still uncertain. In the current study, we aimed to systematically review the literature and provide updates on the efficacy and effectivity of orthodontic therapy using aligners.

Materials and Methods: PubMed, Web of Science and Cochrane Oral Health Group's Trials Register databases were systematically searched for relevant literature up to December 2020. All studies reporting aligner therapy in management of dental misalignment were included. The quality was assessed using the methodological index for non-randomized studies (MINORS) criteria and Jadad scale for randomized controlled trials.

Results: Of the initial 550 articles, 18 studies were ultimately included representing a total of 637 patients who were treated with clear aligners. Of the 18 studies, 15 had a retrospective design, one was an observational study, one was conducted as a prospective clinical trial, and one study was a randomized controlled trial. Due to the design and methodology of the studies the quality assessment revealed a high risk of bias. Significant diversity among the outcomes of the studies was observed; however, an underlying consistency was detected within the included studies with regards to the effectivity of aligner therapy in alignment of the anterior teeth, while the pretreatment predictive rates were not significantly different to treatment outcomes. In addition, despite comparable treatment outcomes between aligner therapy and conventional appliance technique, aligner therapy resulted in increased rates of patient satisfaction.

Conclusion: Aligner therapy seems to be a viable alternative to conventional orthodontic therapy for correction of mild to moderate malocclusions in non-growing nonextraction patients. However, it should be taken into consideration that due to the high risk of bias, results should be interpreted with caution.

Keywords: Orthodontics; Aligner; Tooth movement; Clinical effectivity.

Introduction

In 1945, Kesling et al. introduced the idea of utilizing thermoplastic tooth positioners to move misaligned teeth to appropriate positions [1]. Since its introduction, the idea of manufacturing aligners to move the teeth

to an ideal position has gained significant attention. Recent, orthodontic advancements in the last decades have resulted in an increased patient demand for esthetic interventions. Furthermore, adult patients have also increasing

sought out more comfortable treatment alternatives to conventional fixed appliances [2,3]. Due to the stigma that conventional techniques are accompanied with compromised facial esthetics and a more painful treatment process, more and more adults have requested more comfortable and esthetic interventions such as aligners and splints [4,5].

Despite the variety of the aligners regarding the production process and designs, the main goal of the treatment remains the same, which is the improvement of the tooth alignment through feasible and affordable techniques [6-8]. While clear aligner therapy offers some advantages such as increased comfort and esthetics of patients during treatment, several disadvantages including questionable treatment efficacy, inability to correct particular types of malalignments and risk of root resorption of this treatment modality are still debatable [8,9]. In a 2014 study, Rossini et al. systematically reviewed the available literature with regards to the various features of the aligners and provided evidence related to the efficacy of clear aligner treatment in controlling some orthodontic tooth movements such as intrusion and posterior buccolingual inclination. Authors claimed that clear aligners are not effective in achieving anterior extrusion or controlling anterior buccolingual inclination as well as rotation of the rounded teeth [10]. Several systematic reviews have been published during the recent years, that have emphasized the efficacy of particular products in different tooth movements, or have focused on specific clinical side effects, such as root resorption [9-13]. On the other hand, recent advancements and rapid progression in the development of new products and subsequently published articles should be addressed through reevaluation and reassessment in order to update treatment approaches and clinical algorithms. The current systematic review aimed to evaluate the available literature from 2014 to 2020 in order to provide updates on the efficacy of aligner orthodontic therapy.

Materials and Methods

The study modeled the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines [14].

Search strategy and selection criteria

A systematic literature search of Medline (PubMed), Cochrane Oral Health Group's Trials Register and ISI Web of Science databases was conducted by the combination of the following search term groups: “(aligner therapy OR aligner) AND (Orthodontic OR “Or-

thodontic treatment” OR alignment)”. The search was restricted to all relevant studies published after 2014. The last search was performed in December 2020. The study question was formulated based on the Population, Intervention, Comparison, Outcome and Study design (PICOS) strategy. Studies were included in the study if they met the following criteria:

- Population: Orthodontic patients with malalignment of teeth.
- Intervention: Aligner, regardless of type, stage of treatment, and manufacturer.
- Comparison: None.
- Outcome: Relevant post-treatment outcomes, including tooth movement, and patient satisfaction.
- Study design: All study designs were eligible for inclusion.

Experimental studies, letters, comments, editorials, case reports, and case series were excluded. Double publications and review articles were crosschecked and excluded to prevent reporting repetitive cases. The reference lists of the retrieved articles were screened for additional relevant studies.

