

코입술주름치료의 개요

이상열

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Prominent Nasolabial Fold: An Overview of Treatments

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One of the prominent signs of aging in the midface is deepening and lengthening of the nasolabial folds, which makes people look old and aesthetically displeasing. There have been many treatment modalities to manage prominent nasolabial folds, but there is no single most effective one yet, because every method has its own efficacy and limitations. In order to select the optimal method to meet the desire of patient, several factors such as the age of the patient, his or her aesthetic needs, other aging stigmata, downtime and even economic status should be considered. In this article, treatment modalities are classified into three categories according to the extent of their invasiveness: minimally invasive, moderately invasive, and most invasive techniques. The purpose of this article is to review various methods currently used to manage prominent nasolabial folds, to describe the anatomic structures relevant to the fold formation and to help surgeons select the appropriate method for prominent folds.

(Archives of Aesthetic Plastic Surgery 17: 143, 2011)

Key Words: Nasolabial Folds, Aging, Midface

The nasolabial crease is the facial line between the upper lip and cheek, and the nasolabial fold is the bulging of the skin and fat pad lateral to the crease. The nasolabial fold is absent in newborns, who have a sheath of subcutaneous fat covering the entire face.¹ The fold first becomes obvious around the age 25 and more apparent with aging although there is great individual variation.² The key to successful treatment of the nasolabial fold is to diagnose the cause of the deep fold accurately. The development of a prominent

nasolabial fold with aging is multifactorial. A nasolabial fold becomes prominent from attenuation of retaining ligaments, atrophy of cheek fat, and repeated facial animation. In order to improve prominent folds, many techniques have been developed and modified as the sole or ancillary procedure (Table I). Until a diverse dermal filler was introduced in the clinical fields, the available options were bovine collagen fillers, autologous tissue graft such as fat, dermofat, temporalis fascia, and face lift. Even though

Received September 24, 2011

Revised September 25, 2011

Accepted September 26, 2011

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* The author has no financial interest in any of the products, or devices mentioned in this article.

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Table I. Treatment Modalities Used for Correcting Prominent Nasolabial Fold

Minimally Invasive	<ol style="list-style-type: none"> 1. Botulinum Toxin 2. Dermal Filler <ol style="list-style-type: none"> a. Synthetic Filler: Hyaluronic Acid b. Allogeneic Filler: Cymetra, Fascian c. Xenogeneic Filler: Zyderm/Zyplast, Evolence, Permacol d. Alloplastic Filler: Radiesse, Sculptra, ArteFill
Moderately Invasive	<ol style="list-style-type: none"> 1. Microfat Graft 2. Subcision 3. Autograft-Dermofat, Temporalis Fascia, SMAS 4. Allograft-Acellular Dermal Matrix (Alloderm) 5. Alloplastic Implant-expanded PTFE (Gore-Tex) 6. Laser Lipolysis-1,444nm Nd:YAG (AccuSculpt) 7. Barbed Thread-Aptos Thread, Contour Thread, Quill SRS
Most Invasive	<ol style="list-style-type: none"> 1. Deep Plane, Composite Face Lift 2. Extended SMAS Face Lift 3. Subperiosteal Midface Lift

conventional face lift techniques have been modified, most of them showed variable results in softening the prominent fold. It often drove surgeons to add an adjuvant procedure to the face lift technique for an alteration of the fold. During the last decade, the advent of various synthetic fillers as well as injectable bioimplants provided surgeons with another treatment modality. In addition, a variety of minimally invasive techniques such as subcision, laser lipolysis, and barbed thread suspension have also been tried. Understanding the various treatment techniques as well as the relevant anatomy of nasolabial fold formation will be very helpful in managing the prominent nasolabial fold.

I. NOMENCLATURE: FOLDS AND CREASES

There has been confusion on the nomenclature used to describe the various skin folds and creases in surgical literature. It is necessary to clarify this issue as it is related to the current understanding of anatomic principles and clinical application. A crease is a visible line in the skin, whereas a fold is a redundancy of skin that is often in conjunction with connective tissue attachments.³ Creases are frequently described as folds in discussions of the eyelids, the nasolabial area, and the submammary area.

