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Surgical Treatment of Keloids in the Ear: Prospective and Randomized Study Comparing Direct Surgical Excision vs. Keloid Fillet Flap

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

Introduction: Keloids and hypertrophic scars are characterized by abnormal responses to the healing process and involve intense production and deposition of collagen and glycoproteins in the dermis, resulting in the development of a pathological scar. To compare the techniques for keloid resection preserving the epidermis and superficial dermis, *Keloid Fillet Flap (KFF*), with direct surgical excision treatment for resecting all the scars with primary closure.
Methods: The design of the study was a prospective and randomized study in a single-center with patients who had keloids in the auricular area. All of the participant patients were randomly divided into two groups: direct surgical excision-RC (n = 36 patients); and the group Keloid Fillet Flap-KFF (n = 37 patients). In both groups, neoadjuvant treatment of infiltration with triamcinolone 20 mg/ml until the end of the clinical activity of the keloid was performed, and the treatments were followed by the adjuvant treatment of 10 sessions of Beta Ray Therapy.
Results: The present study enrolled 73 patients, of which 37 comprised the KFF group and 36 the RC group. Following the use of the scar measuring scales to define the recurrence rate, our study demonstrated a recurrence rate of the total sample of 62%, with the KFF group presenting a rate of 76% and the RC group presenting a rate of 40%. In the KFF group, the mean volume of the recurrent lesions was 56 cm3, versus 13.25 cm3 in those that did not recur. In the RC group, the

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mean volume was 57 cm3 in the recurrent lesions and 1.6 cm3 in the non-recurrent lesions. These volumetric differences were statistically significant (p 0.05), that is, the volume of relapses is much higher than that of non-relapsed ones.

Keywords: Keloid; surgical flaps; ear; wound healing; skin.

1. INTRODUCTION

Through historical narratives, keloid was first described by Egyptian doctors in 1700BC, in the *Smith papyrus* [1]. There are authors in the literature who affirm that collagen synthesis is bigger than the lise [2] and others who say that it is uncertain if the main mechanism for keloid generation is the increased synthesis or a smaller reabsorption of collagen, caused by a relative decrease in the production of collagen or a direct inhibition of such an enzyme. The combination of these mechanisms can be considered the reason for the histopathological findings in keloids [3].

Due to a lack of understanding about the factors that stimulate and trigger the formation of a keloid, several treatment methods have been proposed in the literature, but none of them has been proven to be ideal for the management of keloids [4].

The link between pediculated keloid, total wound resection, and the technique described by Kim et al. as "Keloide fillet flap" [5] may be mentioned among the surgical procedures. This technique uses a keloid dermis-epidermis flap for primary closure of the wound and macroscopic total resection of the keloidal bulk regardless of localization and clinical activity.

Relevant aspects are: the classification according to Muir [6], in which the ear keloid is a scar of mixed types, and which the nodular is the one with a better prognosis. Also, considering the innervation present in the keloid as a factor for trophism, with denervation of the dermioepidermal flap for smaller thickness and larger resection of its bulk. This, consequently, leads to a reduction in the neurogenic [7] stimuli. Therefore, as an indication, one must consider the kind of phenotypical expression of the fibroblasts, from peripheral to central ones, as well as from shallow and deep ones [8].

Thus, one learns a treatment protocol for ear keloid by comparing the recurrence levels and post-surgical satisfaction of clients between the two techniques above mentioned.

1.1 Objective

To compare the keloid resection technique with preservation of the superficial dermis and epidermis-Keloid Fillet Flap (KFF) with direct surgical excision treatment with primary closure.

2. METHODS

The study design was a prospective, randomized, double-blind, controlled, single-center study with patients presenting unilateral or bilateral ear keloid and who were treated at the Plastic Surgery outpatient clinic. The subjects were selected according to the inclusion criteria and totalled 73 patients.

A consent form was used. They were all informed about the surgical procedure, its risks, and potential complications, and gave permission for image use.

Such procedures occurred, according to the regulations of the Ethics in Research Committee and the regulations of Declaration of Helsinki.

The sorting of the groups and surgical procedures took place from April 2013 to November 2014, and the follow-up was carried out up to December 2016.

The inclusion criteria were patients with an age of equal or above 13 years, both genders, with primary or recurrent, unilateral or bilateral ear keloid with signs of minimum inflammatory activity or inactivity (without pain and/or pruritus and/or reactive hyperemia and/or scar growth, with an index on analogical scale and variation from 0–10, lower or equal to 4). Patients with prior corticotherapy use were included only if treatment was equal to or greater than three months prior to entering the trial.

