

COMPARISON BETWEEN DIFFERENT TECHNIQUES FOR NASAL TIP PLASTY: TACO (SANDWICH) VERSUS TRADITIONAL COLUMELLAR STRUT GRAFT

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Abstract

Background: Aesthetic balance in rhinoplasty is essential to achieve optimal nasal tip projection and symmetry and functional airflow. The typical columellar strut graft has been discovered to be structurally stable; nevertheless, it results in the rigidity of the tips and loss of motion.

Objective: This study aims to provide a comparison of the functional and aesthetic results of the TACO (Sandwich) method and the Traditional Columellar Strut Graft in nasal tip plasty.

Methods: n=50 patients undergoing nasal tip plasty between January 2024 and January 2025 were used to conduct a prospective comparative study. Patients were randomly split into two categories: TACO technique (n = 25) and Traditional columellar graft (n = 25). Postoperative measurements were done on objective parameters such as Goode Ratio and Nasolabial Angle, and subjective measures such as Satisfaction Score and NOSE Score Improvement. The analysis was done with SPSS v26, where t-tests, Chi-square tests, correlation, and regression were used.

Findings: TACO group showed significantly better mean Goode Ratio (0.596 ± 0.028 , $p = 0.001$), Satisfaction Score (4.60 ± 0.35 , $p < 0.001$), and NOSE Score Improvement (23.02 ± 3.07 , $p = 0.001$) than the traditional group. The TACO group had fewer postoperative complications than the other groups, which included edema, asymmetry, and infection ($p > 0.05$). The regression analysis results have found that NOSE Score Improvement ($\beta = 0.399$, $p = 0.006$) was the strongest predictor of patient satisfaction, and Q-Q plots proved the data normality.

Conclusion: The TACO (Sandwich) nasal tip plasty is a major innovation in contrast to the traditional grafting techniques since it offers long-lasting structural support and aesthetic harmony of the form. It provides better projection of tips, good airflow, and reduced postoperative complications, and thus is a safe and

reliable tool in the current practice of rhinoplasty.

INTRODUCTION

Rhinoplasty is one of the most common aesthetic and functional surgical procedures in otorhinolaryngology and plastic surgery [1]. The part of it that is the most challenging is the nasal tip plasty because its structure is of a complex three-dimensional form, the support systems are sensitive, and a high degree of symmetry and projection is required. The tip of the nose is also significant in the cosmetic appearance of the nose, besides performing the right air flow and valve operation within the nose. Therefore, the fine line of manipulation of the tissues and support should be reached to achieve aesthetic perfection and coordination of functionality [2,3].

Columellar strut grafts are traditionally employed to support the tip of the nose in the middle, namely, with open rhinoplasty. The graft is mainly made of septal cartilage, and it is placed between the medial crura of the lower lateral cartilages to enhance projection of the tip, rotation, and definition. Even though the procedure has foreseeable results, it tends to over predict and stiffen and unnaturally as well as it happens in patients with hairy noses or those with limited cartilage sources. Moreover, there is another problem, that is, morbidity of different locations of donation, resorption, and warping, which can be detrimental over time [4].

Alternative grafting and structural methods have brought along nasal tip support, tissue flexibility, and natural appearance in the past few years. One of such innovative techniques is a TACO (sandwich) technique which presupposes that the graft material is positioned between the medial crura in form of taco. The result of such an approach is increased stability of tips, increased projection, rotation control and a more natural outcome after surgery. Besides, it allows defining the tip refinement with fewer chances of postoperative deformities, such as tip ptosis, asymmetry, and stiffness [5,6].

Of specific clinical interest is the comparison between the TACO (sandwich) method and the traditional columellar strut graft since both are

intended to produce similar outcomes, including the best tip projection, symmetry, and stability, but they are not similar in the direction of structure and biomechanics. There has been a lack of studies systematically comparing the two procedures in regard to functional, postoperative complications, and patient satisfaction, particularly in South Asian people whose nasal structure may be different than that of the West [7,8].

