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Determining postoperative outcomes after cleft palate repair: A systematic review and meta-analysis☆

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Abstract *Background:* A lack of high-level evidence exists on the outcomes of different cleft palate repair techniques. A critical appreciation for the complication rates of common repair techniques is paramount to optimize cleft palate care.
Methods: A literature search was conducted for articles on the measurement of fistula and velopharyngeal insufficiency (VPI) rates following cleft palate repair. Study quality was determined using validated scales. The heterogeneity between studies was evaluated using the I^2 statistic. Random-effect model analysis and forest plots were used to report pooled relative risks (RRs) with 95% confidence intervals for treatment effect. *P*-values of 0.05 were considered statistically significant.
Results: Of 2386 studies retrieved, 852 underwent screening and 227 met inclusion criteria (130 studies (57%) on fistulas and 122 studies (54%) on VPI). Meta-analyses were performed using 32 studies. The Furlow technique was associated with less postoperative fistulae than the von Langenbeck and Veau/Wardill/Kilner techniques (RR = 0.56 [0.39-0.79], $p < 0.01$ and RR = 0.25 [0.12-0.52], $p < 0.01$, respectively). One-stage repair was associated with less fistulae compared to two-stage repair (RR = 0.42 [0.19-0.96], $p = 0.04$). The Furlow repair was also associated with a less VPI than the Bardach palatoplasty (RR = 0.41 [0.23, 0.71], $p < 0.01$), and

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the one-stage repair was associated with a reduction in VPI rates compared to two-stage repair (RR = 0.55 [0.32, 0.95], $p = 0.03$).
Conclusion: The Furlow repair is associated with less risk of fistula formation than the von Langenbeck and Veau/Wardill/Kilner techniques and less VPI compared to the Bardach repair. One-stage repair is associated with less risk of fistula formation and VPI than two-stage repair.

Introduction

Clefting is the most common craniofacial birth defect in children, with significant effects on facial growth, hearing, speech, and psychosocial well-being.[1] The management of a patient with a cleft is complex and requires a multidisciplinary team, which includes plastic surgeons, maxillofacial surgeons, orthodontists, otolaryngologists, speech-language pathologists, and pediatricians, among others. Surgical repair of the cleft palate is typically performed after the age of 9–10 months as this is associated with optimal speech outcomes.[2] The techniques used for cleft palate repair vary depending on the length and width of the palate as well as the type of cleft palate according to the Veau classification. The objective is to close the cleft defect and realign the levator veli palatini, palatopharyngeus, and palatoglossus muscles.

The most common surgical techniques include the Furlow double-opposing Z-plasty, the von Langenbeck palatoplasty, the V-Y Pushback, and the Bardach palatoplasty. A recent poll of cleft surgeons in the United Sates demonstrated that the most frequently used techniques were the Furlow Palatoplasty and the Bardach palatoplasty with an intravelar veloplasty (IVVP) (87% of all cases), and the most common timing or surgery was between 6 and 12 months (74% of all cases).[3] Any repair of a cleft palate carries a risk of postoperative complications, the most common being velopharyngeal insufficiency (VPI) (10–30%),[4,5] maxillary hypoplasia, (approximately 25% of patients require further orthognathic surgery after the completion of skeletal growth),[6] and fistula formation (5.2–11.6%).[7–9]

Significant efforts have been made to both standardize and maximize the outcomes of the care of cleft palate patients, but despite this, the surgical technique, perioperative management, and outcomes remain highly variable between centers. To date, there is a paucity of high-level evidence comparing both surgical technique and timing for cleft palate repair. Existing literature is largely retrospective in nature, and conclusions are mixed. The purpose of this review was to systematically examine the rates of fistula formation and VPI for the most commonly used cleft palate surgical repair techniques.

