

Dispelling the Myths of Isotretinoin and Implications for Rhinoplasty

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Summary: Despite concerns from 1980s case reports, oral isotretinoin, a derivative of vitamin A, has largely proven to be safe in surgical procedures, with the exception of deep skin resurfacing. Isotretinoin modulates thinning skin and internal scarring in select rhinoplasty patients who may otherwise have poor definition and excessive scarring. A review of patients undergoing surgical interventions, including rhinoplasty, in the setting of concomitant isotretinoin use was performed to examine safety and therapeutic potential. A total of 49 studies were reviewed. Isotretinoin use appears to be safe in a wide variety of surgical procedures relying on internal scar formation. In rhinoplasty, oral isotretinoin was used to thin skin and improve appearance, and resulted in patient and surgeon satisfaction. As such, the clinical potential for using oral isotretinoin in select rhinoplasty candidates—such as those with thick, glabrous, sebaceous skin; male sex; certain races or ethnicities; or revision cases—could mitigate internal scarring processes. Further studies examining the optimal dosing regimen and long-term benefits are warranted. (*Plast. Reconstr. Surg.* 155: 689e, 2025.)

The long-held belief that oral isotretinoin, or 13-cis-retinoic acid, causes aberrant scarring or hinders wound healing originates from a small subset of case series ($n = 3$) published in the mid-1980s.^{1–3} Early investigators reported keloid formation or delayed wound healing using dermabrasion or argon laser treatment in the setting of oral isotretinoin therapy. These reports posited that it would take skin tissue months to revert to normal physiologic healing, and thus recommended delaying elective dermatologic or surgical interventions at least 6 to 12 months after oral isotretinoin use.^{1–3}

The notion that all procedures warrant a significant delay after oral isotretinoin therapy use has been perpetuated by the medical community since these early cases. However, the growing body of literature since these initial concerns questions the persisting dogma.^{4,5} In 2017, the evidence for using oral isotretinoin in the setting of external resurfacing procedures was examined by experts from the American Academy of Dermatology and the American Society for Dermatologic Surgery Task Force.^{4,5} In brief, with exception of fully

ablative laser and mechanical dermabrasion, it was determined that there was insufficient evidence to delay other external procedures.^{4,5} Further reviews have substantiated these conclusions, and reported normal healing in internal procedures (ie, surgery).^{6–11}

Not only does perioperative use of oral isotretinoin appear to be safe in surgery involving internal scarring versus resurfacing procedures that rely heavily on reepithelialization, it may be a useful adjunct for the facial plastic surgeon.¹⁰ Purported mechanisms include thinning of thick and sebaceous skin, and potentially modulating the wound-healing response to diminish internal scar formation, dead space, or inflammation.^{10,12–15}

Disclosure statements are at the end of this article, following the correspondence information.

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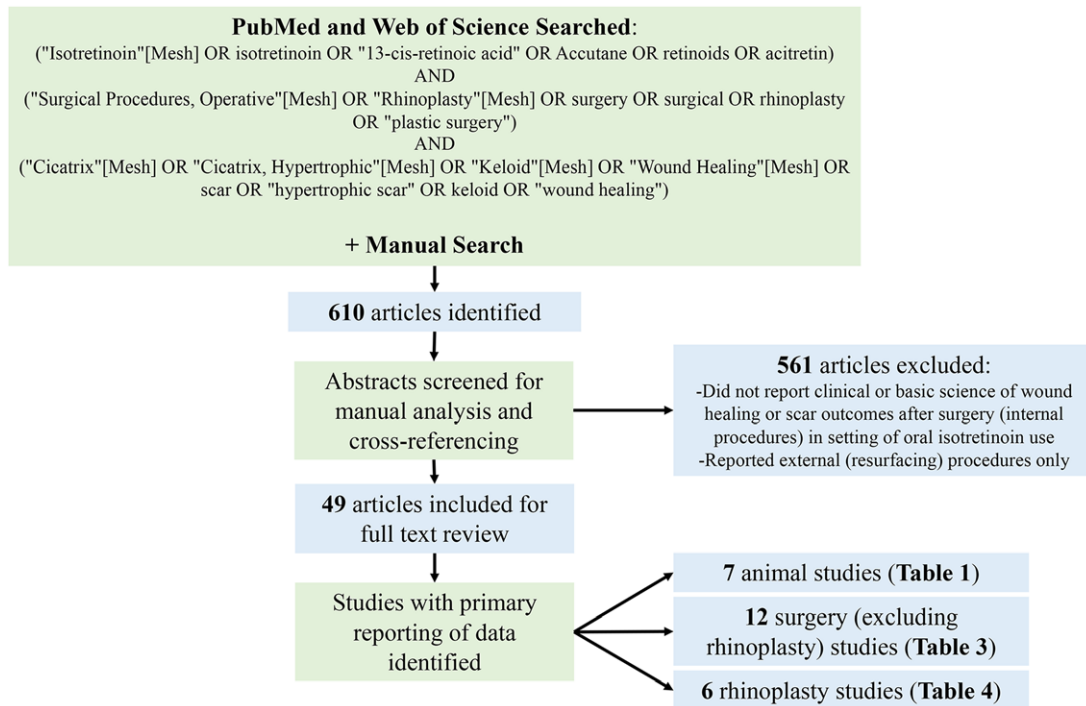


Fig. 1. Article selection process.

