

Comparing the Treatment Outcomes of Absorbable Sutures, Nonabsorbable Sutures, and Tissue Adhesives in Cleft Lip Repair: A Systematic Review

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Abstract

Objectives: To examine the literature and synthesize the available reports for the best possible option between absorbable, nonabsorbable, and tissue adhesives in cleft lip skin closure.

Design: We conducted systematic searches for randomized controlled trials and controlled clinical trials in PubMed, Cochrane, Ovid Medline, and OpenGrey databases. Identified studies were retrieved and assessed for eligibility. All statistical analyses were done with Revman, version 5.4.

Interventions: The intervention considered in this systematic review were techniques of cleft lip repair using resorbable sutures, nonabsorbable sutures, medical adhesives, or any combination of these.

Outcome Measures: The primary outcomes assessed in the trials had to include any combination of the following: wound healing cosmesis and wound healing complications. While secondary outcomes considered were quality of life, direct and indirect costs to patients and health services, and participant satisfaction.

Results: Only 6 studies met all inclusion criteria and were selected for qualitative analysis. A more favorable wound healing cosmesis was seen when nonabsorbable suture was used in cleft lip repair compared to absorbable sutures and tissue adhesives (CI, 0.65-4.35). This advantage was overshadowed by the significantly higher prevalence of postoperative complications when nonabsorbable sutures are used.

Conclusion: Although the results point to more favorable cosmesis with nonabsorbable sutures and an overall more favorable outcome with either absorbable sutures or tissue adhesives, the 6 selected studies were assessed at an unclear risk of bias; therefore, the results of this study should be interpreted with caution and regarded as low-certainty evidence.

Keywords

absorbable suture, nonabsorbable suture, tissue adhesives, cleft lip repair, systematic review

Introduction

Orofacial clefts (OFC) encompass a range of congenital abnormalities of the orofacial region, which commonly presents as cleft lip with or without palate (CLP) or isolated cleft palate (CP). Orofacial cleft is recognized as the most common craniofacial diagnoses in humans, with a worldwide prevalence of 1.2 per 1000 live births (Oginni & Adenekan, 2012) but can be up to 1 per 700 live births (Shkoukani et al., 2013).

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Cleft lip repair is complicated by the distortion of multiple anatomical structures, including the skin and muscle attachments of the upper lip, columella, nasal floor, and alar, which can occur with varying severity. The goal of CLP repair is to address the functional and cosmetic deformity of CLP (De La Pedraja et al., 2000). In order to achieve such goals, the repair should include the creation of an intact and appropriately sized upper lip to compensate for the loss of philtral height on the cleft side, repair of the underlying muscular structure for normal oral competence and function, and primary repair of nasal deformity in complete cleft cases (De La Pedraja et al., 2000). Another major aspect in the management of CLP is the follow-up period as esthetic results from definitive surgical repair are only evident after some time has passed (Shkoukani et al., 2013). Therefore, it may be necessary for the patient to return to the operating room for revisions to improve function and appearance of the repair (Pham & Senders, 2006). Facial cosmetic results are one of the most concerning issues for the parents of patients with cleft lip. Moreover, the postoperative care of the surgical site, the discomfort associated with the suture removal, and additional visit for suture removal are other reasons that encourages one to use any new treatment method that may replace the need for suture placement and removal (Shkoukani et al., 2013).

These concerns have led to recent changes in practices characterized by some surgeons advocating the use of absorbable sutures in place of the traditionally used nonabsorbable sutures, eliminating the need for suture removal postoperatively, which often necessitates sedation or general anesthesia (Choudhary & Cadier, 2000; Kudur et al., 2009). Studies have also proposed the use of tissue adhesives as an adjunct technique for skin closure as opposed to sutural cleft lip repair (Knott et al., 2007; Collin et al., 2009). These studies showed that adhesives, such as Dermabond (J & J Healthcare Systems), offer equivalent mature wound cosmesis similar to traditional suture closure in the repair of cleft lip and have the added benefit of avoiding additional dressing changes or suture removal under sedation (Knott et al., 2007; Collin et al., 2009).

Results of the above studies (Choudhary & Cadier, 2000; Knott et al., 2007; Collin et al., 2009; Kudur et al., 2009) emphasize the need to determine which of these treatment options provide the best treatment outcome in terms of wound healing cosmesis, postoperative complications, and postoperative surgical care. Despite several studies (Choudhary & Cadier, 2000; Knott et al., 2007; Collin et al., 2009; Kudur et al., 2009) elucidating the need to understand these comparative outcomes, to our knowledge, there has been no systematic review of the available evidence to provide an evidence-based decision on the best option for cleft lip repair based on the above parameters. Such evidence will inform clinical decisions regarding the choice of material for cleft lip repair as this will lead to a more favorable treatment outcome. Therefore, the aim of this systematic review was to examine the literature and synthesize the available reports for the best possible option between absorbable, nonabsorbable, and tissue adhesives in

cleft lip skin closure. Outcomes evaluated included cosmesis, complications, and ease of surgical care.

Methodology

This systematic review and meta-analysis were conducted and presented according to the methods of the Cochrane guideline for systematic reviews (Akl, 2019) and according to the protocol registered in the PROSPERO 2018 database: CRD42020202893.

