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Review

Outcomes of surgical management of TMJ ankylosis: A systematic review and meta-analysis

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ABSTRACT

Background: Temporomandibular joint (TMJ) ankylosis can be surgically managed by a number of approaches. This systematic review compared the clinical outcomes among various treatment options, i.e., gap arthroplasty (GA), interpositional gap arthroplasty (IGA), reconstruction arthroplasty (RA) and distraction osteogenesis (DO).

Methods: PubMed, Ovid, Embase, Web of Science, Scopus and Cochrane central register of controlled trials were searched till April 2018. Randomized controlled trials, cohort studies and retrospective studies in subjects with acquired TMJ ankylosis reporting re-ankylosis with a follow-up period of $\geq$12 months were included.

Results: Twenty-six studies with 1197 subjects were included. The higher recurrence rate was observed with GA compared to both IGA and RA ($p < 0.05$). Comparable results were obtained with IGA, RA and DO ($p > 0.05$). Among interpositional materials, alloplastic materials showed higher recurrence rate compared to autogenous materials ($p < 0.05$). However, for reconstruction, both autogenous grafts and alloplastic prosthetic implants gave similar results ($p > 0.05$). The highest improvements in MMO (maximum mouth opening) resulted with IGA but the differences regarding post-operative changes in MMO were clinically similar in all other groups.

Conclusion: IGA with autogenous material and reconstruction using either autogenous grafts or total joint replacement by alloplastic prosthetic implants provide similar clinical outcomes for TMJ ankylosis management.

1. Introduction

Temporomandibular joint (TMJ) ankylosis is a restraining ailment categorized by a restricted functional capacity of the jaw with limiting movements owing to bony or fibrous adhesions between the condyle and either glenoid fossa, disc and/or eminence (Rowe, 1982; Long et al., 2005). It affects the quality of life by interfering with mastication, speech, maintenance of oral hygiene and poor esthetics (Engel, 1948; El-Sheikh et al., 1996). TMJ ankylosis often occurs in young age and hampers the growth resulting in facial deformity and poor airway space. The etiological factors include trauma (most commonly), infection, previous TMJ surgery and systemic illnesses like psoriasis, rheumatoid arthritis, etc. (Chidzonga, 1999; Obiechina et al., 1999).

The management of TMJ ankylosis is surgical and is composed of various options, i.e., gap arthroplasty (GA), interpositional gap arthroplasty (IGA), reconstruction arthroplasty (RA) and distraction osteogenesis (DO) (Katsnelson et al., 2012; Al-Moraissi et al., 2015; Ma et al., 2015a,b; De Roo et al., 2016; Jiang et al., 2018). GA is an age-old method which is technically simple and short but had largely been abandoned due to a higher risk of associated failures (Topazian, 1966). The preferred method of treatment is mostly IGA or RA depending on age and associated facial deformity (Balaji, 2003; Sahoo et al., 2012; Al-Moraissi et al., 2015; Ma et al., 2015a). Both IGA and RA have been reported to employ a wide range of autogenous and alloplastic materials (Balaji, 2003; Mehrotra et al., 2008; 2012; Mercuri et al., 2008; Elgazzar et al., 2010; Sahoo et al., 2012; De Roo et al., 2016). DO is frequently

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applied before, after or simultaneously with ankylosis release for correction of facial deformities accompanying TMJ ankylosis (Mehrotra et al., 2016; Hu et al., 2017). Recently, DO has been employed as a primary management option for ankylosis and neocondylogenesis (Sahoo et al., 2012; Jiang et al., 2018).

The choice of any of the surgical methods and materials for either interpositioning or reconstruction is primarily guided by the surgeon's own experiences, skills, and subjective expert opinions. There exist no expert consensus or evidence-based guidelines and only a few comparative studies have been published. Few meta-analyses have also been published to quantify the magnitude of evidence if any favouring one or other technique (Katsnelson et al., 2012; Al-Moraissi et al., 2015; Ma et al., 2015a,b; De Roo et al., 2016). But, none of the meta-analyses has compared all of the techniques; furthermore, distraction osteogenesis has not been included in any of the meta-analyses. Also, the published meta-analyses have focused on most commonly used materials, i.e., temporalis myofascial flap (TMF) and costochondral grafts (CCG); while a comprehensive array of materials have been reported to be employed for both IGA and RA. The choice of surgical approach depends on the age of the subjects, but it has not been addressed in any of the meta-analyses. These facts very clearly underline the need of a methodologically sound systematic review to build the evidence for clinically important outcomes, i.e., the incidence of relapse/re-ankylosis and maximal mouth opening (MMO) and in relation to age of patients.

Bearing in mind the above-mentioned facts, the present systematic review and meta-analysis were planned to compare the various surgical modalities for treatment of acquired TMJ ankylosis, i.e. GA, IGA, RA and DO with the following objectives:

1. *Primary objective:* Identify and compare recurrence after a follow up of 12 months.
2. *Secondary objectives:*
   a. Identify and compare the post-operative change in maximum mouth opening (δMMO).
   b. Identify and compare recurrence and δMMO amongst autogenous and alloplastic materials in IGA and RA.
   c. Identify and compare the above-stated outcomes in subjects aged ≤18 years.

2. Material and methods

2.1. Material

Randomised controlled trials, quasi-randomised controlled trials, clinically controlled trials, non-randomised cohort studies and retrospective studies employing either GA, IGA, RA and/or DO in subjects with acquired TMJ ankylosis and reporting re-ankylosis as an outcome measure with a follow-up period of at least 12 months were eligible to be part of this meta-analysis. Further, reports with the study population comprising subjects with congenital TMJ ankylosis, TMJ ankylosis as part of any known syndrome or acquired TMJ ankylosis owing to systemic diseases were not eligible. Also, sub-groups intended to be part of the analysis with the number of subjects <5 were not included.

2.2. Methods

2.2.1. Locating the eligible studies

The potentially eligible studies (considering the above-mentioned inclusion and exclusion criteria) were searched using electronic databases, i.e., Pubmed, Ovid, Embase, Web of Science, Scopus and Cochrane central register of controlled trials (CENTRAL) till April 2018. The search terms were TMJ, TMJ ankylosis, interpositional arthroplasty, gap arthroplasty, reconstruction, distraction osteogenesis, neocondylogenesis, temporalis, costochondral grafts, coronoid grafts, autogenous grafts, allogenous grafts, prosthesis, condylectomy, and joint resection.

Hand searching was performed for mainstream journals pertaining to the subject of Oral and Maxillofacial Surgery. Further, reference lists of all included studies and any published systematic reviews and meta-analysis were searched to identify any additional studies. Searches were performed independently and in duplication by two investigators. Any disagreements on the eligibility of article/s were resolved by discussion with the most senior investigator.

2.2.2. Data extraction

The data extraction was performed on a pre-designed excel spreadsheet (Microsoft Excel, Microsoft Office 10, Redmond, Wash, USA) with provision to record study characteristics, details of intervention and details of study participants.

2.2.3. Quality assessment of included studies

The quality of included studies was evaluated based on Newcastle Ottawa Scale and accordingly a numeric score (NOS Score) was assigned (Deeks et al., 2003).

2.2.4. Statistical analysis

The risk difference with a 95% confidence interval (95% CI) was calculated for binary outcomes, and the mean difference with 95% CI was calculated for continuous outcomes. A fixed effects model (Mantel-Haenszel method) was used if there was no heterogeneity ($p > 0.05$ or I-squared ≤24%), otherwise a random effects model (Der Simonian-Laird method) was used (Higgins and Green, 2011). The publication bias was evaluated using a funnel plot (Egger et al., 1997). Subgroup analysis was performed for the younger age group (≤18 years) for inter-comparison among various treatment groups, i.e., GA, IGA, RA and DO. Further subgroup analysis was done for IGA and RA for the type of material used, i.e., autogenous or alloplastic. All statistical analyses were performed using the RevMan 5.3 (Cochrane Collaboration, Software Update, Oxford, UK).

2.2.5. Heterogeneity assessment

Statistical heterogeneity was calculated on the basis of Chi^2 and I^2 tests which measure the degree of inconsistencies across studies (Higgins et al., 2003). The heterogeneity on the basis of I^2 test was categorized as 0–24% = no heterogeneity, 25–49% = moderate heterogeneity, 50–74% = large heterogeneity; and 75–100% = extreme heterogeneity. A significant p value of <0.05 on the Chi^2 test meant high heterogeneity.