Early experience indicates that it may be a potent complement in rhinoplasty for patients with thick, sebaceous skin; certain races or ethnicities; male sex; or those undergoing revision procedures, in particular.^{10,12–14,16–22}

This article reviews the evidence for performing resurfacing procedures in the setting of perioperative oral isotretinoin, aims to familiarize the plastic surgeon with oral isotretinoin as it pertains to wound healing and surgery, and discusses its implications as an adjunct in rhinoplasty and other surgical procedures for skin quality and internal scar modulation.

METHODS

The PubMed and Web of Science electronic databases were used to search for articles from database inception to November of 2023 using selected MeSH search terms for articles related to surgery and concomitant perioperative isotretinoin use, including human, animal, and in vitro studies (Fig. 1). Articles were cross-referenced with previous systematic reviews and on manual search of “isotretinoin AND (surgery OR rhinoplasty)” for comprehensive analysis. Articles were reviewed, and dosing and timing data for isotretinoin were recorded when available. Outcomes of interest included normal healing versus delayed or aberrant wound healing. Level of evidence was determined using the American Society of Plastic

Surgeons Rating Levels of Evidence and Grading Recommendations.

RESULTS

Search results yielded 270 PubMed and 51 Web of Science publications using MeSH terms. After manual review and cross-referencing, 49 publications were included for analysis related to surgery and concomitant oral isotretinoin use, including human, animal, and in vitro studies. Six studies reported surgical outcomes on unique rhinoplasty patients. Tables 1 and 2 and the tables in the Supplemental Digital Content summarize findings of animal, surgical, and rhinoplasty studies. (See Table, Supplemental Digital Content 1, which presents a summary of animal studies reporting wound-healing outcomes with isotretinoin use, <http://links.lww.com/PRS/H506>. See Table, Supplemental Digital Content 2, which shows a summary of literature reporting surgical outcomes for patients undergoing nonrhinoplasty surgical procedures with isotretinoin use, <http://links.lww.com/PRS/H507>.)

DISCUSSION

Isotretinoin: Mechanism of Action and Modulation in Wound Healing

Isotretinoin is a first-generation oral retinoid that was approved by the US Food and Drug

Table 1. Summary of Dermatologic Panel Recommendations in External (Skin-Resurfacing) Procedures

Procedural Intervention	Consistency of Evidence	Recommendation ^a	Associated Risk	GRADE Strength ^b
Dermabrasion				
Mechanical and full face	Inconsistent	Not recommended	Wound-healing complications, keloid formation, hypertrophic scarring	B to D
Superficial manual and microdermabrasion	Consistent	Insufficient evidence to delay	NA	B
Chemical peels				
Superficial peels	Consistent	Insufficient evidence to delay	NA	B
Medium or deep peels	Inadequate	Not enough data available	NA	B to D
Cutaneous surgery				
LASIK surgery	Inconsistent	Not recommended	Dry eyes	D
Incisional and excisional surgical procedures	Inconsistent	Insufficient evidence to delay	NA	D
Lasers and energy devices				
Fractional lasers (eg, laser hair removal)	Consistent	Insufficient evidence to delay	NA	B
Nonfractional lasers (fully ablative)	Consistent	Not recommended	Abnormal scarring and healing	B to C

GRADE, Grading of Recommendations Assessment, Development, and Evaluation; LASIK, laser-assisted in situ keratomileusis; NA, not available.

^aRecommendation to patients while on isotretinoin or within 6 months after isotretinoin cessation.

^bGRADE strength of recommendation scale of A to D based on quality of available evidence, with A = high, B = moderate, C = low, and D = very low.

Administration to treat severe nodulocystic acne in 1982 after originally being synthesized in the 1960s to prevent skin cancer.²³ Today, the off-label indications for isotretinoin have expanded to mild to moderate acne, inflammatory skin conditions such as rosacea and rhinophyma, genodermatoses, skin cancer prevention, other skin disorders, and neoplasms including cutaneous T-cell lymphomas and neuroblastoma.²⁴ This is ascribed to its anti-inflammatory, immunomodulatory, and antineoplastic properties.^{24,25} Pharmacologically, isotretinoin is believed to act as a prodrug, with its metabolites (including tretinoin) binding the nuclear retinoic acid receptors (RAR and RXR), thereby influencing gene expression and ultimately the cell cycle, differentiation, and apoptosis.^{15,23,24} Clinically, it targets multiple etiologies of acne, with remarkable long-term remission or improvement (Fig. 2).^{15,23,24,26} Specific mechanisms of action include pilosebaceous unit involution, diminished sebum production, thinning of sebaceous skin, decreased comedogenesis, dekeratinization through shedding of desmosomes, anti-inflammation, and decreased *Propionibacterium acnes* skin microbiome.

Early concerns regarding isotretinoin's influence on wound healing prompted investigators to elucidate these mechanisms as well. Vitamin A balance has been well-documented to influence the integumentary system and wound healing

through the stimulation of angiogenesis, collagen metabolism, epithelialization, and fibroplasia.^{7,27–35} Retinoids are vitamin A derivatives synthesized to harness the therapeutic benefits while limiting the toxicity profile.²⁷ Their influence on wound healing is incompletely understood, but basic science studies indicate potential mechanisms (Fig. 2).^{7,15,27–35} Proposed mechanisms of action include diminished collagen formation by decreasing fibroblast metabolism and procollagen synthesis; inhibition of normal and keloid fibroblast growth; reduced collagenase activity; decreased epidermal cell growth factor; inhibited transforming growth factor- β -mediated short-term growth; altered epidermal cell ultrastructure; accelerated mast cell accumulation, which influences extracellular matrix deposition and remodeling; and overall anti-inflammation.