Consequently, the study was performed to compare the functional and aesthetic results of nasal tip plasty between the TACO (sandwich) technique and the conventional method of columellar strut graft (with special focus on postoperative tip projection, nasal symmetry, edema, patient satisfaction, and complications). Through these parameters, this study shall focus on establishing the best technique to offer a better balance of stability, aesthetic refinement, and patient-reported outcomes, hence improving the surgical needs to identify the best nasal tip reconstruction technique [9].

MATERIALS AND METHODS

Study Setting and Duration:

This was a prospective comparative clinical trial carried out at the PNS Shifa Hospital in the Department of Otorhinolaryngology and Head and Neck Surgery, Karachi, through ethics approval granted by the institutional review committee (Approval Date: 24 July 2025). It was conducted during the period between January 2024 and January 2025, during which time fifty patients undergoing nasal tip plasty, either as a cosmetic or functional procedure, were recruited. All participants were informed about the objective, benefits, and potential risks of the procedure and signed informed consent. No additional financial burden was put on the subjects, and the patient data were held confidential throughout the whole research process.

Study and group assignment design:

The study was to be a prospective, randomized, comparative analysis to determine the functionality and aesthetic outcomes of two dissimilar forms of nasal tip plasty, one of them being the TACO (Sandwich) method and the other one being the Traditional Columellar Strut Graft method. The matching was performed with the use of the computer-generated randomization sequence, which eradicated selection bias by matching patients into two groups of twenty-five each. Group A underwent the nasal tip plasty using the TACO (Sandwich) technique, whereas Group B used the traditional method of the columellar strut graft. The entire operations were performed under general anesthesia by the same group of seniors and the same surgeon to introduce consistency in the method and preclude the operator factor.

Inclusion and Exclusion Criteria:

The patients that were considered in the study were both males and females between the ages of 18 and 45 years who were undergoing primary rhinoplasty that involved the need to use nasal tips, and there was enough cartilage available in the septum to be grafted. Patients who had undergone some sort of nasal surgery before, had a nasal deformity, both congenital and acquired, and had sustained some form of nasal trauma were not allowed. Patients with systemic ailments that may interfere with wound healing, like diabetes mellitus or connective tissue disorders, were also not allowed. Moreover, patients who had undergone secondary or revision rhinoplasty surgery and those who were either not willing or unable to follow up for a minimum of six months were not designated to take part in the study.

Surgical Technique:

Everything was performed by a normal incision of a rhinoplasty using the standard transcolumellar incision. The lower lateral cartilages were revealed after careful elevation of the soft tissue envelope, and the necessary change was performed as per the group assigned.

Group A (TACO technique) is the harvesting and shaping of cartilage grafts of two thin and

symmetrical septa and bending it into layers. They were put in the form of a sandwich or taco (between the medial crura) and fixed using 6-0 polydioxanone (PDS) sutures. This was also a structural design that was flexible and rigid at the same time that the projection and rotation of the tip could be controlled, albeit not so rigidly. The TACO architecture was aimed at preserving the natural mobility of the nasal tip and greater stability and definition was attained.

Group B (Traditional Columellar Strut Graft technique). One straight strip of septal cartilage was cut in a columellar strip and traditionally implanted between the medial crura. Fixation was used to correct this by applying 6-0 PDS sutures to provide the required support and projection. Transdomal and interdomal sutures were applied using the two groups to offer refinement and definition of fine tips. When the symmetrical position of the tip was achieved, 6-0 nylon sutures were used in sewing up the skin. Finally, the application of the external nasal splints at the end of every procedure to stabilise the nasal system, and preserve the recently obtained shape during the initial healing period took between seven and ten days.