Study selection and data extraction

The titles and abstracts of the retrieved articles were independently screened by two authors (Mahboubeh Hasheminasab and Mana Naeim). The full articles of interest were then reviewed by the other author (Mahsa Mortazavi) to select the articles and extract the data. In cases of disagreement, discussions occurred among the three reviewers and further with other authors until agreements were made. The interobserver agreement was excellent during the screening of titles and abstracts. and detailed assessment of the relevant studies. Study characteristics (study designs, year of the study, sample size, and country), study arms and study outcomes (including tooth movement, mean gingival index and patients' satisfaction) were extracted.

Quality assessment

The quality of each study was assessed by two independent reviewers using the methodological index for non-randomized studies (MINORS) [15]. Quality was determined based on eight MINORS items. The scoring system was, as follows: 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). An overall score of more than 12 points indicated a high quality, studies with scores lying between 8 to 12 points

had intermediate quality, and studies with less than 8 points had low quality. To evaluate the methodological quality of randomized controlled trials, the Jadad score was used [16]. This score evaluated several important items such as randomization (0-2 points), blinding and its technique (0-2 points), and dropouts and withdrawals (0-1 point). Finally, scores were classified, as follows: 'poor' quality: 0-2, 'good' quality: 3-4, 'high' quality: 5.

Results

Description of studies

The literature search yielded 550 potentially eligible studies from screened databases. 239 papers were omitted after duplicates and 293 articles with irrelevant redundant information were eliminated. 18 articles were finally selected for inclusion in this systematic review. Of the 18 enrolled studies, 15 studies had a retrospective design, one was an observational study, one was conducted as a prospective clinical trial, and only one study was randomized controlled trial. All included studies were written in English. Sixteen studies utilized the Invisalign® system and the remaining two articles utilized either F22 aligners or the Nuvola® system. The extracted data from the included studies is described in Table 1. Sample sizes ranged from 16 to 225, with a total of 637 subjects who were treated with clear aligners. 10 out of 18 articles evaluated predictability of movements of teeth with clear aligners. Eight articles compared treatment outcome of aligners with fixed appliance therapy.

Quality analysis

Among the enrolled articles, 17 were non-randomized studies with an acceptable follow-up and are categorized as level 2B evidence according to the Oxford Centre for Evidence-Based Medicine criteria. One study was a RCT and is classified as 1B evidence level due to its small sample size. All studies are considered as low quality according to MINOR and Jadad scales (Table 2).

Aligner therapy and its predictability of tooth movements

Chisari et al. performed a controlled prospective trial to evaluate the factors influencing dental movement with aligners. Their results revealed that aligners produced only 57% of the predicted labiolingually movement measured at the central incisors [17]. Similarly, the mean predictive accuracy of anterior torque movements, premolar derotation, and molar distalization

was reported to be 59.3% by Simon. Authers reported that premolars rotated more than 15 degrees which caused a decrease in outcome accuracy when clinical presentation was compared to simulated treatment goal [18]. Zhang et al. reported a significantly lower root movement in both upper and lower arches compared to that of the crown after clear aligner therapy [19]. A retrospective study was carried out by Charalampakis and colleagues, in which authors have evaluated the accuracy of specific tooth movements in 20 cases (398 teeth) [20]. Extrusion and horizontal movements of all incisors resulted in insignificant differences between predicted and achieved movements. Intrusion was significantly less accurate with a median difference of 1.5mm. All achieved rotations were considerably less than predicted rotations, with the maxillary canines showing the maximum differentiation of 3.05° ($P < 0.001$).

Grünheid and colleagues determined the accuracy of Invisalign in accomplishing predicted tooth positions in 30 patients treated from 2013 to 2016 [21]. Plaster models after treatments were digitized then compared to predicted ClinCheck® models. Authors reported that Invisalign is able to achieve predicted tooth positions with high accuracy in non-extraction cases. However, predicted and achieved tooth positions were significantly different for all teeth types with the exception of the maxillary lateral incisors, canines and first premolars. Anterior teeth were located more occlusal than predicted simulations, total rotation of rounded teeth was not completed, and movements of posterior teeth were not fully achieved in all dimensions.