2.2.6. Sensitivity analysis

The sensitivity analysis was conducted by the leave-one-out approach by removing studies with the highest weight (Higgins and Green, 2011).

3. Results

3.1. Characteristics of included studies and interventions

A total of 50 full text potentially eligible studies were selected from the search results of 8424 titles from all sources [Fig. 1]. From these, 26 studies including 7 non-randomized controlled trials and 19 retrospective studies were finally selected for inclusion in the

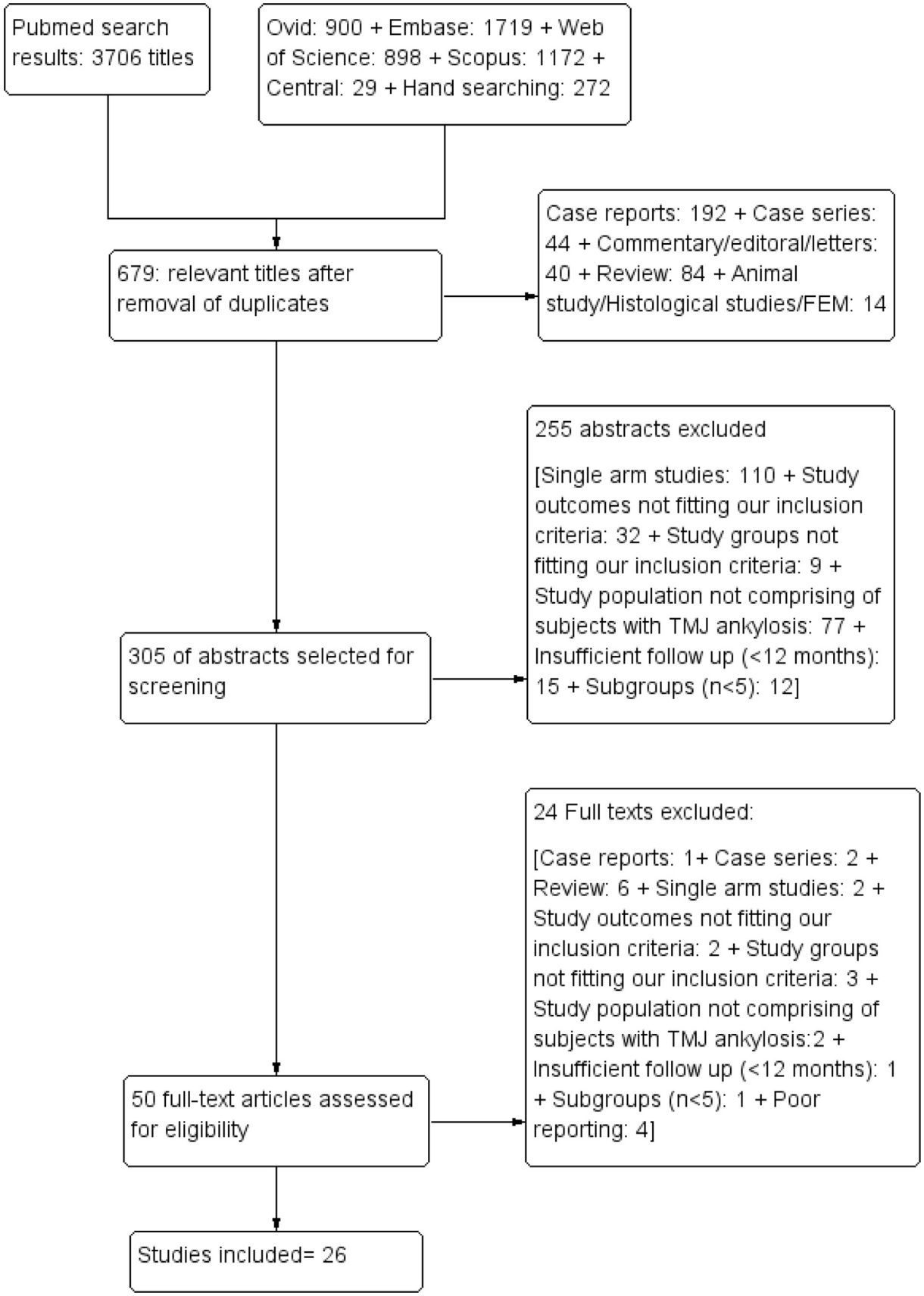


Fig. 1. Flow diagram depicting the process of final selection of studies.

present review [Table 1]. The subjects of the study population of this meta-analysis (n = 1197) were treated by various surgical modalities, i.e., gap arthroplasty (n = 455/1197; 38.01%), interpositional arthroplasty (n = 404/1197; 33.75%), reconstruction arthroplasty (n = 316/1197; 26.40%) and distraction osteogenesis (n = 22/1197; 1.84%) [Table 1]. The data for younger subjects (≤18 years) could be extracted from only 8 studies with 161 subjects. Surgical interventions comprised of GA (n = 29), IGA (n = 41), RA (n = 84) and DO (n = 7).

3.2. Comparative surgical outcomes in GA and IGA

3.2.1. Recurrence rate [Table 2]

The incidence of recurrence was lower in the IGA group compared to the GA group but it was statistically not significant (p = 0.06) [Fig. 2a]. When the studies with shorter follow up, i.e., <24 months were removed from the analysis, the reported incidence of recurrence was significantly less in the IGA group compared to the GA group (p = 0.03) [Fig. 2b]. To identify the effect

Table 1
Individual characteristics of included studies and interventions.[a]

Author, year of publication	Study design	Number of subjects (Males/Females)	Age range (years); Mean age ± SD	Surgical technique/s employed	Follow up[b]	Study quality (NOS Scale)
Valentini et al. (2002)	NRCT	60 (35/25)	3–62; 33.52 ± 14.67	GA (n = 37) IGA (n = 23)	12–60; MD	6
Balaji (2003)	Retro	31 (21/10)	7–37; 22.03 ± 9.64	IGA (n = 22) RA (n = 9)	36–72; MD	6
Souza and Mariani (2003)	NRCT	14 (9/5)	5–65; 19.71 ± 15.1	IGA (n = 5) RA (n = 9)	12–53; 28.8	6
Hu et al. (2005)	Retro	55 (MD)	MD; 17	GA (n = 41) IGA (n = 14)	4–180; MD	6
Tanrikulu et al. (2005)	Retro	24 (11/13)	1–13; 12 ± 1.96	GA (n = 8) IGA (n = 9) RA (n = 7)	12–180; 25.36 ± 34.19	7
Qudah et al. (2005)	Retro	22 (13/9)	7.1–11.3; 8.4 ± 1.3	IGA (n = 8) RA (n = 14)	12–96; 44.5 ± 21.4	7
Ramezanian and Yavary (2006)	NRCT	48 (21/37)	MD; 19.5 ± 8.9	GA (n = 22) IGA (n = 26)	MD; 58.8	7
Erol et al. (2006)	Retro	59 (23/36)	7–40; 18 ± 6.4	GA (n = 34) IGA (n = 15) RA (n = 10)	12–180; MD	6
Güven (2008)	Retro	14 (8/6)	4–11; 6.93 ± 1.9	GA (n = 6) RA (n = 8)	12–60; 33.43 ± 15.2	6
Danda et al. (2009)	NRCT	16 (9/7)	6–21; 9.09 ± 4.46	GA (n = 8) IGA (n = 8)	6–42; 23.1	7
Kummoona (2009)	NRCT	26 (14/12)	4–26; 10.81 ± 6.51	RA Auto (n = 16) RA Allo (n = 10)	24–360; 99.23 ± 93.27	6
Vasconcelos et al. (2006)	Retro	15 (9/6)	7–35; 22.21 ± 9.07	GA (n = 10) RA (n = 5)	24–60; 40.21 ± 17.48	6
Zhi et al. (2009)	Retro	42 (20/22)	5–55; 22.5	GA (n = 25) IGA (n = 12) RA (n = 5)	12–132; MD	6
Elgazzar et al. (2010)	Retro	101 (42/59)	2–41; 19.43 ± 8.5	GA (n = 11) IGA (n = 25) RA (n = 73)	14–96; 28.8	6
Loveless et al. (2010)	Retro	36 (11/25)	MD; 40 ± 13.1	IGA (n = 22) RA (n = 14)	0.3–105; 12	7
Sahoo et al. (2012)	Retro	64 (38/26)	0.83–42; 13.16 ± 7.95	IGA (n = 19) RA (n = 37) DO (n = 8)	12–132; 56.64	6
Shaikh et al. (2013)	NRCT	20 (6/14)	5–25; 15.17 ± 5.66	GA (n = 10) IGA (n = 10)	12; 12	6
Bhatt K et al. (2014)	Retro	261 (137/124)	1–49; 12.9 ± 7.1	GA (n = 206) IGA (n = 55)	12–192; 45.36 ± 36	7
Kumar et al. (2014)	Retro	45 (23/22)	2–50; 26	IGA (n = 30) RA (n = 15)	12; MD	6
Ahmad I et al. (2015)	NRCT	28 (16/12)	1–15; 10.68	GA (n = 7) IGA (n = 8) RA (n = 13)	12–36; MD	7
Bhardwaj and Arya (2016)	Retro	22 (5/17)	6–36; 15.18 ± 8.13	IGA (n = 10) RA (n = 12)	24–96; MD	6
Denadai et al. (2016)	Retro	15 (10/5)	14–46; 23.1 ± 8.4	IGA (n = 8) DO (n = 7)	36–84; 62.4 ± 15.6	8
Shakeel et al. (2016)	Retro	105 (MD)	MD; 13.85	GA (n = 30) IGA (n = 37) RA (n = 38)	12; MD	6
Dad and Uppal (2017)	Retro	30 (11/19)	MD; 14.53	IGA (n = 30)	12; 12	7
Jiang et al. (2018)	Retro	18 (7/11)	5–13; 9.33 ± 2.20	RA (n = 11) DO (n = 7)	12–50; 24.83 ± 9.88	6
Xu et al. (2017)	Retro	18 (9/9)	10–37; 17.11 ± 7.76	IGA (n = 8) RA (n = 10)	12–24; MD	7