Eligibility Criteria

Types of studies. Only randomized controlled trials (RCTs) and controlled clinical trials (CCTs) as described by the authors in the manuscript methodology comparing either resorbable sutures to nonabsorbable sutures or comparing medical adhesives to any type of sutures were included in this systematic review.

Types of participants. Participants were individuals of all ages, but majorly included children less than 1 year of age with confirmed diagnoses of CLP.

Types of interventions. The intervention was any technique of cleft lip repair using resorbable sutures, nonabsorbable sutures, medical adhesives, or any combination of these. We also included secondary cleft lip repair and revisit cleft lip repair cases.

Types of outcome measures. The outcomes assessed in the trials had to include any combination of the following:

Primary outcomes:

- Wound healing cosmesis
- Wound healing complications

Secondary outcomes:

- Quality of life
- Direct and indirect costs to patients and health services
- Participant satisfaction

Search Strategy and Selection of Studies

We conducted systematic searches for RCTs and CCTs in PubMed (NLM), Cochrane, Ovid Medline, and OpenGrey databases. The US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) and the World Health Organization (WHO) International Clinical Trials Registry Platform (WHO clinical trials registry) were also searched for ongoing and past studies. Additional searches were done; the reference sections of eligible studies were hand-searched for other relevant studies and purposeful Google Scholar searches for relevant additional studies were done. Only articles written in English or with English language translations were considered for the review. There were no publication conditions. All databases were searched to June 2020.

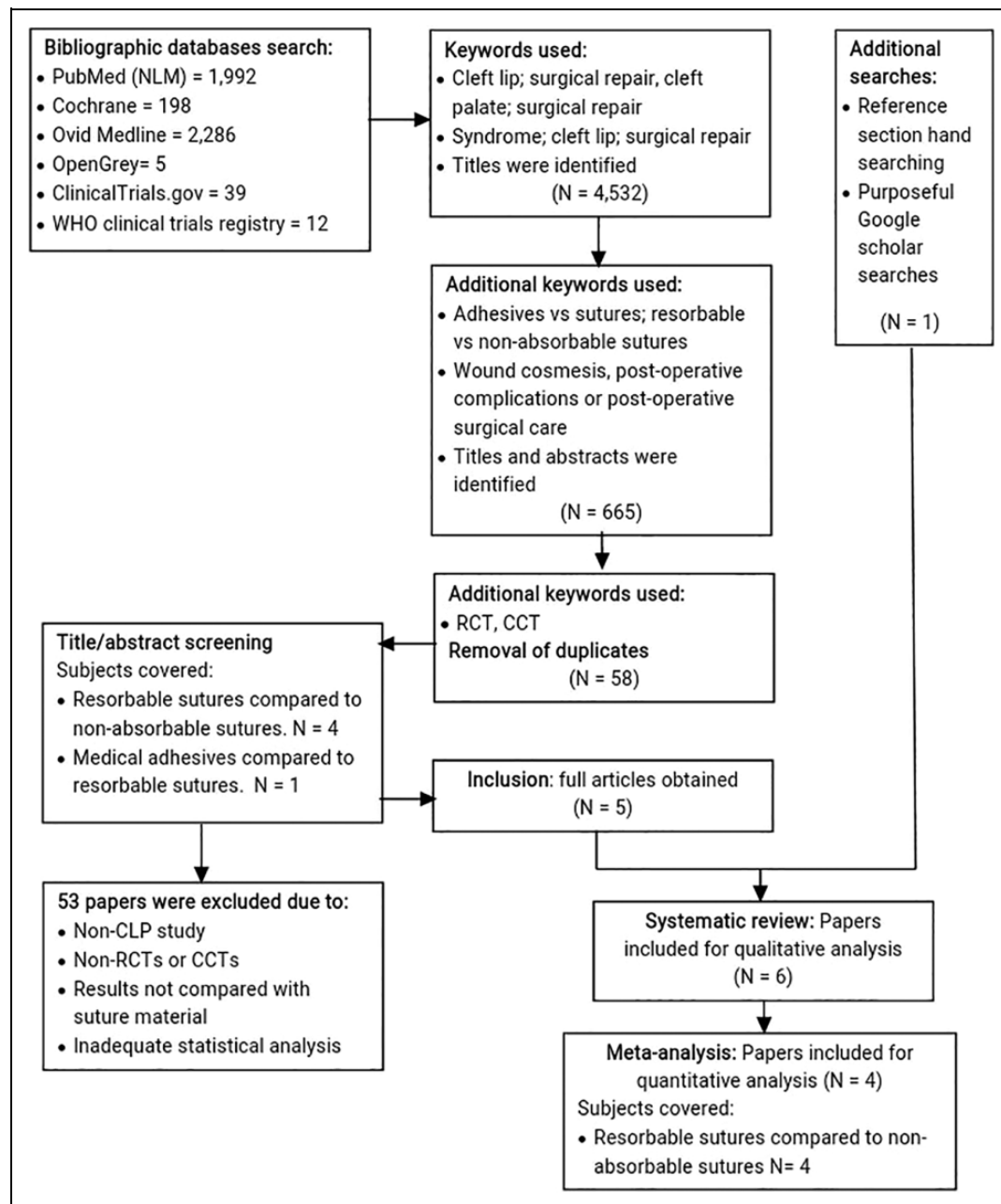


Figure 1. Flowchart of the study search strategy and selection process.