Methods

Literature search

The systematic review and meta-analysis were conducted according to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) guidelines. The study protocol was registered with PROSPERO (PROSPERO 2017: CRD42017082365) and published in *Systematic Reviews*.[10]

A comprehensive electronic database search was performed using PubMed (MEDLINE), Embase, and the Cochrane Central Register of Controlled Trials from inception to November 2016. A clinical trial registry (www.clinicaltrials.gov) was searched, and reference lists were created for all eligible trials. Randomized controlled trials (RCTs), cluster RCTs, nonrandomized controlled clinical trials, interrupted time series, and prospective and retrospective comparative cohort studies were included, whereas case series and case reports were excluded. Data-specific search strategies were created to index the rates of fistula development and VPI. Key search terms, which included "cleft palate," "palatoplasty," "fistula," and "velopharyngeal insufficiency," were developed using various combinations of Boolean operators "AND," "NOT," and "OR." All studies on cleft pathology were included, including those on submucous clefts. Additional searches were also performed using reference lists of relevant studies. The investigation was limited to human studies and those articles in English or French.

Study selection

The retrieved articles were uploaded to RefWorks software (Publisher, Amsterdam) and deduplicated. Updated results were then uploaded into Covidence software (Publisher, New York) for primary screening. Article abstracts were independently screened by two independent reviewers (Z.Z and C.M) and filtered on the basis of predetermined inclusion/exclusion criteria. Full articles were obtained for all those that met the inclusion criteria. These were then reviewed independently by each reviewer, and any area of disagreement was resolved by consensus.

Data extraction

Three reviewers (Z.Z, M.F, and M.S) extracted information independently and in duplicate from each eligible study and populated a standardized template. Data extracted included study design, surgical technique, gender, syndromic vs. non syndromic, Veau cleft classification, one or two stages of repair, timing of repair, adverse events, and rates of fistula development and VPI.

Risk of bias

All reviewers independently assessed the risk of bias for each eligible study by using a modified Cochrane

Collaboration risk of bias tool[11] and provided a score based on the Methodological Index for Nonrandomized Studies (MINORS) criteria.[12] Studies were scored on the basis of seven domains to be deemed at low, high, or unclear risk of bias, and data points were collected in a predesigned Microsoft Excel template (Appendix 1).

Quality of evidence

The Grading of Recommendations Assessment Development and Evaluation System (GRADE) classification was used to report the quality of evidence of all reported outcomes (GRADEpro, Version 20. McMaster University, 2014) (Appendix 2). Using this approach, study outcomes were scored as high, moderate, low, or very low.[13,14]

Statistical analysis

The study findings were tabulated and summarized using the statistical software RevMan 5.1 (Publisher, Amsterdam), according to reference guidelines in *The Cochrane Handbook for Systematic Reviews of Interventions*. Primary outcomes included the rates of palatal fistula development and VPI and timing of repair. Complication rates were compared using relative risk (RR) ratios with 95% confidence intervals.

Heterogeneity was evaluated for each pooled analysis using the I^2 statistic, thus representing variability secondary to true differences as opposed to sampling error.[15] Clinical heterogeneity was tested by considering the variability in participant trial variables. If high levels of heterogeneity existed among the trials ($I^2 \geq 50$ or $P < 0.1$), the study design and characteristics of the included studies were analyzed. If studies were sufficiently homogeneous with respect to design and compactor, a meta-analysis was performed using a random effects model. Subgroup analyses on postoperative outcomes were not conducted if there were three or less studies.

Results

Study characteristics

The literature search yielded 2386 studies, of which 852 underwent primary screening. Full-text screening resulted in 227 studies, which met the inclusion criteria (Figure 1). The majority of eligible studies (160/227) were published after 2000 and published in Asia (24%), Europe (39%), and North America (30%) (Figure 2). With respect to study design, five studies (2%) were RCTs, 15 studies (7%) were prospective cohort studies, and 207 (91%) were retrospective cohort studies. Data were sufficient to perform a meta-analysis on 32 of these studies, which included an analysis of 4151 repaired cleft palates (Table 1, 45.6% of which were nonsyndromic, 6.91% were syndromic, and the others were unspecified (41.3%).

The vast majority of cleft palates underwent one-stage repair (88%), with either the Veau/Wardill/Kilner V-Y pushback (14%), the Von Langenbeck (20%), or the Furlow double-opposing Z-plasty (20%). Postoperative fistula formation was reported in 130 studies (57%), VPI in 122 studies (54%), and maxillary hypoplasia in 100 studies (44%).

Table 1 Study characteristics.