[a] Abbreviations: NRCT = Non randomized controlled trial, Retro = retospective study, MD = Missing data, GA = Gap arthroplasty, IGA = Interpositional arthroplasty, RA = Reconstruction arthroplasty, DO = Distraction osteogenesis, NOS = Newcastle Ottawa Scale.
[b] Follow up expressed as range; mean ± SD (in months).

Table 2
Primary outcome recurrence rate in various study groups.[a]

Contributing Studies	Comparison groups	Incidence of recurrence	Total Risk difference [95% Confidence intervals]	P value
GA versus IGA				
1) Valentini et al. (2002); 2) Hu et al. (2005); 3) Tanrikulu et al. (2005); 4) Erol et al., (2006); 5) Ramezanian and Yavary (2006); 6) Danda et al. (2009); 7) Zhi et al. (2009); 8) Elgazzar et al. (2010); 9) Shaikh et al. (2013); 10) Bhatt et al. (2014); 11) Ahmad et al. (2015); 12) Shakeel et al. (2016)	GA (n = 439) IGA (n =242)	GA group = 6/439; 17.31% IGA group = 29/242; 11.98%	0.05 [−0.00, 0.11]	0.06
Studies with ≥ 24 months of follow up 1) Tanrikulu et al. (2005); 2) Ramezanian and Yavary (2006); 3) Elgazzar et al. (2010); 4) Bhatt et al. (2014); 5) Ahmad et al. (2015)	GA (n = 254) IGA (n =123)	GA group = 53/254; 20.87% IGA group = 18/123; 14.63%	0.10 [0.01, 0.18]	0.03
GA versus IGA Auto				
1) Valentini et al. (2002); 2) Tanrikulu et al. (2005); 3) Erol et al., (2006); 4) Danda et al. (2009); 5) Zhi et al. (2009); 6) Elgazzar et al. (2010); 7) Shaikh et al. (2013); 8) Bhatt et al. (2014); 9) Ahmad et al. (2015); 10) Shakeel et al. (2016)	GA (n = 376) IGA Auto (n = 179)	GA group = 56/376; 14.89% IGA Auto group = 13/179; 7.26%	0.08 [0.02, 0.13]	0.01
GA versus IGA (Subjects ≤ 18 years of age)				
1) Tanrikulu et al. (2005); 2) Danda et al. (2009); 3) Ahmad et al. (2015)	GA (n = 23) IGA (n = 24)		0.02 [−0.25, 0.22]	0.88
GA versus RA				
1) Tanrikulu et al. (2005); 2) Erol et al., (2006); 3) Güven (2008); 4) Vasconcelos (2009); 5) Zhi et al. (2009); 6) Elgazzar et al. (2010); 7) Ahmad et al. (2015); 8) Shakeel et al. (2016)	GA (n = 131) RA (n = 159)	GA group = 19/131; 14.5% RA group = 6/159; 3.77%	0.13 [0.05, 0.22]	0.003
Studies with ≥ 24 months of follow up 1) Tanrikulu et al. (2005); 2) Güven (2008); 3) Vasconcelos (2009); 4) Elgazzar et al. (2010); 5) Ahmad et al. (2015)	GA (n = 42) RA (n = 106)	GA group = 9/42; 21.43% RA group = 5/106; 4.72%	0.17 [0.02, 0.31]	0.03
GA versus RA Auto				
1) Tanrikulu et al. (2005); 2) Erol et al., (2006); 3) Zhi et al. (2009); 4) Elgazzar et al. (2010); 5) Shakeel et al. (2016)	GA (n = 108) RA Auto (n = 122)	GA group = 10/108; 9.26% RA Auto group = 4/122; 3.28%	0.10 [0.01, 0.19]	0.04
GA versus RA (Subjects ≤ 18 years of age)				
1) Tanrikulu et al. (2005); 2) Güven (2008); 3) Ahmad et al. (2015)	GA (n = 22) RA (n = 28)	GA group = 5/22 (22.73%) RA group = 1/28 (3.57%)	0.15 [−0.10, 0.41]	0.24
IGA versus RA				
1) Balaji (2003); 2) Souza & Mariani (2003); 3) Qudah et al. (2005); 4) Tanrikulu et al. (2005); 5) Erol et al., (2006); 6) Zhi et al. (2009); 7) Elgazzar et al. (2010); 8) Loveless et al. (2010); 9) Sahoo et al. (2012); 10) Kumar et al. (2014); 11) Ahmad et al. (2015); 12) Bhardwaj and Arya (2016); 13) Shakeel et al. (2016); 14) Xu et al. (2017)	IGA (n = 230) RA (n = 266)	IGA group = 11/230 (4.78%) RA group = 10/266 (3.76%)	0.02 [−0.02, 0.06]	0.39

Table 2 (*continued*)

