Evidence-Based Medicine: Unilateral Cleft Lip and Nose Repair

Matthew R. Greives, M.D.
Liliana Camison, M.D.
Joseph E. Losee, M.D.

Pittsburgh, Pa.

Learning Objectives: After reading this article, the participant should be able to: 1. Describe the anatomical malformations found in unilateral cleft lip deformity. 2. Discuss current methods of measuring the deformity and subsequent outcomes. 3. Discuss preoperative assessments, workup, and the use of early interventions before definitive cheiloplasty (e.g., preoperative orthopedics, lip adhesion). 4. Discuss the different techniques used for cheiloplasty and nasal repair. 5. Discuss the use of postoperative splints, taping, or molding. 6. Discuss the outcomes and evidence of cleft lip repairs and identify areas for future research.

Summary: The Maintenance of Certification module series is designed to help clinicians structure their individualized course of study to specific areas appropriate to their clinical practice. This article was prepared to accompany practice-based assessment of preoperative evaluation, anesthesia, surgical treatment plan, perioperative management, and outcomes. In this format, the clinician is invited to compare his or her methods of patient assessment and treatment, outcomes, and complications, with authoritative, information-based references. This information base is then used for self-assessment and benchmarking in parts II and IV of the Maintenance of Certification process of the American Board of Plastic Surgery. This article is not intended to be an exhaustive treatise on the subject. Rather, it is designed to serve as a reference point for further in-depth study by review of the reference articles presented. (*Plast. Reconstr. Surg.* 134: 1372, 2014.)

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CLINICAL SCENARIO

A 1-week-old male infant with a complete unilateral cleft lip and nose presents to the clinic for an initial evaluation and management plan (Fig. 1). What is the best evidence to guide your management of this patient?

The management of the cleft lip and nasal deformity is the quintessential operation of the plastic surgery repertoire. The surgical correction of this deformity has evolved from merely filling the defect into a complex reconstructive process to create the lost architecture of the upper lip. The incorporation of the aesthetic and functional elements into the repair has resulted in increased awareness of the complexity of the deformity and its lifelong ramifications for these patients.

From the Children's Hospital of Pittsburgh and the Department of Plastic Surgery, University of Pittsburgh Medical Center.
Received for publication March 3, 2014; accepted May 8, 2014.

DOI: 10.1097/PRS.0000000000000721

PATIENTS AND METHODS

A literature search of PubMed was performed to obtain the best evidence for the topic of complete unilateral cleft lip and nose deformity. Emphasis was placed on those articles whose subject focused on the preoperative assessment of the deformity, interventions, and measurements of outcomes. The following terms were used for the search and combined as appropriate: "unilateral cleft lip," "cleft lip and nose deformity," "cleft lip incidence," "complete cleft lip," "unilateral cleft lip repair," "embryology," "anatomy," "preoperative assessment," "nasal molding," "lip adhesion," "outcomes," and "surgical technique." The initial searches focused on those studies that were meta-analyses, randomized controlled and clinical trials, case-controls studies, and case series, although other studies deemed important to the topic were included as needed. All studies were published in English or were available with English translation. Studies selected for inclusion were then subjected

Disclosure: *The authors have no financial interest to declare in relation to the content of this article.*

Fig. 1. (*Left*) Anteroposterior view and (*right*) worm's-eye view showing complete unilateral cleft lip and nose.

to quality and validity metrics and assigned a level of evidence based on the American Society of Plastic Surgeons Evidence Rating Scales (Tables 1 and 2). All studies included in this Maintenance of Certification article are identified by the level of evidence and the clinical question addressed (Therapy or Diagnosis). Studies included for background and discussion purposes were not assigned a level of evidence.

