



ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΕΣΣΑΛΙΑΣ
ΤΜΗΜΑ ΙΑΤΡΙΚΗΣ



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<<COMPARISON OF PIEZOELECTRIC AND CONVENTIONAL OSTEOTOMY IN RHINOPLASTY: A SYSTEMATIC REVIEW AND META-ANALYSIS>>

<<ΣΥΓΚΡΙΣΗ ΤΗΣ ΠΙΕΖΟΗΛΕΚΤΡΙΚΗΣ ΚΑΙ ΣΥΜΒΑΤΙΚΗΣ ΟΣΤΕΟΤΟΜΙΑΣ ΣΤΗΝ ΡΙΝΟΠΛΑΣΤΙΚΗ: ΜΙΑ ΣΥΣΤΗΜΑΤΙΚΗ ΑΝΑΣΚΟΠΗΣΗ ΚΑΙ ΜΕΤΑ-ΑΝΑΛΥΣΗ>>

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2019

Abstract

Background The osteotomy of nasal bones during rhinoplasty is connected with postsurgical morbidities. Recent evidence suggests that a new surgical method, applying piezoelectric ultrasound waves for lateral osteotomies in rhinoplasty, reduces soft tissue damage and results in less edema and ecchymosis post-surgically.

Purpose The purpose of this study was to compare and analyze the clinical outcomes in the early postoperative period of lateral osteotomies executed with either piezoelectric or conventional instruments in rhinoplasty.

Methods We searched PubMed, CENTRAL and Web of Science from 2005 up to 17 August 2019. We included studies comparing results of patients subjected to piezoelectric or conventional lateral nasal osteotomies in rhinoplasty. For outcomes we considered the assessment of postoperative eyelid edema and periorbital ecchymosis as well as of postsurgical pain and mucosal injury. The quality assessment was performed using the Cochrane risk of bias for randomized studies.

Results Data from 347 cases were considered for the qualitative synthesis and data from 246 cases for the quantitative synthesis. Eyelid edema within the first three postoperative days (SMD = -0,65; 95% CI = [-1,18, -0,12]) and on postoperative Day 7 (SMD = -0,69; 95% CI = [-1,47, -0,09]) were statistically lower in the treatment group in comparison with the control group. Accordingly, periorbital ecchymosis within the first three postoperative days (SMD = -0,85; 95% CI = [-1,42, -0,28]) and on postoperative Day 7 (SMD = -0,52; 95% CI = [-0,79, -0,24]) were statistically lower in the treatment group in comparison with the control group. Similar results were reached after subgroup analysis, taking into consideration the osteotomy visibility (blind osteotomy versus osteotomy under direct vision), but the difference in edema and ecchymosis in osteotomies under direct vision was statistically lower between the control and intervention group. Intraoperative mucosal injury was statistically lower during piezoelectric osteotomies (OR = 0,06; 95% CI = [0,01, 0,53]). Finally, pain during the first three postoperative days was also statistically lower in the treatment group versus the control group (SMD = -0,99; CI [-1,78, -0,11]).

Conclusions The quantitative synthesis demonstrated that lateral piezoelectric osteotomy in rhinoplasty decreases postsurgical periorbital edema and ecchymosis, postsurgical pain and intraoperative mucosa injuries compared to the conventional osteotomy technique with a chisel. Piezoelectric osteotomies are especially connected with less postoperative edema and ecchymosis in osteotomies that are not executed under direct vision. The overall results of this study suggest that piezoelectric instruments could be the surgical instrument of choice for lateral osteotomies in rhinoplasty, especially for those not under direct vision, but a definite recommendation favoring piezoelectric osteotomy cannot be made until more studies with higher numbers become available.

Key words Rhinoplasty, Osteotomy, Piezo surgery, Piezoelectric, Edema, Ecchymosis, Pain, Meta-analysis

Περίληψη

Εισαγωγή Η οστεοτομία των ρινικών οστών κατά την διάρκεια της ρινοπλαστικής συνδέεται με μετεγχειρητικές επιπλοκές. Πρόσφατα δεδομένα υποδεικνύουν ότι μια νέα χειρουργική μέθοδος, η οποία χρησιμοποιεί κύματα υπερήχων για τις πλάγιες οστεοτομίες στην ρινοπλαστική, περιορίζει τον τραυματισμό των μαλακών ιστών και οδηγεί σε λιγότερο μετεγχειρητικό οίδημα και εκχύμωση.

Στόχοι Ο σκοπός αυτής της μελέτης ήταν η σύγκριση και η ανάλυση των κλινικών αποτελεσμάτων της πρώιμης μετεγχειρητικής περιόδου σε πλάγιες οστεοτομίες που πραγματοποιούνται είτε με πιεζοτόμο είτε με συμβατικά όργανα σε ρινοπλαστικές.

Μέθοδοι Αναζητήσαμε βιβλιογραφία στο PubMed, CENTRAL και Web of Science από το 2005 μέχρι 17 Αυγούστου 2019. Συμπεριλάβαμε μελέτες που συνέκριναν τα αποτελέσματα σε ασθενείς που υποβλήθηκαν σε πλάγια οστεοτομία με πιεζοτόμο ή συμβατικά εργαλεία κατά την διάρκεια ρινοπλαστικής. Ως αποτελέσματα λάβαμε υπόψιν το μετεγχειρητικό βλεφαρικό οίδημα και περικογχική εκχύμωση, τον μετεγχειρητικό πόνο καθώς και τον διεγχειρητικό τραυματισμό βλεννογόνων. Η ποιοτική αξιολόγηση των δεδομένων έγινε χρησιμοποιώντας την Cochrane risk of bias για τυχαιοποιημένες μελέτες.

Αποτελέσματα Δεδομένα από 347 ασθενείς χρησιμοποιήθηκαν σε αυτήν την μελέτη. Το περικογχικό οίδημα τόσο κατά τις τρεις πρώτες μετεγχειρητικές ημέρες (SMD = -0,65; 95% CI = [-1,18, -0,12]) όσο και στην έβδομη μετεγχειρητική ημέρα (SMD = -0,69; 95% CI = [-1,47, -0,09]), ήταν στατιστικώς λιγότερο στην ομάδα παρέμβασης έναντι της ομάδας ελέγχου. Ομοίως, η περικογχική εκχύμωση τόσο τις τρεις πρώτες μετεγχειρητικές ημέρες (SMD = -0,85 ; 95% CI = [-1,42 , -0,28]) όσο και την έβδομη μετεγχειρητική ημέρα (SMD = -0,52 ; 95% CI = [-0,79, -0,24]) ήταν στατιστικώς λιγότερο στην ομάδα παρέμβασης έναντι της ομάδας ελέγχου. Ανάλογα αποτελέσματα εξήχθησαν έπειτα από ανάλυση υποομάδων(subgroup analysis), λαμβάνοντας υπόψιν την ορατότητα της οστεοτομίας (τυφλή ή υπό άμεση ορατότητα). Ο διεγχειρητικός βλεννογονικός τραυματισμός ήταν στατιστικά χαμηλότερος κατά τις οστεοτομίες με πιεζοτόμο (OR = 0,06; 95% CI = [0,01, 0,53]). Τέλος, ο πόνος κατά τις τρεις πρώτες μετεγχειρητικές ημέρες ήταν στατιστικά χαμηλότερος στην ομάδα παρέμβασης από ότι στην ομάδα ελέγχου (SMD = -0,99; CI = [-1,78 , -0,11]).