	$N = 4151$
Gender	
Male	1062 (25.7%)
Female	964 (23.2%)
Undisclosed	2125 (51.2%)
Associations	
Syndromic	286 (6.9%)
Nonsyndromic	1893 (45.6%)
Undisclosed	1972 (47.5%)
No. of stages	
One-stage procedure	3648 (87.9%)
Two-stage procedure	427 (10.3%)
Undisclosed	76 (1.8%)
Veau classification	
Type I	474 (11.4%)
Type II	404 (9.7%)
Type I/II (listed as cleft involving hard palate)	367 (8.8%)
Type III	**1062 (25.6%)**
Type IV	526 (12.7%)
Type III/IV (listed as cleft lip and palate)	95 (2.3%)
Submucous	151 (3.6%)
Undisclosed	**1072 (25.8%)**
Repair technique	
Bardach palatoplasty	**880 (21.2%)**
Von Langenbeck palatoplasty	**848 (20.4%)**
Furlow double-opposing Z-plasty	**844 (20.3%)**
Veau-Wardill-Kilner V-Y palatoplasty	**598 (14.4%)**
Vomer flap	179 (4.3%)
Other	802 (19.3%)

Postoperative fistula formation

A comparison of the RR of postoperative fistula formation was performed between the common techniques of cleft palate repair. The meta-analyses performed for comparison of each group are documented in Table 2. The Furlow palatoplasty was associated with a statistically significant reduction in fistula formation compared to the von Langenbeck and the VY pushback techniques (Table 2 and Figure 3). No other statistically significant relationships were noted between repair techniques. A statistically significant reduction in fistula rate was noted when the palatoplasty was performed in a single stage as opposed to two stages (0.42 [0.19-0.96], $p = 0.04$).

Velopharyngeal insufficiency

The RR ratio for VPI based on the cleft repair technique is presented in Table 3. There was a statistically significant

