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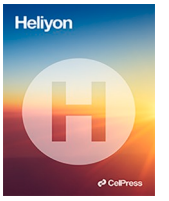

Review article

Does cyanoacrylate have the best postoperative outcomes after third molar extractions when compared to conventional sutures? A systematic review and meta-analysis

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ABSTRACT

Purpose: Tissue synthesis is extremely important for the attenuation of postoperative discomforts, as it keeps the tissues coapted, accelerates the healing process, and reduces the bleeding period of the surgical wound. Thus, this study aimed to systematically review the results of clinical trials that compared the use of cyanoacrylate with conventional sutures after third molars extraction.
Materials and methods: Searches were conducted on MEDLINE (via PubMed), Cochrane Central Registry of Controlled Trials (CENTRAL), Virtual Health Library (VHL), and Web of Science. Articles published up to February 20, 2022, were included. No restrictions were imposed on data or language of publication.
Results: A total of 8 studies (5 randomized controlled trials and 3 non-randomized comparative clinical studies) were included in this review and five studies were included in the meta-analysis, comprising 440 patients. The use of cyanoacrylate promoted better results in pain reduction in the first postoperative day when compared to the use of conventional suture (SMD: −1.01; 95%CI -1.90 to −0.12). Cyanoacrylate group promoted significant but borderline edema reduction compared to conventional sutures in the 7th postoperative day (SMD: −0.24, 95%CI -0.46 to −0.01, I2 = 0 %). For the trismus outcome, in all periods evaluated no differences were found between the groups.
Conclusion: Although promising results, there is no high-quality evidence to suggest the use of cyanoacrylate was better than conventional sutures.

1. Introduction

Third molar (3 M) extraction is a common procedure in dental practice [1]. The surgical time and the trauma caused to the oral

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tissues are considerable factors for the onset of pain, edema, trismus, and bleeding after 3Ms extractions [2]. Tissue synthesis is extremely important for the attenuation of postoperative discomforts, as it keeps the tissues coapted, accelerates the healing process, and reduces the bleeding period of the surgical wound [3,4].

The suture is the most traditional and used method for closing surgical wounds [5]. Although this method does not present adverse effects, the presence of the suture stitches can cause food accumulation and discomfort to the patient and can provoke an exaggerated inflammatory response at the site [6]. Furthermore, in certain areas, the dentist may have difficulty performing the conventional suturing technique. In addition, there is a need for subsequent removal of the stitches from the operated area [7].

As an alternative method of wound synthesis, cyanoacrylates are a group of low-cost, easy-to-apply chemical adhesives that have been widely used for the coaptation of the edges of surgical wounds involving skin and mucous membranes [8–10]. These materials are not absorbable, polymerization takes place in 10–15 s, and they last for 7–10 days after the adhesive is applied [11]. The main advantages of these adhesives are their easy application, hemostasis, fast adhesion, and bacteriostatic effect [12]. In dentistry, these adhesives are used to close flaps, fixation of gingival grafts, and pulp capping [13–15].

There are different approaches for closing the surgical wound and cyanoacrylate can be promising to contribute to 3Ms extractions, due to its easy application [1]. Randomized controlled trials (RCTs) that evaluated the use of cyanoacrylate in 3Ms extractions compared to conventional sutures are still controversial in reducing postoperative complications [1,6,7,12]. Taking into account the posterior location of 3Ms and that the presence of conventional sutures can cause food accumulation and exaggerated inflammatory response our hypothesis is that cyanoacrylate may present good results when compared to conventional ones. Thus, this study aimed to systematically review the results of clinical trials that compared the use of cyanoacrylate with conventional sutures after 3Ms extraction.

2. Materials and methods

2.1. Protocol and registration

This systematic review was conducted in accordance with the guidelines outlined in the Cochrane Handbook [16] and adhered to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [17]. The research protocol was registered with PROSPERO under the registration number CRD42022295538.

2.2. Eligibility criteria

2.2.1. Inclusion criteria

The main question of this study was: "Does cyanoacrylate present better efficacy for pain, edema, trismus, and bleeding after third molar extractions when compared to conventional sutures?"

The PICOS (population, intervention, comparator, outcome, study design) strategy was applied as follows: (P) patients over 18 years of age without systemic diseases who underwent third molar surgery; (I) use of cyanoacrylate or conventional sutures to close the surgical wound after third molar extraction; (O) studies with primary outcomes of pain, edema, trismus, and bleeding and secondary outcomes of dehiscence and wound infection; and (S) randomized controlled trials and comparative clinical studies.

2.2.2. Exclusion criteria

The exclusion criteria were as follows: (1) observational studies (case–control, cohort, and cross-sectional), case reports, narrative reviews, systematic reviews, letters to the editors, short communications, *in vitro* studies, animal studies, and noncomparative studies; (2) studies that used an adhesive other than cyanoacrylate; and (3) studies that included patients with harmful oral habits, such as smoking and chewing tobacco, patients undergoing chemotherapy and/or radiotherapy, and pregnant women.

2.2.3. Search strategy

The MEDLINE (PubMed), Cochrane Central Registry of Controlled Trials (CENTRAL), Virtual Health Library (VHL), and Web of Science databases were searched from inception until February 20, 2022, without data or publication language restrictions. We conducted supplementary searches for additional studies in the gray literature using the Google Scholar and OpenGrey platforms. Furthermore, we reviewed the reference lists of the included articles to identify additional relevant studies. The https://ClinicalTrials.gov/platform was checked for ongoing clinical trial records. MeSH terms, keywords, and other free terms were used as follows: ((Cyanoacrylate) OR (Cyanoacrylates) OR (Bucrylate) OR (Enbucrilate) OR (Enbucrilates) OR (Tissue Adhesive) OR (Tissue Adhesives)) AND ((Molars, Third) OR (Third Molar) OR (Third Molars) OR (Tooth, Wisdom) OR (Wisdom Tooth) OR (Teeth, Wisdom) OR (Wisdom Teeth) OR (oral surgery) OR (maxillofacial surgery) OR (surgery, maxillofacial) OR (exodontics)) AND ((suture) OR (sutures)). When the authors lacked proficiency in a foreign language, Google Translate was employed for translation purposes. Comprehensive descriptions of the search strategies are available in Supplementary File 1.