The first 2 authors (U.P.E. and O.A.) independently screened the titles and abstracts (when available) of all reports identified through the electronic searches. The search was designed to be sensitive and included RCTs and CCTs. Noncontrol clinical trials, retrospective cohorts, and cross-sectional studies were filtered out in the selection process. As studies involving CLP are often included with those of Mendelian syndromes such as van der Woude syndrome, we undertook a broad search to include all possible studies. For studies appearing to meet the inclusion criteria, or for which there were insufficient data in the title and abstract to make a clear decision, we obtained the full report. The full reports were independently assessed by

the first 2 authors (U.P.E. and O.A.) to establish whether or not the studies met the inclusion criteria. Disagreements were resolved by a third review author (A.A.A.). The search strategies and search terms used, as well as the exclusion criteria for selection of studies are illustrated in Figure 1.

Data Extraction and Management

Two review authors (U.P.E. and A.A.A.) independently extracted data from the included studies without disagreement. The data extraction forms were piloted on several papers and modified as required before use.

For each study, we recorded the following data (where available):

- Authors name, year of publication, year of first participant recruitment, country of origin, study design, and source of funding
- Sociodemographic characteristics of participants, criteria for inclusion and exclusion, characteristics of CLP (unilateral, bilateral; partial, complete; palatal involvement; syndromic, nonsyndromic), duration of review, evaluation of wound cosmesis, presence of postoperative complications, and ease of postoperative surgical care
- Details of treatment duration, dosage, cost, and follow-up
- Details of the outcomes evaluated, including assessment measures and time intervals

Assessment of Risk of Bias in Included Studies

We independently assessed the risk of bias in included studies using a design-specific risk of bias tool modified from the adapted risk of bias criteria for individual studies in systematic reviews of health care intervention by Viswanathan et al. (2008). We proposed 7 criteria for the assessment: (1) sequence generation (selection bias), (2) allocation method (selection bias), (3) performance bias, (4) attrition bias, (5) detection bias, (6) reporting bias, and (7) other bias.

Statistical Analysis

Measures of treatment effect. The primary outcome most frequently and reliably reported was post-op cosmesis, measured via the Visual Analog Scale (VAS). Visual Analog Scale was first described in 1921 and referred to at the time as a “graphic rating method” (Okitsu et al., 2014). They are psychometric response scales used to measure subjective characteristics or attitudes and have been used in the past for a multitude of disorders, as well as in market research and social science investigations, among others. (*A Comparison of Multi-Item Likert and Visual Analogue Scales for the Assessment of Transactionally Defined Coping Function*, n.d.; Funke, 2004.) In this case, it tells us the characteristics of the physical appearance of the postsurgical lip repair based on the assessment of parents or the managing physicians. Also, in some studies, the Hollander Wound Evaluation Scale was used by the managing physician to evaluate cosmetic outcome (Quinn J et al., 1997; Ong et al., 2002; Wan et al., 2014).

We entered these data into the meta-analysis using the generic inverse variance method. For each outcome reported, the mean and SD for each group and *P* values were extracted or calculated based on the methods proposed by Parmar and colleagues (Parmar & Torri, 1998). For studies reporting median and range, we planned to estimate mean and SD using the currently most accepted method in the literature for this purpose by Elbourne et al. (2002) and Wan et al. (2014).

Assessment of heterogeneity. Meta-analyses was conducted only for similar studies with similar comparisons reporting the same outcome measures. We assessed the significance of any discrepancies in the estimates of the treatment effects from the different studies using the Higgins Index (I^2 ; Whitehead et al., 2004) and we investigated any heterogeneity.

Data synthesis. We combined mean and SD using random-effect (RE) models. Random-effect models summary estimates were preferred to fixed effects to achieve the most conservative estimates. Standardized mean difference was used as effect measure in preference to mean difference because similar outcomes were measured with different methods and scales. Meta-analysis was only conducted for combinable data. Variables that determined combinability included primary lip repair, type of absorbable sutures used (polyfilament), outcome evaluated, follow-up period, and type of assessment (professional). Due to the different natural history and treatment regimens for CLP, we planned to analyze different CLP types separately, if possible. All statistical analyses were done with Revman, version 5.4 (Cochrane, 2020).

Results

Description of Studies

We identified 58 research papers through our database search after inclusion of all the key words and removal of all duplicate studies. We retrieved full-text copies of these articles for detailed review. Additional searches were also done. Finally, only 6 trials (Shinohara et al., 1996; Spauwen et al., 2006; Bhuiyan et al., 2010; Datarkar et al., 2014; Rao et al., 2016; Alawode et al., 2018) met all inclusion criteria, and they were selected for qualitative analysis. A total of 299 participants who underwent CLP repair were included in the outcome evaluations. Of the 6 trials included in this review; 5 (Shinohara et al., 1996; Bhuiyan et al., 2010; Datarkar et al., 2014; Rao et al., 2016; Alawode et al., 2018) compared resorbable sutures with nonabsorbable sutures and only 1 (Spauwen et al., 2006) compared tissue adhesives with resorbable sutures. Table 1 details characteristics of included studies.