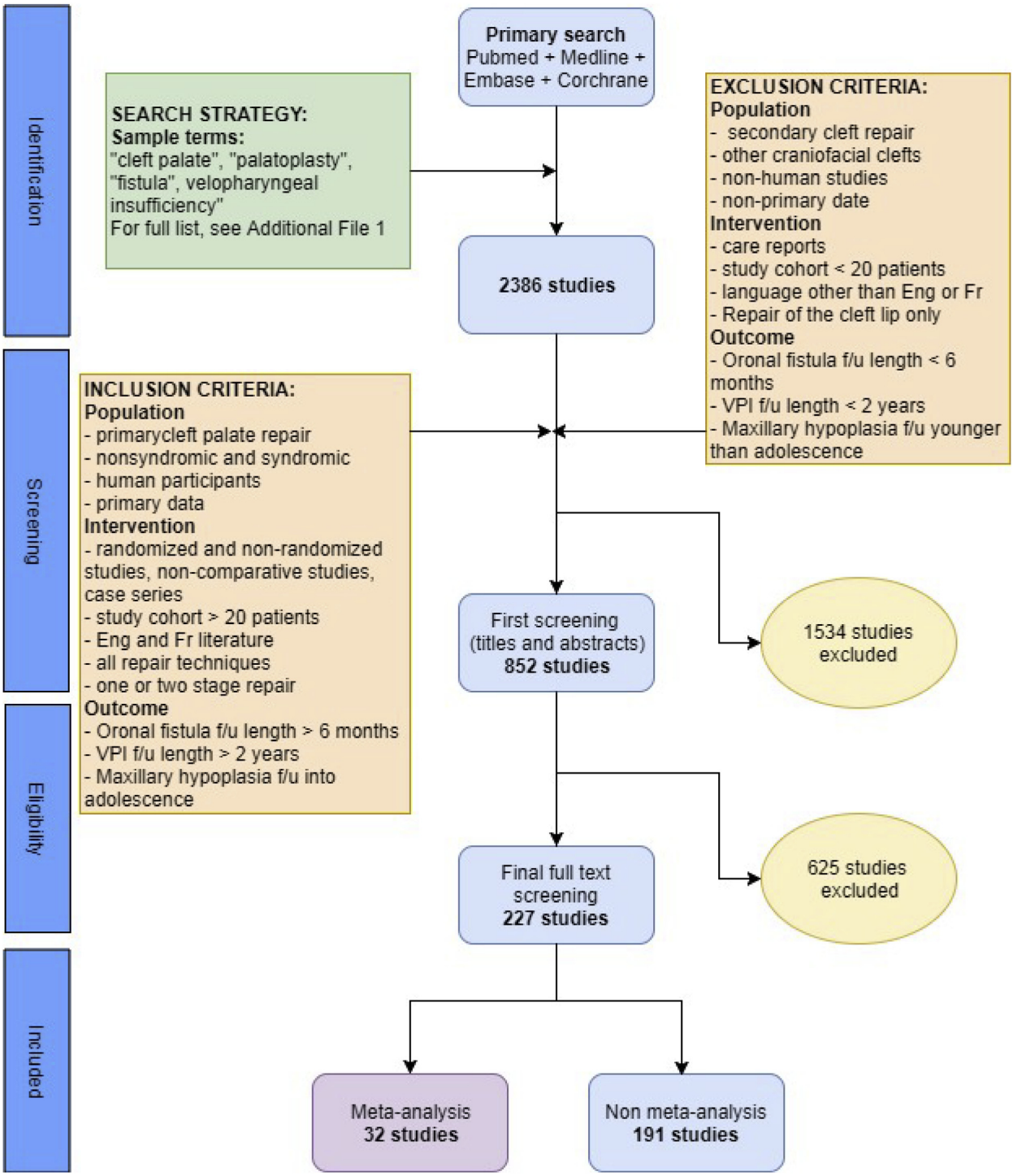

Figure 1 Literature search results and article exclusion process.

reduction in the RR of developing VPI when the Furlow palatoplasty was used compared to the Bardach repair (0.41 [0.23, 0.71], $p < 0.01$) (Figure 4). Although the Furlow palatoplasty was associated with a reduced risk for VPI when compared to the von Langenbeck and Veau-Wardill-Kilner repairs, these associations were not statistically significant. A one-stage cleft palate repair was associated with a statistically significant reduction in VPI when compared to a two-stage repair (0.55 [0.32, 0.95], $p = 0.03$).

Discussion

Despite significant advancements in both the technical and peri- and postoperative management of cleft patients, postoperative fistula formation and VPI remain significant problems following cleft palate surgery.

Previous literature on the rates of fistula formation and VPI has yielded mixed conclusions. Furthermore, the overwhelming majority of these studies are retrospective. The

Table 2 Relative risk ratios for palatal fistula based on cleft repair technique.

Surgical techniques	Number of studies	Number of patients	I^2 (%)	Relative risk (RR)	Total (95% confidence interval)	*p* value (*Z* value)
Furlow vs. von Langenbeck	5	788	0	**0.56**	**[0.39-0.79]**	***p* < 0.01** (3.22)
Furlow vs. Wardill-Kilner	9	575	0	**0.25**	**[0.12-0.52]**	***p* < 0.01** (3.67)
Furlow vs. Bardach	5	513	0	1.42	[0.65-3.13]	$p = 0.38$ (0.88)
Wardill-Kilner vs. von Langenbeck	6	525	0	0.98	[0.60-1.62]	$p = 0.95$ (0.07)
Wardill-Kilner vs. Bardach	3	698	44	0.54	[0.09-3.11]	$p = 0.49$ (0.69)
Bardach vs. von Langenbeck	5	844	0	0.80	[0.40-1.62]	$p = 0.54$ (0.61)
One-stage vs. two-stage repair	5	368	70	**0.42**	**[0.19-0.96]**	***p* = 0.04** (2.07)

Table 3 Relative risk ratios for velopharyngeal insufficiency based on cleft repair technique.