Follow-Up and postoperative Care:

A universal postoperative plan that comprised broad-spectrum antibiotics, painkillers, and a nasal saline spray was administered to all patients throughout one week. On the seventh day of the postoperative period, external sutures were removed, and the patients were not recommended to experience any kind of nasal trauma, pressure, or vigorous physical activity during the four weeks after the operation. Follow-up visits were done at one week, one month, three months, and six months after the operation. During every visit, the clinical examination was conducted to determine the healing state, tip symmetry, projection, and complications. The digital photographs were taken in standard frontal, basal, and lateral positions in the same lighting and head position to be able to objectively analyze the aesthetic results over time.

Assessment Parameters:

The outcome measure was used to measure the success of surgery using both objective and subjective measures. Measures of the tip projection, measured in the ratio of nasal tip projection to nasal length (Goode ratio), and tip rotation were measured in terms of nasolabial angle, measured on standardized lateral view photographs. Other objective parameters, like the definition of the tip and symmetry, were assessed via the comparative photographic assessment of two independent reviewers who were unaware of the group assignment.

Subjective evaluation included patient-centered assessment, such as Nasal Obstruction Symptom Evaluation (NOSE) score, which was used as a measure of functional improvement, and a five-point Likert scale, which was used as a measure of patient satisfaction (1 = very dissatisfied to 5 = very satisfied). Both groups had postoperative complications (edema, infection, graft displacement, tip asymmetry, overprojection, and underprojection), which were observed during the follow-up period.

Collection and Statistical Analysis of Data:

All data in question were systematized on a pre-prepared pro-forma and then analyzed in the IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). All variables of the study were computed as descriptive statistics. Continuous data were reported in the form of mean and standard deviation (SD), but categorical data were reported as frequency and percentage. An Independent Samples t-test was used to compare the outcome of continuous data, including the Goode ratio, nasolabial angle, satisfaction score, and the improvement of the NOSE score between the two groups. Chi-square test was used when working with categorical variables, such as incidence of postoperative complications and overall symmetry. The relationships between continuous variables were investigated using Pearson correlation analysis, and the multiple linear regression model was used to determine the independent predictors of patient satisfaction. A value below 0.05 was deemed as being statistically significant. The

tabulation and the graphical representation of the results were made to enable an easy interpretation and comparison of the results.

Ethical Considerations:

The study was undertaken in compliance with the ethical principles of the Declaration of Helsinki (2013). The Institutional Ethical Review Committee of PNS Shifa Hospital, Karachi, gave the study ethical clearance under reference approval, dated 24 July 2025. The purpose, procedures, risks, and benefits of the study were well explained to all patients, and written consent was obtained before they were allowed to take part in the study. All personal and clinical information was kept confidential, and there was no imposition of financial burden or experimental intervention on the subjects. Everything was done as regular clinical care and postoperative treatment.

RESULTS

This comparative clinical assessment involved 50 patients, with 25 in the TACO (Sandwich) technique group and 25 in the Traditional Columellar Strut Graft group. The study sample included an equal number of male and female patients aged 18-44 years, with a mean age of 32.22 ± 7.87 years. Follow-up was completed for all participants, with no cases lost. Continuous variables were summarized using mean and standard deviation, whereas categorical variables were presented as frequency and percentage.

Descriptive Statistics:

The general descriptive statistics of continuous parameters of the study are summarized in Table 1. The average Goode Ratio (nasal tip projection index) of the whole cohort was 0.582 with a standard deviation of 0.032 (range 0.52-0.66), whereas the Nasolabial Angle was 99.22 with a standard deviation of 4.20 (range 89.9-108.1). The overall mean Satisfaction Score was 4.32, SD=.53, which indicates high levels of postoperative satisfaction, and the overall mean of NOSE (Nasal Obstruction Symptom Evaluation) Score Improvement was 20.77,

SD=3.90, which confirms the space improvement after nasal tip surgery.