II. RELEVANT ANATOMY OF THE NASOLABIAL FOLD

A. Lip Elevator Muscle

The nasolabial crease is formed by the insertion of the lip elevator muscles with their dermal insertion to the crease.⁴ The nasolabial fold correlates with the muscles of smiling, which are responsible for the shape and depth of the fold.¹ There are four major lip elevator muscles: levator labii superioris, zygomaticus, levator labii superioris alaeque nasi, and levator anguli oris, which interdigitate with the orbicularis oris muscle, and they are innervated by the zygomatic and buccal divisions of the facial nerve.⁵ Of these muscles, the levator labii superioris muscle and levator labii superioris alaeque nasi muscle may play a significant role in forming the prominent nasolabial fold. Each muscle affects a specific area of the fold. The levator labii superioris alaeque nasi muscle defines the medial (proximal) nasolabial fold while the levator labii superioris muscle, which is the principal elevator of the upper lip, is related with the formation of the middle nasolabial fold.⁶ The other muscles have a minimal effect on the nasolabial fold. The zygomaticus major muscle has a slight effect by deepening the lateral (distal) fold, whereas the levator anguli oris in the deepest level of the facial musculature has no

discernible effect on the fold.⁶

B. Retaining Ligament

Facial skin is supported by retaining ligaments that run from deep, fixed facial structures to the overlying dermis. Two types of retaining ligaments are (1) osteocutaneous ligaments (e.g., zygomatic and mandibular ligaments) and (2) supporting ligaments (e.g., parotidocutaneous and masseteric cutaneous ligaments). The significance of the retaining ligaments lies in the fact that as people age, the support from this ligamentous system becomes attenuated, leading to many of the stigmata of the aging face.⁷ Prominent nasolabial folds are partly related to the downward descent of malar fat pad caused by attenuation of the zygomatic ligaments.

C. SMAS (superficial musculo-aponeurotic system)

The nasolabial fold is a confluence of the superficial musculo-aponeurotic system (SMAS), the dermis, and the muscle fascia overlying the muscles of facial expression.⁸ Since the anterior attachment of the SMAS can affect the nasolabial fold, precise definition of the SMAS around the fold is critical to the development of surgical procedures that could be used to diminish the nasolabial fold. The SMAS was first reported by Mitz and Peyronie to end at the nasolabial fold as a distinct layer.⁹ However, the SMAS was reported in cadaveric studies not to terminate just medial or lateral to the nasolabial fold, but to be present through the entire upper lip, and fibrofatty tissue was found as a distinct layer above the muscle.^{10,11}

D. Modiolus

Modiolus is a dense, compact, mobile fibromuscular structure playing the role of decussation between the orbicularis oris and labial tractors ending in the modiolus, and located lateral and slightly superior to each angle of the mouth. The following muscles contribute to it: orbicularis oris, buccinator, levator anguli oris, depressor anguli oris, zygomaticus major, and risorius. It plays a great role in the formation of the nasolabial fold and prevents the appearance of facial aging.¹² The trophic modiolus was noted to prevent the appearance of other facial aging in

addition to the nasolabial fold.¹

III. TREATMENT

A. Minimally Invasive Modalities

1) Botulinum Toxin

The nasolabial fold has been the most controversial and uncomfortable area for treatment with botulinum toxin. Currently it is not popularly used for correcting deep nasolabial folds. Because botulinum toxin injection into the lip elevator muscle causes an unpleasant smile, it should be injected cautiously in the selected cases. As the levator labii superioris alaeque nasi is most responsible for forming the medial nasolabial fold, it should be the target muscle for botulinum toxin injection. However, as some patients are dissatisfied with loss of lip elevation after injection, botulinum toxin injection is currently not offered to patients, except in unusual cases in which there is a great deal of incisor show or gummy smile.¹³ The zygomaticus and the levator labii superioris muscles can be also injected with low dosages of botulinum toxin near the origins of these muscles to efface the fold effectively, but the risk-benefit ratio is high, with potential comorbidity as unpleasant smile and unnatural lip position.^{14,15}

2) Dermal Filler

There are many different types of dermal fillers available today. As shown in Table II, dermal fillers can be classified into the temporary, longer-lasting or permanent dermal fillers according to the duration of these fillers. The duration of effect is variable depending upon the type of filler, the area of injection, and the injection technique. Temporary fillers include two categories: collagen and hyaluronic acid fillers. Collagen fillers usually last 2~4 months while hyaluronic acid fillers can last 6~9 months. Longer-lasting and permanent dermal fillers are used to correct deeper facial lines and creases. These fillers generally include microsphere particles suspended in a liquid or gel formulation. Longer-lasting dermal fillers typically last between 12~18 months while permanent fillers can last 5 years or more.

