

ORIGINAL ARTICLE

Triple steps acne scar revision technique: A new combination therapeutic modality for atrophic acne scars

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Abstract

Background: Atrophic acne scarring is an unfortunate, permanent complication of acne vulgaris, associated with significant psychological distress.

Objective: A new complementary treatment of atrophic acne scars using subcision and injection of hybrid cooperative complexes of high and low molecular weight hyaluronan (hybrid H-HA/L-HA).

Methods: This study included eighty-two patients divided into two groups with predominantly atrophic acne scarring. Group 1 received subcision with saline injection, while group 2 received triple steps acne scar revision technique (TSASRT). After topical anesthesia, the procedure of combining subcision and hybrid H-HA/L-HA technique was done in which the first step started using subcision technique done to release fibrous cords at the dermal or deep dermal, subcutaneous plane using Nokor needles-18 g. The second step is to inject the scar's atrophic dermal component with a 29 g needle, applying an average amount of hybrid H-HA/L-HA (0.02–0.1 mL) to the dermal component. The third step was to fill the subcised space with hybrid H-HA/L-HA (0.02–0.1 mL) using a 25 g cannula.

Results: Clinical improvement was achieved in both groups. There were statistically significant improvements in the TSASRT versus subcision ($p \leq 0.05$) in acne scar severity index and qualitative scarring grading system.

Conclusion: The triple step acne scar revision technique appears to be a safe and effective way to treat atrophic acne scars on the face.

KEYWORDS

acne scar, hyaluronic acid, hybrid cooperative complexes of high and low molecular weight hyaluronans, nokor, subcision

1 | INTRODUCTION

This is because of the high prevalence and significance of scarring [up to 95% of acne patients¹], causing mutilation and a significant emotional impact on quality of life.^{2,3} Atrophic acne scars are still the most frequent form, and the most basic and practical system categorizes atrophic acne scars into three major types: ice pick, rolling, and boxcar.² Over the decades, various therapeutic approaches have improved acne scars.⁴

For many years, subcutaneous incisionless (subcision) surgery has treated various skin depressions, including atrophic acne scars, depressed scars, and fine lines. Scar improvement mechanisms include the release of fibrotic cords beneath scars, blood organization in the induced dermal pocket, and the formation of connective tissue in the region.^{5,6} Hyaluronic acid (HA) regulates tissue moisturization and permeation to small and large molecules.⁷ Intradermal injection of hybrid H-HA/L-HA resulted in human fibroblast manipulation and a significant reduction in acne scars.⁸

We wanted to study patients with atrophic acne scars, so we decided to use subcision and injection of hybrid cooperative complexes of high and low molecular weight hyaluronan (hybrid H-HA/L-HA), a novel patented (WO/2012/032151) NAHYCOTM technology-based filler⁹ commercially available as hybrid H-HA/L-HA for treating acne scars as a triple step acne scar revision technique (TSASRT).

2 | PATIENTS AND METHODS

2.1 | Patients

The Research Ethical Committee approved the interventional, randomized, parallel-group study. The study was conducted in the Dermatology Outpatient Department for a year following the Helsinki Declaration guidelines, and all patients provided informed written consent. Healthy participants with predominantly atrophic acne scarring who presented to our outpatient clinic were invited to participate in the study. After computer-based randomization, we selected 101 patients and ended the study with 82 patients (Figure 1). Patients with acute inflammatory lesions, keloidal tendency, immunosuppression, energy-based therapies filler injections within the previous 6–12 months, infections such as herpes labialis, and those on systemic isotretinoin were excluded from the analysis. Before beginning therapy, patients underwent a full history, general and systemic examination, with a particular emphasis on local dermatological examination to assess the scars' number, location, and size. Even during the study period, patients were instructed not to use any therapies.