INCIDENCE

The incidence of isolated unilateral cleft lip with or without cleft palate is calculated to be 0.1 to 2.1 children per 1000 births, making it one of the most common birth defects.[1,2] Variations have been shown to occur based on ethnicity, with Asian and Native American groups having an incidence of one in 450, versus one in 1000 in Caucasian and one in 2000 in African American populations. Male patients have a higher incidence of cleft lip and palate, whereas female patients are more likely to be affected by cleft palate alone. Unilateral clefts of the lip are more commonly found on the left side, and their incidence is nine times as frequent as bilateral cleft lips. Associated malformations and birth defects are found in almost 30 percent of patients who present with unilateral cleft lip.[3–6] Many syndromes have been linked to the formation of cleft lip, with the most common being Van der Woude syndrome, an interferon regulatory factor 6–linked mutation that results in congenital lip pits and cleft lip.[7,8] Overall, Van der Woude syndrome occurs in 7.6 percent of cleft lip patients and, as it is autosomal dominant, has a 50 percent inheritance pattern.[9] Other genes implicated in the formation of unilateral cleft lip are *MSX1* and *TBX22* located on chromosomes 4 and X, respectively.[10–12] Of all the risk factors associated with the development of unilateral cleft, family history shows the highest correlation. For parents with one child with a cleft lip, the risk to subsequent children is 4 percent for the next child and 9 percent for each thereafter. If either parent has a cleft lip, the risk to their first child is 4 percent and jumps to 15 percent for a second child if the first is affected.[13,14]

Other nongenetic risk factors have been implicated in the development of cleft lip and palate. Maternal smoking has long been implicated as a cause of cleft lip, and a dose-response increase in the risk of cleft lip and/or palate was shown in a review of national birth records for 3.8 million patients (**Level of Evidence: Risk, III**).[15] Other epidemiologic studies have shown that this association only holds up for cleft palate alone and not cleft lip.[16] Alcohol use during pregnancy has been a concerning risk for the development of cleft lip, but this elevated incidence is not statistically significant.[17]

UNILATERAL CLEFT LIP AND NOSE EMBRYOLOGY AND ANATOMY

In normal development, the nostrils are formed from the fusion of the medial and lateral nasal processes. The bilateral medial nasal prominences join in the midline to form the intermaxillary segment, which subsequently develops into the columella, nasal tip, philtrum, frenulum, labial tubercle, and primary palate.[18–20] The orbicularis oris muscle, which originates at the bilateral oral modioli, circumnavigates the mouth. Medially, its fibers split into two insertions: superficially, they fuse into the skin at the philtrum; deeply, they terminate on the anterior nasal spine.[21,22]

Table 1. American Society of Plastic Surgeons Evidence Rating Scale for Diagnosis*

Level of Evidence	Qualifying Studies
I	High-quality, multicenter or single-center cohort study validating a diagnostic test (with a criterion standard as reference) in a series of consecutive patients; or a systematic review of these studies
II	Exploratory cohort study developing diagnostic criteria (with a criterion standard as reference) in a series of consecutive patients; or a systematic review of these studies
III	Diagnostic study in nonconsecutive patients (without a consistently applied criterion standard as reference); or a systematic review of these studies
IV	Case-control study; or any of the above diagnostic studies in the absence of a universally accepted criterion standard
V	Expert opinion; case report or clinical example; or evidence based on physiology, bench research, or "first principles"

*Reprinted from Sullivan D, Chung KC, Eaves FF III, Rohrich RJ. The level of evidence pyramid: Indicating levels of evidence in *Plastic and Reconstructive Surgery* articles. *Plast Reconstr Surg.* 2011;128:311–314.

Table 2. American Society of Plastic Surgeons Evidence Rating Scale for Therapy*

Level of Evidence	Qualifying Studies
I	High-quality, multicenter or single-center randomized controlled trial with adequate power; or systematic review of these studies
II	Lesser-quality randomized controlled trial; prospective cohort study; or systematic review of these studies
III	Retrospective cohort or comparative study; case-control study; or systematic review of these studies
IV	Case series
V	Expert opinion developed via consensus process; case report or clinical example; or evidence based on physiology, bench research, or "first principles"

*Reprinted from Sullivan D, Chung KC, Eaves FF III, Rohrich RJ. The level of evidence pyramid: Indicating levels of evidence in *Plastic and Reconstructive Surgery* articles. *Plast Reconstr Surg.* 2011;128:311–314.