In vitro findings in animal studies have not translated to changes in wound healing or aberrant scarring of full- and partial-thickness injuries, including in dog, rat, rabbit, and pig models (see Table, Supplemental Digital Content 1, <http://links.lww.com/PRS/H506>).^{27,35–40} One study did, however, demonstrate delayed wound healing with very-high-dose isotretinoin (10 mg/kg/day) in a guinea pig model.³⁴

The pathogenesis of delayed wound healing after partial-thickness injury, a process reliant on reepithelialization, is explained by isotretinoin's

Table 2. Isotretinoin Use in Rhinoplasty

Source	Study Design (Total <i>n</i>)	Level of Evidence	Isotretinoin Timing	Isotretinoin Duration	Isotretinoin Dose	Outcome
Allen and Rhee, 2005 ⁵⁹	Case series (<i>n</i> = 3)	V	Postoperative (7 mo to 2 yrs)	Not specified	Not specified	Nasal tip deformities and skin thinning in 3 cases associated with postoperative isotretinoin
Cobo and Vitery, 2016 ¹⁸	Case series (<i>n</i> = 17)	IV	Postoperative	4 to 6 mo	0.25 mg/kg to 0.5 mg/kg (<i>n</i> = 15); 0.5 mg/kg to 1.0 mg/kg (<i>n</i> = 2)	Normal healing and scarring; enhanced nasal tip definition and overall posttreatment appearance
Heppt et al., 2018 ¹⁰	Case series (<i>n</i> = 17)	IV	Preoperative	6 to 10 mo	“Low-dose”	Normal wound-healing in rhinoplasty patients; diminished acne flares, tip shaping, and reduced edema
Sazgar et al., 2019 ¹⁷	Randomized controlled trial (<i>n</i> = 48)	II	Postoperative (1 mo)	3 mo	0.5 mg/kg QOD for 1 mo, then QD 2 mo (<i>n</i> = 24)	Normal healing and scarring; improved patient satisfaction and surgeon rating at 3 to 6 mo postoperatively; equivalent to placebo at 1 yr postoperatively
Yahyavi et al., 2020 ¹²	Prospective cohort (<i>n</i> = 303)	III	Concomitant	2.5 mo (2 wk preoperatively to 2 mo postoperatively)	0.3 mg/kg (20 mg/d; <i>n</i> = 149)	Normal healing and scarring including alar-base excisions; no increased revision rate or cartilaginous deformity; improved patient satisfaction at 1 and 3 mo postoperatively, but equivalent thereafter
Silveira et al., 2023 ⁶⁰	Randomized controlled trial (<i>n</i> = 24)	II	Concomitant (held 15 d preoperatively and continued 3 to 5 d postoperatively)	6 mo (2 mo preoperatively to 4 mo postoperatively)	20 mg/d (<i>n</i> = 12)	Normal healing and scarring; enhanced nasal appearance without deformity; substantial thinning of epidermis and dermis at the dorsum, tip, and alae at 6 mo; higher patient satisfaction scores versus control group

inhibition of keratinization and pilosebaceous unit involution. Delayed wound healing, in contrast, has a propensity for hypertrophic scar and keloid formation.¹⁵ However, the exact influence of oral isotretinoin on full-thickness injury and internal scarring is less established clinically. As discussed, surgical wound healing in the setting of isotretinoin use appears to be safe according to available human and animal studies. Nonetheless, in vitro studies demonstrate the differential influence of isotretinoin on fibroblast and extracellular matrix regulation. Oral isotretinoin appears to modulate the fibroproliferative and remodeling phases of wound healing, but the extent of each remains unclear and likely is dose-dependent.¹⁵ Therefore, isotretinoin may modulate internal scar formation, serving as a useful adjunct in scar management.

Safety and Guidelines for Isotretinoin Use in External Procedures

This up-to-date review on perioperative systemic isotretinoin use and safety in external skin resurfacing and surgical interventions largely corroborates previous reviews and recommendations on the topic, including 2017 consensus statements

by the American Academy of Dermatology and the American Society for Dermatologic Surgery Task Force (Table 1).^{4,5} Studies since 2017 are in keeping with their reports.^{41,42} There is insufficient evidence for medical practitioners to delay manual or focal dermabrasion, microdermabrasion, laser hair removal, fractional ablative laser, nonablative laser, fractional radiofrequency microneedling, or superficial chemical peels in the setting of oral isotretinoin use.^{4,5} In fact, many studies have demonstrated the synergistic benefits of performing these procedures to combat acne vulgaris and acne scarring for patients with severe nodulocystic acne requiring concomitant isotretinoin.^{4,5,41} In contrast, deeper skin resurfacing procedures relying on extensive reepithelialization (eg, non-fractional ablative lasers, mechanical or rotary dermabrasion, medium to deep chemical peels) should be delayed 6 to 12 months to minimize the risks of aberrant wound healing and scarring.^{4,5}

Safety and Guidelines for Isotretinoin Use in Internal Procedures (Surgery)

Despite studies including recent systematic reviews demonstrating the safety of performing