Risk of Bias of Included Studies

The risk of bias of included studies was assessed via the design-specific risk of bias modified from the adapted risk of bias criteria for individual studies in systematic reviews of health care intervention by Viswanathan et al. (2008). Of the 6 trials, 3 were RCTs (Datarkar et al., 2014; Rao et al., 2016; Alawode et al., 2018) and 3 were CCTs (Shinohara et al., 1996; Spauwen et al., 2006; Bhuiyan et al., 2010).

Sequence generation (selection bias). Of the 3 RCTs, 2 (Datarkar et al., 2014; Alawode et al., 2018) reported adequate randomization sequence generation methods and were assessed as being at low risk of bias for this domain. In 1 trial (Rao et al., 2016), the method of sequence generation was unclear

Table 1. Characteristics of Selected Studies.

Author, year	Study Design	Country	Sample size Age range Surgery type	Type of CLP	Treatment protocol and technique	Treatment groups	Outcome evaluated follow-up	Evidence/result
Resorbable vs nonabsorbable sutures								
Alawode et al., 2018 ²² First patient recruited May 2013	Randomized controlled trial Single center Nigeria		N = 60 (32 males, 28 females) 3 Months to 48 years (68% <1 year) Primary and secondary repair	Unilateral cleft lip and alveolus (N = 23) Unilateral cleft lip and palate (N = 26) Bilateral cleft lip and alveolus (N = 3) Bilateral cleft lip and palate (N = 8)	Surgical repair under GA (N = 57) Surgical repair under LA (N = 3) Dressing: Sufla-Tulle gauze Surgical repair UCLP: MRA or TRT Surgical repair BCLP: MFFT	1.5 metric Ethicon-coated Vicryl (Polyglactin 910) 4/0 suture, cutting needle 17.5 mm (N = 30) 1.5 metric Nylon 4/0 suture, cutting needle 17.5 mm; removed POD 7 (N = 30)	Wound healing complications, including hemorrhage, tissue reactivity, wound dehiscence, local wound infection. POD 3, 7, 14	POD 3, 7, 14: Vicryl vs nylon Hemorrhage: 3.3%, 0%, 0% vs 0%, 0%, 0% (no P value) Tissue reactivity: 40%, 40%, 6.7% vs 26.7%, 6.7%, 0% (P value = .27, .002, .49, respectively) Wound dehiscence: 10%, 6.7%, 3.3% vs 6.7%, 3.3%, 3.3% (P value = 1.0, 1.0, 1.0, respectively) Infection: 3.3%, 3.3%, 0% vs 0%, 0%, 0% (no P value) No significant difference in cosmetic appearance of scars between both groups (quantitative data not given) Stitch abscess: Nylon 14% > absorbable 0% (P value = .007)
Shinohara et al., 1996 ²³ First patient recruited 1990 (month not stated)	Controlled clinical trial Single center Japan		N = 103 (sex distribution not stated) Age distribution not stated Primary repair	Unilateral and bilateral CLP (sample size per type not stated)	Treatment protocol and technique for surgical repair not stated. Material for dressing not stated.	Absorbable material N = 47: (polydioxanone N = 43; polyglyconate N = 2, or both N = 2) Nonabsorbable (buried monofilament nylon); removed at POD 5 (N = 56)	Wound cosmesis Wound healing complication; stitch abscess 12 months	POD 7, 30, 180, and 1 year: Vicryl vs nylon Hypo/hyperpigmentation: 10%, 40%, 70%, 60% vs 20%, 60%, 20%, 10% (P value = .277, .361, .002, .010, respectively) Hypertrophic scar: 10%, 70%, 70%, 60% vs 0%, 30%, 20%, 20% (P value = .165, .098, .008, .036, respectively) Abnormal scar pliability: 80%, 80%, 70%, 50% vs 80%, 50%, 30%, 10% (P value = .330, .292, .021, .104, respectively) Infection: At POD 7; 0% Vicryl < 10% nylon (P value > .05)
Rao et al 2016 ²⁴ First patient recruitment date not stated	Randomized controlled trial Single center India		N = 20 (sex distribution not stated) 3-18 months Primary repair	Nonsyndromic unilateral cleft lip complete or incomplete (sample size per type not stated)	Surgical repair under GA for all patients (GA or sedation also used for suture removal in the nylon group) Modified MRA technique and primary rhinoplasty (for complete CLP) used for all patients	Absorbable suture material (Vicryl Rapide or irradiated Polyglactin 910; N = 10) Nonabsorbable suture material (nylon or polyamide; removed at POD 7 (N = 10)	Wound cosmesis (hypo/ hyperpigmentation, hypertrophic scar, abnormal scar pliability) Infection: 1 week, 1 month, 3 months, 6 months, 1 year	Mean VAS (Vicryl vs prolene) 1 month, 6 months, 1 year: 88.27, 88.27, 91.93 vs 91.17, 91.17, 93.17 (P value > .05) Wound infection: Vicryl (6.67%) vs prolene (6.67%), P value > .05 Wound dehiscence: Vicryl (0%) vs prolene (10%), P value > .05 Hypertrophic scar: Vicryl (3.33%) vs prolene (3.33%), P value > .05
Datarakar et al., 2014 ²⁵ First patient recruited June 2010	Randomized controlled trial Single center India		N = 60 (no difference in sex of participant) Mean age of 3 months Primary repair	All patients had unilateral primary cleft lip	Surgical repair under GA for all patients (GA or sedation also used for suture removal in the prolene group) Standard MRA technique used for all patients	CLP repair using absorbable suture (Vicryl Rapide; N= 30) CLP repair using nonabsorbable suture (Prolene); removed at POD 7 (N = 30)	Wound cosmesis (measured via 100-mm VAS) Wound healing complication (infection, dehiscence, hypertrophic scar) 1 month, 6 months, 1 year	