Συμπεράσματα Η ποσοτική σύνθεση κατέδειξε ότι η πλάγια οστεοτομία με πιεζοτόμο στην ρινοπλαστική ελαττώνει το μετεγχειρητικό βλεφαριδικό οίδημα, την περικογχική εκχύμωση, τον μετεγχειρητικό πόνο και τον διεγχειρητικό τραυματισμό βλεννογόνων σε σύγκριση με την οστεοτομία με συμβατικά εργαλεία. Οι πιεζοηλεκτρική πλάγια οστεοτομία συνδέεται ιδιαίτερα με λιγότερο μετεγχειρητικό οίδημα και εκχύμωση σε οστεοτομίες που δεν εκτελούνται υπό άμεση όραση. Τα συνολικά αποτελέσματα της μελέτης υποδεικνύουν ότι οι πιεζοτόμοι θα μπορούσαν να αποτελούν χειρουργικό εργαλείο εκλογής για τις πλάγιες οστεοτομίες στην ρινοπλαστική, ειδικά σε αυτές όχι υπό άμεση όραση, αλλά μια οριστική πρόταση υπέρ της οστεοτομίας με πιεζοτόμο δεν μπορεί να πραγματοποιηθεί μέχρι περισσότερες μελέτες με περισσότερους συμμετέχοντες γίνουν διαθέσιμες.

Λέξεις Κλειδιά Ρινοπλαστική, Οστεοτομία, Πιεζοχειρουργική, Πιεζοηλεκτρικός, Οίδημα, Εκχύμωση, Πόνος, Μετα-ανάλυση

Introduction

Osteotomy of the nasal bones is the most challenging and critical step in rhinoplasty. The shaping of the nasal bony structures is the key for a successful operation. (7-8) The type of osteotomy (medial, lateral, or transverse) depends on the nasal deformity to be addressed in order to achieve the desired esthetic and functional outcome. (2,9)

Lateral osteotomy in particular, is the last step of rhinoplasty and its precision is the key to its success. The main indications of lateral osteotomy include the open roof deformity correction after removing the nose hump, the narrowing of the nasal pyramid and the straightening the nasal bones. (19-20,24) In this phase, the mobilization of nasal bones along with minimizing the damage of supporting tissue and avoiding the excessive narrowing, are the main goals of lateral osteotomy (21). Various techniques for lateral osteotomies have been described for the desired aesthetic and functional results, with major goal the reduction of soft tissue damage during rhinoplasty. There is still ambiguity regarding the optimal one. (10,25,26)

Apart from surgical approaches, various different techniques and methods, including percutaneous, trans-oral and endo-nasal procedures, have been suggested to make this step less traumatic by reducing soft tissue damage during osteotomies (1,3-5,8 ,10-13). Each technique has both advantages and limitations. Soft-tissue trauma in particular may lead to prolonged postoperative edema and ecchymosis, as well as apparent irregularities in nasal bone owing to the thin overlying skin. Therefore, a precise and safe osteotomy technique is the desideratum for the preservation of bony structures and the protection of adjacent soft tissues. (18)

Piezoelectric surgery is a new method commonly used during osteotomies, which takes advantage of ultrasonic piezoelectric vibrations in order to decrease the severity of morbidities (6). Its ability to minimize tissue trauma and its associated morbidity, along with its cutting effectiveness, has rendered Piesosurgery popular for several clinical applications in various surgical fields during the last decades. (22) This method is considered though a relatively new alternative for bony procedures in craniofacial surgeries. (27)

It was first introduced by Horton et al in alveolar bone surgery in 1975 (14-15) Since then the technique has improved rapidly and has extended its indications (17). In 2007 Robiony et al was the first to report nasal osteotomy using piezoelectric devices, achieved by adjusting the power and frequency of ultrasound waves employed. (16) Since then, several studies have been conducted indicating that piezoelectric instruments are connected with fewer morbidities in both external and internal lateral osteotomies. (28,29,30-36). This instrument was capable of performing osteotomies with precision, minimizing the damage of surrounding soft tissues and critical structures (nerves, vessels, and mucosa), and avoiding osteonecrosis. (23)

Although several studies have compared the difference in postsurgical morbidities between piezoelectric and conventional osteotomy, none of them have reached a clear conclusion regarding the superiority of either method. (21,30-36). According to the majority of them, the number of samples in these studies was quite limited. Therefore, there were no definitive results on which of the two methods is more effective in reducing for edema and ecchymosis.

A meta-analysis offers readers an overview of competing treatments and potentially ranks them combining the results of Randomized Controlled Studies.

This approach could help us gain an insight of the results of Piezosurgery in rhinoplasty by critically appraising key comparisons drawn from randomized trials in a robust way. Thus, in the current meta-analysis, we sought to assess the main intraoperative and postoperative morbidities of piezoelectric and conventional osteotomy on lateral osteotomies in rhinoplasty by comparing these two techniques.

Materials and Methods

Inclusion and Exclusion Criteria

In this meta-analysis were included only Randomized Clinical Trials, investigating the intraoperative and postoperative morbidities of lateral osteotomy in rhinoplasty using either a Piezoelectric device or a conventional osteotome. We chose only studies where the patients were subjected to lateral nasal osteotomies during rhinoplasty (open or closed), either with a conventional osteotome (control group) or with an ultrasonic piezoelectric device (intervention group). The comparison of the piezoelectric with the conventional osteotomy applied for either intraoperative morbidities (mucosal injury) or postoperative morbidities (eyelid edema, periorbital ecchymosis and postoperative pain). We excluded trials which studied the effects of piezoelectric osteotomy on different surgical procedures or trials which did not present quantifiable data.