In a retrospective research by Tepedino et al. researchers assessed the predictability of aligner therapy (Nuvola®) for achieving buccolingual movement for anterior teeth [22]. Their findings showed that the central and lateral incisor in maxillary arch achieved 88.7% and 94.4% of the predicted movement retrospectively. Whereas, this amount was 98.6% and 100% for the mandibular central and lateral incisors. In this study no statistically considerable difference existed between predicted and achieved buccolingual inclination for anterior teeth. Duncan et al. reported that Invisalign resulted in an increased intercanine, interpremolar, and intermolar width post-treatment in non-extraction patients regardless of their initial presentation of mandibular crowding [23]. Houle observed 72.8% and 87.7% accuracy of expansion for the maxillary and mandibular teeth respectively, with cusp tips having more predictable transverse changes than gingival margins [24]. They recommended overcor-

rection of expansion in posterior region of the maxillary arch. Lombardo et al. assessed the predictability of F22 aligners for rotations, vestibulo-lingual tipping and mesio-distal tipping in 16 patients (345 teeth) from 2014 to 2017 [25]. The mean predictability of this therapeutic method was 73.6%. Mesiodistal and vestibulo-lingual tipping achieved 82.5% and 72.9% predictability, respectively. Noteworthy, mesiodistal tip on the lower premolars and upper molars were achieved with the most predictability, 96.7% and 93.4%, respectively. Correction of the rotation of the lower canines was reported a greatly unpredictable movement (54.2%).

A retrospective report conducted by Dai et al. compared the predicted versus achieved maxillary central incisor and molar tooth movement in 30 invisalign cases treated with first premolar extraction [26]. They found that the central incisors achieved greater lingual crown torque and less retraction than predicted. Maxillary first molars tipped and translated mesially more than predicted by 5.86 degrees and 2.26mm, respectively. Occluso-gingivally, the mesial cusp of the molars was intruded more than predicted by 0.61mm while the distal cusp was stable. Maxillary central incisors were tipped more than predicted (5.16 degrees), and translated less than predicted (2.12mm).

Aligners therapy versus fixed appliance therapy: different impacts on outcomes

Grunheid et al. observed a significantly higher increase in compared measurements of intercanine distance for aligner patients versus fixed appliance patients. They reported that fixed appliances contributed to more upright canines [27]. Gu et al. revealed that both Invisalign and fixed appliance treatments are able to improve various malocclusions however the aligner treatment group had a 30% reduced treatment time when compared to the fixed appliance group. There was no statically significant difference in the posttreatment weighted Peer Assessment Rating Index (PAR score) between the two treatment modalities. However, based on the change of PAR points the the likelihood of achieving "great improvement" in a malocclusion appears to be better with fixed appliances [28]. The survey by Lanteri et al. showed similar results. They reported that both fixed appliances and aligners improved the Peer Assesment Rating (PAR) index. No stationaly significant differences were found in posttreatment and follow-up PAR indices between the two treatment modalities, however the duration of treatment was 4 months longer in patients who were treated with fixed appliances [29]. Hennessy et al. performed a RCT on

44 patients to compare treatment outcomes in patients treated with clear aligner therapy versus fixed labial appliances [30]. The mean crowding values in the clear aligner and fixed appliance groups were 2.5 ± 1.3 mm and 2.1 ± 1.3 mm, respectively. The final mean values of mandibular incisor proclination were not statistically significant for patients with mild crowding.

Sfonrini et al. conducted a retrospective study to compare the torque values of upper incisors in 75 orthodontically treated cases which utilized conventional brackets, aligners, and self-ligating appliances (25 patients in each group) [31]. Conventional brackets had the greatest variation of upper incisors inclination over treatment but there were ultimately no statistically considerable differences among these therapeutic options ($p > 0.05$). A comprehensive study was conducted by Issa et al. to compare the gingival parameters in patients who underwent aligner treatment versus other types of brackets [32]. The mean gingival index in the conventional metal bracket group, conventional ceramic group, metal self-ligating group, and aligner group were 1.26, 0.85, 0.76; and 0.008 respectively. The clear aligner treatment had better treatment outcomes in comparison to conventional brackets and conventional ceramic brackets, but not considerable difference than self-ligating brackets.