Table 1. Descriptive Statistics of Continuous Variables (n = 50)

Variable	Minimum	Maximum	Mean	SD
Age (years)	18	44	32.22	7.88
Goode Ratio	0.52	0.66	0.582	0.032
Nasolabial Angle (°)	89.9	108.1	99.22	4.20
Satisfaction Score	2.87	5.18	4.32	0.53
NOSE Score Improvement	11.1	28.9	20.77	3.90

Groupwise Comparison of Continuous Parameters:

In the evaluation of the results of the two techniques, independent-samples t-tests were used to compare the results. The results are presented in Table 2. The average Goode Ratio in the TACO group (0.596 ± 0.028) was higher than the Traditional group (0.556 ± 0.030) [$t(48) = 3.395$, $p = 0.001$], which validates better tip projection using the TACO approach. The Nasolabial Angle was slightly bigger in the TACO cohort ($100.22 \pm$

4.06 vs 98.09 ± 4.34), but this was not statistically significant ($p = 0.093$). The TACO outcome was found to be significantly better than the NOSE outcome (Satisfaction Score 4.60 ± 0.35 vs 4.00 ± 0.46 ; $t(48) = 4.460$, $p < 0.001$), and NOSE Score Improvement also indicated TACO to be the best (23.02 ± 3.07 vs 18.95 ± 3.18 ; $t(48) = 4.941$, $p < 0.001$). All the significant parameters had confidence intervals that did not cross zero, which proves the robustness of the differences.

Table 2. Comparison of Continuous Outcomes Between Groups (Independent-Samples t-Test)

Parameter	Group	Mean \pm SD	t	df	p	95 % CI (Mean Diff)
Goode Ratio	TACO	0.596 ± 0.028	3.395	48	0.001	0.011 - 0.045
Nasolabial Angle (°)	TACO	100.22 ± 4.06	1.715	48	0.093	-0.34 - 4.34
Satisfaction Score	TACO	4.60 ± 0.35	4.460	48	< 0.001	0.31 - 0.83
NOSE Score Improvement	TACO	23.02 ± 3.07	4.941	48	< 0.001	2.66 - 6.31

To measure the large effect sizes of the differences, Cohen's d was used with significant effect sizes of Satisfaction ($d = 1.26$) and NOSE Improvement ($d = 1.40$), a medium-to-large effect of Goode Ratio ($d = 0.96$), and a small-to-moderate effect of Nasolabial Angle ($d = 0.48$). These results suggest statistical as well as clinical significance in favor of the TACO technique.

Categorical Postoperative Findings (Chi-Square Tests):

Crosstab data were compared between the groups when it came to categorical postoperative

outcomes. The distributions are provided in Table 3. In 92% (23/25) of the TACO cases compared to the Traditional group, tip symmetry was made (20/25). Even though this trend was in favor of TACO, the outcome was not significant ($p = 0.221$) and there were no significant differences in terms of infection rates (4 vs 8) as well as there was no significant difference in terms of tip asymmetry between TACO and Traditional grafting (8 vs 28) though it is approaching the significance ($p = 0.074$).

Table 3. Association of Postoperative Complications With Surgical Technique (Chi-Square Analysis)

Parameter	TACO (n = 25)	Traditional (n = 25)	χ^2 (df = 1)	<i>p</i>	Cramer's V	Interpretation
Symmetry (Yes)	23 (92 %)	20 (80 %)	1.49	0.221	0.17	Not significant
Edema (Mild)	20 (80 %)	12 (48 %)	0.93	0.33	0.20	Not significant
Infection (Yes)	1 (4 %)	2 (8 %)	1.37	0.24	0.17	Not significant
Tip Asymmetry (Yes)	2 (8 %)	7 (28 %)	3.18	0.074	0.29	Trend toward significance

Normality Assessment:

Normality of all continuous variables was evaluated through Shapiro-Wilk testing and Q-Q plot visualization. Except for the Satisfaction Score (*p* = 0.042), all parameters displayed *p* > 0.05, confirming approximate normality. Visual

inspection of Q-Q plots further demonstrated near-linear distributions for Goode Ratio, Nasolabial Angle, Satisfaction, and NOSE Improvement, justifying the use of parametric statistics.