The unilateral cleft lip and nose deformity occurs because of the failure of fusion of the medial nasal and maxillary prominences during normal development around the fourth to sixth weeks of gestation. The orbicularis muscle is malpositioned, as it does not traverse the cleft lip defect. The lateral lip element orbicularis inserts into the alar base, displacing it laterally, posteriorly, and inferiorly. The medial lip element orbicularis inserts into the base of the columella and anterior nasal spine. The caudal septum is displaced out of the vomerine groove and into the contralateral (noncleft) nasal vestibule, and twisting the nasal tip to the ipsilateral (cleft) side.[23] The nasal septum is bowed into the ipsilateral (cleft) side nostril. The alar cartilage on the cleft side is hypoplastic, with a short medial crus. The columella is vertically deficient on the cleft side[24–27] (Fig. 1).

PREOPERATIVE ASSESSMENTS OF THE CLEFT LIP AND NOSE DEFORMITY

The ability to accurately quantify the degree of anatomical aberration in the unilateral cleft lip and nose deformity is essential for measuring the success of current therapies. Most studies addressing this are single-center reports and have developed their own methods for the assessment of the deformity. Very few studies apply tools consistently, both across raters and across centers. This lack of universal evaluation makes large outcome studies difficult to perform.

Some centers have developed anatomical metrics to analyze the degree of deformity found in the unilateral cleft lip and nose. Boorer et al. showed that the cleft lip deformity is a deficiency of both vertical and horizontal dimensions. The height of the medial element is less than the noncleft side by 2.1 mm, and the transverse length is less than the noncleft side by 2.7 mm.[28] Sitzman and Fisher showed that, within the cleft lip, the medial lip element vermilion is significantly deficient compared with the lateral lip element vermilion by an average of 1.3 mm.[29] When comparing the noncleft side to normal lips in age-matched controls, Chou et al. found no significant differences in the noncleft side lateral lip length and philtrum height; only a 0.5-mm deficiency (p = 0.035) in vertical lip height was found in the noncleft side compared with normal lips in the controls.[30]

On a larger scale, the Americleft study sought to assess outcomes in treating unilateral cleft lip across multiple centers (**Level of Evidence: Therapeutic, III**).[31] Their metric of choice was the Asher-McDade rating system, which has been proven to be a reliable and validated tool for the scoring of unilateral cleft lip repairs.[32] The Asher-McDade system uses standardized photographs of cleft patients and stratifies them into a seven-point scale in each of the following categories:

1. Nasal form (frontal view).
2. Symmetry of the nose.
3. Shape of the vermillion.
4. Nasal profile including the upper lip.

The Americleft study, along with its counterpart, the Eurocleft study, demonstrated the power of using a single rating system across multiple

centers, a feat that has been sorely lacking in the cleft literature. However, criticisms of the study include the fact that only a limited number of anatomical points were used in the Asher-McDade scale, and these do not always represent the true nature of the deformity. Also, as technology continues to advance, the use of three-dimensional imaging may prove to be more fruitful in the understanding of the exact degree of distortion in the unilateral cleft lip and nose.

USE OF PRESURGICAL INFANT ORTHOPEDICS

Before definitive cleft lip and nose repair, many surgeons use presurgical infant orthopedics (i.e., lip-nose molding or lip-nose adhesion) to shape the unilateral cleft lip and nose deformity into a "lesser deformity." This is performed in an attempt to make wide complete clefts into "incomplete clefts"—with the belief that the definitive cleft lip and nose repair will be "easier" to perform and that better outcomes will be obtained. A cleft lip and nose adhesion is a surgical procedure performed at approximately 2 months of age, where the nostril sill and medial edge of the cleft lip are closed (Fig. 2, *above*, *left*). Briefly, the cleft side lip and cheek are elevated using a standard buccal incision and mobilized medially. Incisions are then made on the medial and lateral cleft margins, staying within the hypoplastic vermillion segments. A large horizontal mattress permanent suture is then passed through the medial incision, capturing the orbicularis and passing out of the buccal mucosa. The suture is then returned through the cheek to exit within the medial incision, and passing in a similar fashion across the cleft defect and into the lateral incision. The same method of capturing the orbicularis is used on the second side and the suture is secured within the cleft itself. The mucosal edges are then reapproximated around the suture.[33] Although this "repair" does not definitively reconstruct the orbicularis or other anatomical elements (i.e., white roll, Cupid's bow, or nasal cartilages), it does narrow a wide cleft and repairs the deformity in stages.[27]