The non-inclusion criteria were: history of allergy to any local anaesthetic substance, patients with any hepatopathy, refusal of the patient and/or parent/responsible for being part of the study, previously transfused patients in a period of less than one month, cardiopathy patients, chronic dermatological patients, pathological

photosensitivity, metabolical disease, collagen disease, degenerative autoimmune disease, pregnant women, lactating women, patients who stopped breastfeeding in less than six months, current or former presence of any kind of malignant neoplastic disease and any other kind of chronic disease in treatment.

All the participants were numbered and randomized, by sortition through the website www.randomizer.org, into two groups: group RC (which used the classic treatment with the primary closing of the wound and the adjuvant Beta-Therapy): n = 36 patients, and group KFF (which used the *Keloid Fillet Flap* technique followed by adjuvant Beta Ray Therapy): n = 37 patients.

The patients gathered in the RC group were submitted to the treatment considered standard in the literature, with resection of the scar and primary closure, whenever it was possible to join the edges of the wound without excessive tension, so that there would be no aftermost dehiscence or propensity to keloid recurrence. As adjuvant therapy, all the patients received Beta Ray Therapy for a maximum of 24 hours, following the protocol of 10 sessions with a 1-day hiatus.

The randomized patients of group KFF were only different from the RC group by the fact that they were submitted to the Keloid Fillet Flap [5] technique in which local flaps using the tissues that coat the keloid itself were performed, therefore, without the need for skin grafting or the confection of local flaps.

The aspects related to the quality of life were analyzed through a validated instrument (Qualifibro-Plastic Surgery-UNIFESP) [9,10], which was applied in the pre-surgery and post-surgery phases for all the patients who took part in the study.

There were two different scales used, one proposed by Yeong et al. [11] and the other by Singer et al. [12].

In order to obtain a more uniform analysis, Yeong et al. [11] proposed the Seattle Scar Scale (SSS), a numeric scale based on a group of 24 colored standard pictures that evaluate the differences in the scar surface, the thickness of the edge height, and the difference in color between the scar and the adjacent normal skin. The scale varies in whole numbers from -1 to 4, with 5 variables for analysis: surface, border, thickness, and colour, which vary from (-4 --Zero-- +16) increasing the gravity, in which zero is indicative of a normal scar. The recidive is determined when the sum of the values is higher than 4.

The instrument, named the *Stony Brook Scar Evaluation Scale (SBSES),* was proposed by Singer et al. [12], and the scar is evaluated according to five items. It gathers the evaluations of individual attributions (thickness, height, color, suture marks, and general appearance), with a binary response (0 or 1) for each of the items, resulting in a score that varies from 0 (worst) to 5 (best). The lesion shall be considered a recidive when the sum of items responded to is less than 3.

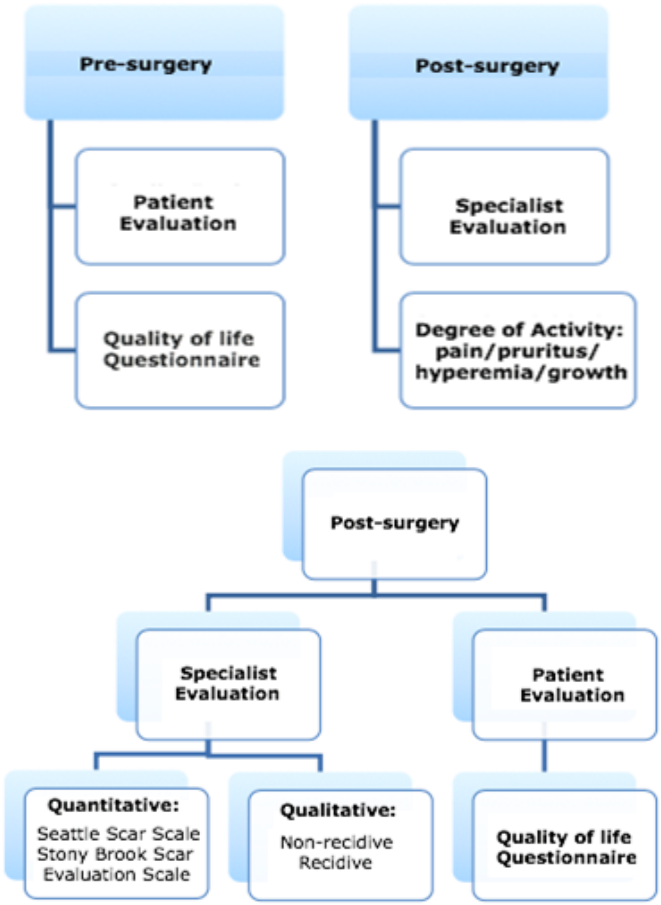
The scales were applied by three distinct plastic surgeons, and neither of them had access to the evaluations made by the other two. All surgeons, like the patients themselves, were blinded to which surgical technique was used on each patient. The data used for the statistical analysis was the mean number calculated from the three evaluations.