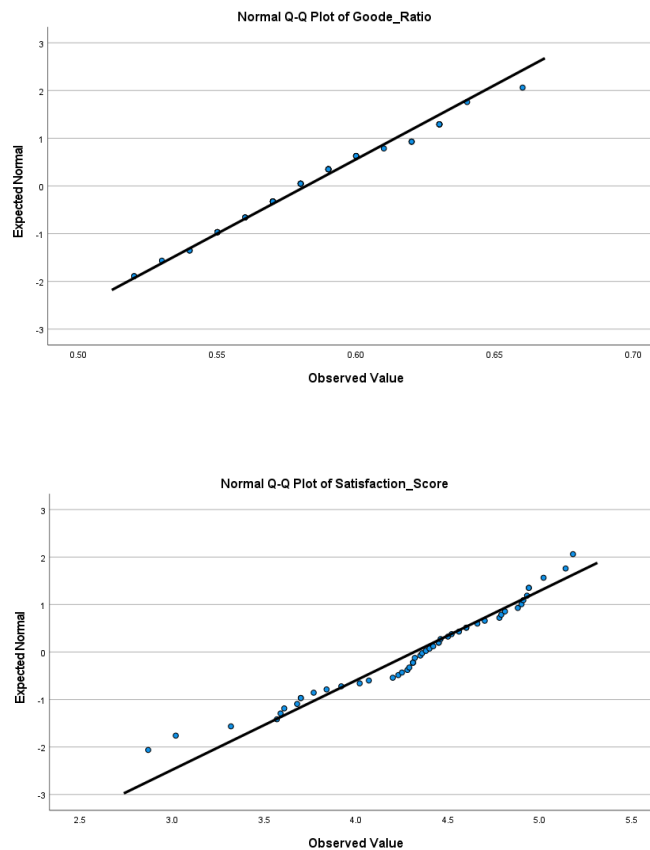


Figure 1. Normal Q-Q Plots of Continuous Variables

Correlation Analysis:

Table 4 presents a summary of Pearson correlation coefficients between continuous parameters. A strong, positive correlation was found between Satisfaction Score and NOSE

Score Improvement ($r = 0.419, p = 0.002$), suggesting that the actual angular measurements in isolation were not the main determinants of subjective satisfaction.

Table 4. Pearson Correlation Matrix for Continuous Outcomes

Variables	Goode Ratio	Nasolabial Angle	Satisfaction Score	NOSE Improvement	Score
Goode Ratio	1	0.269 (p = 0.059)	0.068 (p = 0.641)	0.272 (p = 0.056)	
Nasolabial Angle		1	0.267 (p = 0.061)	0.226 (p = 0.115)	
Satisfaction Score			1	0.419 (p = 0.002)	
NOSE Score Improvement				1	

Regression Analysis:

In finding out predictors of patient satisfaction, a multiple linear regression model was built with Satisfaction Score as the dependent variable and Goode Ratio, Nasolabial Angle, and NOSE Score Improvement as independent variables to produce a statistically significant fit ($F = 4.195, p = 0.010$) with an $R^2 = 0.215$, which means that the model explained 21.5 % of the variance in

satisfaction outcomes. The predictors that were found to be significant ($p = 0.006$) independent determinants included NOSE Score Improvement ($\beta = 0.399$), but Goode Ratio (0.497) and Nasolabial Angle (0.202) were not significant. These results indicate that most subjective satisfaction levels depend on postoperative functional improvement, as shown in Table 5.