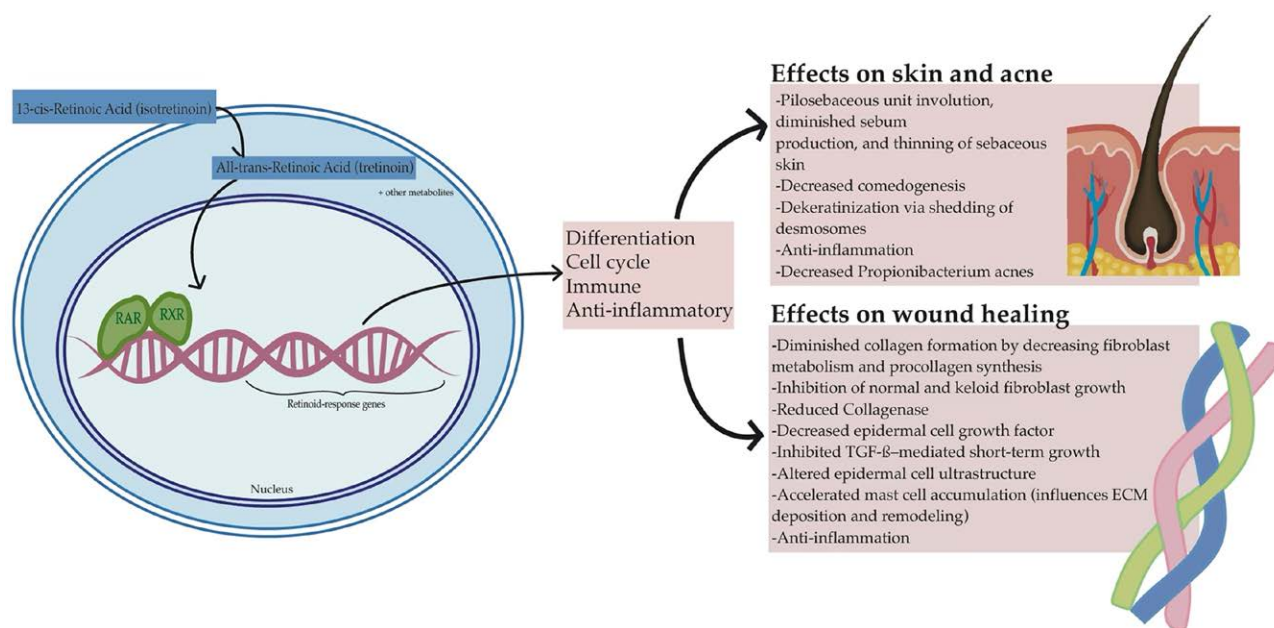


Fig. 2. Isotretinoin mechanisms of action. *ECM*, extracellular matrix.

surgery on patients actively taking isotretinoin, many plastic surgeons and health care providers remain unaware of its safety profile and may unnecessarily delay surgical treatments.^{6–11} Patients receiving isotretinoin have undergone various surgical procedures without wound-healing problems, including blepharoplasties, liposuction, fat transfers, face lifts, skin excisions, scar revision, abdominoplasty, breast surgery (including reductions), hidradenitis excisions, and shoulder arthroscopy (see Table, Supplemental Digital Content 2, <http://links.lww.com/PRS/H507>).^{4,5,8,10,11,36,43–50} Reviews largely corroborate these findings; however, some authors proposed that isotretinoin may weaken maturing scars and could increase risk of postoperative alveolar osteitis in wisdom tooth extractions.^{4,5,7–11,45,51,52}

There is a paucity of studies evaluating isotretinoin effects on the healing of other tissue types. Myalgias and rhabdomyolysis after exercise are known effects on skeletal muscle. Previous authors have surmised that patients taking isotretinoin may represent a high risk for muscle flap failure by rhabdomyolysis, particularly if they demonstrate elevated creatine phosphokinase levels preoperatively. In an assessment of cartilage and tendon thickness by ultrasound, one study reported cartilage thinning at the lateral femoral condyle after isotretinoin use, but at no other locations.⁵³ Other authors reported thinning of cartilage graft and total ossicular replacement prosthesis extrusion after initiation of isotretinoin, but discussed that this could be related to thinning of the dermal coverage.⁵⁴ Isotretinoin

does not appear to impair bony healing, and may accelerate healing or even promote hyperostosis, according to some studies.^{55–57}

This review supports the notion that isotretinoin is not prohibitive of wound healing for surgical patients, and there is no clear evidence to delay surgery. Nonetheless, surgeons and patients should have an informed discussion on a case-by-case basis.

Indications and Mechanisms for Isotretinoin in Rhinoplasty and Facial Plastic Surgery

Isotretinoin may have tremendous clinical potential in the setting of facial plastic surgery and select rhinoplasty procedures. In addition to rhinoplasty, isotretinoin is a potentially useful adjunct to improve skin quality and results after face lift and resurfacing procedures in select patients.¹⁰ However, the data regarding adjunctive isotretinoin in nonrhinoplasty facial cosmetic surgery are limited to a single study (12 blepharoplasty and 9 face lift procedures), demonstrating enhanced skin quality.⁵⁰ Primary implications of isotretinoin in rhinoplasty are twofold: thinning of thick and sebaceous skin and the hypothesized modulation of wound healing to limit internal scarring (dead space scar volume) and diminish swelling.^{10,12,15–18} Thinning of sebaceous, glabrous skin is a well-established effect in patients with acne vulgaris, hyperkeratinization, or sebaceous hyperplasia.^{23,24,29} To what effect isotretinoin limits internal scarring and optimizes healing is unknown.¹⁵

Indications for systemic isotretinoin use in rhinoplasty may include select patients with thick and sebaceous skin, especially those with acne vulgaris or rosacea; ethnic rhinoplasty; male sex; or surgical revision.^{10,14,16,20,21} Patients with severe acne vulgaris or rosacea typically exhibit thick, inflamed, and sebaceous skin. Populations receiving ethnic rhinoplasty with a propensity for glabrous or thick skin include Black, Indian, Hispanic, or Middle Eastern patients; however, there is significant diversity within these groups.¹⁹ Male patients are also more likely to have thick soft-tissue envelopes.²⁰ Patients receiving revision rhinoplasty require meticulous dead-space closure and are at higher risk for cicatricial problems in the setting of weaker cartilage framework due to excessive dead-space scarring, so they may benefit from exerted effects of isotretinoin on internal scarring.⁵⁸