A qualitative analysis also took place at every appointment, and the recurrence was defined as an elevation of the scars that reached beyond the original surgical wound. A scar that did not show signs of elevation or extension was considered non-recidive.

The organization of the applied questionnaire mentioned above is illustrated in the flowchart.

A digital pachometer (precision of 0,01 mm; OTMT Machines, NY, USA) was used to measure the wound in pre-surgery using the metrical system. The measures were taken in three dimensions: height, width, and length, so that it was possible to compare the volume of the wound in all its diverse forms.

The ear(s) were then anesthetized with Lidocaine® 2% vasoconstrictor, and the surgical procedure was chosen at random without the knowledge of the doctor or the patient.



Flow Chart 1. Pre and post surgery implications

After sorting out which surgical technique would be used, the surgeon analyzed the possibilities for the use of the particular technique assigned. When it turned out to be impractical, it was considered a failure of treatment, and the patient was then treated according to the best indication for the case, thus avoiding any negative consequences for the patient.

The suture of the surgical wound resulting from the scar resection was also randomly chosen, and the possible methods were primary closure with the use of Mononylon 5.0/6.0, or dermis-epidermis snips, according to the Keloid Fillet Flap [5], followed by dressing.

The obtained data were analyzed using the Mann-Whitney tests for intergroup comparisons and the Wilcoxon test for intragroup comparisons using the free software BioEstat 5.3®. When the value of p was less than or equal to 0.05, the data were considered statistically significant.

The follow-up of the patients is at intervals of 6, 12, 24, and 36 months. On the scar qualification scales, a photographic, register was created.

3. RESULTS

The present study included 73 patients, of whom 37 were in the KFF group and 36 were in the RC group. These patients ranged in age from 24 to 42 years old, with 41 (56,16%) being male and 32 (43,83%) being female.

Thirteen patients were considered treatment failures because they could not be operated on using traditional techniques due to the risk of serious aesthetic sequelae, and thus their data could not be used for statistical analysis. The number of operated ears was 77, and of the 60 operated patients, 17 had bilateral lesions.

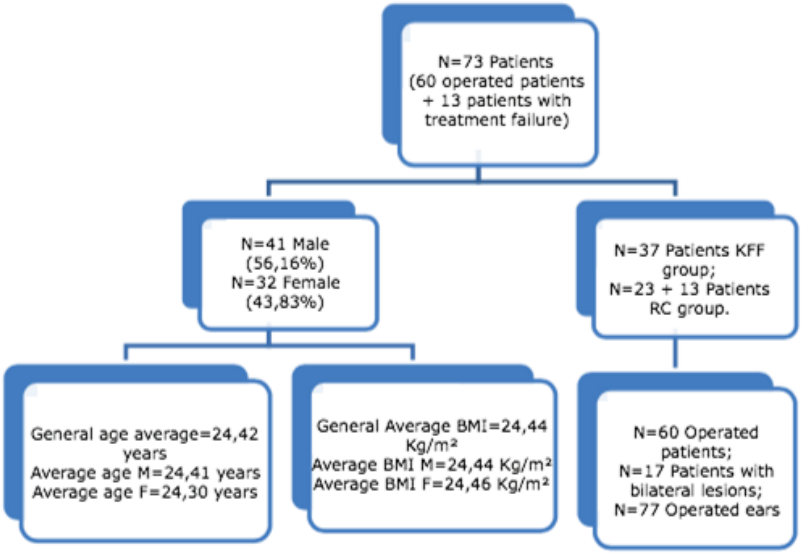
Previous treatments were examined and randomized in the different groups, resulting in homogenous and similar groupings.