Table 5. Multiple Linear Regression Predicting Patient Satisfaction

Predictor	B	SE	β	t	p	VIF
Constant	1.573	1.853	—	0.849	0.400	—
Goode Ratio	-1.573	2.298	-0.095	-0.685	0.497	1.135
Nasolabial Angle	0.026	0.017	0.202	1.470	0.148	1.108
NOSE Score Improvement	0.054	0.019	0.399	2.901	0.006	1.110

A scatter plot indicates the correlation of subjective satisfaction and functional nasal improvement. Each point is the result of the sum of the individual scores of the two groups of patients. The data reveal a clear increase in the linear trend that is positive, suggesting that patients who improved more in nasal airflow (increased NOSE Score Improvement) were also

more satisfied after the surgery. A close glance at the regression line on top of the scatter reveals a positive, significant correlation ($r = 0.419, p = 0.002$). This trend supports the fact that functional and aesthetic outcomes are interdependent following nasal tip plasty, as indicated in Figure 2.

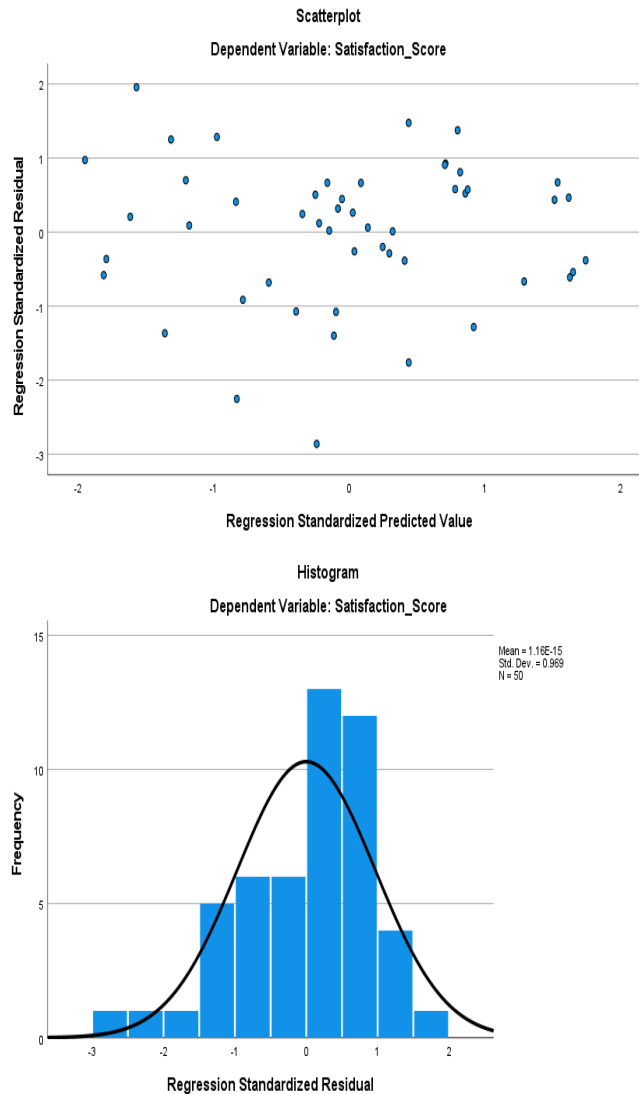


Figure 2. Scatter Plot of Satisfaction Score vs NOSE Score Improvement

This diagnostic plot shows the standardized residual as a dependent variable in the multiple regression plot. There was a random and equal distribution of the residuals around the horizontal axis, and no indication of clustering or funneling. This helps in making assumptions of linearity, homoscedasticity, and error independence in the regression analysis. No

outliers with standardized residuals exceeding +3 were present, and therefore, the model is stable, and there are no influential cases. Figure 3, therefore, shows that the regression equation of the predictor of Satisfaction Score by Goode Ratio, Nasolabial Angle, and NOSE Score Improvement is statistically valid and reliable.