2.2.4. Study selection process

Three reviewers (MRFS, MWAG, and MTBAG) independently conducted electronic searches and managed the entire study selection process. The identified references were imported into EndNote® software (Clarivate Analytics®, version X8), and duplicate records were purged. Subsequently, titles and abstracts were meticulously scrutinized to exclude studies that deviated from the scope of this review. The preselected articles were then rigorously examined and assessed against the eligibility criteria. Any discrepancies arising during the study selection process were resolved through consultation with a fourth reviewer (SGMF).

2.2.5. Data extraction

Data extraction was performed by the same three researchers (MRFS, MWAG, and MTBAG) independently. They searched for the following information: author, year of publication, country, study design, sample size, number of surgeries, eligibility criteria, study conclusions, characteristics of the participants (age and sex), characteristics of the analyzed outcomes (pain, edema, trismus, bleeding, dehiscence, and wound infection), instruments used to measure the outcomes, brand name of cyanoacrylate, type of silk used in the suture, and medications used (pre- and postsurgery).

2.2.6. Risk of bias

Two independent reviewers (MRFS and MWAG) assessed the risk of bias in the included studies, focusing on the assessed outcomes according to the Revised Tool for Assessing Risk of Bias in Randomized Trials (RoB 2.0) [18]. Disagreements between the review authors were resolved by discussion with a third reviewer (SGMF).

2.2.7. Data analysis

The meta-analysis was performed using Stata software (version 3). The measure of effect used was the standardized mean difference (SMD), and 95 % confidence intervals were used to present results in every case. Heterogeneity was measured using the inconsistency statistic (I^2). The fixed-effects model was used when $I^2 = 0$, and the random-effects model was used when $I^2 > 0$. Publication bias was assessed according to the symmetry demonstrated by funnel plots since at least ten studies were included in the meta-analysis [16].

2.2.8. Certainty of evidence

The Grading of Recommendation Assessment, Development, and Evaluation (GRADE) tool was utilized to evaluate the certainty of evidence using Gradepro software (https://gradepro.org). This assessment was grounded in high-quality evidence and involved the examination of study design limitations, inconsistency, imprecision, indirect evidence, and the potential existence of publication bias. The level of evidence certainty was adjusted downward by one or two levels as appropriate. Subsequently, the quality of the evidence was categorized as high, moderate, low, or very low.

3. Results

3.1. Study selection

Initially, 226 studies were identified. Of these, eight were included in the qualitative analysis [1,6,7,12,19–22] and five in the quantitative analysis [1,6,12,19,20]. The selection process and reasons for exclusion are shown in the PRISMA flow diagram (Fig. 1).

3.1.1. Characteristics of the included studies

Of the included studies, five were RCTs [1,12,20–22], and the others were non-randomized comparative clinical studies [6,7,19]. Five used the split mouth method [6,7,19,21,22]. The studies were published between 2009 and 2021, from different countries (Table 1). In total, 220 participants were included in the experimental group and 220 in the control group, with a follow-up period ranging from 1 day to 4 weeks after surgery. The main methodological characteristics of the studies are described in Table 1. The characteristics of the participants are described in Table 2.

The pain variable was evaluated in six studies [1,6,7,12,19,20], edema in four [1,6,12,20], trismus in three [1,12,20] and bleeding in seven studies [1,6,7,12,19,20,22]. Both dehiscence variables [1,12,21] and wound infection [1,6,21] were evaluated in three studies. The tools for evaluating the outcomes and the pre-and postoperative medications used are described in Table 3. All studies included only mandibular 3Ms.

Of the eight studies included in the systematic review, three could not be included in the meta-analysis, as they did not present sufficient data [7,21,22]. Five studies were included in the meta-analysis, with a total of 320 patients [1,6,12,19,20]. Only the pain, edema, and trismus outcomes could be evaluated. The bleeding, dehiscence, and wound infection outcomes also could not be evaluated through meta-analysis, because the studies only presented standard error data and percentages.

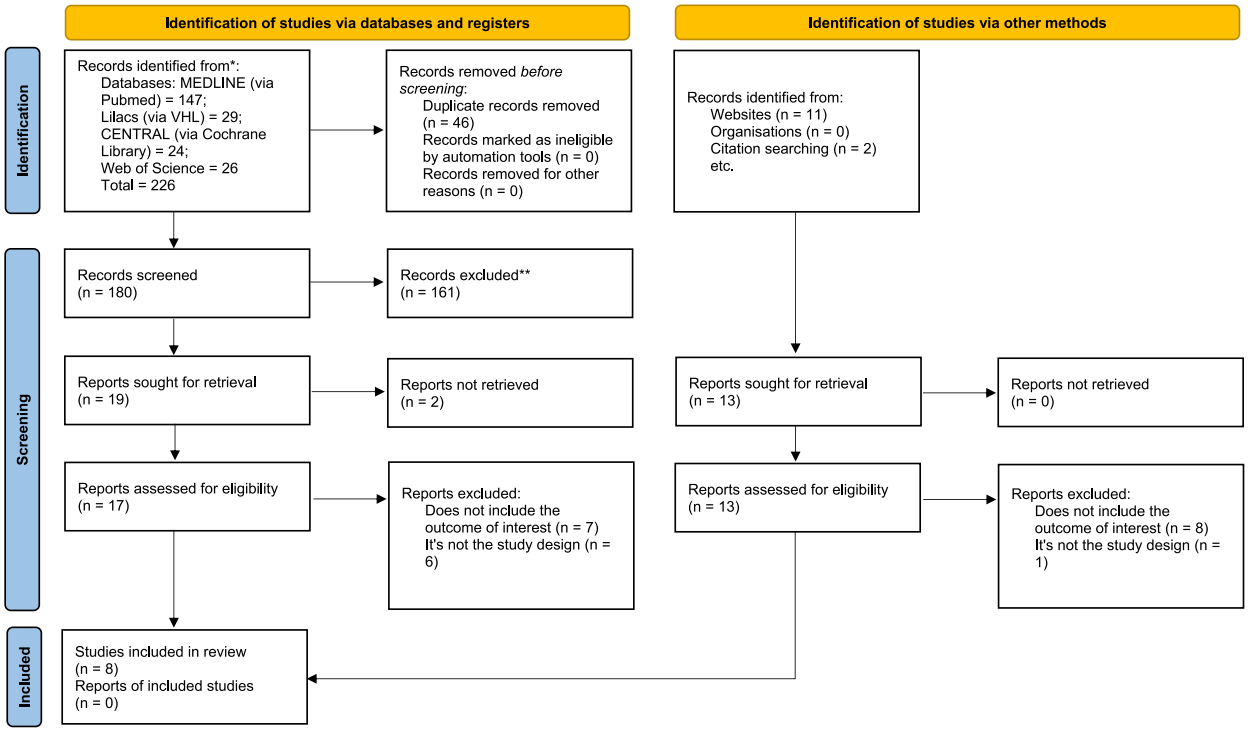

Fig. 1. Flowchart of study selection.