3.1 Characterization of Pre-surgery Sample

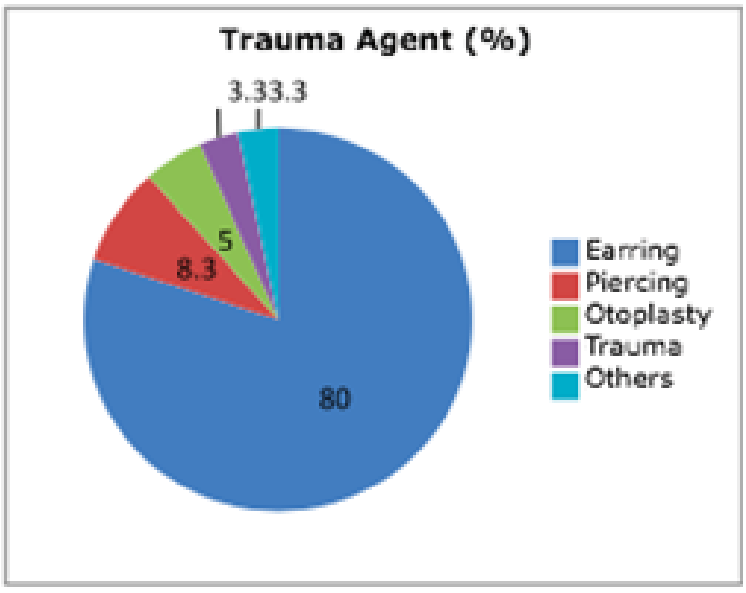
The main agents as causal factors were earrings (ear lobe) (80%), followed by piercings (ear helix) (8.3%). The most commonly afflicted areas by ear keloid were the posterior lobes of the right ear (48%) and the left ear (40%).

3.2 Characterization of Post-surgery Sample

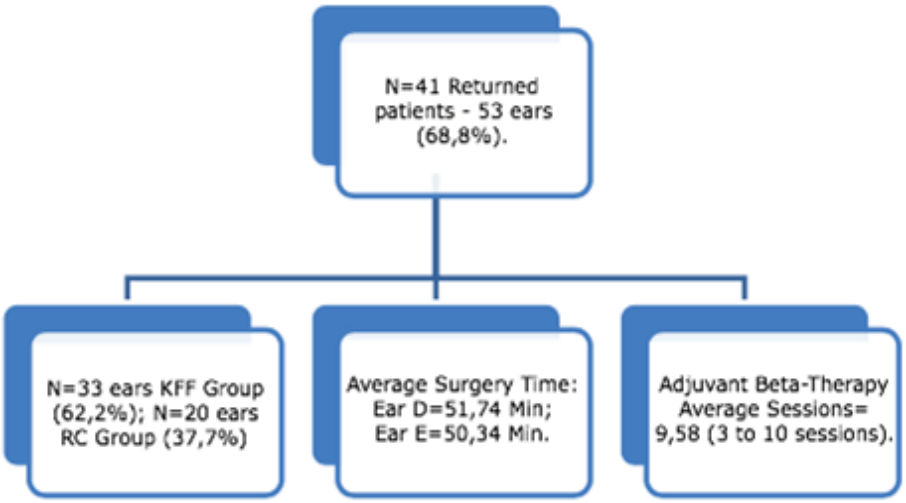
Nineteen of the 60 patients did not return for their appointments and therefore were excluded from the study. This way, the samples considered 41 patients, totaling 53 ears.



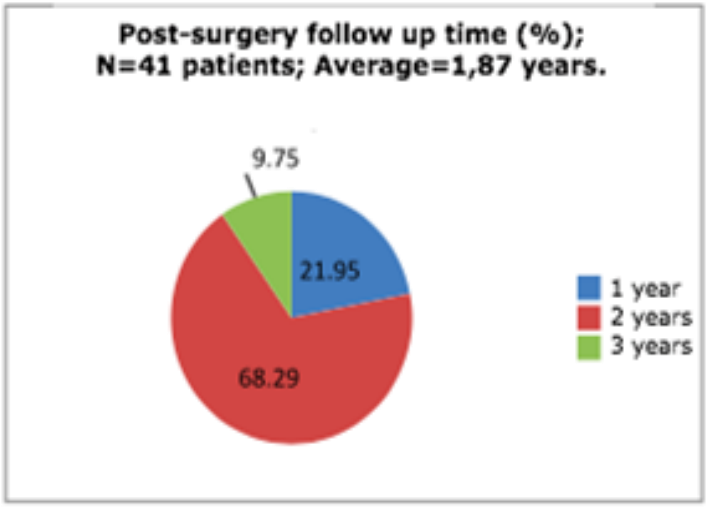
Flow Chart 2. Study protocol



Graph 1. A diagram depicting the trauma agents that induce keloids in the auricular area. All of the patients had keloid formation owing to direct trauma, whether from earrings, surgical procedures, or local trauma. Earrings: injury to the earlobe. Piercing: injury caused to other anatomical parts of the ear, mainly the helix