(continued)

Table 1. (continued)

Author, year	Study Design Country	Sample size Age range Surgery type	Type of CLP	Treatment protocol and technique	Treatment groups	Outcome evaluated follow-up	Evidence/result
Bhuiyan et al. 2010 ²⁶ First patient recruited January 2003	Controlled clinical trial Multicenter (2) Bangladesh	N = 26 (15 males, 11 females) 3 months to 10 years Primary repair	UCLP (central CLP = 1, lateral CLP = 25). Patients with UCLP with grossly deformed face and UCLP with major associated anomaly were excluded from the study	Surgical repair under GA for all patients (GA used for suture removal only in 71.5% of patients in the polypropylene group) Standard MRA technique used for lateral defects. For central defect, linear closure was done	CLP repair using absorbable suture (fast absorbable irradiated Polyglactin 910; N = 12) CLP repair using nonabsorbable suture (polypropylene); removed at POD 7 (N = 14)	Wound cosmesis (measured by clinical examination) Discomfort (pain/itching) Participant/parent satisfaction Total cost 4 weeks	Excellent wound cosmesis: IRPG 910 (91.6%) < polypropylene (92.9%), P value > .05 Discomfort: IRPG 910 (16.7%) < polypropylene (21.4%), P value < .05 Participant satisfaction: IRPG 910 (100%) > polypropylene (35.7%), P value < .01 Cost of suture material: IRPG 910 (300taka) > polypropylene (200taka), P value < .01 Cost of hospital stay: IRPG 910 (200taka) < polypropylene (700taka), P value < .001 Extra cost for suture removal: 1000taka
Medical adhesives vs resorbable sutures							
Spauwen et al. 2006 ²⁷ First patient recruitment date not stated	Controlled clinical trial Single center Netherlands	N = 30 (16 males, 14 females) 5.3-6.4 months Primary repair	Unilateral cleft lip and/or alveolus (N = 12) Unilateral cleft lip and palate (N = 10) Bilateral cleft lip and palate (N = 8)	Surgical repair under GA for all patients Surgical repair UCLP: MRA Surgical repair BCLP: Manchester type of closure	Intradermal sutures at midlevel of the lip (Monocryl 6.0) and Dermabond (ocyl-2- cyanoacrylate) at epidermal level. N = 15 4 intradermal plus 2-3 epidermal sutures of Monocryl 6.0. N = 15	Wound cosmesis (measured via 100-mm VAS) Complications at 8 weeks Complications at 2.2 years, 8 weeks, 1.8-2.7 years (mean 2.2 years)	Mean VAS parents assessment: Dermabond (81.33) > Monocryl 6.0 (80.87), P value = .922 Mean VAS professionals assessment: Dermabond (65.12) > Monocryl 6.0 (64.9), P value = .983 Complications at 8 weeks: Suture granuloma: Dermabond (0%) < Monocryl 6.0 (6.7%), P value > .05 Hyperpigmentation: Dermabond (20%) < Monocryl 6.0 (40%), P value > .05 Hypertrophic scar: Dermabond (20%) < Monocryl 6.0 (26.7%), P value > .05 Complications at 1.8-2.7 years: Suture granuloma: Dermabond (13.3%) < Monocryl 6.0 (20%), P value = .624 Hyperpigmentation/ hypertrophy: Dermabond (40%) > Monocryl 6.0 (20%), P value = .232 Overall complications at ~2.2 years: Dermabond (53.3%) > Monocryl 6.0 (40%), P value = .273

Abbreviations: BCLP, bilateral cleft lip and/or palate; GA, general anesthesia; LA, local anesthesia; MFFT, Millard fork flap technique; MRA, Millard rotation advancement; POD, postoperative day; TRT, Tension-Randall technique; UCLP, unilateral cleft lip and/or palate; VAS, Visual Analog Scale.

and was assessed as being at unclear risk of bias. One CCT (Spauwen et al., 2006) reported adequate strategy for recruiting participants and was assessed as being at low risk of bias for the sequence generation domain while the remaining 2 CCTs (Shinohara et al., 1996; Bhuiyan et al., 2010) were assessed at an unclear risk of bias.

Allocation method (selection bias). Of the 3 RCTs, only 1 (Datarakar et al., 2014) reported adequate allocation concealment and was assessed as being at low risk of bias for this domain. The 3 CCTs (Shinohara et al., 1996; Spauwen et al., 2006; Bhuiyan et al., 2010) did not report their strategies for including participants and were assessed as being at unclear risk of bias for this domain.

Performance bias. Blinding of participants and clinicians is not feasible in surgical trials and was not assessed. In the 6 trials assessed, researchers ruled out any impact from concurrent interventions and unintended exposures and maintained fidelity to their intervention protocol. They were assessed as being at low risk of bias for this domain.

Attrition bias. We assessed 6 trials as being at low risk of bias with regard to incomplete outcome data because all the participants were adequately accounted for in the outcome evaluation.