3.2. Synthesis of results – results of outcome variables

1 -Pain

3.3. Descriptive results

For the pain outcome, divergent results were found among the studies that could not be included in the meta-analysis, totaling 86 patients. Two of them showed better results for pain in the cyanoacrylate group at all postoperative times [6,12], while another showed no differences in this outcome between the groups [7].

3.3.1. Risk of bias

A high risk of bias was observed only for the evaluation of the pain outcome, during the measurement of the outcome [19,20], and deviations from intended interventions [1]. Overall, all studies showed some concerns in the selection of the reported result (Fig. 2A).

3.3.2. Meta-analysis

A total of 170 patients were evaluated in this meta-analysis. The overall analysis for the pain outcome showed better results for the cyanoacrylate group than conventional sutures (SMD: −0.45, 95%CI -0.75 to −0.15, $I^2 = 82$ %). In the sensitivity analysis by subgroups, only in the first postoperative day (24 h after the surgery), the use of cyanoacrylate promoted better results when compared to the use of conventional sutures (SMD: −1.01, 95%CI -1.90 to −0.12, $I^2 = 88$ %) with very low certainty of evidence (Fig. 3 and Supplementary file 2).

2 -Edema

3.4. Descriptive results

A total of 210 patients were evaluated. Three studies showed that there was no difference between the groups in the evaluated periods [1,12,20]. One study found significant differences in the reduction of edema in the group that used cyanoacrylate in the first postoperative day (24 h after the surgery) [6].

3.4.1. Risk of bias

In the evaluation of the edema outcome, two studies [1,6] showed some concerns in the randomization process and one study [6] in deviations from intended interventions. Overall, all studies showed some concerns in the selection of the reported result (Fig. 2B).

Table 1
Main methodological characteristics of the included randomized controlled trials.

Author, year	Country (n)	Study Design	Sample size Intervention/ control (n/n)	Events Intervention/ control (n)	Inclusion Criteria		Exclusion Criteria	Conclusion
					Patients	3 M		
Ghoreishian et al., 2009 [7]	Iran (16)	Clinical trial (split mouth)	16/16	32	All patients needed ostectomy and odontotomy bilaterally, had good general health (ASA I) and good oral hygiene, were nonsmokers, and were cooperative with the study and with postoperative follow-up. They had no contraindication to the drugs or anesthetic in the surgical protocol.	Similar bone impaction and inclination of mandibular third molars on the right and left sides. All patients needed ostectomy and odontotomy bilaterally.	NR	The efficacies of cyanoacrylate adhesive and suturing in wound closure were similar. However, the use of cyanoacrylate adhesive had some advantages such as simplicity, higher speed, and better hemostasis.
Joshi et al., 2011 [19]	India (30)	Clinical trial (split mouth)	30/30	60	No systemic diseases; non-smokers, not allergic to the drugs or anesthetic agents used in the surgical protocol.	Mesio-angularly or horizontally impacted mandibular third molar (Position B Class II, PELL & GREOGERY classification 1933, with difficulty index-5).	NR	Cyanoacrylate is a better alternative for intraoral minor surgical procedures as tissue glue, was found to be hemostatic in nature, was helpful in reducing pain and patients didn1t need to visit again for suture removal. This procedure was comfortable even for the surgeon.
Oladega et al., 2018 [1]	Nigeria (120)	RCT	60/60	120	18 years old and above with mesio-angularly impacted mandibular third molar; non-smokers; without known systemic diseases such as Bleeding dyscrasia and immunosuppression (like Diabetes mellitus and AIDS); not allergic to the drugs or anesthetic agents in the surgical protocol; good oral hygiene.	Mesio-angularly impacted mandibular third molar.	NR	Cyanoacrylate tissue adhesive compares favorably with silk suture as a wound closure material and may therefore be a suitable alternative to silk suture for wound closure following extraction of an impacted lower third molar. Cyanoacrylate may have some beneficial hemostatic effects with significant effect on postoperative bleeding.
Setiya et al., 2014 [6]	India (50)	Clinical trial (split mouth)	50/50	100	Age between 18–35 years old, without any systemic disorders, non-smokers, not allergic to the drugs or anesthetic agents used in the surgical protocol.	Bilaterally symmetrical impacted mandibular third molars (classified as per George Winter's classification).	NR	Sutureless closure of wounds after surgical removal of impacted mandibular third molars using cyanoacrylate glue to be more beneficial when compared to the conventional suturing technique. The use of cyanoacrylate adhesive had certain advantages over conventional suturing technique as follows: it was hemostatic, reduced pain and edema, avoids a second visit for suture removal, and was an expeditious procedure.
Rewainy et al., 2015 [12]	Egypt (20)	RCT	10/10	20	Age between 18–30 years old.	Impacted mesioangular mandibular third molar (Class II position B, according to Pell and Gregory's classification).	Any systemic diseases, signs of pericoronitis or active infection, smoking, addiction, and mouth breathing,	The use of the N-butyl cyanoacrylate (PeriAcryl 90) for the closure of mucoperiosteal flaps is a reliable method that can overcome most of complications faced on using conventional silk

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Table 1 (*continued*)

Author, year	Country (n)	Study Design	Sample size Intervention/ control (n/n)	Events Intervention/ control (n)	Inclusion Criteria		Exclusion Criteria	Conclusion
					Patients	3 M		
							pregnant or lactating woman	sutures in addition to easy manipulation, time-saving, and safety factors.
Al-Moraissi, 2011 [20]	Yemen (20)	RCT	10/10	20	Age between 18–24 years old.	Patients with impacted lower third molars	NR	The efficacy of cyanoacrylate tissue adhesive and suture material in wound closure after mandibular third molar surgery was similar concerning the severity of postoperative trismus and facial edema, However, the efficacy of tissue adhesive in reducing pain and bleeding is superior to black silk suture material in wound closure after lower third molar surgery.
Jafaou and Brad, 2018 [21]	Syria (25)	RCT (split mouth)	25/25	50	Age between 17–30, not suffering from any general diseases, non-smokers, non- alcoholics, women not pregnant.	The presence of an impacted lower third molar medially depth.	NR	The use of a tissue adhesive as an alternative to sutures after surgical extraction of impacted lower third molars does not provide an additional benefit in reducing the complications following surgical extraction, such as wound dehiscence and wound infection.
Heshmah and Choker, 2021 [22]	Syria (19)	RCT (split mouth)	19/19	38	Age between 19–30, not suffering from any general diseases, non-smokers, non- alcoholics, women not pregnant.	Patients with bilateral and symmetrical impacted lower third molars	Any pre-existing pathology or systemic diseases.	The (iceberg-glue) tissue adhesive effectively minimizes post-surgical bleeding after surgical removal of lower third molars.