Although cleft lip and nose molding is a time-tested way to perform presurgical infant orthopedics, the relatively recent rendition of nasoalveolar molding obtains the desired reapproximation of the lip and alveolar segments, and improves the overall nasal symmetry.[34–36] Nasoalveolar molding uses an intraoral appliance that molds the maxillary alveolar segments into alignment across the cleft segment. Alternative modifications have allowed for increased nasal tip projection, alar cartilage repositioning, and lengthening of the columella. The overall goal of nasoalveolar molding is establish the "ideal" relationship of the bony and soft-tissue elements across the cleft defect, thus facilitating the definitive surgical repair.[37]

In a recent poll of practicing cleft and craniofacial surgeons, the use of cleft lip and nose adhesion in the repair of unilateral cleft lip is low, with only 4 percent of surgeons reporting that they "always use it" in their algorithm of care. Of the 26 percent of surgeons who do use it for "some cases," only 25 percent of their patients undergo this additional surgical intervention.[38] Although the use of lip and nose adhesion remains low, those who practice it have shown the powerful nature of its ability to shape the lip and nasal anatomy before definitive cleft lip and nose repair (Fig. 2, *above*, *right*, and *below*). The use of the lip and nose adhesion technique has been shown to significantly improve the vertical height of the hypoplastic cleft lip element. The discrepancy between the noncleft and cleft sides improved by 17 percent on the medial lip and 10 percent on the lateral lip after a 3-month interval.[39]

Nasoalveolar molding has become extremely popular as a method of nonsurgically preparing the cleft lip and nose for the definitive repair. A recent survey found that preoperative orthopedic devices are used routinely by 13 percent and occasionally by 71 percent of surgeons who perform unilateral cleft lip and nose repairs.[38] Timing of the preoperative molding is important for taking advantage of early compliance of the nasal alar cartilage, which is thought to be attributable to the presence of circulating maternal estrogens. Shetty et al. demonstrated that although superior outcomes are seen in those patients who undergo molding before age 1 month, good improvements are obtainable in patients presenting after this time.[40]

Barillas et al. reported excellent long-term symmetry of the nose following nasoalveolar molding in patients with unilateral cleft lip.[41] Although their follow-up was 9 years, these results represent a single center's experience only. Bongaarts et al. conducted a multicenter, randomized, controlled trial to analyze the effects of preoperative orthopedics on facial appearance in patients with complete unilateral cleft lip and palate. Treatment with infant orthopedics by means of passive plates was carried out in one arm until surgical palatal closure was performed at an average of 52 weeks. They showed that, initially, all observers, both professionals and nonprofessionals, chose the treated patients as having improved facial aesthetics;

Fig. 2. (*Above*, *left*) Following cleft lip and nose adhesion. (*Above*, *right*) Following cleft lip and nose adhesion with nasal stents. (*Below*, *left*) Three months after cleft lip and nose adhesion. (*Below*, *right*) One month after definitive cleft lip and nose repair.

however, by 6 years of age, only the professional group appreciated the difference. They concluded that this additional therapy was irrelevant to the final outcomes, as the patients generally interacted with nonprofessional individuals in their daily life (**Level of Evidence: Therapeutic, II**).[42]

Recently, a call for unified research on the use of nasoalveolar molding in unilateral cleft lip and nose was made.[43] The authors found that although extensive research populates the literature, consensus on the timing, process, technique, and even outcomes measured was not standardized across studies analyzed. Although most studies analyzed reported a positive effect of the nasoalveolar molding, a few showed no difference. Because of the difficulty in drawing conclusion from some disparate data sets, the authors were unable to provide a consensus statement regarding its use.

COMPARISON OF CURRENT SURGICAL TECHNIQUES OF PRIMARY CLEFT LIP AND NOSE REPAIR

It seems that few, if any, cleft surgeons truly perform the same operation. Operations to reconstruct the unilateral cleft lip and nose deformity are based on training bias, and evolve over time with individual experience. Also, the particular aesthetic deformity that presents with each unique patient subtly alters the execution of the procedure. Therefore, subtle variation in surgical technique, and the wide spectrum of clefts, results in an extremely difficult arena for outcomes research. As one surgeon is likely to perform a single "type" of reconstruction that slowly evolves over time, most research is limited to single-surgeon experience and consequently of little use to the scientific community.