Literature search

We performed a literature search including the following electronic databases from 2005 up to 17 August 2019: PubMed, Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Science. In these database searches, we applied no language restrictions. We also considered reference lists of relevant studies. Furthermore, we searched ClinicalTrials.gov for completed unpublished comparative studies. This search was conducted using Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. For the search strategy we used the following terms: “piezosurgery”, “piezoelectric”, “rhinoplasty”, “osteotomy”. We adapted this search to each included database.

Study selection

One review author searched for records. The titles and abstracts of these records were screened for eligibility. For the eligible articles, we obtained the full texts and assessed them for potential inclusion. We included only Randomized Controlled Trials in the meta-analysis. Totally, we retrieved 138 articles. (59 articles from Web of Science, 28 articles from PubMed, 14 articles from CENTRAL, 37 from clinicaltrials.gov). Additionally, we reached another 35 articles from other sources such as references from other studies and systematic reviews. Duplicate studies were removed and 131 articles were left for assessment. The initial screening discarded studies that were not related to piezoelectric osteotomy in rhinoplasty. Totally 28 articles were topic relevant. Full-text articles were obtained for all potentially relevant studies. Out of them only 7 were randomized and used controlled groups to assess the effect of piezoelectric osteotomy in rhinoplasty with quantifiable data. Figure 1 depicts the strategy used for study identification.

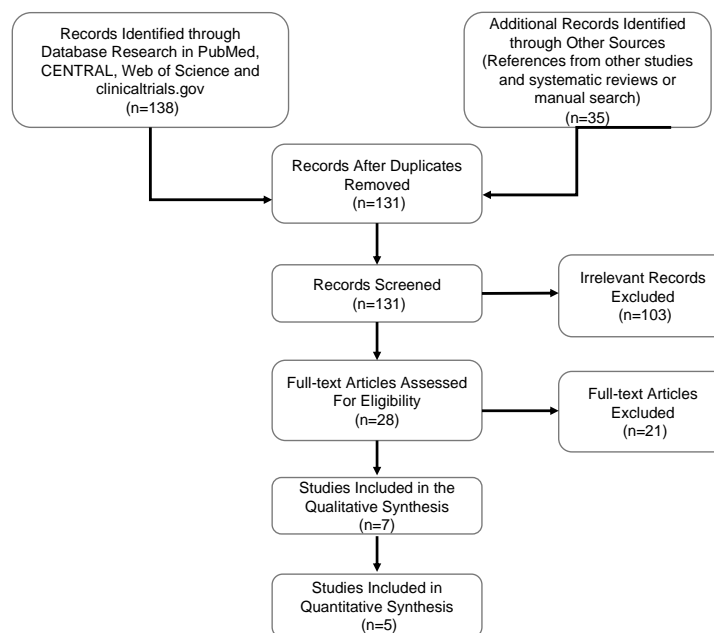


Fig. 1 Flow diagram of the study selection procedure

Data extraction

One reviewer extracted the data. We recorded the following data: the year of publication, the comparators in the control group as well as the number and the demographics of patients in the included intervention groups. We also extracted information about the intervention characteristics, follow-up and study outcomes (Figure 2, Figure 3). In particular, were assessed intraoperative morbidities (mucosal injury) as well as postsurgical morbidities such as eyelid edema and periorbital ecchymosis (within 3 days or on day 7 postoperatively) and postoperative pain (within 3 days postoperatively). Eyelid edema and periorbital ecchymosis were evaluated separately using graded scales. Postoperative pain was assessed with a pain score. More specifically, assessment of the outcomes was conducted as follows:

- Mucosa injury: Patients were subjected to endoscopic examination on day 4 postoperatively.
- Pain: Postoperative pain was assessed by visual analogue scale (VAS). A ten-point ruler was given to patients in which zero showed least pain and 10 represented the most severe pain.
- Edema: Eyelid edema was evaluated by a 4-grade visual scale as described by Kara and Gökalan (41). Grade 1 showed no coverage of iris with eyelids, Grade 2 slight coverage of iris with swollen eyelids, Grade 3 full coverage of iris with swollen eyelids, and Grade 4, full coverage of the eye (41).
- Ecchymosis: Eyelid ecchymosis was assessed by a 3-grade visual scale as described by Kara and Gökalan (41). Grade 1, represented

ecchymosis up to the medial one-third part of lower and /or upper eyelid, Grade 2 ecchymosis up to the medial two-third part of the lower and/or upper eyelid and Grade 3, ecchymosis up to the full length and /or upper eyelid (41).

Study (year)	Country	Inclusion criteria	Exclusion criteria	Number of patients	chronicity	age	males/females
Tirelli et al. (2015)	Italy	History of maxillofacial trauma with specific nasal involvement, consensual deviation of both the nasal septum and pyramid, presence of a wide nasal dorsum and prominent hump and associated nasal respiratory dysfunction	Patients who had already undergone a previous rhinoplasty procedure, or who presented a narrow nasal dorsum and a minimal hump were excluded.	22	from January through September 2013		12women/10men
Illhan et al. (2016)	Turkey		Patients who were current smokers; patients with chronic rhinosinusitis, chronic dermatologic or rheumatologic diseases, nasal polyposis, asthma, or allergic rhinitis; and patients who had previously undergone septoplasty or rhinoplasty. Patients were screened preoperatively for coagulation by evaluating prothrombin time, partial thromboplastin time, and bleeding/ coagulation time. Patients with values outside reference ranges were excluded from this study.	56	from November 2014 to February 2015	26,07 ± 6,48	48women/8men
Taskin et al. (2017)	Turkey		Previous nasal surgery, use of anticoagulant drugs, hypertension, bleeding diathesis with chronic disease, chronic skin allergy, or inflammatory sinus disease.	90	between June 2015 and March 2016	25,6±5,6	55female/34 male
Kocak et al. (2017)	Turkey		History of rhinoplasty, an extremely wide nasal roof, need for double lateral osteotomy, a narrow nasal roof and coagulopathy, smoking, systemic diseases	49	between January 2016 and July 2016	25,7 ± 5,4 for conventional osteotomy 28,5 ± 3,1 for Piezosurgery	32 women / 17men
Koc et al. (2017)	Turkey		History of smoking, presence of systemic diseases (such as cardiac disease, diabetes mellitus, hypertension, bronchial asthma, neurologic diseases) and use of medications	65	between May 2015 and January 2016	23±5,71	36women/29men
Ghavimi et al. (2018)	Iran	Absence of contraindication for rhinoplasty surgery. Indication of the internal lateral osteotomy, no anesthesia contraindication (ASA I and II) and	Current smokers, patients with chronic rhinosinusitis, chronic diseases of the skin or rheumatology, nasal polyps, asthma, allergic rhinitis, patients with prior septoplasty or nasal beautification surgeries, ecchymosis or edema before surgery for any reason as well as the patients who did not come back for postoperative examinations were excluded. Patients with a thick skin or with lateral bone thicker than 3 mm were excluded from the study.	66	from March to November 2017		33women/33men
			Pregnant patients, on antidepressants, or appeared non-			24±1,63 for conventional	