3 M: third molar; RCT: Randomized controlled clinical.

Table 2
Participant's characteristics.

Author, year	Age				Gender			
	EG		CG		EG		CG	
	Mean ± SD (years)	Age range (years)	Mean ± SD (years)	Age range (years)	Male (n)	Female (n)	Male (n)	Female (n)
Ghoreishian et al., 2009 [7]	NR	18–24	NR	18–24	7	9	7	9
Joshi et al., 2011 [19]	NR	20–32	NR	20–32	11	19	11	19
Oladega et al., 2018 [1]	27.2 (6.9)	NR	27.2 (6.9)	NR	NR	NR	NR	NR
Setiya et al., 2014 [6]	NR	NR	NR	NR	NR	NR	NR	NR
Rewainy et al., 2015 [12]	24	18–30	24	18–30	6	4	6	4
Al-Moraissi, 2011 [20]	21.3 (1.2)	18–24	22.2 (1.5)	18–24	6	4	5	5
Jafaou and Brad 2018 [21]	NR	17–29	NR	17–29	8	17	8	17
Heshmah and Choker, 2021 [22]	NR	NR	NR	NR	NR	NR	NR	NR

EG: experimental group; CG: control group; SD: standard deviation; NR: Not reported.

3.4.2. Meta-analysis

A total of 210 patients were evaluated in this meta-analysis. The overall analysis for the edema outcome showed better results for the cyanoacrylate group than conventional sutures (SMD: −0.21, 95%CI -0.33 to −0.09, $I^2 = 0$ %). In the sensitivity analysis by subgroups, the use of cyanoacrylate promoted better results when compared to the use of conventional suture in the 7th postoperative day (SMD: −0.24, 95%CI -0.46 to −0.01, $I^2 = 0$ %), with moderate certainty of evidence (Fig. 4 and Supplementary file 2) (Fig. 4 and Supplementary file 2).

3 -Trismus

3.5. Descriptive results

A total of 160 patients were evaluated. Two studies did not find significant differences between the two groups evaluated in all postoperative periods [1,20]. One study found better results for cyanoacrylate after the first, third and 7th postoperative days [12].

3.5.1. Risk of bias

In the evaluation of the trismus outcome, one study showed some concerns in the randomization process [20]. Overall, all studies showed some concerns in the selection of the reported result (Fig. 2C).

3.5.2. Meta-analysis

A total of 160 patients were evaluated in this meta-analysis. For the trismus outcome, in all periods evaluated (one day, two days, and seven days after surgery) no differences were found between the groups (Fig. 5), with very low certainty of evidence (Supplementary file 2).

4 -Bleeding

3.6. Descriptive results

A total of 275 patients were evaluated for this outcome. Regarding the bleeding outcome, three studies were favorable to the use of cyanoacrylate only in the first 24 h, with no difference between the groups in the other periods evaluated [1,6,22]. Two studies showed better results in the group that used cyanoacrylate up to two days (48 h) after surgery [7,19]. Two others showed better results for the use of cyanoacrylate up to three days (72 h) after surgery [12,20].

3.6.1. Risk of bias

Three studies showed some concerns in the randomization process [6,7,19]. Overall, all studies showed some concerns in the selection of the reported result (Fig. 2D).

3.7. Wound dehiscence and infection

3.7.1. Descriptive results

A total of 360 (165 wound dehiscence and 195 wound infection) patients were evaluated for this outcome. All three studies that assessed the wound dehiscence and infection outcome found no difference between the cyanoacrylate and suture groups at all postoperative periods [1,12,21]. When evaluating wound infection, all studies also concluded that there was no difference between the groups in all periods evaluated [1,6,21].

Table 3
Outcomes' characteristics.