Surgical techniques	Number of studies	Number of patients	I^2	Relative risk (RR)	Total (95% confidence interval)	*p* value (*Z* value)
Furlow vs. von Langenbeck	4	765	0%	0.51	[0.19, 1.36]	$p = 0.18$ (1.35)
Furlow vs. Wardill-Kilner	8	460	0%	0.66	[0.32, 1.35]	$p = 0.25$ (1.14)
Furlow vs. Bardach	3	199	0%	**0.41**	**[0.23, 0.71]**	***p* < 0.01** (3.17)
Wardill-Kilner vs. von Langenbeck	5	401	0%	0.74	[0.44, 1.24]	$p = 0.26$ (1.13)
Wardill-Kilner vs. Bardach	Insufficient	N/A	N/A	N/A	N/A	N/A
Bardach vs. von Langenbeck	Insufficient	N/A	N/A	N/A	N/A	N/A
One-stage vs. two-stage repair	8	840	58%	**0.55**	**[0.32, 0.95]**	***p* = 0.03** (2.12)

N/A = Insufficient studies for meta-analysis.

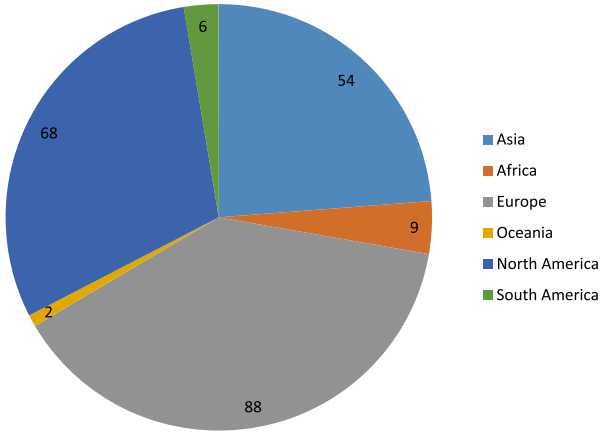

Figure 2 Publications by geographic location.

aim of this meta-analysis was to provide a comprehensive review of fistula and VPI rates to date. These data were then used to compare complication rates between the most common cleft palate repair techniques.

A variety of studies have assessed fistula rates following cleft palate repair. A single-center review of postoperative fistula formation by Cohen et al. demonstrated that the Furlow repair was associated with markedly reduced fistula formation relative to the VY pushback and the von Langenbeck techniques.[16] Later however, Gunther et al. compared the Furlow palatoplasty with IVVP and noted no significant difference in the frequency of fistulae.[17] A recent systematic review by Timbang et al. comparing fistula rates between the Furlow palatoplasty and straight-line IVVP techniques did not also show any difference in fistula rates.[18] Others reported that the fistula rate is strongly associated with the cleft width and the cleft width to total palatal width ratio;[19]

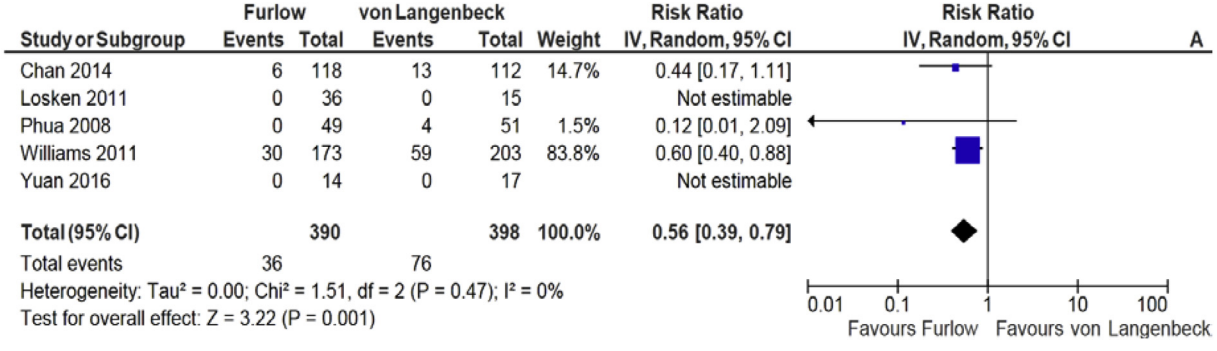

Figure 3 Furlow vs. VY pushback (postoperative fistula formation).