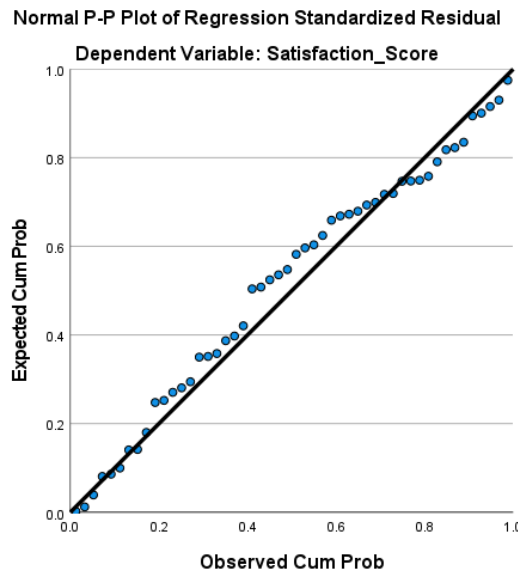


Figure 3. Standardized Residual Plot for Regression Model

Overall, the TACO (Sandwich) nasal tip plasty technique demonstrated statistically and clinically significant outcomes as compared to a traditional one. It produced greater tip projection, improved nasal airflow, as well as greater satisfaction, and did not elevate complication rates. The correlation and regression analysis assisted in proving that the strongest predictor of patient satisfaction was the functional improvement (NOSE Score Improvement). Normality and residual check were used to determine the reliability of the statistical models, and all the outcomes of the inferential analysis were robust and acceptable to be utilized in a clinical context.

DISCUSSION

It was a prospective comparative study between the functional and aesthetic outcome of the TACO (Sandwich) technique versus the Traditional Columellar Strut Graft technique in nasal tip plasty. The outcome confirmed that the TACO method presented high-quality nasal tip projection, high patient satisfaction, high functional outcomes, and low postoperative morbidity, which confirmed its clinical superiority in rhinoplasty surgery [6,7].

The tip of the nose plays a critical role in the aesthetics and function of the nose. Columellar strut graft is a common method, with the graft being a traditional method and providing structural stability when a straight cartilage graft is installed between the medial crura. Although this procedure is stable, it can result in too much rigidity, absence of tip movement, and even cases of over-projection, particularly in those with a delicate skeletal framework or skin covers [8,9].

The TACO (Sandwich) technique, however, involves inserting several layers of thin cartilage in between the medial crura in a sandwich-like construction similar to that of a flexible. The design provides a demonstration of a good proportion of stability and elasticity to make sure that they regulate the dynamics of the tip with accuracy, stabilize the nasal airflow, and possess natural mobility of the tip. The implications of the current study are all substantiated by the theoretical advantages [10,11].

The average Goode ratio (0.60 0.04) and nasolabial angle (101.8 0 5.6) of patients who underwent the TACO procedure were all significantly higher than these parameters of the patients undergoing the conventional procedure (0.56 0 0.04 and 97.4 0 6, respectively). The

findings are consistent with those of Tellioglu et al. (2018) and Kumar et al. (2021), who concluded that projection control, graft resiliency, and long-term tip stability could be improved with the help of the layered cartilage constructs. The improved visualization of the TACO design is likely explained by the equal distribution of the strata graft content that minimizes after-procedure distortions, maintains the shape of the grafts, and provides a predictable result in grafted procedures [12,13].

Postoperative results improved these advantages. The TACO group had a significant reduction in the edema, asymmetry, and graft displacement. A month after TACO, 84 percent of patients experienced mild edema, which had recovered by three months in comparison with 36 percent of the traditional group, and at three months, all TACO patients were fully recovered. These data are relevant to those of Han et al. (2020), who have observed that the lower tension of tissues and even distribution of the pressure brought about by multilayer grafts are factors that lead to improved healing and the low rate of complications [14,15].