2.2 | Preparation of patients for both groups

Procedures were made under the same circumstances, in the same instruments, by the same physician, and with the same technique. Two sessions were held with one month apart and follow-up after 6 months [as maturational or remodeling phase of wound healing process around 6 months (3weeks and up to 12 months)].¹⁰

2.3 | Anesthesia

Under occlusion, topical anesthesia (EMLA cream) was used 1–2 h before the procedure. In patients with a significant number of scars on their cheek(s), an infraorbital nerve block was also conducted. If the lidocaine injection was required, the margins of the scar were labeled to prevent the scar from vanishing after injection, and lidocaine was infused subcutaneously without epinephrine. Povidone-iodine was used to clean the operation area.

2.4 | Patients' position

During the procedures, the patients were in a semi-sitting position, which made the scars, particularly the rolling ones, more visible than in a supine position.

2.5 | Type of needle

Nokor needles were employed 18-gauge.

2.6 | Group (1) Subcision

In the *first step*, we excavated rolling, "superficial and deep box-cars," and pitted scars (except ice-pick scars). For releasing fibrous cords at the dermal or deep dermal, subcutaneous plane, a Nokor needle was inserted adjoining the scar, bevel upward and parallel to the skin surface, into the deep dermis moved back forth in a fan-like movement under the scar. When the fibrous cords were broken, snapping sounds could be heard. Homeostasis was achieved by simply placing a piece of ice without putting any pressure on it. In the *second step*, with a 29-gauge needle, an average amount of saline (0.02–0.1 mL) was applied to the dermal component. The *third step* was filling the subcised space with saline (0.02–0.1 mL) using a 25-gauge cannula.

2.7 | Group (2) the procedure of combining subcision and hybrid H-HA/L-HA technique (Triple steps acne scar revision technique (TSASRT)).

(Figure 2) The *first step* was made up of the previously mentioned subcision technique, but we replaced saline with hybrid H-HA/L-HA. The *second step* was to inject the scar's atrophic dermal component. With a 29-gauge needle, an average amount of hybrid H-HA/L-HA (0.02–0.1 mL) was applied to the dermal component. The *third step* was to fill the subcised space with hybrid H-HA/L-HA (0.02–0.1 mL) using a 25-gauge cannula.

The product under investigation (Profhilo[®], manufactured and scattered by IBSA Farmaceutici Italia Srl, Lodi, Italy) is a health-care device that contains a mixture of HMW-HA and LMW-HA packed in prefilled glass hypodermic needles for local injections. It is based on stable hybrid cooperative complexes of HA produced using a new technology (NAHYCO).⁷ In 2 mL of buffered sodium chloride physiologic solution, the HA concentration is 3.2 percent, with 32 mg of HMW-HA and 32 mg of LMW-HA. The existence of multiple HA molecular weights (high and low) in a single injection solution allows the integration of endogenous HA levels with balanced concentration levels of stabilized HA hybrid compounds.⁷