a. Synthetic Filler

Hyaluronic acid is a glycosaminoglycan polysaccharide composed of alternating residues of the monosaccharide

Table II. Classification of Dermal Filler according to the Duration of Effect

Product name	FDA-Approved year	Special features
Temporary Dermal Filler		
Collagen		
- Zyderm/Zyplast	1981/1985	Bovine collagen-No longer available
- CosmoDerm/CosmoPlast	2003	Human collagen
- Evolence	2003	Porcine collagen
Hyaluronic acid		
- Restylane	2003	
- Juvederm ultra/Ultra plus	2006	
- Perlane	2007	
- Juvederm ultra XC/Ultra plus XC	2010	Contain lidocaine
- Restylane-L and perlane-L	2010	Contain lidocaine
Longer-Lasting Dermal Fillers		
Sculptra aesthetic	2004	Approval for aesthetic use (2009)
Radiesse	2006	Approval for aesthetic use (2008)
Permanent Dermal Filler		
ArteFill	2006	First, only permanent dermal filler (U.S.)

d-glucuronic acid and N-acetyl-d-glucosamine that is normally present in the human body. Owing to their hydrophilic properties, HA filler materials can achieve substantial soft tissue augmentation after injection. In addition to the initial filling effects of HA, it was shown to have an indirect effect to activate the dermal fibroblasts.¹⁶ Hyaluronic acid fillers have become most popular in clinical use for soft tissue augmentation. By 2008, the use of HA fillers had grown to 82.6% of 1,262,848 procedures in the U.S..¹⁷ HA can last for as long as 6 to 9 months or sometimes longer depending on the type of HA filler used. They are less immunogenic, and can be broken down by hyaluronidase. Commercial hyaluronic acid fillers in current use are as Restylane, Juvederm, Hyaform, Perlane, Captique, Puragen, Teosyal. Of these fillers Restylane appeared most often in the relevant studies. Hyaluronic acid has been recently enhanced with the addition of lidocaine in order to reduce patient discomfort during treatment. Most of the adverse reactions related with hyaluronic acid filler are minimal: redness, swelling, ecchymosis, irregularity. However, some serious complications, such as nodular masses, inflammation, necrosis, and dyspigmentation were also reported, and two danger zones that are particularly vulnerable to

tissue necrosis were suggested: the glabella and nasal ala.¹⁸

b. Allogeneic Filler

i) *Dermalogen/CosmoDerm/CosmoPlast*

Dermalogen (Collagen Matrix Technologies, BocaRaton, la.) was the first generation of an injectable allogeneic collagen matrix and was negligible for allergenic risk.¹⁹ CosmoDerm and CosmoPlast (Allergan Aesthetics, Inc., Irvine, Calif.) are manufactured from human tissue that has been grown from a single human fibroblast cell culture in a controlled laboratory environment, and unlike other human derived products, they are not cadaveric in nature.²⁰ However, neither the CosmoDerm family of products nor Dermalogen gained the popularity for clinical use due to their short longevity, which is for 3 to 6 months on average. Currently, most of them have been replaced by new synthetic fillers with longer durability.

ii) *Cymetra*

Cymetra (LifeCell Corp., Palo Alto, Calif.) is the injectable form of human-based micronized acellular dermal matrix. Cymetra is a versatile implant with many applications. It plays a role as a temporary scaffold to encourage revascularization and tissue ingrowth in the body. No

immune response is elicited because cells exhibiting major histocompatibility complexes I and II have been removed. Because of large particle size (100 μm), injections are less smooth than most other implants and can be more painful. The size of the hydrated particles and the needle do not allow intradermal injection, limiting its use to the subcutaneous space. It can potentially result in an embolic event due to large particle size although it is extremely unusual. Injections are not recommended around the glabella and periorbital region because of this concern.²¹ There have been no clinical trials that demonstrate its longevity to be superior to other collagen based implants, but the average longevity was assessed to be 3~9 months.