Patients with thick nasal skin present a challenge for rhinoplasty surgeons due to the difficulty in attaining definition of the underlying osseocartilaginous structure beneath the soft-tissue envelope.²¹ Achieving adequate nasal tip definition, projection, and supratip break (in women) is paramount to modern rhinoplasty aesthetics.^{21,58} Multiple maneuvers are performed to combat poor nasal definition intraoperatively, including strong structural grafts, tip shaping, subcutaneous thinning of the envelope, and meticulous dead-space obliteration; however, the cosmetic outcome often remains suboptimal in these patients.^{10,12–14,16,17,21,58} The senior author (R.J.R.) has written extensively about these maneuvers previously.^{21,58} The ability to thin the soft-tissue envelope itself and further limit dead space and scar formation has prompted the senior author and rhinoplasty surgeons across the world to investigate the application of isotretinoin.^{13,14}

The first report of oral isotretinoin use in the setting of rhinoplasty included concerns by the authors due to patients ($n = 3$) who developed skin thinning and nasal tip deformities.⁵⁹ However, these patients did not start oral isotretinoin until 7 months, 1 year, and 2 years postoperatively. The dosing was not reported. This could be related to various factors such as drug strength, technique of the underlying construct, or failure to obliterate dead space with subsequent internal scar thinning or maturation, resulting in the underlying cartilaginous framework with cicatricial changes. Subsequent studies have not reported wound-healing problems of either columellar or alar-base incisions, cartilaginous deformation, aberrant scar maturation, or other cosmetic issues related to isotretinoin.^{10,12–14,17,18,22} Pertinent to

rhinoplasty, isotretinoin is known to dry the nasal mucosal membrane and increase epistaxis, which could signify the potential for poor mucosal healing. However, there have been no reports of poor nasal mucosal healing outside of a rabbit model.⁴⁰

The optimal dosing regimen and perioperative timing for oral isotretinoin are unknown. Cobo and Vitery¹⁸ published a series of 17 patients with significantly enhanced nasal tip definition and skin appearance when low-dose isotretinoin (0.25 mg/kg to 0.5 mg/kg) was initiated within a few months postoperatively for 4 to 6 months. In a double-blinded placebo-controlled clinical trial, Sazgar et al.¹⁷ trialed a low-dose (0.5 mg/kg) treatment every other day for 1 month starting 1 month postoperatively, then daily for 2 additional months. Patient satisfaction and surgeon-rated outcomes improved significantly with isotretinoin at short-term follow-up (3 and 6 months), but equalized by 1 year.¹⁷ Similar findings were reported by Yahyavi et al.,¹² as 149 of 350 patients underwent 0.3 mg/kg/day (20 mg/day) isotretinoin beginning 2 weeks before surgery and without interruption until 2 months postoperatively. Nearly all patients (98%) underwent alar-base reductions and cartilage grafting without any problems with healing or unexpected framework changes.¹² Improved patient satisfaction was reached early postoperatively (1 and 3 months) with isotretinoin use, but was not significant at 6 and 12 months postoperatively.¹² Early improvements could be related to modulating scar maturation, inflammation, and skin thinning, but late-stage scar maturation propagates after 1 year, and skin changes reverse without an adequate duration of therapy. Silveira et al.⁶⁰ reported similar conclusions in a randomized controlled trial with 12 of 24 patients undergoing isotretinoin 20 mg/kg/day from 2 months preoperatively to 4 months postoperatively. At 6 months, there was significant thinning of epidermis and dermis at the tip, dorsum, and alae on ultrasound evaluation.⁶⁰ Isotretinoin-treated patients also reported higher satisfaction.⁶⁰

Heppt et al.¹⁰ reviewed the utility of retinoids in facial plastic surgery, and described their experience with low-dose isotretinoin for 6 to 10 months to thin the nasal skin preoperatively (held for 6 months before surgery) in 17 patients undergoing rhinoplasty. This study noted optimized tip shaping and visualization, diminished edema, fewer nasal splint-associated acne flares, and improved planning. If the patient was deemed to benefit from restarting isotretinoin postoperatively, it was not initiated until at least 6 months after surgery to allow for adequate healing and to minimize



Fig. 3. Preoperative and 4-month postoperative photographs of a woman who underwent isotretinoin 20 mg/day treatment for 6 weeks preoperatively, followed by secondary rhinoplasty and continued isotretinoin until 4 months postoperatively. Note thinning of her thick, sebaceous skin and enhanced nasal tip definition.

potential adverse effects on wound healing. Kosins and Obagi¹⁴ discussed their experience with thick-skinned rhinoplasty cases and advocated a postoperative low-dose regimen (20 mg/day) starting 3 to 4 weeks after surgery and continuing for 4 to 5 months. See [Table 2](#) for a summary of rhinoplasty data.