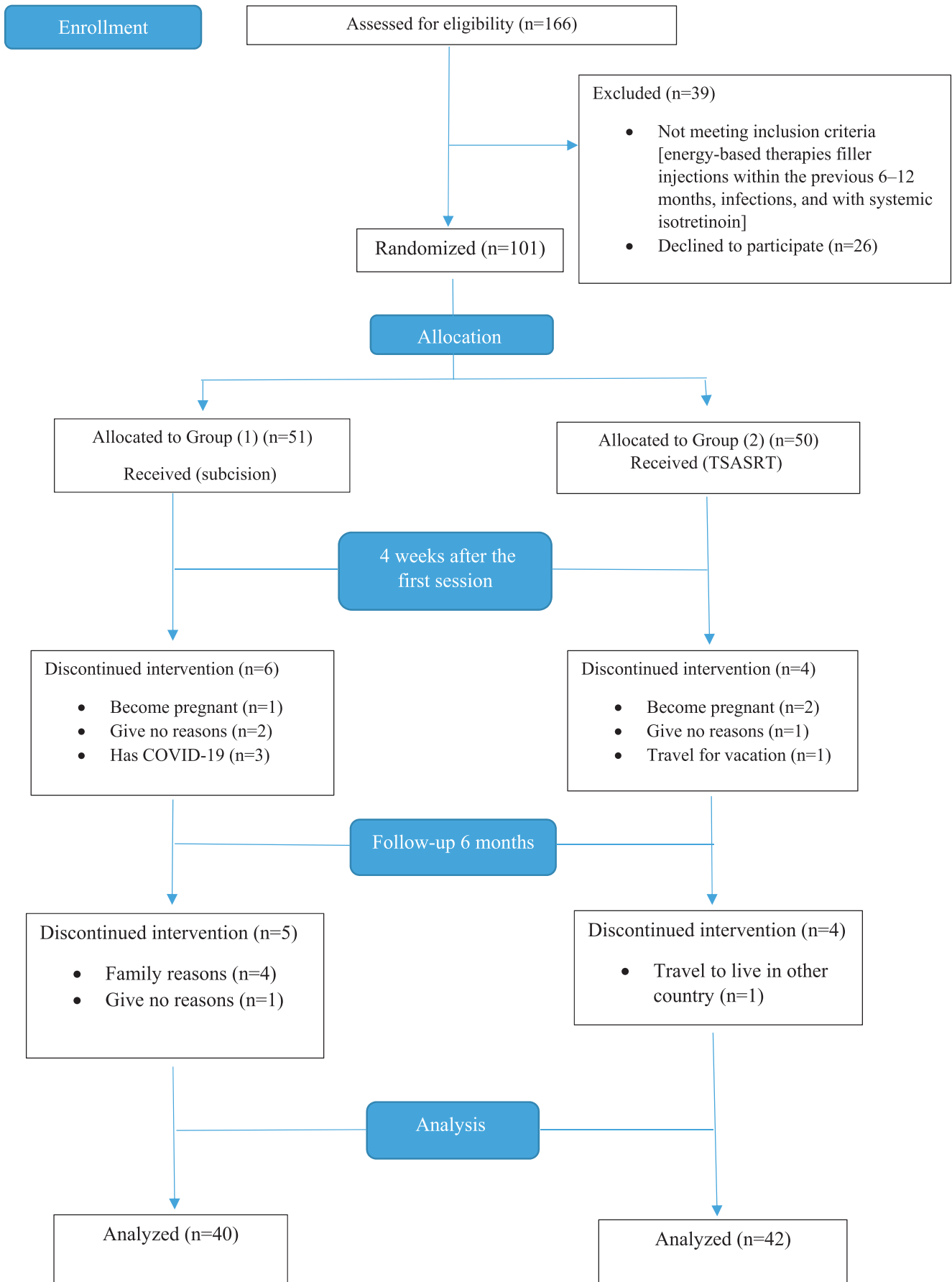


FIGURE 1 Consolidated Standards of Reporting Trials (CONSORT) Flow Diagram

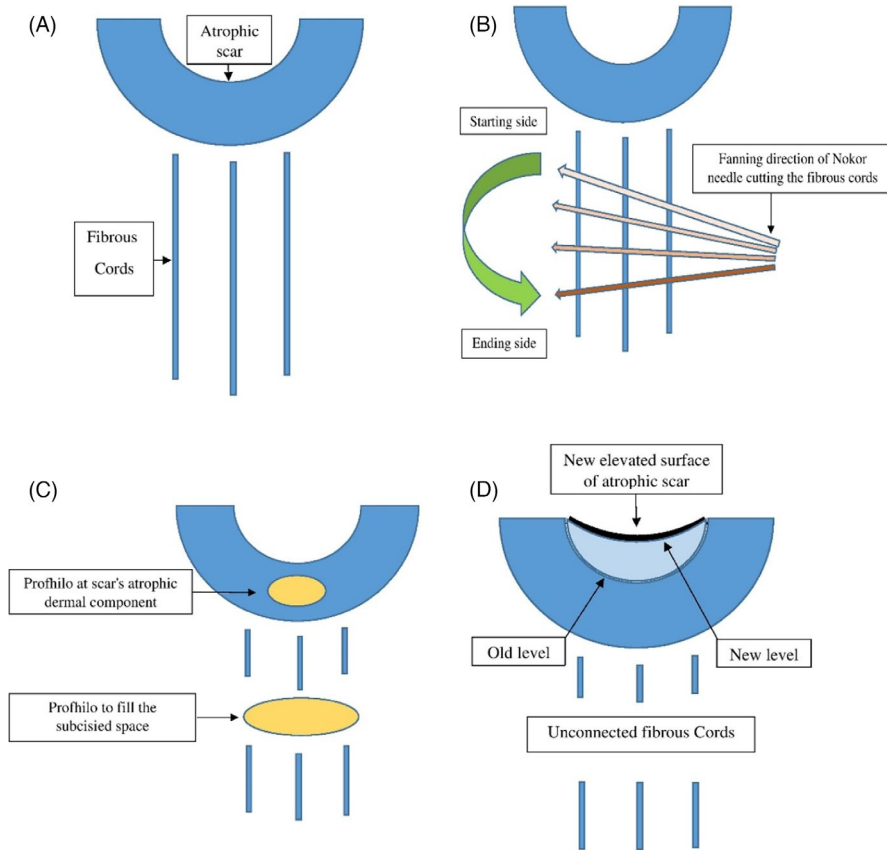


FIGURE 2 Triple step acne scar revision technique. (A) Atrophic scar. (B) First step is cutting the fibrous cords with NOKOR needle 18 g in fanning direction. (C) Second step is to inject the Profhilo® at the scar's atrophic dermal component with a 29 g needle [0.02–0.1 mL]. Third step is filling the subsided space with Profhilo® [0.02–0.1 mL] using a 25 g cannula. (D) New elevated scar surface after healing and new collagen formation

TABLE 1 Goodman and Baron grading scale¹²

Clinical features	Level of disease	Grades of Post Acne Scarring
These scars can be erythematous, hyper- or hypo-pigmented flat marks. They do not represent a problem of contour like other scar grades but of color.	Macular	1
Mild atrophy or hypertrophy scars that may not be obvious at social distances of 50 cm or greater and may be covered adequately by makeup or the normal shadow of shaved beard hair in men or normal body hair if extrafacial.	Mild	2
Moderate atrophic or hypertrophic scarring that is obvious at social distances of 50 cm or greater and is not covered easily by makeup or the normal shadow of shaved beard hair in men or body hair if extrafacial, but is still able to be flattened by manual stretching of the skin (if atrophic).	Moderate	3