Author, year	Outcomes						Trade mark	Suture type	Pre-medication	Post-medication and recomendations
	Pain (tool)	Edema (tool)	Trismus (tool)	Dehiscence (tool)	Bleeding (tool)	Wound Infection (tool)				
Ghoreishian et al., 2009 [7]	VAS 0–5	NA	NA	NA	VAS 0-4	NA	Ethyl-cyanoacrylate (epiglu; Meyer-Haake, Wehrheim, Germany).	3-0 silk	Rinsed with 0.12 % chlorhexidine for 1 min.	Amoxicillin 500 mg, 8/8 h/5 d, acetaminophen 325 mg, 6/6 h/3 d; mouthwash with chlorhexidine (0.12 %) twice daily.
Joshi et al., 2011 [19]	VAS 0-3	NA	NA	NA	VAS 0-3	NA	Amcrylate (Iso Amyl 2-Cynoacrylate, Manufactured by Concord Drugs 3 Ltd, dispensed in ampoules of 0.25, 0.50 and 1 ml).	3-0 silk	Rinsed with 5 % betadine solution.	Amoxicillin 500 mg BD/5 d, diclofenac Sodium 50 mg/3 d; mouthwash chlorhexidine (0.12 %) twice daily.
Oladega et al., 2018 [1]	VAS 0-100	Measurement (in millimeters) of Tragus to Pogonion (ear to chin), Tragus to Oral Commissure (outer corner of the mouth), Outer Canthus to Gonion (angle of the mandible), using a tape measure.	The maximum distance between mesial incisal edges of maxillary and mandibular central incisors in the midline. Measurement (in millimeters) with a vernier-calibrated sliding caliper.	Visual inspection and by gentle probing with a Williams probe.	VAS 0-4	Presence of purulent discharge from the surgical site or there are other signs of infection, such as fever, lymphadenopathy, or persistent swelling and pain that cannot be explained by surgical trauma.	Cyanoacrylate glue [Amcrylate (Iso Amyl 2-Cyanoacrylate) – by Concord Drugs Ltd., Hayathnagar, India, dispensed in ampoules of 0.25 ml].	3-0 silk	Rinsed with 0.12 % chlorhexidine solution for 1 min.	Amoxicillin 500 mg 8/8 h, 5 d, metronidazole 200 mg, diclofenac Sodium 50 mg 12/12 h/3 d, dexamethasone 8 mg stat, then 4 mg 6/6 h in 2 doses.
Setiya et al., 2014 [6]	VAS 0-5	Measurement of the distances between the lateral corner of the eye to gonion, tragus to the outer corner of the mouth, and tragus to pogonion.	NA	NA	VAS 0-4	Score Observation: 1 Nonhealed 2 Gaping 3 Healed adequately 4 Satisfactory	Cyanoacrylate glue [Amcrylate (Iso Amyl 2-Cyanoacrylate) – Concord Drugs Ltd., Hayathnagar, AP, India].	3–0 silk	NR	Amoxicillin 500 mg TID/5d, diclofenac Sodium 50 mg + Paracetamol 400 mg TID/3d; mouthwash (0.12 % chlorhexidine) twice daily.
Rewainy et al., 2015 [12]	VAS 0-4	Measurement of the distance from the attachment of the ear lobe to the soft tissue pogonion, the distance from the ear lobe, to the corner of the mouth, then the	NA	NA	VAS 0-3	NA	PeriAcryl 90 (N-butyl cyanoacrylate and 2-octyl cyanoacrylate).	3–0 silk	Rinsed with 15 ml of 0.12 % chlorhexidine gluconate. Amoxil 500 mg every 8 h started the day before.	Amoxicillin 500 mg, antibiotic every 8/8 h started the day before surgery and lasting for 4d after, diclofenac potassium 50 mg when needed. Ice packs at the operated side extra-

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Table 3 (*continued*)

Author, year	Outcomes						Trade mark	Suture type	Pre-medication	Post-medication and recomendations
	Pain (tool)	Edema (tool)	Trismus (tool)	Dehiscence (tool)	Bleeding (tool)	Wound Infection (tool)				
		distance from the outer canthus of the eye to the angle of the mandible (Gabka and Matsumra's method).								orally, mouthwash with Chlorhexidine (0.12 %) twice daily for 1 week.
Al-Moraissi, 2011 [20]	VAS	3 linear measurements: Tragus-lip line, Gonion-lip line and the Outer canthus of the eye-Gonion line, on the 2nd,5th and 7th postoperative day.	Maximal Interincisal Opening mm/±deviation on the2nd, 5th and 7th postoperative days.	NA	VAS	NA	NR	3–0 silk	NR	NR
Jafaou and Brad 2018 [21]	NR	NR	NR	NR	NR	NR	Glubran 2	3–0 silk	NR	Clamoxyl 1g twice daily for five days, as well as k-flam after eating when needed.
Heshmah and Choker, 2021 [22]	NR	NR	NR	NR	VAS 0-4	NR	Iceberg-Glue	3–0 silk	NR	Clamoxyl 1g twice daily for five days, as well as k-flam after eating when needed.

VAS: Visual analog scale; NR: Not reported; NA: Not applicable; BD: bi-dose; D: days; H: hours.