Most surgeons elect to definitively repair the unilateral cleft lip and nose between 3 and 6 months of age. Although the unoperated cleft lip may initially impede the ability of the infant to feed, most affected children are able to adapt and thrive, even with a wide cleft lip. The justifications of waiting for surgery are to allow the infant to increase in size and weight, and to bypass a period of higher risk for anesthesia.[44] Although not an absolute, some follow the "rule of 10s" proposed by Millard in 1957 and later modified by Wilhelmsen and Musgrave in 1966, which is reached at approximately 3 months of age: hemoglobin level greater than 10 g/dl, weight greater than 10 lb, age older than 10 weeks, and blood cell count less than 10,000 /mm^3.[45,46] Also delaying this process is the use of a cleft lip and nose adhesion or nasoalveolar molding, which in general push the time to primary repair closer to 6 months of age.

Very few high-quality studies have been performed to compare types of primary cheiloplasty techniques. Based on a survey of the members of the American Cleft Palate-Craniofacial Society and the Canadian Society of Plastic Surgeons, most surgeons perform a single repair. Of these, 45 percent use a modified rotation-advancement repair, with 9 percent reporting the use of some variation of triangular flap repair.[38] A previous report of the international community found that 84 percent of practicing cleft surgeons used some variation of the rotation-advancement flap.[47]

The rotation-advancement flap, as originally described[48] or with subtle variations,[49,50] remains the most popular type of primary repair for the unilateral cleft lip. The primary goal of this and all techniques is to perform "philtral subunit reconstruction" and, in so doing, lengthen the columella, restore a functional orbicularis oris muscle, produce a symmetric upper lip with a well-balanced Cupid's bow, and establish continuity of the upper lip vermilion and white roll. In the rotation-advancement technique, the Cupid's bow is balanced by creating a rotation incision on the noncleft side medial lip element that will ultimately mirror the normal philtral column. This incision rotates the Cupid's bow inferiorly, and the lateral lip element on the cleft side is then advanced across the defect. Vertical lengthening of the columella is achieved by transposing a nasal sill–based flap (C flap) into the defect created by the rotation incision, thereby augmenting the cleft side columella. This repair places the incision, and resulting linear scar, along the length of the new philtral column and across the white roll and vermilion. A more detailed description of a modified rotation-advancement repair is detailed in a CME article published in December of 2013 in *Plastic and Reconstructive Surgery*.[20]

The straight-line repair, as modified by Fisher,[51] likely presents the second most popular type of repair. Fisher's repair finds its roots in the Tennison/Randall triangular flap technique of primary cleft lip repair. The key difference from the rotation-advancement technique includes the absence of an incision across the philtrum and the incorporation of a small triangular flap above the white roll, used to balance the Cupid's bow.

Perhaps the largest series comparing different surgical techniques was reported by Gosla Reddy et al., who analyzed a cohort of 1200 patients who had undergone repair using the Millard rotation advancement, the Pfeifer incision (a wavy-line repair that allows vertical lengthening as the curves are approximated into a straight line along the lateral line of the philtrum), or the Afroze incision (a combination of both techniques that uses a Millard incision on the medial lip element and a Pfeifer incision on the lateral lip element). They found that the Afroze repair resulted in superior results for nostril symmetry, white roll approximation, vermilion repair, scar quality, lip length, and Cupid's bow symmetry (**Level of Evidence: Therapeutic, II**).[52] Although this was not a randomized study, the size of the cohort and standardization of the assessment make it the largest seen to date in the literature.

In the distant past, the cleft lip and nose deformity was not addressed at the time of the initial lip repair. This was because of concern over subsequent adverse growth, and whether long-term form and function were improved with early nasal surgery.[53] However, these concerns have been relieved by outcome studies that have demonstrated no adverse growth effects following primary cleft lip and nose deformity correction.[54–59] Also, there are data that support long-term improvement without adverse growth effects following primary septoplasty.[60,61] Studies have documented improvements when comparing primary cleft lip and nose deformity correction to patients who did not have a septorhinoplasty at the time of lip repair.[62,63] Current techniques of primary cleft lip and nose deformity correction focus on repositioning and reshaping the lower lateral cartilages and caudal septum. These can be performed with subcutaneous dissection as in a "closed" rhinoplasty,[64] with access to the nasal tip medially through the cleft lip incision at the base of the columella, and laterally from the alar base. Also, the nasal tip cartilages can be directly accessed through external incisions (i.e., rim and/or Tajima inverted U) and

internal incisions (i.e., intercartilaginous) as in an "open" rhinoplasty.[65–68] Nearly all techniques, both open and closed, incorporate nasal tip cartilage suture maneuvers. The rare complication of nostril stenosis has been reported following the use of circumferential nostril incisions, and the authors of this Maintenance of Certification article believe this is another reason for the routine use of postoperative nasal stents.