Severe atrophic or hypertrophic scarring that is evident at social distances greater than 50 cm and is not covered easily by makeup or the normal shadow of shaved beard hair in men or body hair if extrafacial and is not able to be flattened by manual stretching of the skin.	Severe	4

2.8 | The post-treatment protocol

The use of sunscreen was maintained. Using camouflage makeup was permitted. Each visit, depth, appearance, and the number of acne scars were noted.

2.9 | Evaluation and assessment of results

The outcomes were evaluated with two independent professional observers' global assessments of clinical photographs and participants' self-assessments. Photographic documentation of

results obtained at baseline, before each treatment session, and six months after the last treatment. The following outcomes were evaluated and rated: first, determine the severity of acne scars (mild if the patient had 1–25 scars, moderate if the patient had 26–50 scars, and severe if the patient had more than 50 scars).¹¹ On a quartile weighted scale, improvement was categorized as excellent if scars were reduced by 70%, good if scars were reduced by 51%–70%, fair if scars were reduced by 30%–50%, and poor if scars were reduced by 30%. Second, the qualitative scarring grading system (Goodman and Baron grading scale¹²) was used (Table 1).¹² After the therapeutic interventions, patient satisfaction was measured using a three-point scale (well, fair, and poor).

At every treatment session and follow-up visit, side effect surveys were completed.