Detection bias. Only 1 trial (Spauwen et al., 2006) stated blinding of outcome assessment by evaluators and was assessed at a low risk of bias for this domain.

Reporting bias. We assessed 6 trials as free of selective reporting bias as they reported on expected, prespecified clinically important outcomes.

Other bias. We assessed 6 trials at low risk of other bias because the intervention groups appeared to be similar at baseline.

Overall bias. All trials were assessed at an unclear risk of bias for the outcomes evaluated. Also, the studies reported the use of different sutures materials that react differently with soft tissue conferring additional overall bias on qualitative analysis. A summary of the risk of bias assessment is presented in Figure 2.

Effects of Intervention

Comparison 1: Resorbable sutures versus nonabsorbable sutures. Five trials (Shinohara et al., 1996; Bhuiyan et al., 2010; Datarakar et al., 2014; Rao et al., 2016; Alawode et al., 2018) compared the use of resorbable sutures with nonabsorbable sutures in CLP repair. The trial by Alawode et al. (2018) compared 4/0 Vicryl (Polyglactin 910) sutures to 4/0 nylon sutures; the trial by Shinohara et al. (1996) compared polydioxanone and polyglyconate sutures to monofilament nylon sutures; the trial by Rao et al. (2016) compared Vicryl sutures to nylon sutures; the trial by Datarakar et al. (2014) compared Vicryl sutures to prolene (polypropylene) sutures; and the trial by Bhuiyan et al.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Alawode et al, 2018	+		+		+	+	+
Bhuiyan et al, 2010			+		+	+	+
Datarakar et al, 2014	+	+	+		+	+	+
Rao et al, 2016			+		+	+	+
Shinohara et al, 1996			+		+	+	+
Spauwen et al 2006	+		+	+	+	+	+

Figure 2. Risk of bias summary: Review authors' judgments about each risk of bias item for each included study.

(2010) compared irradiated Polyglactin 910 sutures to polypropylene sutures in CLP repair.

Wound healing cosmesis. Rao et al. (2016) measured wound healing cosmesis in terms of the presence or absence of abnormal pigmentation, hypertrophic scar, and abnormal scar pliability. A significant difference favoring cosmesis of nonabsorbable suture group was seen in abnormal pigmentation measured at 3 months and 1 year ($P = .002, .010$, respectively); hypertrophic scar measured at 3 months and 1 year ($P = .008, .036$); and abnormal scar pliability measured at 3 months ($P = .021$). In the trial by Datarakar et al. (2014), wound healing cosmesis was measured via 100-mm VAS (Okitsu et al., 2014) and reported to be more favorable in the nonabsorbable suture group compared to the resorbable suture group. This difference was, however, not statistically significant ($P > .05$). The trial by Bhuiyan et al. (2010) measured wound healing cosmesis by clinical examination and also reported a difference favoring the nonresorbable suture group that was not statistically significant ($P > .05$). The trial by Shinohara et al. (1996) reported that there was no significant difference in cosmetic appearance of scars between the

resorbable and nonabsorbable suture groups but did not give any quantitative data. The trial by Alawode et al. (2018) did not report wound healing cosmesis.

Wound healing complications. Infection was the most common wound healing complication reported. Alawode et al. (2018) reported 3.3% infection rate in the Vicryl group and no infection in the nylon group (no P value given). Rao et al. (2016) reported a difference in rate of infection favoring the Vicryl group ($P > .05$). Datar et al. (2014) reported an equal rate of infection in both groups ($P > .05$). Shinohara et al. (1996) reported infection in terms of stitch abscesses and showed a statistically significant difference of higher recorded infection in the nonabsorbable suture group ($P = .007$). The trial by Bhuiyan et al. (2010) did not report on infection.

Two trials (Datar et al., 2014; Alawode et al., 2018) reported contradictory results for wound dehiscence. The trial by Alawode et al. (2018) reported more wound dehiscence in the resorbable suture group ($P = 1.0$), while the trial by Datar et al. (2014) reported more wound dehiscence in the nonabsorbable suture group ($P > .05$). Hypertrophic scar assessed at 1 year post-CLP repair was regarded as a complication. Datar et al. (2014) reported an equal prevalence of hypertrophic scar in both groups ($P > .05$), while Rao et al. (2016) reported a statistically significant increase in the presence of hypertrophic scar in the resorbable suture group ($P = .036$). Other complications such as hemorrhage (no P value given) and tissue reactivity ($P = .002$) measured at postoperative day (POD) 7 were reported to be higher in the resorbable suture group by Alawode et al. (2018), while pain/discomfort was reported to be significantly lower ($P < .05$) in the resorbable suture group by Bhuiyan et al. (2010).

Secondary outcomes. Only the trial by Bhuiyan et al. (2010) reported secondary outcomes. Patient satisfaction was significantly higher in the resorbable suture group ($P < .01$) and overall cost to participants was significantly higher in the nonabsorbable suture group ($P < .01$). Though the cost of resorbable suture material is higher than that of the nonabsorbable, the overall costs involved for repeated visits, suture removal, and anesthesia required in the nonabsorbable suture group are quite higher than those of the resorbable suture group.