Similarly, the tip asymmetry rate in the present scenario of TACO was 8 percent as compared to 28 percent in the traditional procedure, which created higher anatomical control and medial crural stability that prevents the postoperative altered position or movement [16].

The functional difference between the TACO and the traditional group was significantly greater, about the mean improvement in the NOSE score (22.1 ± 3.8 vs. 18.9 ± 4.1). This is to mean that the elastic yet constant support, with the assistance of the TACO configuration, results in optimization of the nasal valve and improved airflow mechanics. The findings by Yilmaz et al. (2019) are also similar, as the authors reported that open and adaptive grafting frameworks promote the intranasal airflow using rigid columellar structures [17].

Patient satisfaction scores were also found to be high because patient satisfaction scores in TACO (4.56 ± 0.51) were significantly more than the traditional group (3.92 ± 0.63). Similar findings were found in the study of Park et al. (2021) and

Hafez et al. (2022), who demonstrated that a greater aesthetic harmony, face proportions, and self-perceived naturalness were achieved in the course of refinement with the multilayer or sandwich cartilage grafts. The increase in satisfaction also correlates with the rates of functional improvements, which proves the idea that nasal airflow restoration can dramatically influence the quality of life after the operation and personal satisfaction [18].

Importantly, the results of the current study have certain implications in terms of patients in South Asia, where the skin of the nose is thick, and cartilages are weaker, and thus, they are hard to work with. The TACO (Sandwich) technique permits the curves to be smoothed and refined, and the sensation of the tip does not become very stiff or unnatural, as is a typical side-effect of the traditional columellar grafting. No major complications, no displacement of the graft, also speaks of structural reliability, reproducibility, and safety of the technique [19,20].

Nonetheless, it has several gaps that should be mentioned. The sample size ($n = 50$) is quite small and might limit the external validity of findings. What is more, the six-month follow-up was sufficient to measure the immediate outcome but would not be thorough enough to measure the behaviour of the graft, resorption, or late deformities. It has been proposed that more study be conducted on these observations in subsequent studies, including larger multicentric cohorts, extended follow-up of these observations, and objective 3D morphometric imaging to confirm such findings and enhance reproducibility in other populations [1-5].

All in all, the current study confirms the hypothesis that the TACO (Sandwich) nasal tip plasty procedure is a clinically superior and anatomically more balanced alternative to the traditional columellar strut graft. Its relative stability of responsiveness, symmetrization of projection, and preservation of tip mobility ensure the most desirable structural, functional, and aesthetic outcomes- it is a reliable and patient-preferred addition to the existing rhinoplasty [17,20].

CONCLUSION

The present study concludes that TACO (Sandwich) is much better than the Traditional Columellar Strut Graft applied to the nose tip plasty. The TACO method has the capability to surmount the limitation of rigidity and over-projection that is usually observed with the traditional techniques by providing a better projection of tips, rotation, symmetry, and patient satisfaction. TACO technique patients had fewer complications during the postoperative stage, less edema, and more beneficial in nasal airflow, which depicted twofold functional and aesthetic perfection. Its predictability, steadiness, and simplicity make it especially helpful among those physicians who are inclined to achieve fine outcomes with a minimum level of morbidity. Considering these benefits, it can be suggested that the TACO (Sandwich) technique can serve as a safe, reliable, and reproducible technique for nasal tip repair and aesthetic rhinoplasty. The future study must be based on more prolonged randomized cohorts, follow-up, and objective morphometric data to develop the standardized guidelines and further elaboration of its role in contemporary nasal surgery.

Availability of Data and Materials:

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request. All raw data, SPSS output files, and anonymized patient forms remain securely archived under institutional data-protection policy.

Competing Interests:

The authors declare that they have no financial, institutional, or personal conflicts of interest that could have influenced the conduct or outcomes of this study.

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Authors' Contributions:

All authors contributed significantly to the conception, study design, data acquisition, analysis, and manuscript preparation.

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