3 | STATISTICAL ANALYSIS

Data collection sheets were used to collect, summarize, and report data. They were entered into Microsoft Excel spreadsheets with appropriate tabulation and graphical presentation using SPSS version 25. The Chi-square test was used to compare categorical variables, and numerical variables were compared using the paired *t*-test. The *p*-value (level of significance) was set at 0.05. If the *p*-value is less than 0.05, the results are statistically significant.

4 | RESULTS

Out of 166, only 82 healthy individual post-acne scars were included in the study. Their mean ages were 24.4 ± 2.3 and 26.1 ± 1.2 (19–33) years in (TSASRT) study group and control group, respectively, which was matched ($p > 0.05$), and their mean duration was 10.1 ± 1.3 and 9.2 ± 2.1 (5–13) years in (TSASRT) study group and control group, respectively, which was matched ($p > 0.05$). The Fitzpatrick skin phototype in the experiment was matched ($p > 0.05$). Acne scar severity index and Goodman and Baron grading were matched between the two groups ($p > 0.05$). These observations are summarized in Table 2.

Clinical improvement was achieved in both groups, with minimal adverse effects consisting of mild transient erythema, ecchymosis, and edema immediately following each treatment session. There had been no evidence of scarring or hyperpigmentation due to the treatment.

There were statistically significant differences in the acne scar severity index, Goodman and Baron grading scale, and patient satisfaction evaluation score of both groups before and after treatment. ($p < 0.05$) (Table 3). However, the triple step technique group improved significantly more than the subcision group in terms of acne scar severity index, Goodman and Baron grading scale, and patient satisfaction evaluation score ($p < 0.05$) (Table 3) (Figures 3,4). There were significant improvements in rolling and boxcar scars versus ice-pick scars in both groups ($p < 0.05$) (Table 3).

From the perspective of investigators and patients, “the mean improvement” and “70% improvement or more” were significant in the study group compared with the control group (Table 4). Table 4 shows the statistically and clinically findings. Patients in study group were satisfied with considerable reduction in depth and size of scars and noticeable better appearance of their skin.

The following findings can be attributed to this study:

- Edema diminished within 2–5 days.
- Bruising gradually absorbed within 7–10 days.
- No hyperpigmentation, hypertrophic scar, and Hemorrhagic papule &/or pustule were observed in groups.

TABLE 2 Clinical features of the 82 participants at baseline

Variables		(TSASRT)study group (n = 42)	Control group (n = 40)	<i>p</i> value
Age (years), mean (SD)		24.4 ± 2.3	26.1 ± 1.2	>0.05
Gender	Male	13	16	>0.05
	Female	29	24	>0.05
Fitzpatrick skin phototype, n (%)	II	21.4	25	>0.05
	III	23.8	27.5	>0.05
	IV	28.6	25	>0.05
	V	26.2	22.5	>0.05
Duration of scars (years), mean (SD)		10.1 ± 1.3	9.2 ± 2.1	>0.05
Body mass index mean (SD)		22.1 ± 1.1	23.5 ± 3.3	>0.05
Acne scar severity index (by independent doctors)		1.584	1.324	>0.05
Goodman and Baron grading (by independent doctors)		2.231	2.324	>0.05
Types of scars	Rolling scars	42	40	>0.05
	Boxcar scars	42	40	>0.05
	Pitted scars	42	40	>0.05

Abbreviation: SD, standard deviation.

Significance *p* value ≤ 0.05 .

Non significant *p* value > 0.05 .