iii) Fascian

Fascian (Fascia Biosystems, Beverly Hills, Calif.) is preserved, particulate fascia lata derived from human cadavers. This is the only injectable material that has the potential for collagenesis by the ingrowth of fibroblasts into a collagen matrix.²² There have been no reports of complication related to the material itself. Skin testing is not necessary. Jung²³ reported that 92% of the 35 patients treated with Fascian for deep glabellar wrinkles and nasolabial folds were satisfied with the results at 6 months follow-up. There are no reports to document the longevity of the material yet. The average longevity of Fascian was considered as 6~8 months.

c. Xenogeneic Filler

i) Zyderm/Zyplast

The first widely used Zyderm and Zyplast (Inamed Aesthetics, Santa Barbara, Calif.) was injectable bovine collagen. It was used as the principal dermal filler until the advent of new synthetic fillers during the last decade. In 1997, collagen was used in more than 90% of the 385,427 dermal filler procedures performed in the U.S.,¹⁷ but it is not in clinical use any more because it has several drawbacks such as short longevity and possible immune reaction in the body.

ii) Evolence

Evolence (ColBar LifeScience, Herzliya, Israel), a xenogeneic product derived from porcine tendons, is an injectable dermal collagen. Porcine collagen is supposedly less immunogenic than its bovine counterpart making it highly compatible with human collagen. No allergic responses

have been reported, and allergy testing is unnecessary. Its longevity is equivalent to that of Zyplast collagen, and in fact it may be longer, up to 12 months.²⁰

iii) Permacol

Permacol (Tissue Science Laboratories, Aldershot, United Kingdom) is a porcine dermal collagen matrix graft. It is primarily manufactured as a firm sheet of material that is used for reconstructing human dermal tissue defects. Permacol is the cross-linked micronized formulation of the sheet form. It is intended for urinary bulking for patients with urinary incontinence, but some physicians have used it off-label as dermal filler.²⁰

d. Alloplastic Filler

i) Radiesse (calcium hydroxyapatite, CaHA)

Radiesse (BioForm Medical, San Mateo, CA) is composed of calcium hydroxyapatite microspheres (25 to 45 μm) suspended in an aqueous carboxymethylcellulose gel carrier. When placed into soft tissue, the CaHA particles act as a scaffold for new tissue formation and collagen deposition. To some doctors, Radiesse is the first choice of injectable filler for the nasolabial fold.²⁴ It has a firm, robust character, and is therefore highly effective in treating men with thicker skin. However, care must be taken to avoid superficial injections because of the possibility of contour irregularities. An important drawback to the use of Radiesse is relatively increased discomfort compared with other injectables. Calcium hydroxyapatite was reported to be significantly more effective than hyaluronic acid in correcting nasolabial folds without serious adverse events.²⁵ Tzikas²⁶ also demonstrated persistence of results at 12 months, and the most frequent adverse events were erythema and ecchymosis, and the formation of nodules was rare and was chiefly confined to the lips.

ii) Sculptra (poly-L-lactic acid, PLLA)

Sculptra (Dermik Laboratories, sanofi-aventis, Bridgewater, NJ) is an injectable device containing poly-L-lactic acid. It was approved for the treatment of the signs of HIV-associated facial lipoatrophy in 2004 and for cosmetic purposes in 2009. Upon injection, PLLA is believed to gradually elicit the stimulation of fibroblasts, which in turn produce collagen, adding substantial volume to the skin.²⁷ The cosmetic improvements were observed in a retrospective study to sustain for up to 24 months in subjects treated

with poly-L-lactic acid for cosmetic purposes, but several treatments sessions are required to obtain maximum benefits.²⁸ The treatment to the perioral and periorbital regions was shown to be associated with an increase risk of papules or nodules in their studies.²⁸

iii) ArteFill (Polymethylmethacrylate, PMMA)

ArteFill (Artes Medical, San Diego, Calif.) is a permanent injectable filler composed of polymethylmethacrylate microspheres that are suspended in a 3.5% collagen gel matrix containing 0.3% lidocaine. It is a third-generation PMMA-based filler product that contains an optimized collagen matrix with microspheres, which have enhanced uniformity and consistency compared to the second-generation PMMA product Artecoll (Artes Medical, San Diego, Calif.). The polymethylmethacrylate filler was demonstrated to be maintained with significant nasolabial fold correction at 5 years.²⁹ The most common complication is lumpiness. Arte Fill is the only U.S. FDA-approved filler with a documented durability over a 5-year period.