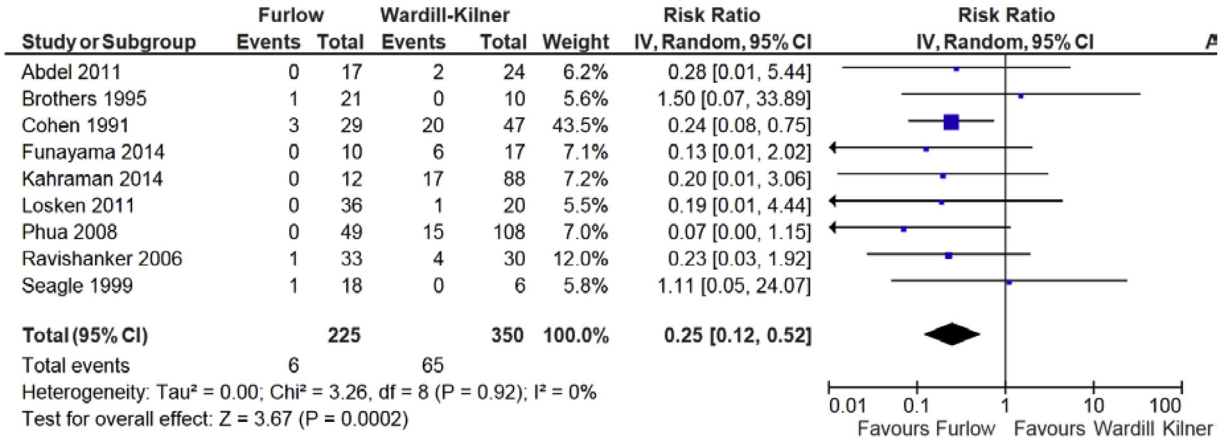

Figure 4 Furlow vs. Bardach repairs (velopharyngeal insufficiency).

however, inconsistent results in these measurements made comparisons difficult. Despite these inconsistencies, sufficient data were available to compare postoperative fistula rates, and we found that the Furlow palatoplasty is associated with a statistically significant reduction in fistula rates compared to both the VY pushback and the von Langenbeck repair techniques.

The rates of VPI have similarly been difficult to compare because of the nonstandardized speech outcome recording techniques. Instead of a binary outcome, hypernasality has been measured subjectively as "good" or "excellent" or by a numerical scale, thus preventing comparison between studies. For this reason, the literature comparing rates of VPI among different procedures is lacking. Furthermore, the majority of studies are retrospective, are nonrandomized, and do not demonstrate clear superiority of one procedure over another. In the present review, we report clear superiority of the Furlow palatoplasty compared to the Bardach technique.

While the majority of surgeons perform a one-stage cleft palate repair, debate remains regarding whether it leads to facial growth restrictions. The two-stage repair entails early soft-palate closure using an anterior obturator and delayed hard-palate closure at a second stage.[20,21] Proponents of the two-stage repair argue that it minimizes facial growth restriction, but disadvantages include an increased risk of oronasal fistula and inferior speech outcomes.[22,23] Our findings corroborate previous studies arguing for single-stage repair. We demonstrated that a two-stage repair is associated with an increased risk of both fistula development and VPI compared to a single-stage repair.

To the best of our knowledge, this is the first systematic review and meta-analysis to compare the different techniques of cleft palate repair with respect to fistula formation and VPI. Strengths of the present study as compared to previous reviews of postoperative complications in cleft palate surgery include a more restricted inclusion criteria and the presence of meta-analyses.

One notable limitation of the study is the ambiguity in the cleft palate nomenclature. For instance, the classical Furlow palatoplasty[24] is described as a double-opposing Z-plasty of the soft palate with primary closure of the hard palate. In reality, however, soft palate reconstruction using the Furlow technique requires an additional technique to close the hard palate if that is also involved. This way, a palate closure with Furlow technique does not provide insight into which way the hard palate was closed, thus potentially obscuring the results.

Conclusions

The Furlow double-opposing Z-plasty is associated with decreased fistula rates when compared to the von Langenbeck and V-Y pushback techniques and decreased VPI rates as compared to the Bardach technique. A one-stage repair of the cleft palate is associated with a decreased risk for both fistula formation and VPI than a two-stage repair. This study illustrates the need for an international collaborative study on cleft palate repair and its outcomes with agreed and validated outcome measures for speech, fistula formation, and maxillary growth.

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Conflicts of interest

None of the listed authors have conflicts of interest or any disclosures.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.bjps.2018.08.019.

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