TABLE 3 Comparing of treatment using the (TSASRT) and subcision with injecting saline before and after 6 months of the second session

Variables		(TSASRT)study group (n = 42)		Control group (n = 40)	
		Before	After	Before	After
Acne scar severity index (by independent doctors)	Healed	0	17	0	10
	Mild	7	19	6	9
	Moderate	12	6	5	21
	Sever	23	0	29	0
p value		0.035*		0.041*	
		0.042*			
Goodman and Baron grading (by independent doctors)	Macular	0	18	0	10
	Mild	4	19	5	9
	Moderate	14	5	8	21
	Sever	24	0	27	0
p value		0.029*		0.035*	
		0.031*			
70% improvement or more assessed by investigators	Rolling scars	42	42	40	31
	Boxcar scars	42	42	40	29
	Pitted scars	42	0	40	0
p value		0.033*		0.049*	
		0.043*			
Patient satisfaction evaluation (by patient) After treatment	A	39		19	
	B	3		21	
	C	0		0	
	D	0		0	
p value		0.029*			

*Significance p value ≤ 0.05 .

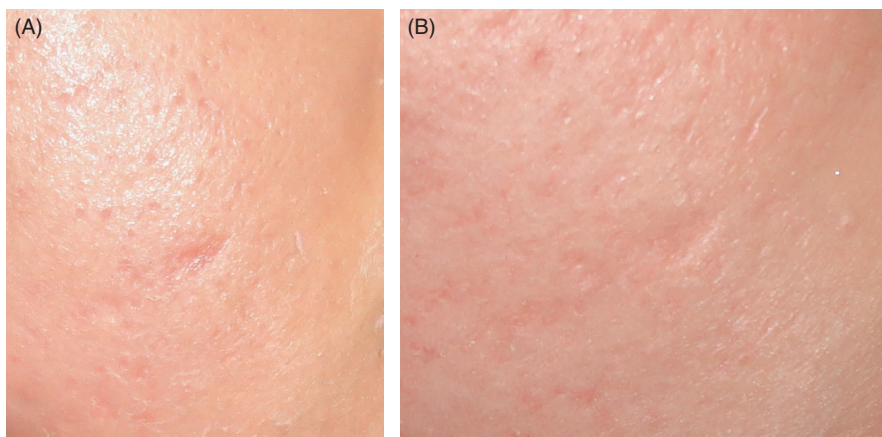


FIGURE 3 Case 1: (A) before treatment; (B) 6 months after two sessions of treatment. [Subcision group]

5 | DISCUSSION

Both the physician and patient found the treatment of post-acne scars to be a significant challenge.^{13–18} A wide range of treatments is available for atrophic acne scars. Skin type, scar type, treatment downtime, efficiency, adverse reactions, treatment plan, improvement perseverance, and patient needs all influence determining the ideal therapy for patients.

There is no single effective therapeutic strategic approach. Because of the disease's upsetting nature and emotional resonance with patients, quick and convenient treatments are highly sought after. Among the therapies for atrophic acne, scarring are surgical techniques (punch graft, punch excision, and subcision), resurfacing procedures (dermabrasion, ablative laser therapy, and exfoliation), other energy-based device therapies, allogenic fat transfer, and hyaluronic acid injections.¹⁹

FIGURE 4 Case 2: (A) before treatment; (B) 6 months after two sessions of treatment. [TSASRT group]

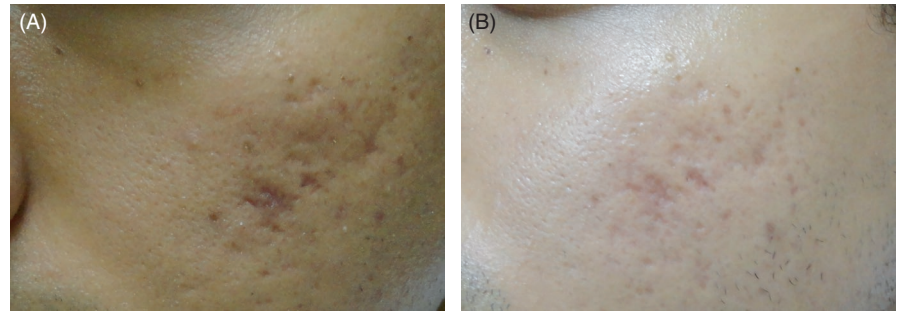


TABLE 4 Comparison of the results of the study and control group statistically and clinically 6 months after the second session