Contributing Studies	Comparison groups	Incidence of recurrence	Total Risk difference [95% Confidence intervals]	P value
Studies with ≥ 24 months of follow up 1) Balaji (2003); 2) Souza & Mariani (2003); 3) Qudah et al. (2005); 4) Tanrikulu et al. (2005); 5) Elgazzar et al. (2010); 6) Sahoo et al. (2012); 7) Ahmad et al. (2015); 8) Bhardwaj and Arya (2016)	IGA (n = 106) RA (n = 174)	IGA group = 8/106; 7.55% RA group = 5/174; 2.87%	0.02 [−0.05, 0.09]	0.55
IGA Auto versus RA Auto 1) Balaji (2003); 2) Tanrikulu et al. (2005); 3) Qudah et al. (2005); 4) Erol et al., (2006); 5) Zhi et al. (2009); 6) Elgazzar et al. (2010); 7) Sahoo et al. (2012); 8) Kumar et al. (2014); 9) Bhardwaj and Arya (2016); 10) Shakeel et al. (2016); 11) Xu et al. (2017)	IGA Auto (n = 183) RA Auto (n = 214)	IGA Auto group = 6/183; 3.28% RA Auto group = 8/214; 3.74%	−0.00 [−0.05, 0.05]	0.95
IGA versus RA (Subjects ≤ 18 years of age) 1) Qudah et al. (2005); 2) Tanrikulu et al. (2005); 3) Ahmad et al. (2015); 4) Bhardwaj and Arya (2016)	IGA (n = 34) RA (n = 43)	IGA group = 7/34; 20.59% RA group = 2/43; 4.65%	0.14 [−0.06, 0.33	0.16
IGA versus DO 1) Sahoo et al. (2012); 2) Denadai et al. (2016)	IGA (n = 27) DO (n = 15)	IGA group = 5/27 (18.52%) DO group = 0/15 (0%)	0.25 [−0.23, 0.73]	0.30
RA and DO 1) Sahoo et al. (2012); 2) Jiang et al. (2018)	RA (n = 48) DO (n = 15)	RA group = 2/48; 4.17% DO group = 0/15; 0%	0.03 [−0.11, 0.18]	0.66
IGA using autogenous material (IGA Auto) versus IGA using alloplastic material (IGA Allo) 1) Valentini et al. (2002); 2) Shakeel et al. (2016); 3) Dad & Uppal (2017)	IGA Auto (n = 52) IGA Allo (n = 38)	IGA Auto group = 0/52; 0% IGA Allo group = 9/38; 23.68%	−0.22[−0.42,0.02]	0.03
RA using autogenous material (RA Auto) and RA using alloplastic material (RA Allo) 1) Kummoona (2009); 2) Bhardwaj and Arya (2016)	RA Auto (n = 23) RA Allo (n = 15)	RA Auto group = 0/23; 0% RA Allo group = 2/15; 13.33%	−0.11[−0.31,0.10]	0.31

[a] Abbreviations: same as Table 1.

of the choice of interpositioning material in the IGA group, another subgroup analysis between the GA and the IGA Auto (IGA with autogenous material) group depicted significantly higher ($p = 0.01$) incidence of recurrence in the GA group compared to the IGA Auto group [Fig. 2c]. No significant differences were reported for recurrence rate between the GA group and the IGA group for subjects ≤18 years of age ($p = 0.88$).

3.2.2. Postoperative changes in maximum mouth opening (δMMO) [Table 3]

Significantly higher δMMO was reported in both groups, i.e., the IGA group [Fig. 2d] and the IGA Auto group [Fig. 2e] compared to the GA group ($p = 0.01$). However, in subjects ≤18 years of age, the cumulative mean difference between the GA group and the IGA group was not significant ($p = 0.75$).

3.3. Comparative surgical outcomes in GA and RA

3.3.1. Recurrence rate [Table 2]

Significantly less incidence of recurrence was reported for the RA group compared to the GA group ($p = 0.003$) [Fig. 3a]. When studies with a follow up period less than 24 months were excluded, the incidence of recurrence was again significantly lower ($p = 0.03$) in the RA group compared to the GA group [Fig. 3b]. The subgroup analysis comparing recurrence rate between the GA and the RA Auto group (RA using autogenous material) also reported a significantly lower incidence of recurrence in the RA Auto group compared to the GA group ($p = 0.04$) [Fig. 3c]. However, no significant differences were reported for subjects <18 years of age ($p = 0.24$).

3.3.2. Postoperative changes in maximum mouth opening (δMMO) [Table 3]

Although the δMMO was higher in the RA group compared to the GA group, the difference between the two groups was statistically not significant ($p = 0.22$) [Fig. 3d]. Likewise, insignificant differences ($p = 0.77$) were reported for δMMO between the GA group and the RA Auto group [Fig. 3e]. For subjects <18 years of age, there was no significant difference in δMMO between the GA group and the RA group ($p = 0.86$).

3.4. Comparative surgical outcomes in IGA and RA

3.4.1. Recurrence rate [Table 2]

A similar incidence of recurrence rate was reported in the IGA group and the RA group, respectively ($p = 0.39$) [Fig. 4a]. Pooling of data from studies with ≥24 months of follow up also showed the insignificant difference in recurrence rate between two groups

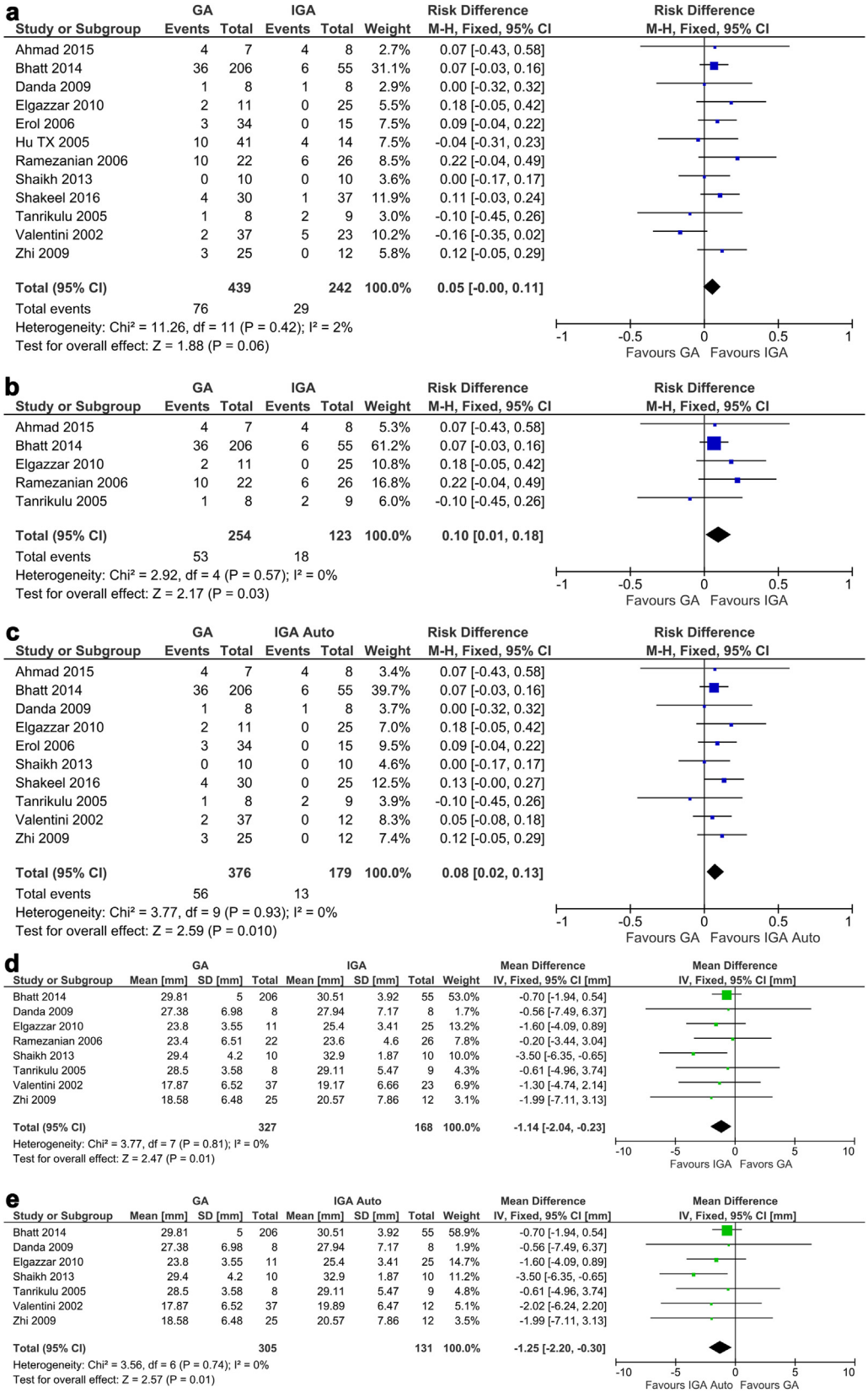


Fig. 2. a: Inter-comparison of recurrence rate in GA and IGA. b: Inter-comparison of recurrence rate in GA and IGA after ≥24 months follow up. c: Inter-comparison of recurrence rate in GA and IGA Auto. d: Inter-comparison of postoperative change in mouth opening (δMMO) in GA and IGA. e: Inter-comparison of postoperative change in mouth opening (δMMO) in GA and IGA Auto. Green colour in forest plots is for depicting primary outcome 'Recurrence rate'. Blue colour is for depicting secondary outcome, 'postoperative change in mouth opening (δMMO)'. The black diamond is for depicting pooled outcome.