Quantitative analysis. Quantitative analysis for all the different outcomes was based on a generic inverse variance method and RE model using log odds and the SE data entry. For cosmesis, only 3 studies (Bhuiyan et al., 2010; Datar et al., 2014; Rao et al., 2016) fulfilled the criteria for combinability reporting cosmesis result of polyfilament absorbable sutures compared with nylon/prolene sutures measured at 1 year postoperation by the attending physician. Test of overall effect of the pooled data showed a statistically significant difference in cosmesis favoring the nonabsorbable suture group ($P < .008$). For overall complications, only 3 studies (Datar et al., 2014; Rao et al., 2016; Alawode et al., 2018) fulfilled the criteria for combinability reporting complications of polyfilament absorbable sutures compared with nylon/prolene sutures

measured at POD 7 by the attending physician. Test of overall effect did not show any statistically significant difference in the rate of complications between the 2 groups measured at POD 7. Figure 3 represents the meta-analysis of absorbable and nonabsorbable comparison.

Comparison 2: Medical adhesives versus resorbable sutures. Only 1 study (Spauwen et al., 2006) compared the use of medical adhesives with resorbable sutures in skin apposition of CLP repair. The trial by Spauwen et al. (2006) compared the use of intradermal Monocryl 6/0 sutures and Dermabond (octyl-2-cyanoacrylate) at epidermal level for CLP repair with the use of Monocryl 6/0 sutures.

Wound healing cosmesis. Spauwen et al. (2006) reported wound healing cosmesis measured by both the parents and the professional via the 100-mmVAS (Okitsu et al., 2014). There was no significant difference between the overall cosmetic result of medical adhesive (81.33; 65.12) and resorbable sutures (80.87; 64.9) judged by both parents and professionals, respectively ($P = .922, .983$, respectively).

Wound healing complications. In the trial by Spauwen et al. (2006), immediate complications like suture granuloma (0%, 6.7%), hyper pigmentation (20%; 40%), and hypertrophic scar (20%; 26.7%) were recorded less in the Dermabond group compared to the Monocryl suture group, respectively. However, overall complications measured between 1.8 and 2.7 years showed a complication predilection favoring the Dermabond group (53.3%) compared to the Monocryl suture group (40%). Both results were not statistically significant ($P > .05$).

Secondary outcomes. The trial by Spauwen et al. (2006) did not report secondary outcomes.

Quantitative analysis. No quantitative analysis was done for this group due to insufficient data.

Discussion

This systematic review was undertaken to answer the question, "Between absorbable sutures, nonabsorbable sutures, and medical adhesives, which will give the best clinical outcome when used for CLP repair?" Some studies (Choudhary & Cadier, 2000; Collin et al., 2009; Kudur et al., 2009) have reported an improved clinical outcome when CLP repair is performed with absorbable sutures and/or tissue adhesives over nonabsorbable sutures, while others have reported an inconclusive result (Knott et al., 2007; Alawode et al., 2018). Therefore, an evidence-based answer to this question will guide clinical and surgical practices and also lead to an improved surgeon and patient/parent satisfaction after CLP repair. Six trials with a total of 299 participants with CLP were included. All included trials had an overall unclear risk of bias.

Several studies (Choudhary & Cadier, 2000; Magee et al., 2003; Mourougayan, 2006; Paige, 2006; Collin et al., 2009; Knott et al., 2007; Kudur et al., 2009; Ruotolo & Fearon, 2009; Cooper & Malhotra et al., 2016) have advocated the