Table 1 Qualitative characteristics of analyzed studies

Study (year)	Outcome measure	Surgical Technique, Control Group	Surgical Technique, Intervention Group	Osteotomy approach / Soft tissue dissection
Tirelli et al. (2015)	Eyelid edema, Periorbital ecchymosis, Operative time, Mucosal injury	Lateral Osteotomy with conventional em 3-mm-guided-curved Osteotome	Lateral Osteotomy with VarioSurg-3-Piezo-Instrument	External approach / Limited dissection
Illhan et al. (2016)	Eyelid edema, Periorbital ecchymosis	Lateral Osteotomy with no further defined, conventional Instruments	Lateral Osteotomy with micro-saw OT7 tip (Mectron, Carasco, Italy) Piezo- Instrument	Intranasal approach / Limited dissection
Taskin et al. (2017)	Eyelid edema, Periorbital ecchymosis	Osteotomy with no further defined, conventional Instruments	Lateral Osteotomy with Piezo-Instrument	Intranasal approach / Wide dissection
Kocak et al. (2017)	Eyelid edema, Periorbital ecchymosis, Operative time, Pain score, Mucosal injury	Osteotomy with conventional em 2-mm-guarded, straight Osteotome	Lateral Osteotomy with Piezo-Instrument	Intranasal approach / Limited dissection
Koc et al. (2017)	Eyelid edema, Periorbital ecchymosis, Operative time, Pain score	Lateral nasal osteotomy by using two stab incisions by utilizing a 2mm osteotome	Lateral nasal osteotomy after two stab incisions with 2mm using the Viosurg device from NSK Company with a lateral osteotomy pen.	External approach/ Limited dissection
Ghavimi et al. (2018)	Eyelid edema, Periorbital ecchymosis	Lateral osteotomy with external percutaneous approach with a 2-mm traditional osteotome	Lateral osteotomy with external percutaneous approach with the Piezosurgery Medical Device	External approach/ Limited dissection
Fallahi et al. (2019)	Eyelid edema, Periorbital ecchymosis, Operative time, Pain score	Lateral osteotomy with a standard chisel	Lateral osteotomy with Piezo-Instrument	Intranasal approach / Wide dissection

Table 2 Qualitative characteristics of analyzed studies

Quality assessment

One investigator performed the quality assessment of individual trials using the Cochrane Collaboration's "risk bias". (37) For the assessment of the included trials, we considered the following domains: randomization; Allocation concealment, blinding of patients, blinding of personnel and blinding of outcome

assessors. We judged each domain as either low, unclear, or high risk of bias. Furthermore, we assessed the quality across studies. For each domain of the Cochrane's risk of bias tool, if more than half of the information was from studies at a low risk of bias, we judged the domain to be at a low risk of bias. If most information was from studies at an unclear/high risk of bias, we considered the domain to be an unclear/ high risk of bias, respectively. For all study outcomes, we considered the domain of masking the outcome assessors to be crucial (38). Finally, we contacted the corresponding authors of the included studies to request additional information in regard to the quality assessment. We resolved the discrepancies about the risk of bias assessment through discussion.

Study(Year)	Type of study	Randomization	Allocation concealment	Blinding of participants	Blinding of personnel	Blinding of outcome assessors	Overall Risk of Bias
Tirelli et al. (2015)	RCT	LOW	UNCLEAR	LOW	UNCLEAR	LOW	LOW
Ihlan et al. (2016)	RCT	LOW	UNCLEAR	LOW	UNCLEAR	LOW	LOW
Taskin et al. (2017)	RCT	UNCLEAR	UNCLEAR	UNCLEAR	UNCLEAR	LOW	UNCLEAR
Koçak et al. (2017)	RCT	LOW	UNCLEAR	UNCLEAR	UNCLEAR	LOW	UNCLEAR
Koc et al. (2017)	RCT	LOW	UNCLEAR	LOW	UNCLEAR	LOW	LOW
Ghavimi et al. (2018)	RCT	UNCLEAR	UNCLEAR	LOW	UNCLEAR	LOW	UNCLEAR
Fallahi et al. (2019)	RCT	LOW	LOW	LOW	LOW	LOW	LOW

Table 3 Quality assessment

Statistical analysis

We used the Review Manager (RevMan) Software (version 5.3) to perform pair-wise meta-analysis (39). For continuous outcomes (comparison of means and standard deviations between control and treatment groups), we conducted random effects quantitative synthesis utilizing the effect size of Standardized Mean Difference (SMD) and calculated 95% confidence intervals (Cis) according to the inverse variance method. For dichotomous outcomes, we conducted a random effects meta-analysis using the Mantel-Haenszel method and considered the effect measure of odds ratio (OR). In this review, a *p* value of less than 0,05 indicated statistical significance. We explored for statistical heterogeneity using the *Q* statistic and measured the extend of heterogeneity using the *I²* statistic. We considered the following classification of statistical heterogeneity (39):

- $I^2 = 0-40\%$: not important heterogeneity
- $I^2 = 30-60\%$: moderate heterogeneity
- $I^2 = 50-90\%$: substantial heterogeneity
- $I^2 = 75-100\%$: considerable heterogeneity

We avoided using funnel plot for publication bias detection, because in our analysis we included only 5 studies. When there are fewer than 10 studies the power of the tests is too low to distinguish chance from real asymmetry (69).

Synthesis of the results

For clinical outcomes, we avoided combining data from different study designs. Instead we excluded perspective cohort studies and included exquisitely randomized controlled trials, with the aim to supplement the results of our meta-analysis (68).

Subgroup and sensitivity analyses

We accounted for the impact of the osteotomy visibility (blind osteotomy versus osteotomy under direct vision), depending on the width of the incision performed (3mm or lower) by conducting a prespecified subgroup analysis. Furthermore, we performed a sensitivity analysis, in which we excluded trials of an unclear and high risk of bias.

Clinical interpretation of the results

The classification of the effect sizes in the meta-analysis was (42):

- SMD <0.4: small effect
- $0.4 < \text{SMD} < 0.7$: moderate effect
- $0.7 < \text{SMD}$: large effect

For the clinical interpretation of the results we accounted for the level of evidence and statistical power of the analysis.