Table 3
Secondary outcome post-operative change in MMO (δMMO) in various study groups.[a]

Contributing Studies	Comparison groups	Cumulative mean difference [95% Confidence intervals]	P value
GA versus IGA			
1) Valentini et al. (2002); 2) Tanrikulu et al. (2005); 3) Ramezanian and Yavary (2006); 4) Danda et al. (2009); 5) Zhi et al. (2009); 6) Elgazzar et al. (2010); 7) Shaikh et al. (2013); 8) Bhatt et al. (2014)	GA (n = 327) IGA (n =168)	−1.14 [−2.04, −0.23]	0.01
GA versus IGA Auto			
1) Valentini et al. (2002); 2) Tanrikulu et al. (2005); 3) Danda et al. (2009); 4) Zhi et al. (2009); 5) Elgazzar et al. (2010); 6) Shaikh et al. (2013); 7) Bhatt et al. (2014);	GA (n = 305) IGA Auto (n = 131)	−1.25 [−2.20, −0.30]	0.01
GA versus IGA (Subjects ≤ 18 years of age)			
1) Tanrikulu et al. (2005); 2) Danda et al. (2009);	GA (n = 16) IGA (n = 16)	−0.61 [−4.40, 3.19]	0.75
GA versus RA			
1) Tanrikulu et al. (2005); 2) Güven (2008); 3) Zhi et al. (2009); 4) Elgazzar et al. (2010);	GA (n = 50) RA (n = 93)	−2.62 [−6.83, 1.59]	0.22
GA versus RA Auto			
1) Tanrikulu et al. (2005); 2) Zhi et al. (2009); 3) Elgazzar et al. (2010)	GA (n = 44) RA Auto (n = 74)	−0.94 [−7.29, 5.40]	0.77
GA versus RA (Subjects ≤ 18 years of age)			
1) Tanrikulu et al. (2005); 2) Güven (2008);	GA (n = 14) RA (n = 15)	−0.90 [−10.61, 8.80]	0.86
IGA versus RA			
1) Balaji (2003); 2) Souza & Mariani (2003); 3) Qudah et al. (2005); 4) Tanrikulu et al. (2005); 5) Elgazzar et al. (2010); 6) Loveless et al. (2010); 7) Sahoo et al. (2012); 8) Bhardwaj and Arya (2016)	IGA (n = 120) RA (n = 175)	0.87 [−1.71, 3.45]	0.51
IGA Auto versus RA Auto			
1) Balaji (2003); 2) Tanrikulu et al. (2005); 3) Qudah et al. (2005); 4) Elgazzar et al. (2010); 5) Sahoo et al. (2012); 6) Bhardwaj and Arya (2016)	IGA Auto (n = 93) RA Auto (n = 136)	1.05 [−1.43, 3.53]	0.95
IGA versus RA (Subjects ≤ 18 years of age)			
1) Qudah et al. (2005); 2) Tanrikulu et al. (2005); 3) Bhardwaj and Arya (2016)	IGA (n = 26) RA (n = 30)	1.20 [−0.11, 2.50]	0.07
IGA versus DO			
1) Sahoo et al. (2012); 2) Denadai et al. (2016)	IGA (n = 27) DO (n = 15)	−5.10 [−12.39, 2.18]	0.17
RA versus DO			
1) Sahoo et al. (2012); 2) Jiang et al. (2018)	RA (n = 48) DO (n = 15)	−2.57 [−4.61, −0.53]	0.01
IGA Auto versus IGA Allo			
1) Shakeel et al. (2016); 2) Dad & Uppal (2017)	IGA Auto (n = 27) IGA Allo (n = 26)	1.69 [−2.75, 6.12]	0.46
RA Auto versus RA Allo			
1) Kummoona (2009); 2) Bhardwaj and Arya (2016)	RA Auto (n = 23) RA Allo (n = 15)	−3.03 [−9.00, 2.94]	0.32

[a] Abbreviations: same as Table 1.

(p = 0.55) [Fig. 4b]. The subgroup analysis between the IGA Auto group and the RA Auto group again depicted the statistically insignificant difference between the two groups (p = 0.95) [Fig. 4c]. Similarly, for subjects ≤18 years of age statistically comparable incidence of recurrence was reported for the IGA group and the RA group (p = 0.16).

3.4.2. Postoperative changes in maximum mouth opening (δMMO) [Table 3]

The cumulative mean difference δMMO between the IGA group and the RA group was statistically not significant (p = 0.51) [Fig. 4d]. Moreover, the subgroup analysis to compare δMMO in the IGA group and the RA Auto group also showed a statistically

insignificant difference ($p = 0.41$) [Fig. 4e]. Further, for subjects ≤18 years of age, even though the δMMO was higher in the IGA group compared to the RA group, it did not reach statistical significance ($p = 0.07$).

3.4.3. Comparative surgical outcomes in IGA and DO [Tables 2 and 3]

The cumulative risk difference for recurrence rate between the two groups did not achieve statistical significance ($p = 0.30$) [Table 3]. The reported δMMO was higher in the DO group compared to the IGA group, but the difference between the two groups was statistically not significant ($p = 0.17$) [Table 3].

3.4.4. Comparative surgical outcomes in RA and DO [Tables 2 and 3]

The recurrence rate was statistically similar ($p = 0.66$) in the two study groups [Table 2]. Significantly higher δMMO was reported for the DO group compared to the RA group ($p = 0.01$) [Table 3]. Only one study (Jiang et al., 2018) with a sample size of 18 subjects was identified which compared RA ($n = 11$) and DO ($n = 7$) for subjects ≤18 years of age. In this study, no recurrence rate was reported in any of the groups, but significantly higher δMMO was reported for the DO group compared to the RA group ($p = 0.002$).

3.4.5. Comparative surgical outcomes in IGA using autogenous material (IGA Auto) and IGA using alloplastic material (IGA Allo) [Tables 2 and 3]

Significantly lower recurrence rate was reported in the IGA Auto group compared to the IGA Allo group ($p = 0.03$) [Table 2]. The comparative analysis of δMMO between the two groups did not show a significant difference ($p = 0.46$) [Table 3].

3.4.6. Comparative surgical outcomes in RA using autogenous material (RA Auto) and RA using alloplastic material (RA Allo) [Tables 2 and 3]

The recurrence rate between the RA Auto group and the RA Allo group was statistically similar ($p = 0.31$) [Table 2]. The total mean difference between the pooled δMMO in the two groups was also not significant statistically ($p = 0.32$) [Table 3].

3.4.7. Sensitivity analysis and funnel plots

The sensitivity analyses performed by removal of studies with high weight did not affect either the significance level or the cumulative risk difference/mean difference to affect the overall results for any of the comparisons performed. However, the sensitivity analysis performed by successive removal of studies with <24 months and <36 months of follow up affected the overall results for recurrence rate between the GA group and IGA group. The recurrence rate between GA and IGA was found to be similar ($p = 0.06$). But, when the studies with <24 months and <36 months of follow up were successively removed, the p-value reached a significance level ($p = 0.03$ for studies with ≥24 months follow up and $p = 0.04$ for studies with ≥36 months follow up). The funnel plots (not shown because of space constraints) for any of the analyses did not show asymmetry suggestive of publication bias.