Variables	(TSASRT) study group (n = 42)	Control group (n = 40)
Mean improvement assessed by investigators	0.042*	
70% improvement or more assessed by investigators	0.038*	
Mean improvement assessed by patients	0.039*	
70% improvement or more by patients	0.043*	
Efficacy between investigators and patients	0.037*	
Acne scar reduction (rolling and boxcar scars)	0.044*	
Duration of bruising	0.063**	
Scar reappearance	0.034*	
Pigmentation, hypertrophic scar, and Hemorrhagic papule and/or pustule	-	

*Significance p value ≤ 0.05 .

**Non significant p value > 0.05 .

Subcision is a simple and painless surgical procedure that can be conducted in any skin area in minutes and has no adverse reactions. Even though scar recurrence is widely recognized as a limiting factor, subcision has a success rate of 15%–80%.^{20–22} In two studies, effectiveness is described as mild (30%),²² while in two others, progress is estimated to be around 50%.^{20,21} Depression in acne scars is caused by atrophy and the formation of fibrous tissue after acne has healed.²³ Scar surfaces separately from the fundamental attachment in subcision due to fibrotic tissue release, and a blood dermal pocket forms beneath the scar. Blood does more than just act as a temporary spacer to keep the tissue from connecting quite shortly.⁴ However, it is believed that subsequent blood organization will result in the formation of connective tissue, revision of the defect, and reconnection.^{1,24} These are the chief reason for injecting hybrid H-HA/L-HA to act as a space-occupying substance during the subcised scar healing process to prevent reconnection, delay dermal wound reconnection, and a more new connective tissue formation in the new higher level of healing. In other words, this method is based on removing the cause of depression as well as the bound-down appearance of scars, and it causes scar augmentation by using the patient's own connective tissue.

The Nokor needle is a common subcision tool.^{21,25} By pinching or stretching the skin, we could subcise various types of acne scars, including rolling, deep and superficial boxcars, and pitted ones (except ice pick).

HA is extensively used in cosmetic procedures like dermal fillers and restoration therapies. The high HA content of the human dermis enables hydration while maintaining proper tissue volume, protecting skin cells from mechanical injury. Alone or other molecules, HA accelerates wound healing (e.g., burn and ulcer).^{7,26} Furthermore, HA has anti-inflammatory and bio-stimulant properties and stimulates other signaling pathways through interactions between various biological membrane receptors.²⁷

Depending on its molecular weight, HA has different effects.²⁸ There is a significant increase in HA immediately following the initial stage of wound healing. HMW-HA accumulates and binds fibrinogen, which itself is required for clot formation. Furthermore, a significant amount of HMW-HA initially opens up tissue spaces, allowing polymorph nuclear cells access to the wound site to remove dead tissue, debris, and bacteria. Following that, during the inflammatory stage, there is a buildup of LMW-HA, which is generated by the degradation of HMW-HA, which produces cytokines and promotes angiogenesis.²⁹

Exogenous HMW-HA or LMW-HA has been studied extensively to know more about the contribution of HA in wound healing and to develop innovative pharmaceutical/cosmeceutical formulations based on HA size.^{27–35}

LMW-HA spurs fibroblast and keratinocyte proliferation by binding to specific receptors, supplying nourishment and deep hydration to aged skin. D'Agostino et al. have described the technology, rheological properties, and biological properties.⁷ HMW-HA, on the

contrary, has a dermal scaffolding effect due to its high potential to bind water molecules and engage with collagen and proteoglycans. Hybrid H-HA/L-HA can stimulate cellular proliferation in facial adipose tissue (Bichat fat pad), an origin of noncommittal staminal cells that differentiate into cutaneous fibroblasts.^{36,37}