Another study by Alajmi et al. evaluated and compared patient experiences regarding daily routine, food consumption, oral and teeth symptoms, treatment satisfaction, and the presence and severity of pain during treatment in patients who underwent clear aligner and conventional fixed orthodontic therapy [33]. Difficulty in speech ($p = 0.035$), necessitating change in speech delivery ($p = 0.003$), was significantly more in clear aligner group. During clear aligner treatment, patients reported better chewing ability ($p < 0.001$), less mucosal ulceration ($p = 0.01$), and less restrictions for routine foods ($p = 0.02$). Therefore, clear aligner therapy is not necessarily more pleasant, but could be considered more tolerable. A study conducted by Kankam et al. assessed postoperative outcomes and edema in 33 patients with conventional fixed appliances (20 cases) or clear aligners (13 cases) who underwent orthognathic surgeries [34]. Results showed that there was not any considerable difference with regards to duration of surgery, the extraction of teeth, duration of hospital stay, or the utilization of narcotic analgesics. Postoperative edema was not significantly different in patients with conventional fixed appliances (44.29 ± 23.16 cm) than those with clear aligners (37.36 ± 31.19 cm) ($P = 0.712$).

Author/ Year/ Type of study	Sample size	Age (year)	Tooth prediction evaluation	Significant Results and clinical bottom lines
• Studies which reported predictability of tooth movement				
Chisari, 2014/ Prospective CT	30 (15 adult and 15 young adults)	27.9 (Median)	Percentage of tooth move- ment goal achieved	<ul style="list-style-type: none"> • CI: 57% of movement occurred of 1 mm labially (0.25 mm per aligner) programmed movement • A cubic relationship between age and tooth movement • Limited correlations with cone-beam computed tomography morphology and rate of tooth movement were detected
Simon, 2014/ Retrospective	30 (60 teeth)/ 4 dorppouts	32.9	Pre- and post-treatment superposition of dental casts	<ul style="list-style-type: none"> • Overall: 59.3% of the planned movement occurred, with the highest accuracy in the group of molar distalization. • PM: derotation with attachement (37.5%), and without attachement (42.4%). • MO: distalization with attachement (88.4%), and without attachement (86.9%). • Inisor: torque with attachement (49.1%), and with power ridge (51.5%). • Accuracy of derotation was reduced >15 degree.
Zhang, 2015/ Retrospective	32	26.7	Discrepancy in the predicted and achieved crown and root positions	<p style="text-align: center;">- Maxillary arch:</p> <ul style="list-style-type: none"> • Crown: mm: 0.376 (SD: 0.041)* • Root: mm: 2.062 (SD: 0.128)* <p style="text-align: center;">- Mandibular arch:</p> <ul style="list-style-type: none"> • Crown: mm: 0.398 (SD: 0.037)* • Root: mm: 1.941 (SD: 0.154)*
Duncan, 2016/ Retrospective	61 (catego- rized base on mandible crowding: a. 20 mild, b. 22 mod- erate c. 19 severe)	-	Digital study models and lateral cephalometric radiographs evaluating Changes in mandibular incisor position and arch width	<p style="text-align: center;">- Mild:</p> <ul style="list-style-type: none"> • Canine: Pretreatment [mm: 25.567], posttreatment [mm: 25.854], difference [mm: -1.2868] • Premolar: Pretreatment [mm: 26.456], posttreatment [mm: 28.031], difference [mm: -1.5752] • Molar: Pretreatment [mm: 32.577], posttreatment [mm: 34.231], difference [mm: -1.6537] <p style="text-align: center;">- Moderate:</p> <ul style="list-style-type: none"> • Canine: Pretreatment [mm: 23.556], posttreatment [mm: 25.331], difference [mm: -1.7742] • Premolar: Pretreatment [mm: 24.943], posttreatment [mm: 27.465], difference [mm: -2.5223] • Molar: Pretreatment [mm: 32.741], posttreatment [mm: 34.606], difference [mm: -1.8653] <p style="text-align: center;">- Severe:</p> <ul style="list-style-type: none"> • Canine: Pretreatment [mm: 24.077], posttreatment [mm: 25.816], difference [mm: -1.7391] • Premolar: Pretreatment [mm: 24.973], posttreatment [mm: 28.168], difference [mm: -3.1952] • Molar: Pretreatment [mm: 31.334], posttreatment [mm: 33.986], difference [mm: -2.6526]