4. Discussion

The present systematic review aimed to compare the surgical outcomes, i.e., recurrence and postoperative improvement in MMO (δMMO) after a minimum follow up period of 12 months among various surgical techniques (GA, IGA, RA and DO) for management of TMJ ankylosis. Additionally, the surgical outcomes in autogenous and alloplastic materials in IGA and RA were also compared. Further, the data for younger subjects (≤18 years of age) were also extracted to help draw evidence for the comparative efficacy of these techniques as the choice of treatment is guided by age of the subjects. The present meta-analysis pooled data from 1197 subjects from 26 studies and it is to date one of the most extensive systematic reviews. None of the previously published systematic reviews analyzed all of the surgical modalities for the management of TMJ ankylosis. Although one meta-analysis (De Roo et al., 2016) compared multiple treatment options and conducted sub-group analysis for children as well, it included only single-arm studies and the included studies suffered from extreme heterogeneity, i.e., >90%. Thus, the findings of their meta-analysis are questionable. The recent systematic reviews included studies published till 2014; while the present meta-analysis is a sequential update as the literature search was conducted in April 2018. The previously published systematic reviews did not attempt to standardize the study population and studies conducted on subjects with systemic illnesses affecting joints were also included which could have affected the analyzed outcomes (Katsnelson et al., 2012; Al-Moraissi et al., 2015; Ma et al., 2015a,b; De Roo et al., 2016). On the other hand, in the present meta-analysis, the included studies were composed of subjects with acquired TMJ ankylosis without any systemic illnesses affecting joints, i.e., osteoarthritis or rheumatic arthritis. None of the meta-analyses except one (De Roo et al., 2016) analyzed the data for a younger age-group, while the present meta-analysis conducted subgroup analyses for subjects <18 years of age as well. Another meta-analysis (Al Moraisi et al., 2015) included studies with 6 months of follow up as well, while in the present meta-analysis studies with a minimum of 12 months follow up were included. Additionally, subgroup analyses by excluding studies with <24 months of follow up were conducted. In this meta-analysis, the inclusion criteria for studies was recurrence rate after a follow-up period of 12 months as an outcome measure while a previously published review included the studies with MMO as an outcome measure. This facilitated pooling of data from a larger number of studies as few studies reported the incidence of recurrence but not MMO. It is obvious that such reports were not included in the previous reviews. Indeed, it is a reasonable approach to consider the recurrence rate as the primary outcome and not the MMO as the average MMOs in all the studies were in the clinically acceptable range of 30–35 mm. Furthermore, the secondary outcome was the post-operative change in MMO (δMMO) while the previously published meta-analyses studied post-operative MMO as the outcome measure, which is logically less robust as it does not consider the pre-operative MMO (Al-Moraissi et al., 2015; Ma et al., 2015a,b).

Amongst GA and IGA, similar rates of recurrence were noted ($p = 0.06$) but when the data of studies with <24 months of follow up were removed, significantly fewer events of recurrence were observed in IGA compared to GA ($p = 0.03$). This suggests that IGA gives stable results while relapses occur over a longer period of time when surgical management has been done using GA. A variety of autogenous and alloplastic materials were used to perform IGA and this could have contributed to heterogeneity. To evaluate if the choice of interpositional material affects the outcome, the outcomes were also compared between GA and IGA Auto and between IGA Auto and IGA Allo. Although IGA Auto and IGA Allo depicted statistically similar δMMO ($p = 0.45$); the recurrence rate was significantly higher in the IGA Allo group compared to the IGA Auto ($p = 0.03$). These findings underline the poor performance of alloplastic materials for interpositioning. The TMF was the commonest interpositioning material in the included studies. As it is known to suffer from inherent drawbacks of scar contraction and reduction in post-operative MMO, it would have been worthwhile to compare TMF with other types of autogenous materials. But, unfortunately, lack of eligible studies precluded such comparison. Low heterogeneity was reported for all of these comparisons except between IGA Auto and

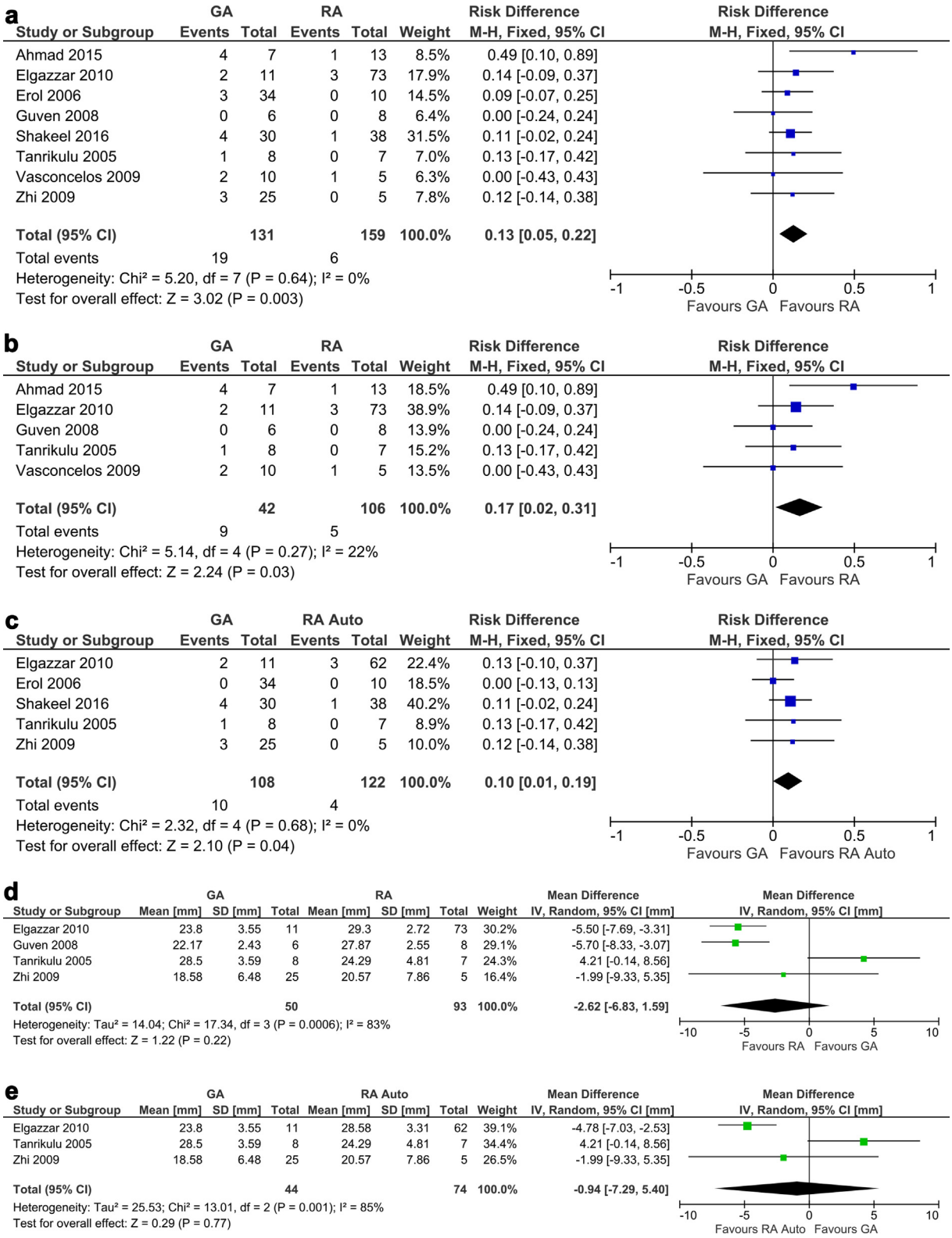
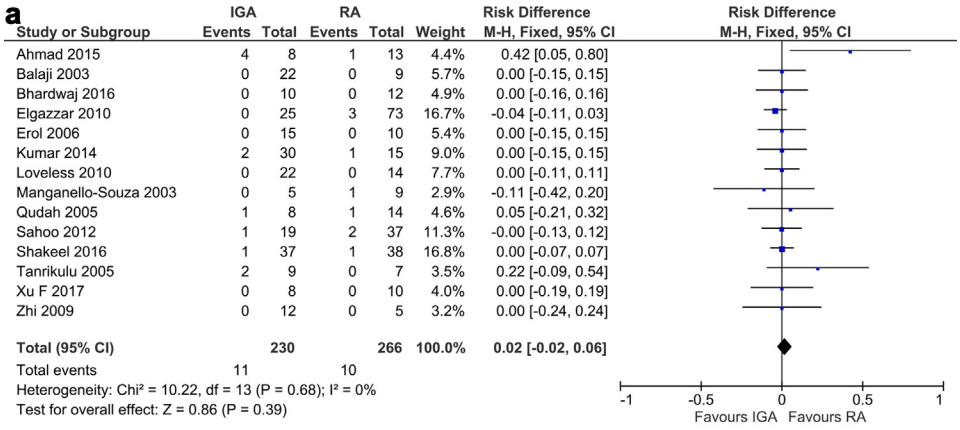
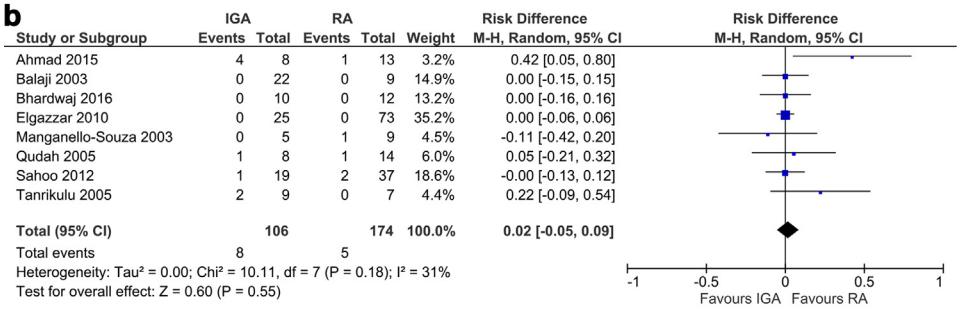
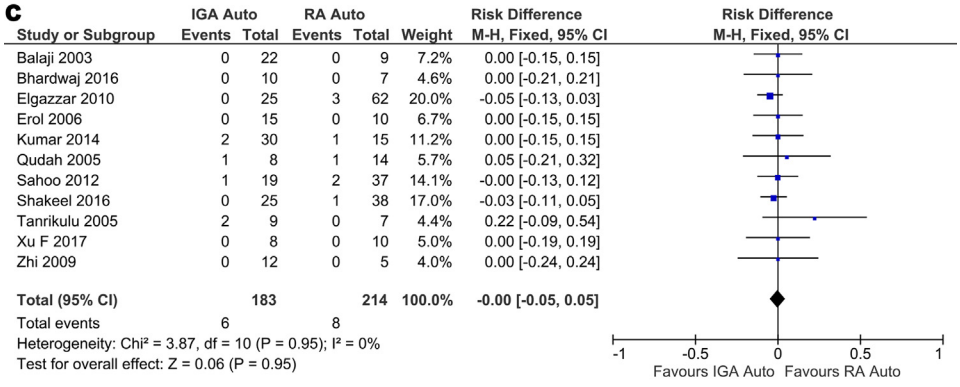