Flow Chart 3. Post-surgery sample analysis



Graph 2. Graph depicting the duration of patient follow-up. The average follow-up in both groups was 1.8 years, indicating that the data has a high level of validity due to the lengthy follow-up

The average follow-up time of these patients was 1.78 years, and 78% of the patients had a follow-up of 2 years or longer.

The recurrence rate was divided into clinical recurrence and recurrence by the application of scar quality scales. In this way, the total sample presented a clinical recurrence rate of 66%, with the average time varying between 7 and 8 months. In the KFF group, this rate was 82%, with time varying between 6 and 7 months, and the RC group presented a clinical recurrence rate of 40% in a period between 9 and 10 months.

When the scales were used to define the recurrence rate, it showed a rate of 62%, with the KFF group presenting a rate of 76% and the group RC at 40%.

3.3 Comparison of results KFF Group x RC Group

The results considered relevant were the average volume of scars that did not have a recurrence during the follow-up time of the study. The average volume of recurrence scar for the KFF group was 56 cm3, while the volume of non-recurrence scar was 13.25 cm3. The average volume for the RC group was 57 cm^3 of

recurrence scar and 1.6 cm3 of non-recurrence scar. Such volumetric differences presented statistical significance (p 0,005), and therefore, the volume of the recurrence scars was much higher than the non-recurrent ones.

Writing down the results for the use of the quality of life questionnaire Quali Fibro-Pro in patients during pre-surgery and post-surgery, we obtained the following results.

Table 1. Data obtained in the KFF and RC groups, comparing lesion dimensions and recurrence rates

Comparison KFF x RC	Total Sample	KFF group	RC group
# of Samples	73	37	36
# of Treatment Failures*	13	0	13
# of Operated Ears	77	48	29
Average Scale of Lesion Activity Degree (0 to 4)	0,68 points	0,78 points	0,52 points
Average Volume of Operated Lesions*	D - 28,07 cm²	D - 38,06 cm²	D - 13,77 cm²
	E - 28,36 cm²	E - 30,33 cm²	E - 24,25 cm²
# of Returning Ears	53	33	20
Average Time of Surgery*	D - 51,74 min	D - 69,38 min	D - 28,6 min
	E - 50,34 min	E - 61,37 min	E - 27,4 min
Average Number of Adjuvant Beta Ray Therapy Sessions (0 to 10)	9,58	9,48	9,75
Average Follow up Time	1,87	1,88	1,87
Rate of Clinic Recidive	66%	82%	40%
Rate of Recidive According to Scales Criteria	62%	76%	40%
Statistically significant = p<0,05.			

The table depicts the data of a sample that is extremely homogeneous in terms of both quantity and attributes. Thirteen patients in the RC group had therapy failure and were not candidates for standard surgery. There were no treatment failures in the KFF group, indicating that the approach may be employed on any size lesion. Because the KFF group did not have any constraints on the amount of the operated lesions, the mean volume of the operated lesions was greater. Without taking into account the 13 patients in the RC group who had treatment failure, the mean volume of the two groups was comparable but not statistically significant

3.4 Qualifibro Pre X Post (Without Recidive)

Table 2. Comparative quality of life data between the KFF and RC group

Total Sample	Pre-surgery	Post-surgery
Average Physical Score	-2,54	-3,0
Average Psychological Score*	-1,07	-3,07
KFF Sample	Pre-surgery	Post-surgery
Average Physical Score *	-2,0	-3,4
Average Psychological Score *	-0,6	-3,2
RC Sample (except for the 13 patients who were deemed to be treatment failures)	Pre-surgery	Post-surgery
Average Physical Score	-2,87	-2,75
Average Psychological Score *	-1,37	-3,0
*Statistically significant = p<0,05.		