For acne vulgaris treatment, isotretinoin is curative long-term for the majority of patients due to lasting effects on sebaceous glands, but as many as 26% of patients required a second round of treatment over the long term.^{23,61} The importance of cumulative dose, cited to be 120 to 150 mg/kg,^{15,23} in acne clearance is discussed extensively, although challenged among some experts. This is traditionally achieved with 4 to 6 months of therapy at 0.5 to 1.0 mg/kg/day.²³ Indeed, the length of sebaceous gland suppression accounts for clearance and relapse rate.¹⁵ High-dose isotretinoin induces sebocyte and sebaceous gland stem cell apoptosis, thereby requiring shorter treatment duration. In contrast, low-dose or microdose (0.1 to 0.2 mg/

kg/day) regimens can achieve excellent outcomes while minimizing side effects, but they require treatment periods of 8 to 12 months to attain adequate duration of sebaceous cell suppression.¹⁵

Without long-term data regarding the dose response of isotretinoin effects on the nasal soft-tissue envelope in rhinoplasty, the data herein are extrapolated from the acne literature. Although short-term thinning is evident, the notion of whether thinning is maintained remains controversial, and likely relates to the degree of sebaceous tissue apoptosis. A sustained diminution in sebum production has been shown at least 1 year after treatment.⁶² Yigit et al.¹⁶ demonstrated that both the nasal dermis and underlying soft tissue are substantially reduced and have improved elasticity in the acne vulgaris population on low-dose isotretinoin. This study reported significant benefit by 2 months of therapy and further benefit within 4 months. The authors reported quicker and more diffuse thinning of the nasal envelope using 0.5 mg/kg/day versus 0.25 mg/kg/day, but both doses were

ultimately efficacious by 4 months, reinforcing the importance of dose response in sebocytes.¹⁶ Unlike the treatment plan for acne vulgaris, which can be monitored clinically to tailor therapy, the end target of treatment is more challenging to ascertain for rhinoplasty candidates; duration and monitoring similar to acne regimens could be considered for skin-thinning response.

Another consideration regarding the ideal regimen relates to reducing internal scar formation, dead-space closure, and swelling. Much remains to be elucidated; however, a dose-dependent effect on internal scar modulation may hold true. In regard to timing, treatment could be initiated preoperatively to take advantage of these potential mechanisms. In the senior author's (R.J.R.) experience with several thick-skinned revision rhinoplasty cases, a low-dose (20 mg/day) therapy may be initiated 1 week to 2 months before surgery and treated through 3 to 6 months postoperatively (until satisfactory thinning and definition is achieved). This entails a discussion regarding the limitations of rhinoplasty due to the soft-tissue envelope, the mitigating potential of isotretinoin, as well as its possible risk profile. No wound-healing issues were reported; in fact, there has been notable improvement in early rhinoplasty results (Fig. 3). As such, surgeons could consider a longer preoperative duration to achieve soft-tissue envelope thinning and elasticity, aiding intraoperative tip and structural shaping with greater predictability. Despite a paucity of evidence to support holding isotretinoin perioperatively, surgeons should use their judgment on a patient-to-patient basis. If isotretinoin is held, patients may not benefit from these purported perioperative advantages. Future studies with long-term outcomes are needed to determine the optimal dose and schedule of treatment perioperatively as it pertains to rhinoplasty.

Isotretinoin Adverse Effects and Monitoring

Plastic surgeons using oral isotretinoin should be aware of the adverse effects and management guidelines. It is recommended to work closely with a board-certified dermatologist due to the required monitoring. The primary side effects of isotretinoin are common, including mucocutaneous problems (eg, cheilitis, xerosis, epistaxis), among others.²³ These are dose-related, which is why many prescribers favor low-dose regimens (≤ 0.5 mg/kg/day). Sun protection and skin moisturizers are paramount. Major contraindications to therapy include pregnancy, inflammatory

bowel disease, hepatitis, drug addiction, and unreliable patients.²³ Isotretinoin is a grade X teratogen and carries a black box warning, thus requiring monthly pregnancy tests in women, 2 forms of contraception or abstinence, and registration with the iPledge monitoring program.²³ Liver function tests, serum cholesterol, and triglycerides must be monitored during use.²³ There is controversy regarding an association with inflammatory bowel disease, depression, and psychosis; meta-analyses have failed to demonstrate this association. Patients should be screened for depression, suicidality, or history of violent behavior.²³ Concomitant tetracycline use is contraindicated due to reports of benign intracranial hypertension.²³

CONCLUSIONS

This review challenges concerns about effects of isotretinoin use on surgical wound healing. Isotretinoin appears to be safe and potentially beneficial in thinning skin and modulating scarring, particularly in rhinoplasty for specific candidates. While further research is needed to define optimal dosing and long-term benefits, this review highlights the potential value of isotretinoin as an adjunct in plastic surgery. Further investigations examining the optimal dosing regimen and long-term benefits are warranted.

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DISCLOSURE

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PATIENT CONSENT

The patient provided written informed consent for the use of her images.

REFERENCES

1. Roenigk HH, Pinski JB, Robinson JK, Hanke CW. Acne, retinoids, and dermabrasion. *J Dermatol Surg Oncol*. 1985;11:396–398.