Ethical Considerations

This study did not enroll human participants for treatment. As a result, there was not a need for informed consent for this systematic review and meta-analysis.

Results

Seven studies with 347 patients were included for qualitative synthesis in this systematic review. Totally 208 of the participants were women and 139 were men. The qualitative data regarding the participants age could not be assessed because of incomplete reporting among the studies. The study characteristics are depicted in Table 1 and Table 2.

Five studies with 246 patients were included for the quantitative synthesis. The extracted data were used for the comparison of intraoperative outcomes (mucosa injury) as well as for the comparison of intraoperative outcomes (eyelid edema, periorbital ecchymosis, postoperative pain).

Intraoperative outcomes

Only two studies provided data regarding intraoperative mucosa injury, examined by endoscopy on day 4 post-surgically. The incidence of intraoperative

mucosal injury (OR = 0,06; 95% CI = [0,01, 0,53]; $p=0,01$; $I^2 = 0\%$; Figure 2) was statistically lower during the piezoelectric in comparison with the conventional osteotomy. The inter-study heterogeneity was not important.

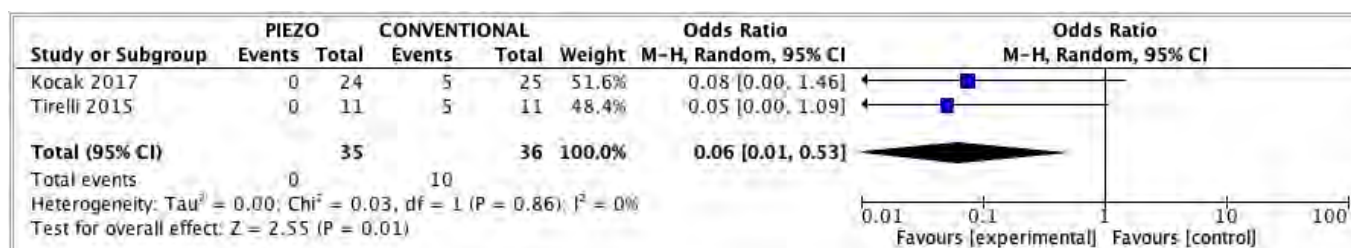


Figure 2 Forest plot of standardized mean differences for the assessment of intraoperative mucosa injury

Postoperative outcomes

Eyelid edema and Periorbital ecchymosis was assessed by the data extracted by four studies.

Eyelid edema in particular, was assessed within the first three postoperative days (SMD = -0,65; 95% CI = [-1,18, -0,12]; $I^2=69\%$; $p=0,02$; Figure 3) as well as on postoperative day 7 (SMD = -0,69 ; 95% CI = [-1,47, -0,09] ; $p=0,08$; $I^2=85\%$; Figure 4). Eyelid edema is statistically lower in patients that underwent piezoelectric osteotomies. The difference in eyelid edema was higher between the control and intervention group on day 7 than within the first three postoperative days. Substantial inter-study heterogeneity was found in these outcomes.

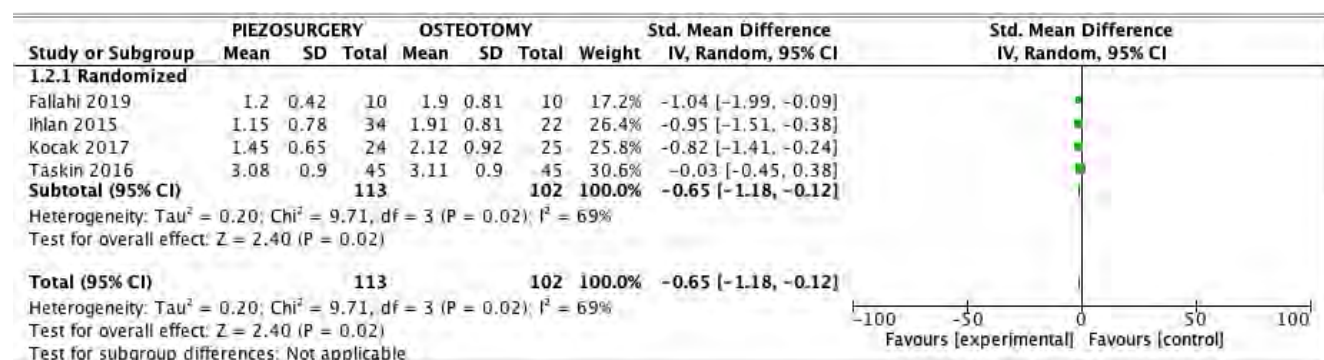


Figure 3 Forest plot of standardized mean differences for the assessment of eyelid edema within the first three postoperative days

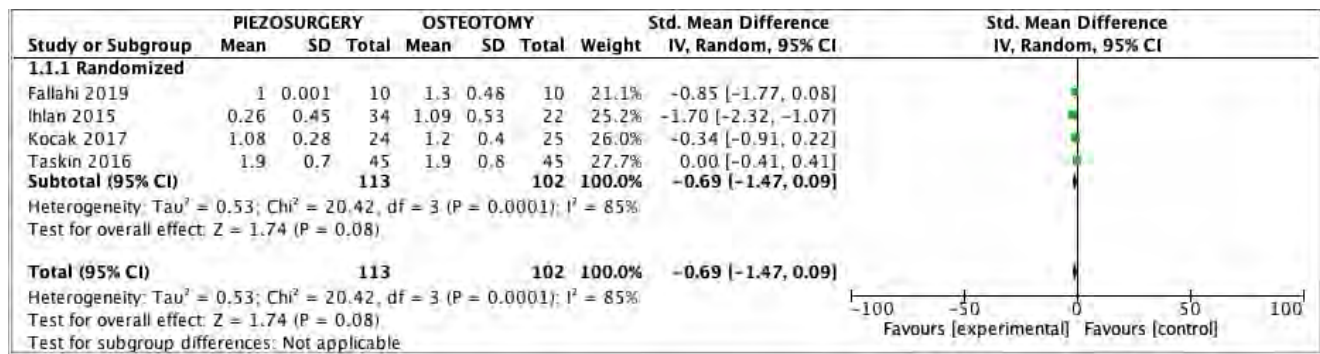


Figure 4 Forest plot of standardized mean differences for the assessment of eyelid edema on postoperative Day 7

Periorbital ecchymosis was assessed also within the first three postoperative days ($SMD = -0.85$; $95\% CI = [-1.42, -0.28]$; $I^2 = 72\%$; $p=0.004$; Figure 5) as well as on postoperative day 7 ($SMD = -0.52$; $95\% CI = [-0.79, -0.24]$; $p=0.0003$; $I^2=71\%$; Figure 6). It is obvious that periorbital ecchymosis is lower at patients that underwent piezoelectric osteotomy. The difference between periorbital ecchymosis was lower between the control and intervention group on day 7 than within the first three postoperative days. Substantial inter-study heterogeneity was found in these outcomes.