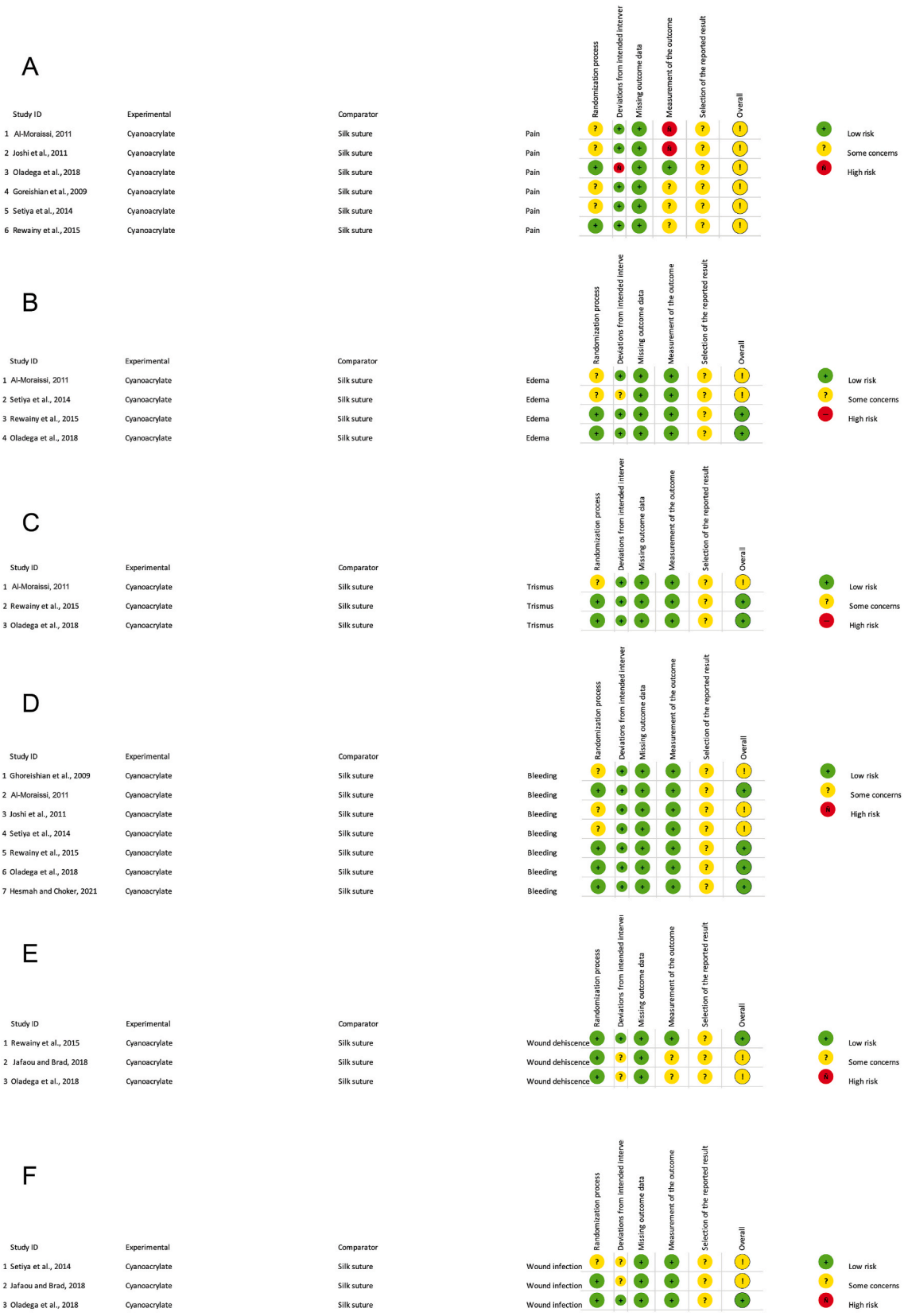

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Fig. 2. Assessment of the risk of bias in the included studies for (A) pain, (B) edema, (C) trismus, (D) bleeding, (E) wound dehiscence and (F) wound infection.

3.7.2. Risk of bias

For wound dehiscence, two studies showed some concerns in deviations from intended interventions [1,21] and measurement of the outcome [1,21]. For wound infection, one study [6] showed some concerns in the randomization process and two studies [6,21] in deviations from intended interventions. Overall, all studies showed some concerns in the selection of the reported result (Fig. 2E–F).

The funnel plots to verify publication bias were not constructed because none of the analysis included more than 10 studies.

4. Discussion

The results presented in this study shows that cyanoacrylate when compared to conventional sutures in lower 3Ms surgeries, can present better results in terms of pain and edema, but with no high-quality evidence.

The group treated with cyanoacrylate showed a significant reduction in pain compared to the control group, 24 h after the surgical procedure. In the remaining postoperative periods, there was no difference between the groups. This may have occurred due to the reduced tissue handling with the use of cyanoacrylate and the wound sealing created by it, which leads to the maintenance of the clot plug inside the alveolus and reduces the exposure of nerve endings [1,23]. Also, after 72 h the signs of inflammation and pain are expected to decrease, which may explain the absence of differences between the groups in the other postoperative periods [24,25].

The mechanisms involved with the use of cyanoacrylate are related to the reaction that occurs between cyanoacetate and formaldehyde and to the formation of a liquid monomer. This monomer penetrates uneven surfaces, and it chemically changes to a polymer in contact with moisture, through an exothermic hydroxylation reaction to form a strong bridge that keeps the wound edges in contact

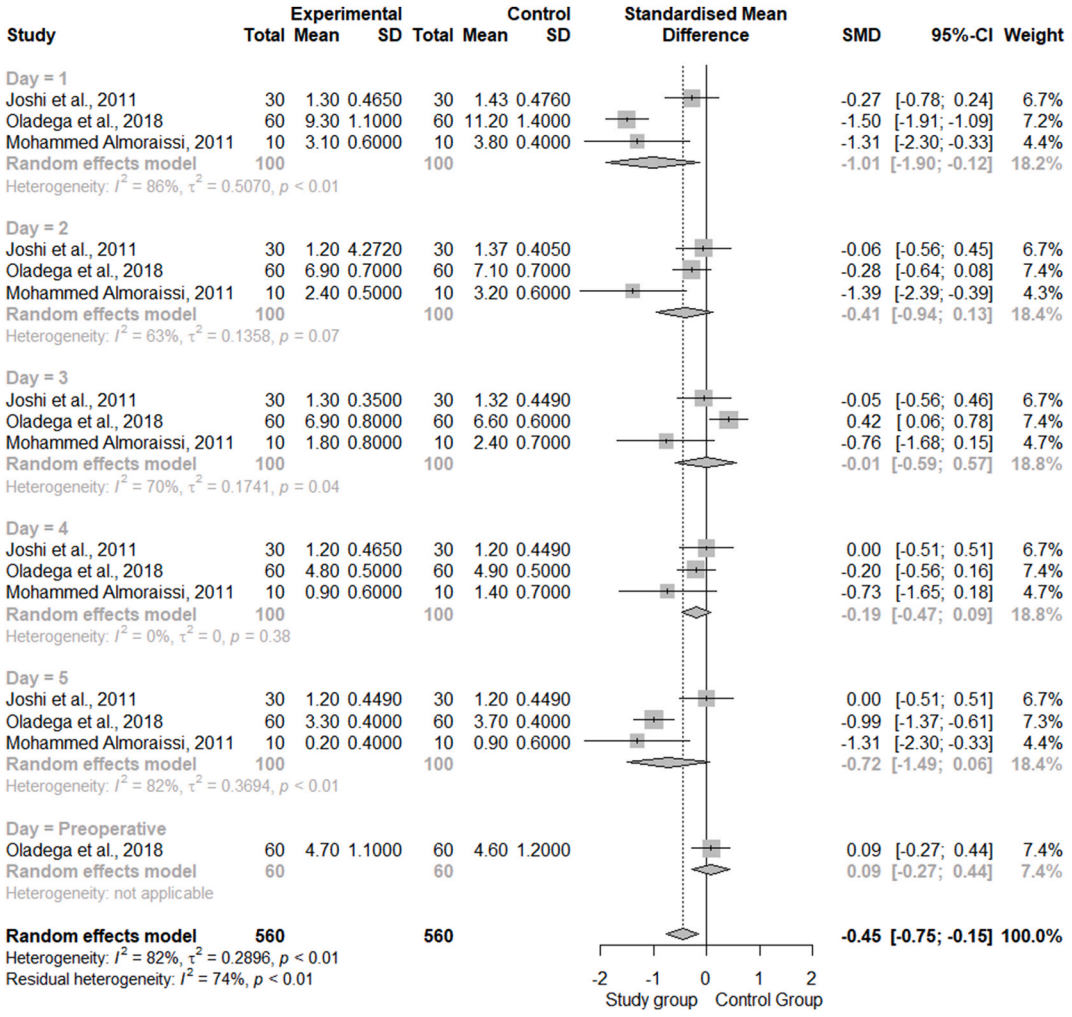

Fig. 3. Forest plots of pain outcome.