Grunheid, 2017/ Retrospective	30 (28 teeth From each patient)	21.6	Changes in meialdistal, faciallingual, occlusogin- gival as well as tip, torque and rotation torque	<p>- Maxillary arch:</p> <ul style="list-style-type: none"> • CI: faciallingual [mm:-0.45 (SD: 0.6)], and also torque [mm: 1.75 (SD:3)] • 2 PM: meialdistal [mm: 0.19 (SD: 0.7)],faciallingual [mm: 0.20 (SD: 0.6)], torque [mm: -1.2 (SD:3)] • 1Mo: meialdistal [mm: 0.27 (SD: 0.3)], faciallingual [mm: 0.23 (SD: 0.6)], torque [mm: -1.5 (SD:3)] • 2 Mo: meialdistal [mm: 0.07 (SD: 0.8)], faciallingual [mm: 0.30 (SD: 0.8)], torque [mm: -2.1 (SD:4)] <p>- Mandibular arch:</p> <ul style="list-style-type: none"> • CI: faciallingual [mm 0.12 (SD: 0.4)], and also torque [mm: -.66 (SD: 2.6)] • 2 PM: meialdistal [mm: 0.13 (SD: 0.6)],faciallingual [mm: 0.09 (SD: 0.6)], torque [mm: -0.74 (SD:3)] • 1Mo: meialdistal [mm: 0.12 (SD: 0.3)], faciallingual [mm: -0.08 (SD: 0.5)], torque [mm: -0.85 (SD:2)] • 2 Mo: meialdistal [mm: -0.02 (SD: 0.5)], faciallingual [mm: -0.17 (SD: 0.4)], torque [mm: -1.1 (SD:2)]
Lombardo, 2017/Retrospec- tive	16 (345 teeth)	28	Rotation and tipping	<p>- Maxillary arch:</p> <ul style="list-style-type: none"> • Canine: Mesio-distal (78.3%), Vestibulo-lingual (54%), rotation (62.3%) • Incisor: Mesio-distal (76.6%), Vestibulo-lingual (64.5%), rotation (61.5%) <ul style="list-style-type: none"> • Premolar: Mesio-distal (70.6%), Vestibulo-lingual (69.6%), rotation (54%) • Molar: Mesio-distal (93.4%), Vestibulo-lingual (52.5%), rotation (78%) <p>- Mandibular arch:</p> <ul style="list-style-type: none"> • Canine: Mesio-distal (86.7%), Vestibulo-lingual (66.4%), rotation (54.2%) • Incisor: Mesio-distal (87.7%), Vestibulo-lingual (86.1%), rotation (67%) <ul style="list-style-type: none"> • Premolar: Mesio-distal (96.7%), Vestibulo-lingual (90.4%), rotation (82.7%) • Molar: Mesio-distal (61.8 %), Vestibulo-lingual (86.2%), rotation (85.4%)
Houle, 2017/ Retrospective	64	31.2	Arch expansion prediction	<p>- Maxillary arch:</p> <ul style="list-style-type: none"> • Overall: 72.8% • Canine: tip (88.7), gingival (67.8%) • 1PM: tip (84.7%), gingival (67.6%) • 2PM: tip (81.7%), gingival (62.3%) • 1MO: tip (76.6%), gingival (52.9%) <p>- Mandibular arch:</p> <ul style="list-style-type: none"> • Overall: 87.7% • Canine: tip (100%), gingival (61%) • 1PM: tip (96.9%), gingival (88.4%) • 2PM: tip (98.9%), gingival (85.5%) • 1MO: tip (100%), gingival (70.7%)