Administration of a high-osmolality compound (e.g., hybrid H-HA/L-HA) into lymphatic vessel-enriched areas promotes diffusion until an osmotic equilibrium is reached. Hybrid H-HA/L-HA draws water molecules thru the lymphatic fenestrated capillary endothelium, allowing them to diffuse thru the interstitium and obtain overall balance, optimal circumstances for dermal cellular proliferation.³⁸

The stabilized hybrid HA cooperative complex formation occurred without the addition of any chemical cross-linking compound. In comparison with HMW-HA and LMW-HA alone, hybrid cooperative complexes have several advantages and distinguishing features, such as:

- a. Hybrid cooperative compounds have a longer half-life because they are more refractory to hyaluronidase than HMW-HA.⁷
- b. Transforming growth factor-1 (TGF-1) is less upregulated in hybrid cooperative compound-treated samples compared with LMW-HA-treated cells, indicating a low inflammatory reaction.⁷
- c. The viscosity of hybrid cooperative compounds is lower than LMW-HA and HMW-HA alone.⁷
- d. The hybrid cooperative compounds increased the expression of type I and type III collagen in fibroblasts and type IV and VII collagen in keratinocytes.³⁹
- e. The upsurge in elastin expression over a more extended period of period (up to 7 days) lends credence to clinically identified improvement in skin elasticity.³⁹
- f. HA concentration is high (64 mg/2 mL).⁹
- g. High controllability.⁷
- h. Tissue diffusion at its best.⁴⁰
- i. 1,4-butanediol diglycidyl ether (BDDE) and other chemical agents are not permitted.⁹
- j. Natural HA that has been thermally stabilized and has a duration comparable to a weakly cross-linked gel.^{7,40}

Hybrid H-HA/L-HA is used for enhancing collagen formation, rejuvenation, and skin lifting in face and body.^{41,42} This study treated 42 patients with atrophic acne scars with hybrid H-HA/L-HA at the scar's floor and filled the gap after subcision.

Hybrid H-HA/L-HA works in three ways. First, it occupies the space left after subcision, preventing the fibrous bands from re-connecting. Second, hybrid H-HA/L-HA creates optimum media for collagen formation. Third, because of the unique properties of hybrid H-HA/L-HA, high-quality collagen is formed, and scars heal at a higher level. Finally, reduce the number of subcision sessions.

Our findings outperformed those of a previous study that used microfat after subcision to treat severe atrophic acne scars and avert the reconnection of fibrous bonds.⁴³ Furthermore, using hybrid H-HA/L-HA after subcision produced better results than using

HA or threads after subcision, and with fewer sessions.⁴⁴ In severe atrophic acne scarring, TSASRT outperforms platelet-rich plasma as an adjunctive therapy to a combined subcision and needling treatment.⁴⁵ When compared to other studies, this study yielded excellent results, fewer sessions, a simple technique, and higher patient satisfaction.⁴³⁻⁴⁵

TSASRT used this gel for atrophic acne scars in conjunction with subcision, resulting in significant objective and subjective improvement. Patients tolerated the treatment well, and complications were minimal. The entire procedure takes 20 min and requires 0.5–2 mL of hybrid H-HA/L-HA.

Some limitations of the study are shared by all self-reported data studies, such as potential social favorability and retrospective recall biases. Furthermore, the sample's characteristics limit the generalizability of the results.

Furthermore, we propose that the study is expanded to include a larger number of people from different ethnic backgrounds and with different types of scars (post-chicken pox scars, burn scars, or surgical scars) to confirm or refute the current findings.

6 | CONCLUSION

The three-step acne scar revision technique (TSASRT) appears to be a safe and effective way to treat atrophic acne scars on the face. The advantages of hybrid H-HA/L-HA-based formulations be attributed to their pro-collagenogenic and pro-adipogenic properties.

CONFLICT OF INTEREST

None declared.

ETHICAL APPROVAL

The Research Ethical Committee of Shaqra university approved the interventional, randomized, parallel-group study.

DATA AVAILABILITY STATEMENT

The data used to support the finding of this study are included within the article.

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