2. Rubenstein R, Roenigk HH, Stegman SJ, Hanke CW. Atypical keloids after dermabrasion of patients taking isotretinoin. *J Am Acad Dermatol*. 1986;15:280–285.
3. Zachariae H. Delayed wound healing and keloid formation following argon laser treatment or dermabrasion during isotretinoin treatment. *Br J Dermatol*. 1988;118:703–706.
4. Spring LK, Krakowski AC, Alam M, et al. Isotretinoin and timing of procedural interventions: a systematic review with consensus recommendations. *JAMA Dermatol*. 2017;153:802–809.
5. Waldman A, Bolotin D, Arndt KA, et al. ASDS guidelines task force: consensus recommendations regarding the safety of lasers, dermabrasion, chemical peels, energy devices, and skin surgery during and after isotretinoin use. *Dermatol Surg*. 2017;43:1249–1262.
6. McDonald KA, Shelley AJ, Alavi A. A systematic review on oral isotretinoin therapy and clinically observable wound healing in acne patients. *J Cutan Med Surg*. 2017;21:325–333.
7. Hatami P, Balighi K, Asl HN, Goodarzi A, Aryanian Z. Isotretinoin and timing of procedural interventions: clinical implications and practical points. *J Cosmet Dermatol*. 2023;22:2146–2149.
8. Davies MJ, Perkins D. Oral isotretinoin (Roaccutane) use during incisional surgery: safe or risky? *Case Reports Plast Surg Hand Surg*. 2022;9:131–134.
9. Patel AA, Lee AH, Spiegel JH. Should isotretinoin be stopped prior to surgery? *Laryngoscope*. 2022;132:724–725.
10. Heppt MV, Kirchberger MC, Ruzicka T, Berking C, Heppt WJ. Indications and use of isotretinoin in facial plastic surgery. *Facial Plast Surg*. 2018;34:75–81.
11. Ungarelli LF, Hetem CMC, Junior JAF. Is it safe to operate on patients taking isotretinoin? *Aesthetic Plast Surg*. 2016;40:139–148.
12. Yahyavi S, Jahandideh H, Izadi M, Paknejad H, Kordbache N, Taherzade S. Analysis of the effects of isotretinoin on rhinoplasty patients. *Aesthet Surg J*. 2020;40:NP657–NP665.
13. Guyuron B, Lee M. An effective algorithm for management of noses with thick skin. *Aesthetic Plast Surg*. 2017;41:381–387.
14. Kosins AM, Obagi ZE. Managing the difficult soft tissue envelope in facial and rhinoplasty surgery. *Aesthet Surg J*. 2017;37:143–157.
15. Rademaker M. Isotretinoin: dose, duration and relapse. What does 30 years of usage tell us? *Australas J Dermatol*. 2013;54:157–162.
16. Yigit E, Rakici IT, Seden N, Manav V, Kaygisiz I, Yigit O. The impact of isotretinoin therapy on the nasal skin thickness and elasticity: an ultrasonography and elastography based assessment in relation to dose and duration of therapy. *Aesthetic Plast Surg*. 2022;46:1760–1770.
17. Sazgar AA, Majlesi A, Shooshtari S, Sadeghi M, Sazgar AK, Amali A. Oral isotretinoin in the treatment of post-operative edema in thick-skinned rhinoplasty: a randomized placebo-controlled clinical trial. *Aesthetic Plast Surg*. 2019;43:189–195.
18. Cobo R, Vitery L. Isotretinoin use in thick-skinned rhinoplasty patients. *Facial Plast Surg*. 2016;32:656–661.
19. Rohrich RJ, Bolden K. Ethnic rhinoplasty. *Clin Plast Surg*. 2010;37:353–370.
20. Rohrich RJ, Mohan R. Male rhinoplasty: update. *Plast Reconstr Surg*. 2020;145:744e–753e.
21. Sieber DA, Rohrich RJ. Finesse in nasal tip refinement. *Plast Reconstr Surg*. 2017;140:277e–286e.
22. Saadoun R, Riedel F, D'Souza A, Veit JA. Surgical and non-surgical management of the nasal skin-soft tissue envelope. *Facial Plast Surg*. 2021;37:790–800.
23. Layton A. The use of isotretinoin in acne. *Dermatoendocrinol*. 2009;1:162–169.
24. Paichitrojjan A, Paichitrojjan A. Oral isotretinoin and its uses in dermatology: a review. *Drug Des Devel Ther*. 2023;17:2573–2591.
25. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol*. 2016;74:945–973.
26. Dispenza MC, Wolpert EB, Gilliland KL, et al. Systemic isotretinoin therapy normalizes exaggerated TLR2-mediated innate immune responses in acne patients. *J Invest Dermatol*. 2012;132:2198–2205.
27. Abdelmalek M, Spencer J. Retinoids and wound healing. *Dermatol Surg*. 2006;32:1219–1230.
28. Abergel RP, Meeker CA, Oikarinen H, Oikarinen AI, Uitto J. Retinoid modulation of connective tissue metabolism in keloid fibroblast cultures. *Arch Dermatol*. 1985;121:632–635.
29. Park H, Del Rosso JQ. Use of oral isotretinoin in the management of rosacea. *J Clin Aesthet Dermatol*. 2011;4:54–61.
30. Oikarinen H, Oikarinen AI, Tan EML, et al. Modulation of procollagen gene expression by retinoids. Inhibition of collagen production by retinoic acid accompanied by reduced type I procollagen messenger ribonucleic acid levels in human skin fibroblast cultures. *J Clin Invest*. 1985;75:1545–1553.
31. Cruz NI, Korchin L. Inhibition of human keloid fibroblast growth by isotretinoin and triamcinolone acetonide in vitro. *Ann Plast Surg*. 1994;33:401–405.
32. Bauer EA, Seltzer JL, Eisen AZ. Inhibition of collagen degradative enzymes by retinoic acid in vitro. *J Am Acad Dermatol*. 1982;6:603–607.
33. Sporn MB, Roberts AB, Roche NS, Kagechika H, Shudo K. Mechanism of action of retinoids. *J Am Acad Dermatol*. 1986;15:756–764.
34. Arboleda B, Cruz NI, Cruz NI. The effect of systemic isotretinoin on wound contraction in guinea pigs. *Plast Reconstr Surg*. 1989;83:118–121.
35. Gencoglan G, Tosun M, Gencoglan O. Isotretinoin-induced effects of mast cells on wound healing. *J Drugs Dermatol*. 2010;9:1207–1210.
36. Larson DL, Flugstad NA, O'Connor E, Kluesner KA, Plaza JA. Does systemic isotretinoin inhibit healing in a porcine wound model? *Aesthet Surg J*. 2012;32:989–998.
37. Dzubow LM, Miller WH. The effect of 13-cis-retinoic acid on wound healing in dogs. *J Dermatol Surg Oncol*. 1987;13:265–268.
38. Frosch PJ, Czarnetzki BM. Effect of retinoids on wound healing in diabetic rats. *Arch Dermatol Res*. 1989;281:424–426.
39. Moy RL, Moy LS, Bennett RG, Zitelli JA, Uitto J. Systemic isotretinoin: effects on dermal wound healing in a rabbit ear model in vivo. *J Dermatol Surg Oncol*. 1990;16:1142–1146.
40. Cengiz AB, Ozyilmaz C, Tabaru A, et al. Effects of oral isotretinoin on normal and wounded nasal mucosa: an experimental study. *Eur Arch Otorhinolaryngol*. 2018;275:3025–3031.
41. Xue H, Ye D, Huang SL, et al. Early acne scar intervention with 1064 nm picosecond laser in patients receiving oral isotretinoin: a randomized split-face controlled pilot study. *Lasers Med Sci*. 2023;38:40.
42. Kim J, Jongudomsombat T, Lee YI, et al. Combined use of energy-based interventions with low-dose isotretinoin for the treatment of inflammatory acne: an retrospective cohort analysis. *J Cosmet Dermatol*. 2022;21:4383–4391.
43. Strock D, Sivesind TE, Dellavalle RP, Mundinger GS. Isotretinoin use in transmasculine patients and its implication on chest masculinization surgery: scoping review of the literature. *JMIR Dermatol*. 2023;6:e45351.
44. Tan SR, Tope WD. Effect of acitretin on wound healing in organ transplant recipients. *Dermatol Surg*. 2004;30:667–673.