Tepedino, 2018/ Retrospective	39 (63 arches)	30.7	Torque Measurement	<ul style="list-style-type: none"> - Maxillary arch: <ul style="list-style-type: none"> • Canine: achieved torque (100%) <ul style="list-style-type: none"> • LI: 94.4% • CI: 88.7% - Mandibular arch: <ul style="list-style-type: none"> • Canine: achieved torque (100%) <ul style="list-style-type: none"> • LI: 100% • CI: 98.6%
Charalampakis, 2018/Retrospec- tive	20 (398 teeth)	37.5	Displacement vertically and horizontally, rotation and widths of inter PM	<ul style="list-style-type: none"> - Maxillary arch: <ul style="list-style-type: none"> • CI: horizontal (79%), extrusion more than 36% rather than predicted, and rotation (57%) • LI: horizontal (77%), extrusion more than 27% rather than predicted, and rotation (66%) <ul style="list-style-type: none"> • Canine: horizontal (76%), and rotation (57%) <ul style="list-style-type: none"> • PM: rotation (74%) - Mandibular arch: <ul style="list-style-type: none"> • CI: horizontal (98%), extrusion (87%), and rotation (76%) • LI: horizontal (98%), extrusion (87%), and rotation (76%) <ul style="list-style-type: none"> • Canine: horizontal (85%), and rotation (71%) <ul style="list-style-type: none"> • PM: rotation (65%)
Dai, 2019/Retro- spective	30	19.4	Tipping, molar and translation of molar arch and also tipping, incisor, and translation of central section	<ul style="list-style-type: none"> - Maxillary arch: <ul style="list-style-type: none"> • Molar angulation (difference of mean: 5.86+3.51) • Molar translation in mesio-distal direction (difference of mean: 2.26 +1.58) • Molar translation(mesialcusp) in occluso-gingival direction (difference of mean: 0.61+0.89) <ul style="list-style-type: none"> - Central: <ul style="list-style-type: none"> • Incisor labiolingual translation (difference of mean: -5.16+5.92) • Incisor torque (difference of mean: 2.12+1.51) • Incisor occluso gingival translation (difference of mean: -0.50+1.17)
• Studies which compared outcome of clear aligners with fixed appliance therapy				
Grunheid, 2016/ Retrospective	Aligners: 30 Fixed-appli- ance: 30	25/26.3	buccolingual inclination of mandibular canines and the intercanine distance	<ul style="list-style-type: none"> - Buccolingual Inclination of Mandibular Canines <ul style="list-style-type: none"> • Fixed appliance (-1.9±5.1) • Aligners (0.7±2.5) - Mandibular Intercanine Distance <ul style="list-style-type: none"> • Fixed appliance (-0.1±2.4) • Aligners (0.7±1.5)
Hennessy, 2016/ RCT	Aligners: 22 Self ligating: 22	26.4	Proclination of incisor of mandibular arch	<ul style="list-style-type: none"> - Proclination of mandibular incisor <ul style="list-style-type: none"> • Aligners (3.4+3.2 degree) • Self ligating (5.3+4.3 degree) • Aligners produced around 64% of proclination in the comparison with Self ligating

Gu, 2017 / Retrospective	Aligners: 48 Fixed-appliance: 48	24	Treatment efficacy in mild to moderate malocclusion using Peer Assessment Rating index	<ul style="list-style-type: none"> - Invisalign: <ul style="list-style-type: none"> • Pretreatment Weighted PAR: Pretreatment [20.81 (SD: 6.79)], posttreatment [4.08 (SD: 4.35)] • Anterioposterior: Pretreatment [2.48 (SD: 1.34)], posttreatment [2.06 (SD: 1.29)] • Transverse: Pretreatment [0.17 (SD: 0.66)], posttreatment [0.06 (SD: 0.43)] • Vertical: Pretreatment [0.02 (SD: 0.14)], posttreatment [0 (SD: 0)] - Fixed-appliance: <ul style="list-style-type: none"> • Pretreatment Weighted PAR: Pretreatment [22.79 (SD: 7.72)], posttreatment [2.69 (SD: 2.23)] • Anterioposterior: Pretreatment [2.44 (SD: 1.29)], posttreatment [1.69 (SD: 1.27)] • Transverse: Pretreatment [0.33 (SD: 0.81)], posttreatment [0.06 (SD: 0.43)] • Vertical: Pretreatment [0 (SD: 0)], posttreatment [0.02 (SD: 0.14)]
Lanteri, 2018/ Retrospective	Invisalign: 100 Fixed-appliance: 125	28/25	Anterior crowding treatment evaluation using the Peer Assessment Rating Index	<ul style="list-style-type: none"> - PAR index <ul style="list-style-type: none"> • Invisalign: Pretreatment [22.5 (SD: 7)], posttreatment [3.5 (SD: 3)] • Fixed appliance: Pretreatment [24 (SD: 6)], posttreatment [4.5 (SD: 4)] - Maxillary Little Index <ul style="list-style-type: none"> • Invisalign: Pretreatment [Moderate: 23%, minimal: 62%], posttreatment [100%] • Fixed appliance: Pretreatment [Moderate: 31%, minimal: 69%], posttreatment [100%] - Mandibular Little Index <ul style="list-style-type: none"> • Invisalign: Pretreatment [Severe: 12%, Moderate: 36%, Minimal: 52%], posttreatment [92%, Minimal: 8%] • Fixed appliance: Pretreatment [Severe: 16%, Moderate: 32%, Minimal: 52%], posttreatment [8%, Minimal: 12%]
Sfondrini, 2018/ Retrospective	Aligners: 25 Self ligating: 25 Fixed-appliance: 25	25.5	Central incisor/palatal plane, central incisor/ occlusal plane, central incisor/True vertical line	<ul style="list-style-type: none"> - Central incisor/ palatal plane <ul style="list-style-type: none"> • Conventional Bracket (6.11±3.91) <ul style="list-style-type: none"> • Self-ligating (5.64±3.27) • Aligner (5.13±3.23) - Central incisor/ occlusal plane <ul style="list-style-type: none"> • Conventional bracket (6.88±4.28) <ul style="list-style-type: none"> • Self-ligating (5.17±3.10) • Aligner (4.60±3.46) - Central incisor/ True vertical line <ul style="list-style-type: none"> • Fixed appliance (1.56±0.47) <ul style="list-style-type: none"> • Self-ligating (1.62±0.66) • Aligner (1.47±0.57)
Sfondrini, 2018 / Retrospective Alajmi S, 2019 / observational study	Invisalign: 30 fixed appliance: 30	23.75	Oral impacts experienced by patients	<ul style="list-style-type: none"> - Pain level <ul style="list-style-type: none"> • Invisalign (5.4 ± 1.8) • Fixed appliance (5.4 ± 2) - Mucosal ulceration <ul style="list-style-type: none"> • Invisalign (36%) • Fixed appliance (70%)