B. Moderately Invasive Modalities

1) Microfat Graft

Since the early 1990s, many reports including the positive results of fat grafting were published, which motivated fat grafting to be applied in the various clinical fields. Coleman³⁰ reported cases of fat grafting to over the 400 nasolabial folds, who demonstrated continued correction with few complications 7 years after one procedure.³¹ Although the fat has several advantages as filler, it is not easy to get a constant good result in the correction of the prominent nasolabial fold. Diffuse infiltration with multiple passes and the placement of extremely small amounts with each pass is one of the keys to successful fat grafting.³¹ In addition to basic principles for fat graft, great attention should be paid to the placement of fat around nasolabial fold, which is strongly attached to the underlying muscles with dense fibrous septa. Fat tends to migrate into the cheek to be placed along the crease. Loeb³² described the technique of fat graft with undermining to prevent displacement of grafted fat into the adjacent lip and cheek tissue. Bucky and Kanchwala²⁴ also described that the treatment of the nasolabial fold with fat injection required the release of the dermal attachments using the V-dissector cannula. On the other hand Kim³³ recommended a counter-

compression technique, which makes similar tissue density between the upper cheek area and lower orbicularis oris area.

2) Subcision

Subcision is subcuticular undermining without incision, which induces the formation of the fibrotic tissue underneath the skin. This technique is helpful to treat depressed scars, wrinkles, folds, cellulite and malar groove, etc. The amount of internal scar tissue formed by subcision seems to depend on various factors. Certain anatomical locations as periorbital, glabellar, labial commissure and upper lip are possible areas of increased skin tension and may have great propensity for fibroplasia.³⁴ It is not a single procedure, for better results it has to be often repeated every two or three months. The instruments commonly used for subcision are wire scalpel and hypodermic needles. The Nokor needle is a kind of modified hypodermic needle looking like a spear. While the wire scalpel developed by Sulamanidze³⁵ is very helpful in undermining long and wide lesions as nasolabial fold, a hypodermic needle is used for small and short lesions. People over forty with prominent nasolabial folds can be candidates for subcision, and the simultaneous subcision in the patients undergoing face lift was presented to give excellent results for the correction of the deep nasolabial fold recalcitrant to standard rhytidectomy.³⁶ Subcision is a very simple and inexpensive procedure, and effective in selected case, but the drawback is that it does not give constant results. The most serious complication is an internal hypertrophic scar, but it rarely occurs if done less intensively. Other complications are minimal. The effect of subcision was reported to improve significantly with the immediate fill such as strips of SMAS, dermis, microfat for deep nasolabial folds.^{37,38}

3) Autograft

Several autogenous tissues such as dermofat,^{39,40} temporal fascia⁴¹ and SMAS^{42,43} are used to improve deep nasolabial folds as a sole procedure or an ancillary procedure combined with rhytidectomy. Dermal grafts may last longer but have a high incidence of cyst formation. The fascial grafts are associated with no complications and may last longer than fat or dermis.⁴⁴ This is because of the rich collagen and fibrous tissue included in the fascia. The appropriate fixation is necessary to prevent their migration.

Table III. Devices Used in Laser Lipolysis with FDA Approval

Trade name	Wave length	Laser type	Pulse duration (μ s)	Power (J)
SlimLipo (USA)	924,975	Diode	Continuous	30
Lipotherme (USA)	980	Diode	Continuous	25
smartLipo (USA)	1,064	Nd:YAG	100	18
SmartLipoMPX (USA)	1064,1320	Nd:YAG	150	20,12
CoolLipo (USA)	1,320	Nd:YAG	100	20-50
AccuSculpt (Korea)	1,444	Nd:YAG	100	12

4) Allograft

Several studies showed good results in the correction of nasolabial folds using acellular dermal matrix with no serious adverse effects such as immune reaction, and the maintenance of its volume was also demonstrated with less absorption in the body.^{45,46}

5) Alloplastic Implant

Expanded polytetrafluoroethylene was reported to be still valuable in the treatment of deep nasolabial folds in relatively young patients.^{47,48} The possible complications are localized swelling, malposition, extrusion, and an unnatural feel.⁴⁹ In addition, the graft is palpable or visible with animation.⁵⁰