Data shows that patients in the KFF group improved their physical and psychological ratings, whereas patients in the RC group improved their psychological scores. The whole sample indicates an improvement in psychological score, indicating that the keloid has an impact on patient quality of life

3.5 Examples of Patients Participating in the Study

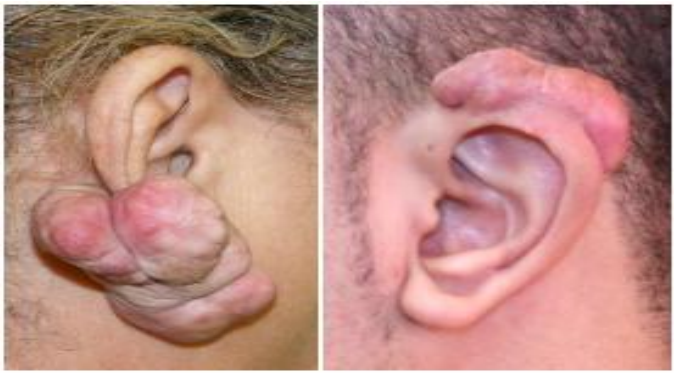


Fig. 1. Examples of patients in RC group excluded for failure in treatment, It would not be possible to perform primary synthesis

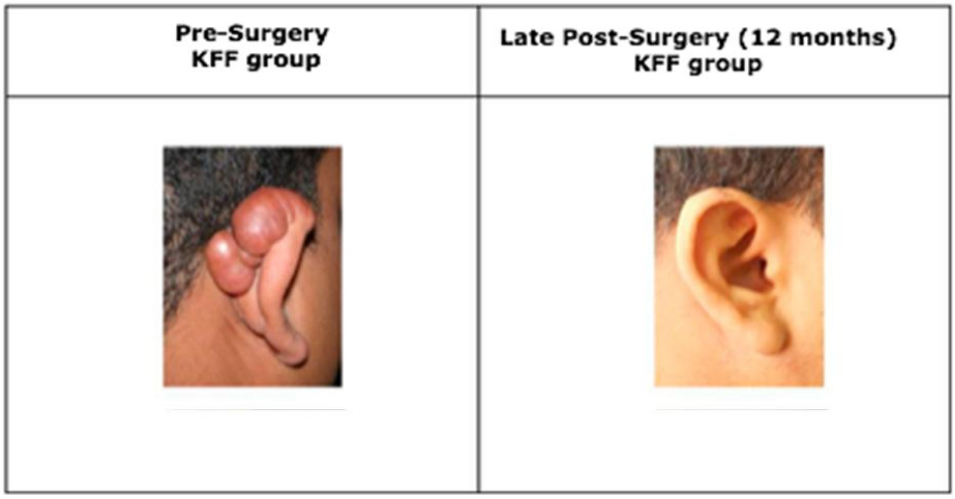


Fig. 2. Example of patient in pre and post-surgery KFF group

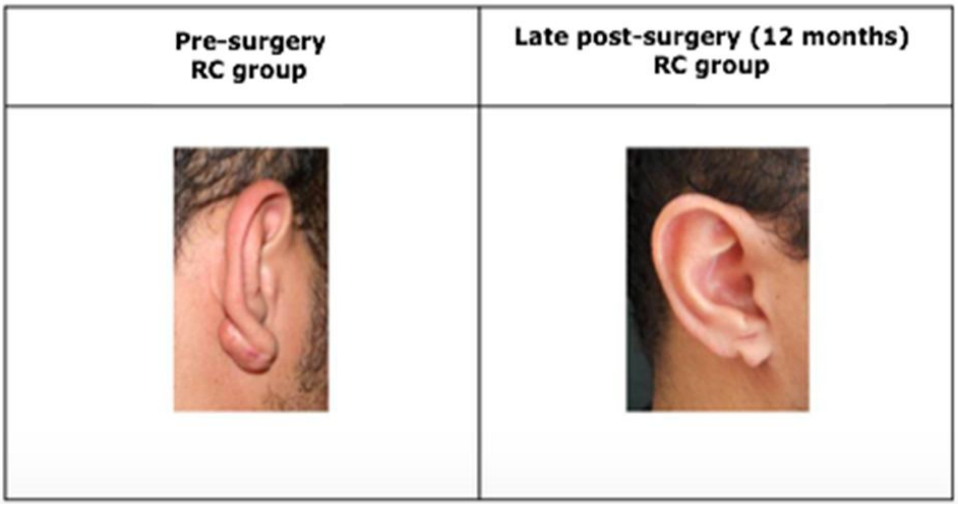


Fig. 3. Example of patient in pre and post- surgery. RC group

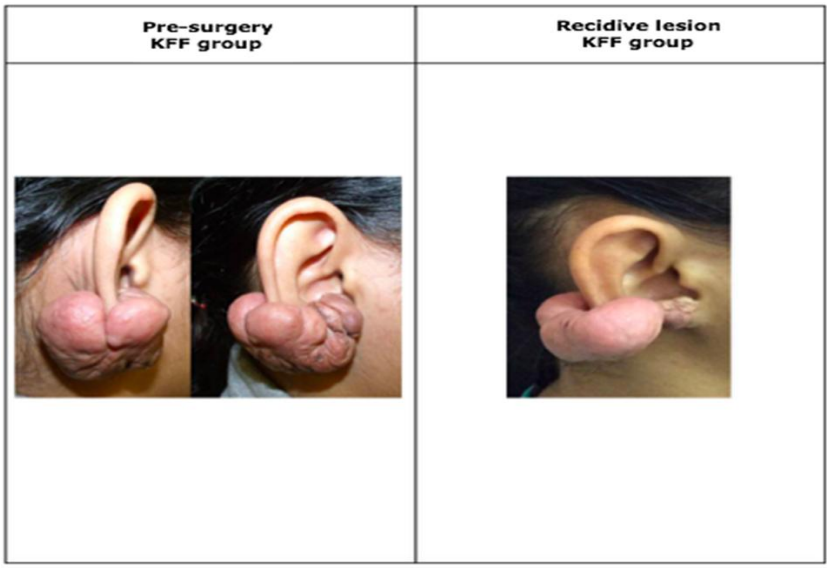


Fig. 4. Example of pre and recidive scars. KFF group

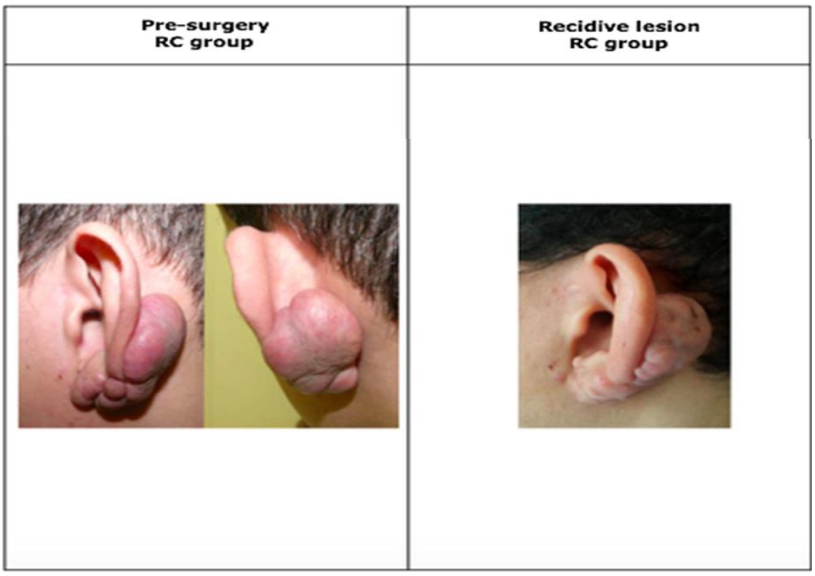


Fig. 5. Example of pre and recidive scars RC group

4. DISCUSSION

Among the abnormal scars, the keloid represents one of the biggest challenges for plastic surgery. Their incidence is higher in African descendants, Hispanics, and Asians, ranging from 4.5 to 16%. [3,13]. As for the symptoms, they may cause pain, pruritus, numbness, and redness in the scar tissue [14,15]. They also significantly affect the self-esteem and quality of life of the patient [9].

As for treatment methods, the isolated surgical excision of the scar presents recurrence rates of 45 to 100% [16,17]. Other treatment methods include scar injections with corticosteroid [18], compression, irradiation of beta ray therapy, laser, cryotherapy, and silicon bandage.

Currently, keloids located on the ear lobes may have as treatment methods, surgical excision, associated with corticoid scar injections and beta ray therapy. With adjuvant corticotherapy, literature reports recurrence rates of 3 to 45% [19].

There are many publications that try to show the best treatment for keloids. Vieira et al. [20],

provided a review of the main options for treatment and an analysis of the recurrence rates of each one. He concluded that, besides the great variety of treatments, no monotherapy is effective and the best therapy is still prevention.
A systematic review, comparing the use of radiotherapy and corticosteroid infiltration adjuvant to excision of ear keloids, published by Shin et al. [21], showed that the existing studies did not have the methodological quality to define an affirmative position on which keloid treatment was the best one. The authors did not find differences between the two therapies, and the recurrence rate was 16%. However, no signs of inflammatory activity in the keloid were found in the pre-surgical nor in the scar dimensions, which in our study proved to be very important for the recurrence rates.