45. Sharma J, Thiboutot DM, Zaenglein AL. The effects of isotretinoin on wisdom tooth extraction. *J Am Acad Dermatol*. 2012;67:794–795.
46. Huoh KC, Chang KW. Lip abscess associated with isotretinoin treatment of acne vulgaris. *JAMA Dermatol*. 2013;149:960–961.
47. Yew YW, Pan JY. Complete remission of recalcitrant genital warts with a combination approach of surgical debulking and oral isotretinoin in a patient with systemic lupus erythematosus. *Dermatol Ther*. 2014;27:79–82.
48. Wootton CI, Cartwright RPE, Manning P, Williams HC. Should isotretinoin be stopped prior to surgery? A critically appraised topic. *Br J Dermatol*. 2014;170:239–244.
49. Mahadevappa OH, Mysore V, Viswanath V, et al. Surgical outcome in patients taking concomitant or recent intake of oral isotretinoin: a multicentric study: ISO-AIMS Study. *J Cutan Aesthet Surg*. 2016;9:106–114.
50. Hernandez-Perez E, Khawaja HA, Alvarez TYM. Oral isotretinoin as part of the treatment of cutaneous aging. *Dermatol Surg*. 2000;26:649–652.
51. Aksoy HM, Aksoy B, Çalikoglu E. Systemic retinoids and scar dehiscence. *Indian J Dermatol*. 2019;64:68–70.
52. Tolkachjov SN, Sahoo A, Patel NG, Lohse CM, Murray JA, Tollefson MM. Surgical outcomes of patients on isotretinoin in the perioperative period: a single-center, retrospective analysis. *J Am Acad Dermatol*. 2017;77:159–161.
53. Yıldızgören MT, Karataş Toğral A, Baki AE, Ekiz T. Effects of isotretinoin treatment on cartilage and tendon thicknesses: an ultrasonographic study. *Clin Rheumatol*. 2015;34:1255–1258.
54. Alwabli M, Alotaibi N, Alamry S. Prosthesis extrusion post total ossicular replacement ossiculoplasty (TORP) following isotretinoin use: a case report and literature review of peri-operative isotretinoin safety. *Ann Med Surg*. 2022;81:104469.
55. De Oliveira HTR, Bergoli RD, Hirsch WDB, Chagas OL, Heitz C, Silva DN. Isotretinoin effect on the repair of bone defects: a study in rat calvaria. *J Craniomaxillofac Surg*. 2013;41:581–585.
56. DiGiovanna JJ. Isotretinoin effects on bone. *J Am Acad Dermatol*. 2001;45:S176–S182.
57. Bergoli RD, Junior OLC, de Souza CEC, et al. Isotretinoin effect on alveolar repair after exodontia: a study in rats. *Oral Maxillofac Surg*. 2011;15:85–92.
58. Savetsky IL, Avashia YJ, Rohrich RJ. The five-step rhinoplasty dead space closure technique. *Plast Reconstr Surg*. 2022;149:679e–680e.
59. Allen BC, Rhee JS. Complications associated with isotretinoin use after rhinoplasty. *Aesthetic Plast Surg*. 2005;29:102–106.
60. Silveira CSC, Azulay-Abulafia L, Barcaui EO, Silva MMM, Roxo ACW. Analysis of the use of isotretinoin as an adjuvant in rhinoplasty. *Int J Dermatol*. 2023;63:224–231.
61. Azoulay L, Oraichi D, Bérard A. Isotretinoin therapy and the incidence of acne relapse: a nested case-control study. *Br J Dermatol*. 2007;157:1240–1248.
62. Hughes BR, Cunliffe WJ. A prospective study of the effect of isotretinoin on the follicular reservoir and sustainable sebum excretion rate in patients with acne. *Arch Dermatol*. 1994;130:315–318.