USE OF POSTOPERATIVE MOLDING

The use of postoperative splints or taping remains controversial. Advocates of postoperative stenting and/or taping point to the retention of corrected form, reduction in tension across the newly repaired cleft lip, and improved nasal symmetry. Opponents view their use as additional difficulties to impose on parents, as the stents and tape require daily cleaning and adjustments, thus making compliance a difficult obstacle to overcome.

Fifty-four percent of surgeons use some form of postoperative splints in their patient populations.[38] Yeow et al. used postoperative silicone nasal splints in their series of patients following unilateral cleft lip repair.[69] Four different techniques of nasal repair using nasal silicone stents postoperatively were compared over time. Although all groups in the study used the postoperative silicone stents, they found that the group using augmented stents on the cleft side nostril for 6 months postoperatively, when combined with preoperative nasoalveolar molding and primary rhinoplasty, produced the most significant result in nasal symmetry. They concluded that overcorrection of the cleft side nostril, both surgically and postoperatively with splints, resulted in the best long-term results.[70]

OUTCOMES ASSESSMENT AFTER PRIMARY CLEFT LIP AND NOSE REPAIR

The majority of outcomes studies published to date remain single-surgeon experiences, using their modification of a single technique. These reports rely on photographic evaluation of postoperative patients and focus on physical findings such as scar placement, lip symmetry, and other anatomical landmarks (**Level of Evidence: Diagnostic, III**).[71] The Eurocleft study, a previously performed, large-scale, multicenter study, demonstrated a lack of correlation between physical metrics, as measured by clinicians and patients, and family satisfaction rates.[72] This was perhaps the first "wake-up call" to cleft surgeons that not all metrics used for outcomes analysis were provider-centered.

As described previously, the Americleft study, using the Asher-McDade rating scale, demonstrated similar nasolabial aesthetics across four large cleft centers, even with different treatment protocols used at each center.[31] This was one of the largest multicenter studies to validate a single metric for outcomes evaluations, and will possibly provide the benchmark for future outcomes studies in cleft lip surgery.

Few large, multicenter studies examining the quality of life and functional status of these patients currently exist. In a large review of the published literature, Eckstein et al. found that outcome studies for these functional metrics are sorely lacking in the cleft literature.[73] They did locate and analyze five such scales for measuring outcomes in the cleft and craniofacial population: the Youth Quality of Life-Facial Differences questionnaire, the Pediatric Voice-Related Quality-of-Life survey, the Cleft Audit Protocol for Speech-Augmented, the Child Oral Health Impact Profile, and the Child Oral Health Quality of Life. Their review analyzed the level of validation for these studies in the cleft population and found that, although all studies covered many elements of the necessary content to make them useful for the cleft population, no single scale was sufficient to encompass all patient-related outcomes. Their conclusion called for the development of a larger and more comprehensive metric for measuring outcomes in the cleft population.

CONCLUSIONS

As is evident from the literature, wide variation in practice, both surgical technique and nonsurgical management, makes high-level research in the field of unilateral cleft lip and nose repair extremely difficult to perform. Although many groups have made a call for unified research on many of these fronts, there are few large, multicenter, randomized, controlled trials currently in progress. The Americleft and Eurocleft projects have examined the largest cohorts studied to date and may represent the best current evidence for the management of these patients.

Joseph E. Losee, M.D.
Division of Pediatric Plastic Surgery
Children's Hospital of Pittsburgh of UPMC
Children's Hospital Drive
45th & Penn Avenue
Pittsburgh, Pa. 15201
joseph.losee@chp.edu

PATIENT CONSENT

Parents or guardians provided written consent for use of the patient's images.

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