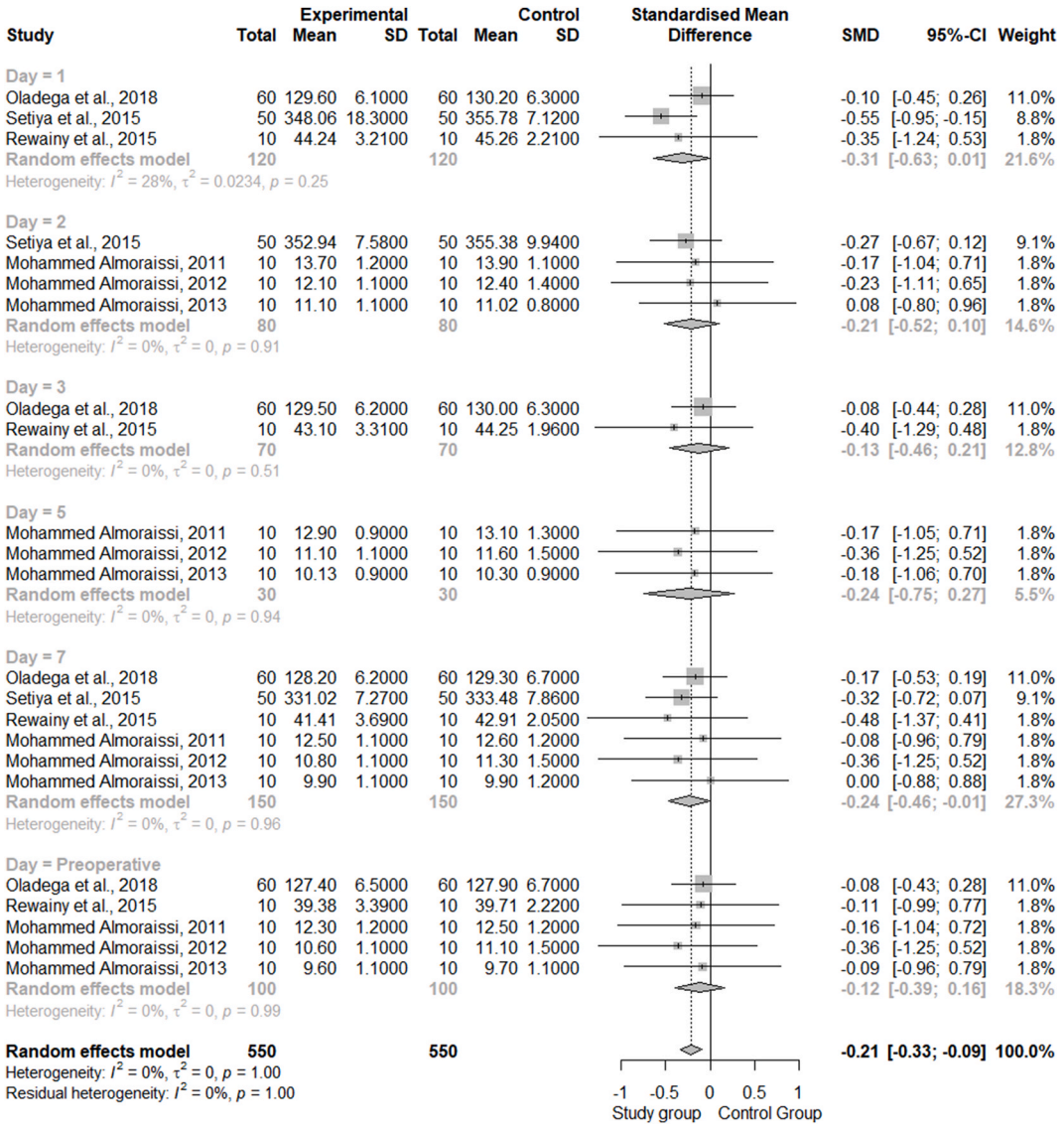

Fig. 4. Forest plots of edema outcome.

[11,26]. The presence of saliva in the intraoral mucosa serves as good moisture for the process involved in the use of cyanoacrylate [11]. The studies included in this review do not address the adverse effects of cyanoacrylate usage. Furthermore, the literature demonstrates that the use of cyanoacrylate does not elicit anti-inflammatory adverse reactions that would contraindicate its use [27].

There was a small significant reduction in the edema assessed in the 7th postoperative day after surgery among patients treated with cyanoacrylate. No differences were found between the groups in the other periods. As in the pain process, is expected edema decreases in the third day (72 h) after the surgical procedure [25]. Edema is among the most common postoperative complications, caused mainly by surgical manipulation. The greater the extension of the surgery and the duration of the surgical procedure, the greater the edema [28]. Its evolution is gradual, with a peak of edema within two days (48 h) after surgery [29]. Cyanoacrylate can contribute to the reduction of edema due to its easy application and reduction of the handling time of the operated site [6].

Our results indicate that trismus was not influenced by the use of interventions at any of the evaluated moments. However, a study that compared the use of conventional sutures with fibrin glue found that postoperative mouth opening was better in the group that used fibrin glue after 24 h [23]. As with the use of fibrin glue, cyanoacrylate is expected to eliminate suture-related harmful effects, such as tissue damage and prolonged surgery time, which are proportionally related to the degree of trismus [23]. Trismus plays an important role in a patient's daily quality of life, since the greater the limitation of mouth opening, there is the possibility to decrease the ability to chew and speak [30]. Primary studies evaluating the trismus outcome are necessary since only three studies accessed this outcome [1,12,20].