Kankam, 2019/ Retrospective	brackets: 20 Conventional ceramic brack- ets: 20 Self-ligating: 20 Aligner: 20	gingival parameters	-Gingival index • Conventional brackets: Mean: 1.2622 , SD: 0.67947 • Conventional ceramic brackets: Mean: 0.8541, SD: 0.49963 • Self-ligating: Mean: 0.7642, SD: 0.48007 • Aligner: Mean: 0.0080, SD: 0.02462 - Gingival bleeding index • Conventional brackets: Mean: 11.2500, SD: 2.76967 • Conventional ceramic brackets: Mean: 4.2000, SD: 3.88790 • Self-ligating: Mean: 0.7000, SD: 1.12858 • Aligner: Mean: 0.0005, SD: 0.00224
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Table 1. Characteristic of enrolled studies.

Author, year	Methodological index for non-randomized studies								Total
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	
Mulla Issa, 2020	2	0	0	1	0	2	0	0	5
Alajmi, 2019	2	0	0	1	0	2	0	0	5
Kankam, 2019	2	0	0	1	0	2	0	0	5
Dai, 2019	2	0	0	1	0	2	0	0	5
Charalampakis, 2018	2	0	0	1	0	2	0	0	5
Lanteri, 2018	2	0	0	1	0	2	0	0	5
Tepedino, 2018	2	2	0	1	0	2	0	0	7
Sfondrini, 2018	2	0	0	1	0	2	0	0	5
Grunheid, 2017	2	0	0	1	0	2	0	0	5
Gu, 2017	2	0	0	1	0	2	0	0	5
Houle, 2017	2	2	0	1	0	2	0	0	7
Lombardo, 2017	2	2	0	1	0	2	0	0	7
Grunheid, 2016	2	2	0	2	0	2	0	0	8
Duncan, 2016	2	2	0	1	0	2	0	0	7
Zhang, 2015	2	0	0	0	0	2	0	0	4
Simon, 2014	2	0	0	1	0	2	0	0	5
Chisari, 2014	2	0	0	1	0	2	0	0	5

Q1: Did the study have a clearly stated aim?, Q2: Were consecutive patients included?, Q3: Were data collected prospectively?, Q4: Were endpoints appropriate to the study?, Q5: Was there an unbiased assessment of endpoints?, Q6: Was the follow-up period adequate?, Q7:

Was loss to follow-up less than 5 per cent?, Q8: Was there a prospective calculation of study size?

0, Not reported; 1, reported but inadequate; 2, reported and adequate.

Jadad scale for quality assessment of RCTs

Author, year	Hennessy, 2016
Was the study described as randomized?	1
Method to generate sequence of randomization (appropriate?)	1
Was the study described as double blind?	0
Method of double blinding (appropriate?)	0
Description of withdrawals and dropouts	1

Higher scores indicate better reporting ('high' quality: 5; 'good' quality: 3-4; 'poor' quality: 0-2).

Table 2. Risk of bias of observational studies.