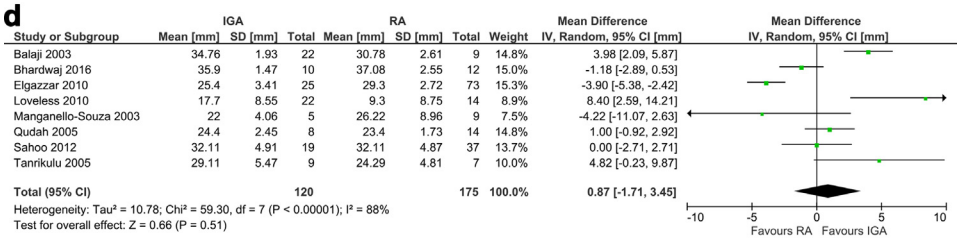
Fig. 3. a: Inter-comparison of recurrence rate in GA and RA. b: Inter-comparison of recurrence rate in GA and RA after ≥24 months follow up. c: Inter-comparison of recurrence rate in GA and RA Auto. d: Inter-comparison of postoperative change in mouth opening (δMMO) in GA and RA. e: Inter-comparison of postoperative change in mouth opening (δMMO) in GA and RA Auto. Blue colour in forest plots is for depicting primary outcome 'Recurrence rate'. Green colour is for depicting secondary outcome, 'postoperative change in mouth opening (δMMO)'. The black diamond is for depicting pooled outcome.

IGA Allo where 57% of heterogeneity was found. Also, only two studies provided data for comparison of δMMO in IGA Auto and IGA Allo. Rather than excluding the comparative data between IGA Auto and IGA Allo on account of heterogeneity, these findings were included in the present meta-analysis with a cautionary note for careful extrapolation. These findings support the long-standing clinical opinion that the resected surfaces should be interposed with a lining material (Kaban et al., 1990). As per the results of the









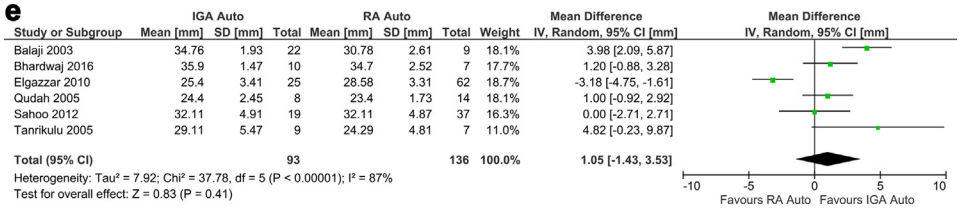


Fig. 4. a: Inter-comparison of recurrence rate in IGA and RA. b: Inter-comparison of recurrence rate in IGA and RA after ≥24 months follow up. c: Inter-comparison of recurrence rate in IGA Auto and RA Auto. d: Inter-comparison of postoperative change in mouth opening (δMMO) in IGA and RA. e: Inter-comparison of postoperative change in mouth opening (δMMO) in IGA Auto and RA Auto. Blue colour in forest plots is for depicting primary outcome 'Recurrence rate'. Green colour is for depicting secondary outcome, 'postoperative change in mouth opening (δMMO)'. The black diamond is for depicting pooled outcome.

analyses, the preferred lining should be of autogenous material. Despite methodological differences, these findings corroborate with those of Al-Moraisi et al. (2015) who reported 3.15 times greater risk of re-ankylosis with GA compared to IGA. However, Ma et al. (2015a) reported a similar incidence of recurrence among GA and IGA, and the differences may be because of the inclusion of recently published reports in our review. Significantly better δMMO values were reported for IGA compared to GA and this agrees with previously published systematic reviews and individual studies (Al-Moraissi et al., 2015; Ma et al., 2015b; De Roo et al., 2016). However, a cumulative difference of 1.14 mm (0.23–2.04; 95% CI) was found and this small difference should not be a guiding factor for choosing the surgical management option.

Similar types of findings were reported when the comparisons were made between GA and RA. Comparable δMMO values were reported for GA and RA ($p = 0.22$) and also for subgroup comparison, i.e., GA and RA Auto ($p = 0.77$). Also, statistically similar δMMO values were reported for RA Auto and RA Allo ($p = 0.75$). But for recurrence rate, surgical intervention with GA resulted in significantly higher rates of recurrence compared to RA ($p = 0.003$), which remained significant when studies with <24 months of follow up were removed from the analysis ($p = 0.03$). The RA Auto depicted significantly less incidence of recurrence compared to GA ($p = 0.04$). But RA Auto and RA Allo showed a comparable incidence of re-ankylosis ($p = 0.75$). It is to be noted here that studies included for comparison of recurrence between 'GA and RA' and between 'GA and RA Auto' showed no heterogeneity but rest of the comparison groups, i.e., recurrence rate between RA Auto and RA Allo and comparative δMMO in GA and RA; GA and RA Auto and RA Auto and RA Allo showed high heterogeneity. Data from only two eligible studies could be pooled to draw comparisons between RA Auto and RA Allo. The authors caution about generalizing interpretations to practice for this subgroup. Only one previously published systematic review by Al Moraisi et al. (2015) compared recurrence rate among GA and RA and published no differences between GA and RA. They included only two studies (Mabongo, 2013; Vasconcelos et al., 2006) with 28 subjects. They did not analyze data from studies by Tanrikulu et al. (2005) and Elgazzar et al. (2010) for comparing outcomes between the GA and RA, even when they included these studies in their review. Regarding comparison between RA Auto and RA Allo, the results in the present meta-analysis were somehow in corroboration with those by Al Moraisi et al. (2015). It is to be noted here that different subsets of studies (Saeed et al., 2002; Tang et al., 2009) with study population comprising subjects with arthritis were included by them. While in the present meta-analysis, the strict inclusion criteria of including papers investigating subjects with acquired TMJ ankylosis precluded the inclusion of studies included by Al Moraisi et al. (2015).