It was not possible to evaluate the bleeding, dehiscence, and wound infection outcomes through a meta-analysis, as the studies

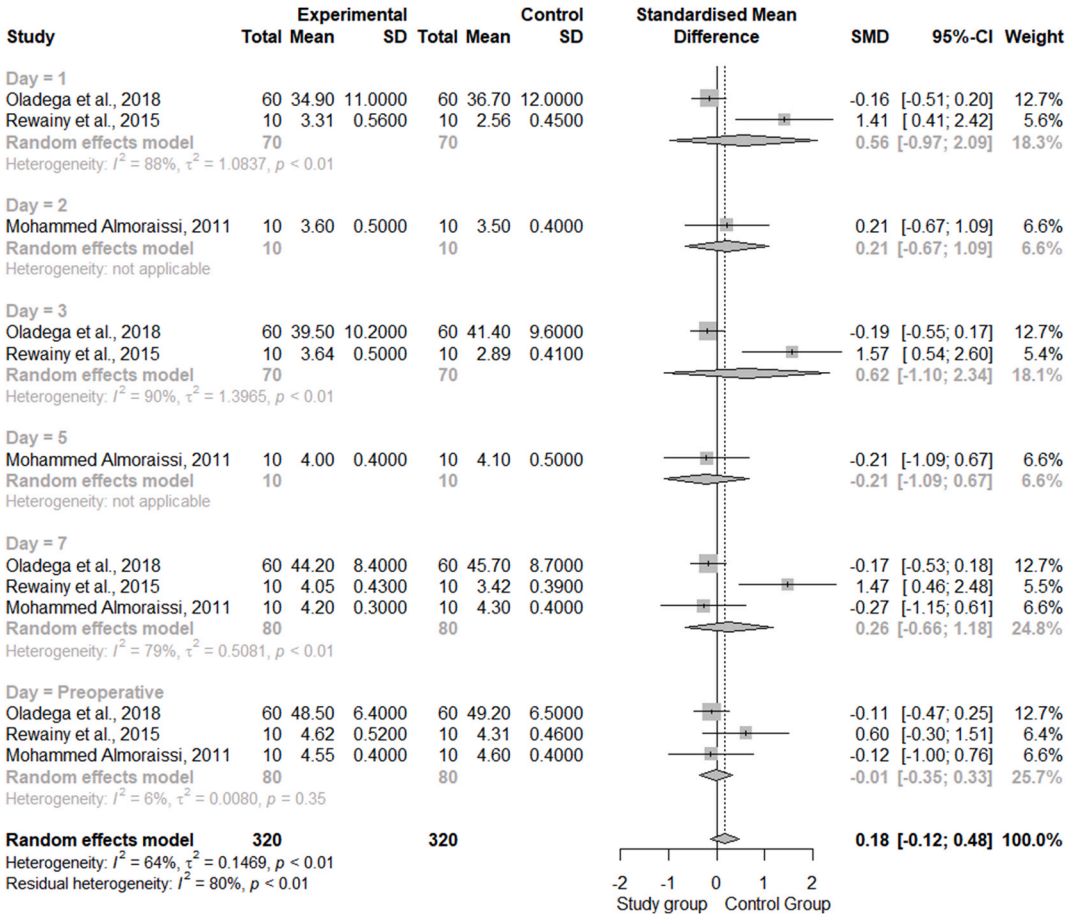

Fig. 5. Forest plots of trismus outcome.

found only presented standard error and percentage data. When evaluating postoperative bleeding, the results of an isolated study showed that the group that used cyanoacrylate presented less bleeding after 24 and 48 h, possibly due to the hemostatic effect of the material in the oral cavity [31]. A considerable hypothesis for the reduction of bleeding is that the ester forms a macrofilm causing a mechanical blockage, which also acts as a surface agent to activate the coagulation cascade [32]. Similarly, the occurrence of dehiscence was not different between the interventions [1,12,21]. However, there must be standardization in the form of measurement of this outcome so that comparisons between future studies are possible. Although not a result supported by meta-analysis, the authors of these studies argue that the use of tissue adhesive is simpler and involves less tissue manipulation related to suture, providing a reduction in wound closure time. This will reduce the operative time and possibly the expected reduction in the rate of postoperative complications [28].

In addition to dehiscence, the assessment of wound infection is another important complication to be evaluated [33]. As cyanoacrylate has a bacteriostatic effect, it is believed to have a favorable effect in reducing wound infection [34]. However, we have not been able to find evidence to support this hypothesis in clinical practice. A systematic review that evaluated the use of tissue adhesives to close skin wounds found more dehiscence in the cyanoacrylate group [35]. Studies assessing the oral cavity were not included. New studies that present the data similarly, so they can be grouped in a meta-analysis, are needed.

Although a favorable result for the use of cyanoacrylate was found, some limitations of this study must be acknowledged. As it is a systematic review, the main limitation is related to the reduced availability of studies on the subject and the lack of standardization of techniques for the assessment of bleeding, dehiscence, and wound infection outcomes. Furthermore, not all included studies were randomized, which may lead to some degree of bias in our findings. In assessing the pain outcome, a high risk of bias was observed during the measurement of the outcome deviations from intended interventions. This fact can be justified since pain is a subjective outcome and patients were responsible for filling out the Visual Analogic Scale (VAS). Furthermore, the use of the conventional suture can be verified by the patient's touch, allowing the intervention to be identified by the participants, unlike the evaluation of other outcomes that were measured by the researcher. Also, the GRADE analysis of certainty of the evidence was very low and moderate for the outcomes evaluated. Although Google Translate was an aid tool for reading and interpreting the studies and it must be recognized as a limitation, at least one of the authors spoke the language of the included studies (SGMF/English and EAAM/Arabic).

On the other hand, some care was taken to increase confidence in our results: three reviewers conducted the screening and data

extraction of the included articles; all recommended steps for the elaboration of a systematic review were followed, whose protocol was previously registered. Finally, all studies included only mandibular 3Ms, which makes the included sample more homogeneous.

For future studies, RCTs with larger samples are needed. In addition, the standardization of data presentation for the assessment of bleeding, dehiscence, and wound infection outcomes is necessary so that the data can be compiled in a meta-analysis.

5. Conclusion

Considering the reported limitations, the use of cyanoacrylate was better for pain reducing in the first postoperative day and edema reducing in the 7th postoperative day after 3Ms surgeries when compared to the use of conventional silk suture. The easy application, bacteriostatic and hemostatic effect of cyanoacrylate should be considered when using this technique as an ally in clinical practice.

Data availability statement

The study data has not been deposited in a publicly accessible repository and will be made available on request.

CRediT authorship contribution statement

Moisés Willian Aparecido Gonçalves: Data curation, Methodology, Writing - original draft. **Marina Rocha Fonseca Souza:** Data curation, Methodology, Writing - original draft. **Marco Túllio Becheleni:** Methodology, Data curation. **Endi Lanza Galvão:** Supervision, Formal analysis, Writing - review & editing. **Essam Ahmed Al-Moraissi:** Conceptualization, Formal analysis, Writing - review & editing. **Saulo Gabriel Moreira Falci:** Writing - review & editing, Supervision, Project administration, Methodology, Investigation, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e23058.

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