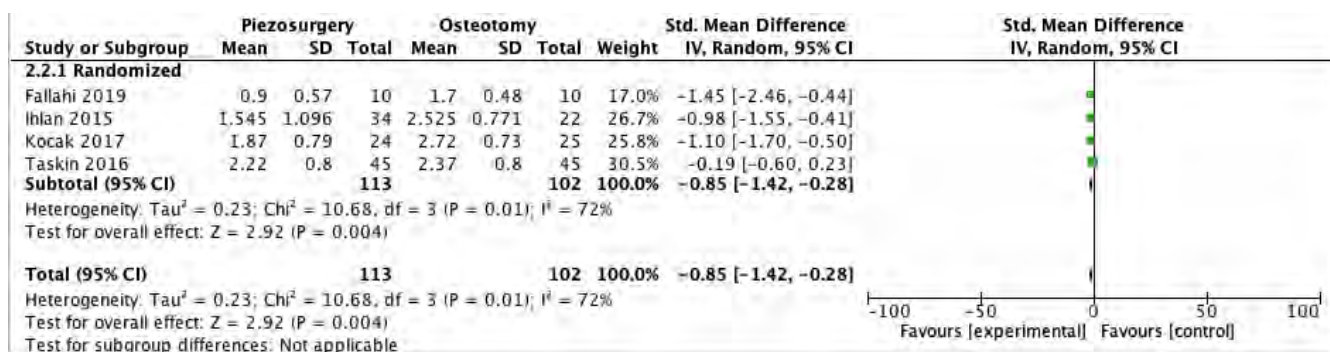


Figure 5 Forest plot of standardized mean differences for the assessment of periorbital ecchymosis within the first three postoperative days

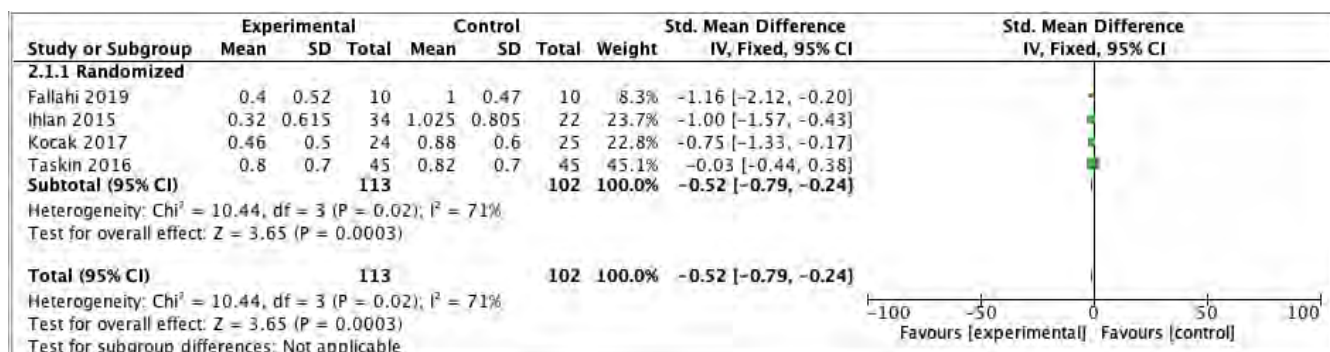


Figure 6 Forest plot of standardized mean differences for the assessment of periorbital ecchymosis on postoperative Day 7

Postoperative pain within the first three days postoperatively, was analyzed using the available data by two studies. (SMD = -0,99; CI [-1,78, -0,11]; I^2 =49%; p =0,01; Figure 11) The postoperative pain was lower in the patients that underwent piezoelectric osteotomy in comparison with those that underwent conventional osteotomy. Moderate heterogeneity was found in this outcome.

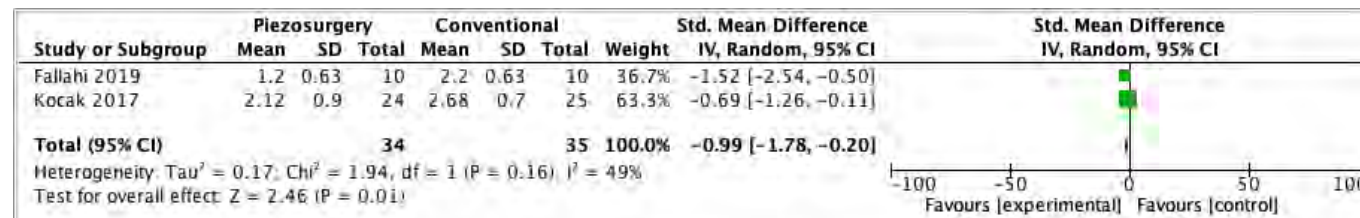


Figure 11 Forest plot of standardized mean differences for the assessment of postoperative pain within the first three postoperative days.

Subgroup Analysis

In both outcomes (eyelid edema and periorbital ecchymosis) was found substantial heterogeneity. In all these Randomized Controlled Trials the same surgical approach was performed (internal lateral osteotomy). However surgical approach deferred in the extend of incision performed. Only in two of the analyzed clinical trials was performed a wide surgical incision (3mm) and thus lateral osteotomy under vision in comparison. On the contrary, in the remaining studies was preferred a narrow surgical incision and the osteotomy was executed blindly. Thus, a subgroup analysis was performed dividing the studies based on the width of the surgical incision.

Overall both postsurgical eyelid edema and periorbital ecchymosis were statistically lower in patients that underwent lateral osteotomies under direct vision. (Figure 7-10). However, piezoelectric osteotomy under direct vision had no significant difference in edema and ecchymosis compared to conventional osteotomy, especially on the postoperative Day 7.

Eyelid edema was assessed within the first three postoperative days separately for patients that underwent lateral osteotomy with a wide surgical incision (SMD = -0,44; CI [-1,41, -0,53]; I^2 =73%; p =0,37; Figure 7) as well as for those who underwent a narrow surgical incision (SMD = -0,89; CI [-1,29, -0,48]; I^2 =0%; p < 0,0001; Figure 7). The Standardized Mean Difference (SMD) was higher in osteotomies with narrow incisions. Also, in this group heterogeneity was insignificant.