Thierauf et al. [22] performed a study comparing multimodal treatment with the association of more than one therapy, using the technique described by Kim [5], with a very reduced number of samples as well as a non-standardized measurement of the volume of the wound. The authors found that the *"Keloid Fillet Flap"* technique by itself represented a factor of recurrence decrease. The study concluded that the association of more than one treatment proved to be the best therapeutic choice for keloid treatment. In our study, which standardized the scar volumes, we managed to identify that, even though the KFF group presented a higher recurrence rate (76%) in comparison to the RC group (40%), the volumes of the KFF group scars were much bigger (35 cm^3) than those of the RC group (19 cm^3).

When we analyzed the decisive rates according to the volumes, we noticed that there was an exponential increase in both groups, with volumes larger than 50 cm^3. The average volume of recidivated wounds in the KFF group was 56 cm^3, while it was 57 cm^3 in the RC group. Thus, we could conclude that wounds with volumes greater than 50 cm3 have high recurrence rates.

The present study also showed that the average wound volumes that were not recurrent in the RC group were 1,6 cm^3 and in the KFF group, 13 cm^3, and this difference was statistically significant. Therefore, when the scars treated in the KFF group were analyzed with volumes equal to the RC group average, a neutral recurrence rate was obtained. This endorses the data brought by Thierauf et al. [23] and Ogawa et al. [24], showing the positive effect of the technique used, as well as the ubiquitous indication, with the possibility of being used in scars of any shape and size.

The interrelationship between keloid and simpathetic sensory innervation becomes clear over time [4,7,25]. This method involves thinning of the skin flap and denervation, which results in a smaller trophic potential and favors non-recurrence of the keloid [26,27]. Furthermore, it is well known that the most proliferative fibroblasts in keloids are the ones in the periphery and in the deep dermis that are eliminated with this surgical method, theoretically endorsing the indication of this practice.

Treatments that have shown promise, such as the one given by Nguyen et al. [28], include improved technology and tissue engineering, as well as chemicals that operate on fibroblast proliferation signaling pathways, such as the activin molecular route. The "in vitro" study by Seungmin Ham et al. [29] utilizing follistatin to disrupt this route is one example. However, such therapies are too expensive for the majority of patients who suffer from fibroproliferative scars.

A very relevant aspect of fibroproliferative scars, or keloids, is the quality of life of the patients due to the associated heavy stigma. There are few studies in the literature about this subject, so the present study brought important features through the application of the quality of life questionnaire, which is specific to keloids [19,27].

In their study, Walliczec et al. [30] that the patients without scar recurrence had greatly improved their quality of life. The study did not show any comparative improvement in distinct groups or in long-term follow-up. Our study, with the application of the pre and post-surgery questionnaire, with a minimum of 12 months after the surgery, showed a significant reduction in psychological suffering (p 0,005). This included a combination of members of the KFF and RC groups. Unfortunately, the physical discomfort, although showing a decreasing trend, did not reach statistical significance.

When analyzed separately, the KFF group presented post-surgery data showing more physical suffering in comparison to the RC group ($p = 0,05$). Perhaps this was because of the greater volume of scars in this group compared to the RC group, due to the fact that 13 patients were excluded for treatment failure.

The intragroup analysis revealed that the KFF group showed great improvement in physical and psychological scores post-surgery. This did not consider the patients who had a recidive, since they did not show any improvement. Improvement in the KFF group reached statistical significance, thus strengthening the benefits to the patients who took the treatment, even if the treatment was associated with high levels of recurrence.

As for the RC group, there was only a significant statistical improvement in psychological suffering (p 0.05), probably due to the smaller scar volume that did not cause great discomfort to the patient. The pre-surgery questionnaire was very similar to the post-surgery one in this group.

5. CONCLUSION

The technique described by Kim [5] is a viable option since it has a low cost and shows recurrence rates equal to or even smaller than other ones when considering the initial volume of the scar. Also, it presents an excellent aesthetic result.

Regardless of the surgical technique used, the initial volume of a keloid scar is directly related to the recurrence rate. For scars larger than 50 cm^3, there is a high rate of recurrence with the combination therapies used in the present study. Therefore, the volume of lesions represents an important predictor of treatment failure.

CONSENT

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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