6) Liposuction

Conventional liposuction has been tried to soften the nasolabial fold concomitantly with rhytidectomy in an aging face, and resulted in consistent improvement.^{51,52} In the early 1990s, laser assisted-liposuction (laser lipolysis) was first introduced as a new modality for the liposculpture (Table III). It was deemed to be ideal for traditionally challenging cases as well as attributable to neocollagenesis leading to skin tightening. The most common advantages of laser-assisted liposuction relate to easier recovery as well as less operator fatigue compared with traditional liposuction. Devices of three wavelengths have been FDA approved in the U.S. for laser lipolysis-980 nm, 1,064 nm, 1,320 nm. A new 1,444 nm Nd:YAG laser, AccuSculpt (Lutronic Corporation, Ilsan, Korea), was recently introduced in the market. This device has been applied to facial sculpture including nasolabial folds more frequently than before. This device has excellent duality of absorption in both fat and water.⁵³ A 1,444 nm device was shown to be superior to 1,064 nm from the viewpoint of lipolysis potential and

requires less energy to produce the same degree of lipolysis.⁵⁴ The facial contouring using the 1,444 nm Nd: YAG laser was described to be a novel treatment modality to enable selective soft tissue removal for great precision in three-dimensional contouring of the face.⁵⁵ The overall effect of the laser device for liposuction is still controversial, but it is a safe technique in experienced hands.

7) Barbed Thread Suspension

The suture suspension technique is minimally invasive and can be performed easily. It is applicable for various age groups to rejuvenate and reshape the midface. The load-bearing ability of facial suspension sutures has increased with the addition of barbs to polypropylene suture. These sutures are as Aptos Threads (Aptos, Moscow, Russia), Contour Threads (Surgical Specialties Corp., Reading, Pa.), Woffles Threads, Silhouette Midface Suture, Quill SRS. Theoretically, the development of a fibrous capsule around each barbed suture should result in adhesion to the adjacent tissues, but it has not yet been clearly elucidated. There are several reports showing good results using barbed polypropylene sutures,⁵⁶⁻⁵⁸ but no objective measurement was assessed for its efficacy and durability. Persistence of good results using 3-0 polypropylene sutures with absorbable cones (Silhouette Sutures; Kolster Methods, Inc., Corona, CA, USA) was obtained at a mean follow-up period of 18 months with high patient satisfaction.⁵⁹ Barbed sutures offer the promise of minimally invasive facial suspension with diminished adverse events, but the data on efficacy, adverse events, and longevity of effect are less clear.

C. Most Invasive Modalities

Face lift techniques have been advanced to provide a

more youthful appearance and maintain the longevity of effect, which was pioneered by Skoog. Skoog demonstrated that his technique undermining the superficial fascia and skin as a unit resulted in better aesthetic improvements, especially in the jowls. However, it gave only minimal improvement in nasolabial area.⁶⁰ Thereafter various SMAS modification techniques with subcutaneous rhytidectomy were introduced, but these techniques did not alter the nasolabial fold to a great extent either.⁶¹ Along with them, many modifications of subSMAS dissection technique have been described focusing on more optimal treatment of the midface, nasolabial fold, and periorbital area. The techniques of deep plane rhytidectomy,^{62,63} the extended subSMAS technique,⁶⁴ and the high-SMAS technique⁶⁵ were demonstrated to improve the nasolabial fold considerably. To improve the infraorbital area as well as the nasolabial fold and obtain a more harmonious appearance, the composite rhytidectomy was introduced.⁶¹ On the other hand, various modified subperiosteal techniques have been developed. Their efficacies on lower lid rejuvenation are well known, but the improvement of the nasolabial fold has not been proved. A prospective randomized study comparing the efficacy of the standard SMAS face lift against the extended SMAS and composite face lift technique demonstrated that all the procedures were lacking in improvement of the midface ptosis and the nasolabial folds.^{61,66} There are still debates in the literature as to which technique is ideal in addressing the aging face on their efficacy and longevity.

IV. CONCLUSION

Although there are many techniques that are used to correct prominent nasolabial folds, the key to consistent results is not the technique itself but rather the surgeon's ability to individualize the treatment plan according to the age of patient, his or her aesthetic needs, other aging stigmata, downtime and even economic status. In order to select the optimal procedure for the patient, a thorough understanding of the diverse techniques currently used in clinical fields is essential.

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