The incidence of re-ankylosis between IGA and RA was similar ($p = 0.39$) and no significant differences were detected even when the studies with <24 months of follow up ($p = 0.55$) were removed from the analysis. The subgroup analysis for autogenous materials, comparing between IGA Auto and RA Auto, again revealed a similar incidence of re-ankylosis amongst the two groups ($p = 0.95$). Further, the δMMO was also similar among IGA and RA ($p = 0.51$) and between IGA Auto and RA Auto ($p = 0.41$). The level of heterogeneity was high among studies included for comparisons for δMMO. These findings are a validation of previously published studies (Al Moraisi et al., 2015; Ma et al., 2015a).

A smaller number of studies on DO could be included, i.e., 2 studies drew comparisons between IGA and DO and 2 studies were included to compare RA and DO. The δMMO was higher in DO compared to both IGA and RA, the differences were significant only for RA versus DO ($p = 0.01$). However, no significant differences were found for recurrence rate between either IGA versus DO ($p = 0.30$) or RA versus DO ($p = 0.66$). Fewer studies coupled with a high heterogeneity does not justify generalizing these results to clinical practice. Nevertheless, promising results with comparable success rates and jaw movements by reconstruction of RCU (ramus condyle unit) employing DO have been published (Xiao et al., 2012; Bansal et al., 2014; Kohli et al., 2017). However, those studies could not be included in the present review because of less follow up (Kohli et al., 2017) or no comparison group (Xiao et al., 2012; Bansal et al., 2014). The most interesting is the analogous trabecular pattern and cancellous bone density of neocondyles generated by DO akin to natural contralateral condyles as reported by Bansal et al. (2014) using cone beam CT. Further, long term stability of neocondyles with 92 months follow up has been confirmed by Xiao et al. (2012).

For younger ages, i.e., ≤18 years of age, the paucity of studies limited the comparisons to GA versus IGA ($n = 3$ studies), GA versus RA ($n = 3$ studies) and IGA versus RA ($n = 4$ studies). No significant differences were reported for any of the comparisons. Also, except GA versus IGA where no heterogeneity was found, the rest of the comparisons depicted high heterogeneity. Thus, no separate conclusions could be drawn for the younger population.

Before the readers go on to extrapolate these findings to clinical practice, it is emphasized that the success of treatment in long run is dependent on supplementing rehabilitation with vigorous and supervised physiotherapy. Some authors have recommended that with aggressive and regular physiotherapy even minimal gap arthroplasty is efficacious (Babu et al., 2013; Ma et al., 2015b). The authors planned to study the effect of physiotherapy but missing data in published studies prevented such analysis. In almost all of the included studies, it was mentioned that physiotherapy was done and exercises were prescribed; but insufficient information was available on adherence to physiotherapy routine, methods, aggressiveness and duration. The importance of coronoidectomy for preventing relapse has been previously emphasized (Kaban et al., 1990). It would have been interesting to study the effect of coronoidectomy on recurrence rate or δMMO, but again, insufficient reporting prohibited this analysis.

Two main outcomes employed routinely to assess success of surgical intervention for management of TMJ ankylosis include relapse and δMMO. The former is assessed by MMO and radiographic evidence of bony union between condyle and glenoid fossa. While the decrease in MMO can also happen as a result of poor compliance and failure to do physiotherapy with recommended vigour and frequency. Thus, a decrease in MMO does not always imply recurrence. Further, to note that the findings in this manuscript are pooled from previously performed research and are dependent on authors reporting where a clear-cut definition of what constitutes relapse might not be available. Also, in some studies only relapse rate was given with no description of MMO. Hence, a lesser number of studies were available for pooling of data for the outcome 'δMMO' compared to the outcome 'recurrence rate'. Also, recurrence and δMMO were the only two outcomes evaluated for determining the post-operative success in the present meta-analysis. But various other important outcomes, i.e., mandibular deviation, malocclusion, undergrowth or overgrowth with CCG reconstruction and mandibular range of motion in addition to mouth opening, i.e., mandibular laterotrusion and protrusion determine the overall success of surgical intervention of TMJ ankylosis. These outcomes could not be investigated in the present systematic review owing to incomplete reporting in included studies.

As per the findings of the present review, both IGA and RA performed similarly. Based on these findings it can be safely stated

that because of the relatively less extensive and simple procedure, IGA should be a preferred modality in non-growing subjects. However, RA is a needed treatment option in subjects with greater deformity and asymmetry. In subjects with remaining growth potential, RA with CCG should be the preferred treatment option. Although CCG has been the standard treatment modality in children, its use is of obvious concern because of its unpredictable growth pattern. The effect of the latter may manifest as undergrowth or overgrowth resulting in a need for subsequent surgery for correction of the ensued deformity. In the present review, only 5/160 (3.13%) subjects developed mandibular asymmetry subsequent to CCG placement. But, as many studies did not report any data on CCG growth and the follow up was only 12 months in some studies, this figure may well underreport the aberrant growth following CCG placement. A recent systematic review (Kumar et al., 2015) reported that 10/96 grafts of CCG showed aberrant growth, i.e., undergrowth in 1 graft, overgrowth in 7 grafts, lateral overgrowth in 1 graft and no growth in 1 graft. The amount of growth has often been correlated with the amount of cartilage implanted and it has been recommended that the amount of cartilage to be used should be <5 mm. However, this is an open-ended recommendation and future trial can approve or disprove it.

In the present meta-analysis, only a smaller number of comparative studies could be included to justify the success of total joint replacement by alloplastic implants (RA Allo). But then, few single arm studies with long-term follow up have reported greater than 90% success rate with TMJ prosthesis (Mercuri et al., 2008; Wolford et al., 2015). It is notable that CCG has a questionable prognosis in older adults and those who have undergone previous surgeries (Mercuri et al., 2008; Al Moraisi et al., 2015; Wolford et al., 2015). The cortical ribs in older adults offer poor osseointegration because of the presence of a small amount of cancellous bone. This is even truer in cases of scarred recipient tissue bed because of previous surgeries, because it is often poor in vascularity needed to support and integrate the graft (Mercuri et al., 2008; Tang et al., 2009; Wolford et al., 2015). In such cases with a previous history of multiple surgeries, failed grafts or older age, mechanical integration of alloplastic implants can provide stable results.

Nevertheless, the present systematic review suffers from limitations. The most problematic is the failure to include any randomized controlled trial (RCT). The RCTs are considered the most appropriate approach to compare any two interventions (Higgins and Green, 2011). However, there is a scantiness of RCTs addressing surgical management of TMJ ankylosis owing to the low incidence of TMJ ankylosis, inability to include a sufficient number of subjects, surgeon's own preferences, ethical aspects in assigning subjects to specific invasive experimental treatment options and requirement of long-term follow-ups which often impose logistics and monetary burdens. Consequently, in the present meta-analysis, the data were pooled from non-randomized studies and retrospective studies. But the included studies were of good quality, i.e., all of them rated ≥6 on NOS. Another restraint was the inability to obtain sufficient data for younger subjects (≤18 years of age). The data for this age group was extracted even from studies which reported results for mixed ages by using data for individual subjects from the tables published in included studies. But this was still not adequate and the included studies suffered from a high level of heterogeneity. Observing the deficiencies of the available literature, we suggest that future RCTs should be conducted with a greater number of subjects. The multicentric trials should be conducted to help recruit a larger number of participants. The role of a predesigned consensus-based physiotherapy regimen should be evaluated. In addition to re-ankylosis and MMO, various other factors should be studied, i.e., amount of lateral excursion, protrusion, pain and overall quality of life.

5. Conclusion

A higher recurrence rate was observed with GA compared to both IGA and RA, while the latter two show equivalent recurrence rate. Unstable results were reported with GA and with GA, relapses tend to occur over time. Comparable results were obtained with DO, IGA, and RA. Regarding the type of material, alloplastic materials gave poor results with higher recurrence rate compared to the autogenous material when used for inter-positioning. For reconstruction, both autogenous grafts and total joint replacement by alloplastic prosthetic implants gave similar results. The highest improvements in MMO result with IGA but the differences regarding post-operative changes in MMO were clinically similar in all groups. No conclusions could be drafted for younger ages due to the paucity of studies. Further, no endorsements could be made for the effect of physiotherapy on the success of surgical treatment due to deficient data in included studies.

Conflicts of interest

Nil.

Acknowledgment

Nil.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcms.2019.03.029.

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