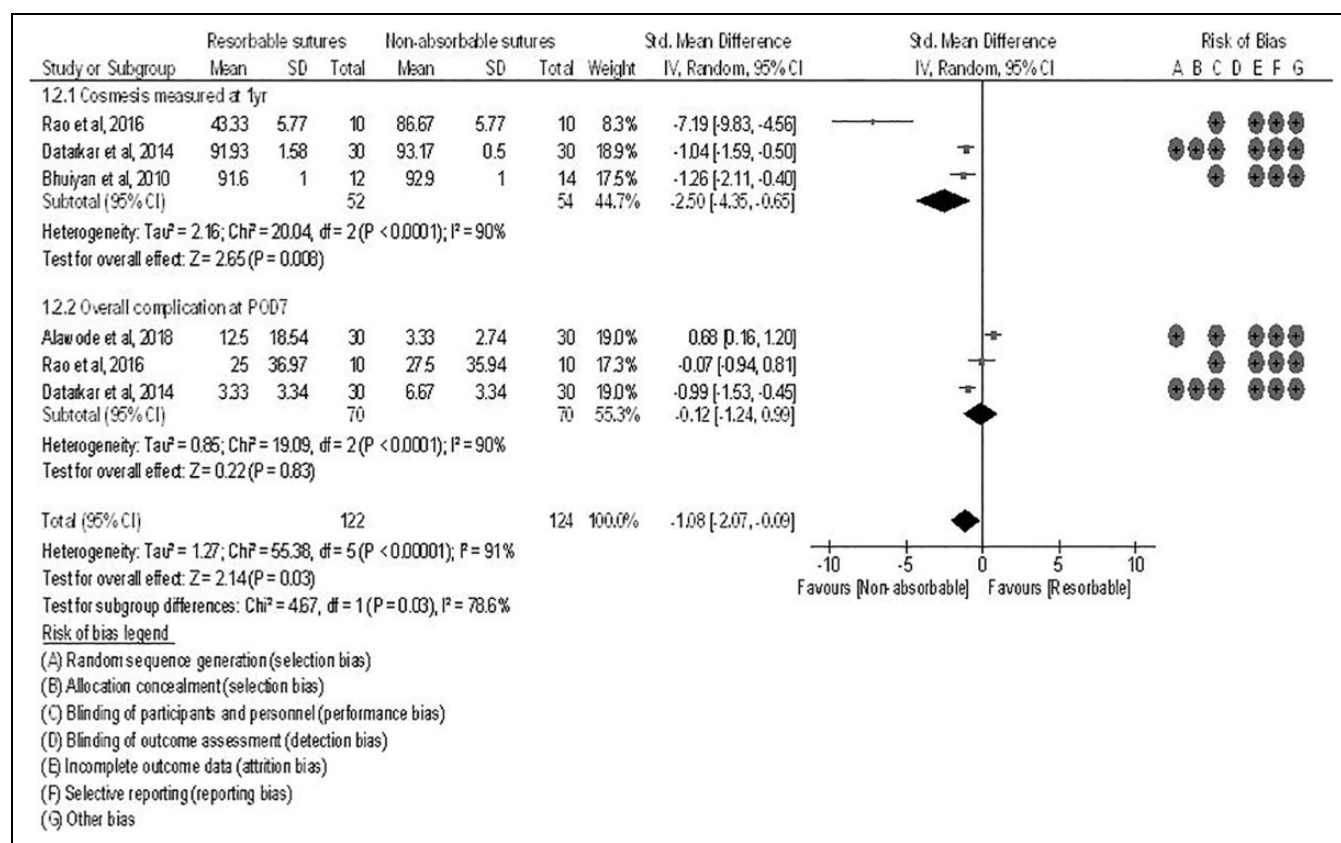


Figure 3. Forest plots of the main quantitative analysis for absorbable sutures versus nonabsorbable sutures showing estimates of each outcome for individual studies, and the pooled estimates of all studies alongside their risk of bias assessments.

elimination of the suture removal stage as this would help reduce cost to patients from additional dressing and anesthesia/sedation, as well as limit the risk of complications arising from multiple visits. Five trials (Shinohara et al., 1996; Bhuiyan et al., 2010; Datarkar et al., 2014; Rao et al., 2016; Alawode et al., 2018) that compared the use of only resorbable sutures with the use of only nonabsorbable sutures in CLP repair were included. In qualitative analysis of wound healing cosmesis, 1 trial (Rao et al., 2016) reported a statistically significant difference in favor of the nonabsorbable arm, whereas the remaining trials did not report any statistically significant difference between the 2 groups. After meta-analysis, a statistically significant difference in wound healing cosmesis measured at 1 year post-CLP repair was noted favoring the nonabsorbable arm ($P = 0.008$). This result, however, should be interpreted with caution and regarded as low-certainty evidence because the pooled data from combined studies had a high degree of heterogeneity ($I^2 = 90\%$; $P < .0001$), which could have affected the result.

Conflicting results were seen in the qualitative analysis of infection rate and no significant difference was noted between the 2 groups. Stitch abscess, however, was reported to be significantly more prevalent in the nonabsorbable suture group ($P = .007$) and this usually occurred when sutures were left beyond POD 7 (Shinohara et al., 1996). Inconclusive results

were reported in the qualitative analysis of other complications such as wound dehiscence, hypertrophic scar, and hemorrhage. No significant difference was noted in the meta-analysis of overall complication rate measured at POD 7. A significant difference in cost and patient satisfaction was also noted ($P < .01$) favoring the resorbable suture group.

Also, several studies (Magee et al., 2003; Cooper & Paige, 2006; Mourougayan, 2006; Ruotolo & Fearon, 2009; Malhotra et al., 2016) have advocated the use of tissue adhesives for CLP repair due to certain advantages such as satisfactory wound healing cosmesis, reduced surgery time compared to suturing technique, limited patient discomfort through elimination of suture removal stage, and simplified postoperative care. This review involved only 1 trial (Spauwen et al., 2006) that compared the use of absorbable intradermal sutures and tissue adhesives for skin apposition for CLP repair. Qualitative analysis reported no significant difference in both wound healing cosmesis and complication rate measured over short- and long-term periods between both groups. Meta-analysis was not conducted as only 1 study fulfilled the inclusion criteria.

Although we planned to analyze different CLP types separately (unilateral, bilateral; complete, incomplete; with or without palatal involvement; syndromic, nonsyndromic), the included studies did not delineate treatment outcomes based on CLP type, making it impossible to do so.

Conclusion

Although the results of this review point to a more favorable wound healing cosmesis for nonabsorbable sutures, similar and satisfactory wound healing cosmesis for absorbable sutures with or without tissue adhesives, a significantly higher prevalence of postoperative complications and poor patient satisfaction for nonabsorbable sutures, and an overall more favorable outcome for either absorbable sutures or tissue adhesives, the 6 selected studies were assessed at an unclear risk of bias. Therefore, the results of this study should be interpreted with caution and regarded as low-certainty evidence. Also, the results of this review were based on only 6 studies due to low quantity of publications available on RCTs in wound closure following cleft lip surgery. A more robust number of studies with low level of bias would have been a better indicator. This emphasizes the need for more RCTs on surgical wound closure following cleft lip repair.

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