The results were also similar for the postsurgical Day 7. In particular, for patients that underwent lateral osteotomy with a wide surgical incision (SMD = -0,32; CI [-1,12, -0,49]; I^2 =63%; p =0,44; Figure 8), the Standardized Mean Difference (SMD) was lower than in patients that undergone narrow surgical incision (SMD = -1,01; CI [-2,34, -0,32]; I^2 =90%; p =0,14; Figure 8). However, in both groups heterogeneity was substantial.

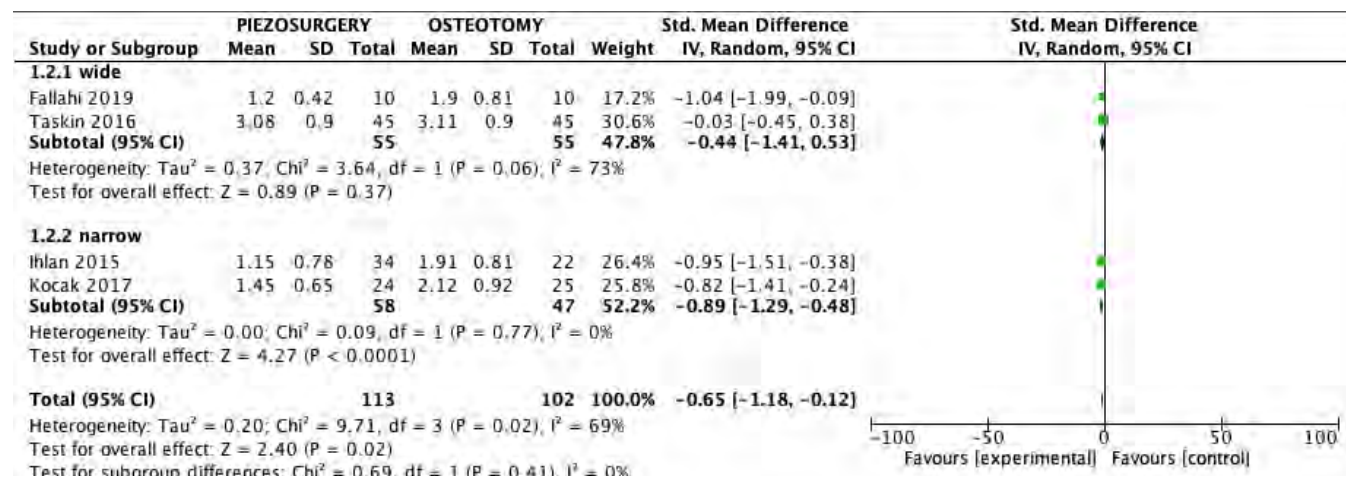


Figure 7 Forest plot of standardized mean differences for the assessment of eyelid edema within the first three postoperative days considering the width of surgical incision

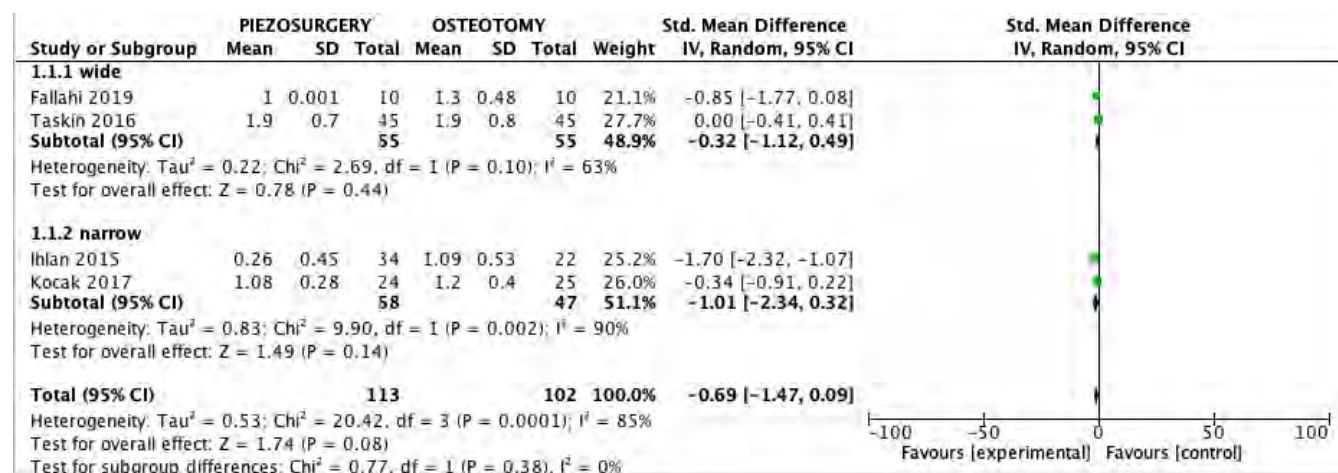


Figure 8 Forest plot of standardized mean differences for the assessment of eyelid edema on postoperative Day 7 considering the width of surgical incision

Similarly, periorbital ecchymosis was assessed within the first three postoperative days separately for patients that underwent lateral osteotomy with a wide surgical incision (SMD = -0,73; CI [-1,96, 0,50]; $I^2 = 81\%$; $p = 0,24$; Figure 9) as well as for those with a narrow surgical incision (SMD = -1,04; CI [-1,45, -0,62]; $I^2 = 0\%$; $p < 0,0001$; Figure 9). The Standardized Mean Difference (SMD) was higher in osteotomies with narrow incisions. Also, in this group heterogeneity was insignificant.

The same assessment was executed also for the postsurgical Day 7 separately for patients that underwent lateral osteotomy with a wide surgical incision (SMD = -0,20; CI [-0,58, 0,18]; $I^2 = 78\%$; $p = 0,29$; Figure 10) as well as for those with a narrow surgical incision (SMD = -0,88; CI [-1,28, -0,47]; $I^2 = 0\%$; $p < 0,0001$; Figure 10). The Standardized Mean Difference (SMD) was higher in osteotomies with narrow incisions. Also, in this group heterogeneity was insignificant.