Discussion

The current systematic review was aimed to review the current literature to evaluate the treatment efficacy of clear aligners for dental malalignment and compare clear aligner therapy with conventional fixed appliance therapy. A comprehensive search strategy was conducted through databases, including PubMed, ISI web of science, and Cochrane library. To assess the risk of bias in the included studies the MINORS quality assessment tool was utilized [35]. However, the majority of the included studies had a retrospective design, (only one was a RCT), which reflected an overall poor methodology of the included studies and regrettably significantly reduced the quality of the evaluated evidence. In terms of aligner brands used, the Invisalign system was the most popular aligner brand, which was used in 16 out of 18 of the studies [17-21,23, 24, 26-34]. However, due to significant heterogeneity of the studies in terms of outcomes and methodologies, we are unable to make the argument that the Invisalign system is more efficacious or offers more clinical advantages than other clear aligner brands. To evaluate the effectivity of clear aligners, two factors including the conformity of the pretreatment prediction compared to treatment outcomes, as well as advantages and disadvantages of aligner therapy in comparison to conventional fixed appliances, were evaluated.

With regards to pretreatment predictability of aligner therapy, five retrospective studies evaluated tooth movement and compared the values among pre and posttreatment time points [20-22, 25,26]. Rotation of the round teeth (such as mandibular canines and premolars), intrusion of the incisors and the molar torque correction were among the least predictable tooth movements [20,21,25]. Although Charalampakis et al. observed no significant difference between predicted and acquired values in terms of extrusion and rotation among incisors, the rotation rate was significantly lower compared to predictions, especially in maxillary canines [20]. The results of the study by Tepedino et al. showed that incisors had significantly more predictable movements compared to the posterior teeth and fulfilled more than 80% of the predicted torque movements [22]. Contrarily, Lombardo et al. demonstrated aligner therapy yielded unpredictable results in terms of lower canine rotation correction, however tipping movements were more predictably achieved in the premolar and molar areas [25]. The current controversy between the outcomes of the Lombardo et al. study and other studies may have arisen due to the different type of the aligners administered in these studies that may

have contributed to the diverse treatment effects. Finally, Dai et al. illustrated that anchorage control and central incisor retraction after aligner therapy in first premolar extraction treatments were not predictable [26]. Although over retraction of the incisors may also happen with the fixed appliances, anchorage control may be more feasible with appliances such as headgear and transpalatal arch (TPA) or temporary anchorage devices (TADs) [36]. Therefore, aligner therapy may provide more predictable treatment outcomes in patients with mild to moderate malocclusions who do not need extraction as a part of their orthodontic treatment.

In order to compare treatment outcomes of aligners versus fixed appliances, eight studies with different endpoints were enrolled, among those only one study being a randomized controlled trial [27-34]. The overall results showed increased patient satisfaction and tolerability during aligner therapy, which may be a consequence of patient's having better chewing ability, less mucosal ulcerations, and fewer restrictions to routinely consumed foods that lead to patients retaining their pretreatment quality of life [33]. Also, Issa et al. reported a significantly lower mean gingival index among patients who underwent clear aligner treatment compared to other techniques, including conventional metal, conventional ceramic, and metal self-ligating brackets [32]. Furthermore, although aligner therapy was associated with speech difficulty that led to a change in speech delivery, it was not characterized as a significant issue by patients [33]. Therefore, considering the feasibility and satisfactory outcomes of aligner therapy as well as comparable outcomes with fixed appliances technique, clear aligners can be a proper treatment modality for orthodontic patients.

Our study faced several limitations. First, the data provided by studies were not unified due to heterogeneity, mainly in designs and regions of the studies. In addition, despite the effort given through systematic search and general search terms, a number of relative studies may not have been included in our survey. Second, the overall sample size of the included studies was small which may have led to a decreased statistical power. Third, the majority of the studies had a retrospective design which contributed to our low quality of the evidence.

Conclusion

Despite significant diversity among treatment outcomes, there was a strong consistency among the included studies regarding superior efficiency of aligner therapy for the alignment of the anterior teeth and

comparable outcomes of pretreatment prediction values with posttreatment outcomes. Rotation correction is the least predictable movement compared to vertical and horizontal tooth movements. In addition, aligner therapy resulted in the increased rate of patients' satisfaction, shorter treatment time, and similar clinical outcomes in non-extraction orthodontic treatment. Therefore, aligner therapy should be considered as a feasible alternative to conventional fixed appliances for patients with mild to moderate malocclusions. However, treatment outcomes should be interpreted with caution due to the high heterogeneity of included studies. Furthermore, more studies and well-designed RCTs are crucial in order to justify strong clinical recommendations.

Conflict of Interest

There is no conflict of interest to declare.

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