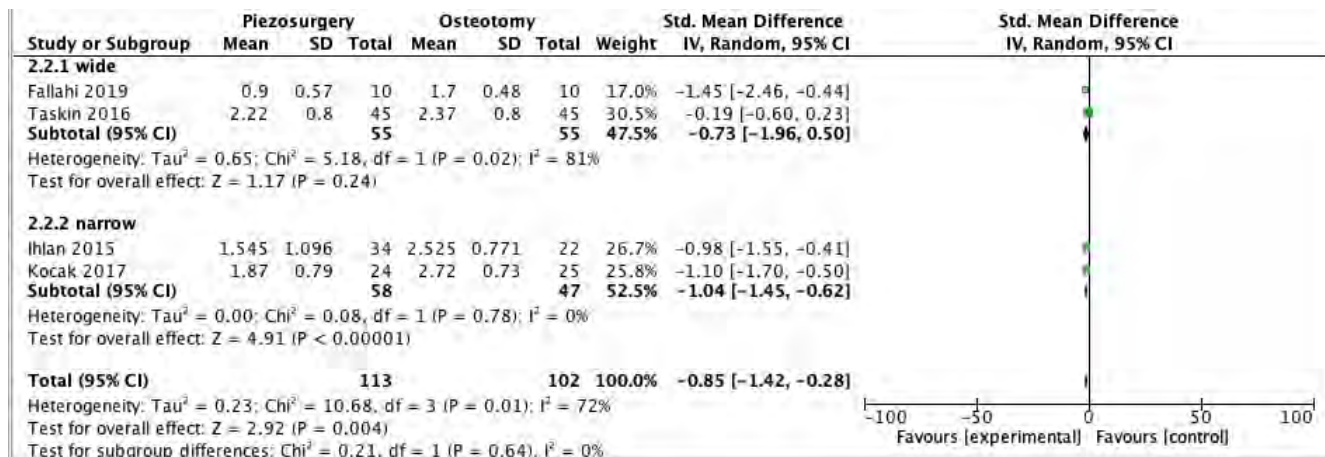


Figure 9 Forest plot of standardized mean differences for the assessment of periorbital ecchymosis within the first three postoperative days considering the width of surgical incision

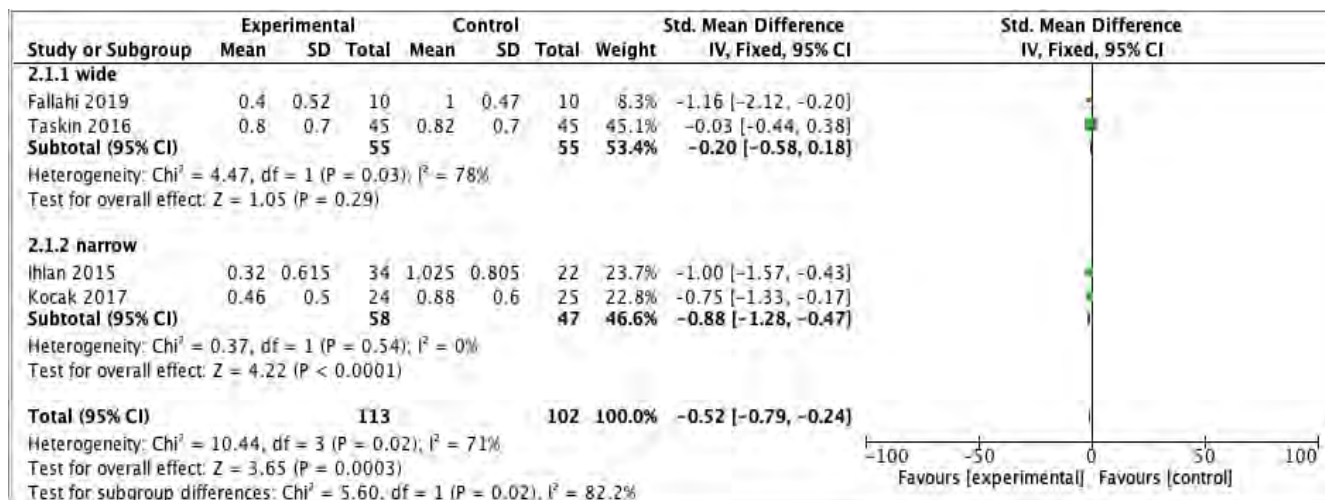


Figure 10 Forest plot of standardized mean differences for the assessment of periorbital ecchymosis on postoperative Day 7 considering the width of surgical incision

Sensitivity analyses

We conducted a pre-determined sensitivity analysis, in which trials of an unclear or high risk of bias were excluded and insignificant heterogeneity levels were detected with the exception of the assessment of eyelid edema on postoperative Day 7 ($I^2 = 55\%$). Statistical differences were detected between primary and sensitivity analysis when we accounted for periorbital ecchymosis and eyelid edema.

The Standard Mean Differences (SMD) calculated after sensitivity analysis were higher in all outcomes in comparison with the primary analysis, thus the differences in postoperative eyelid edema and periorbital ecchymosis between control and intervention groups were more intense for all outcomes.

Specifically, the results for eyelid edema within the first three postoperative days were: (SMD = -0.97; 95% CI = [-1.46, -0.48]; $p < 0.0001$; $I^2 = 0\%$; Figure 12) and

on postoperative Day 7 were: (SMD = -1,34; 95% CI = [-2,16 , -0,52] ; p=0,001 ; $I^2 = 55\%$; Figure 13).

Accordingly, the results for periorbital ecchymosis within the first three postoperative days were (SMD = - 1,10; 95% CI = [-1,59, -0,60]; p<0,0001; $I^2 = 0\%$; Figure 14) and on postoperative Day 7 were: (SMD = - 0,66; 95% CI = [-0,95, -0,37]; p<0,0001; $I^2 = 0\%$; Figure 15).

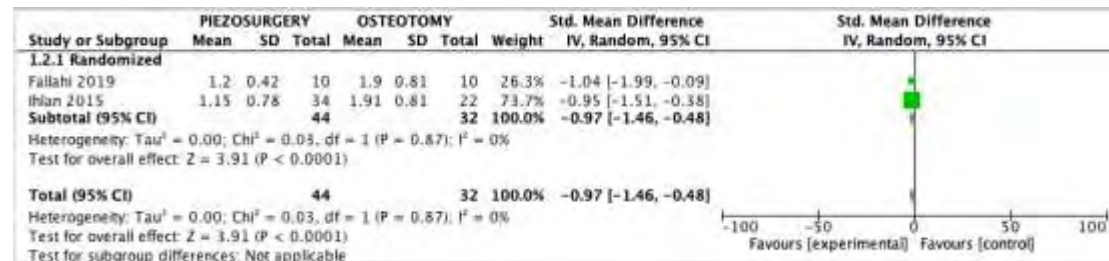


Figure 12 Forest plot of standardized mean differences for the assessment of eyelid edema within the first three postoperative days (sensitivity analysis)

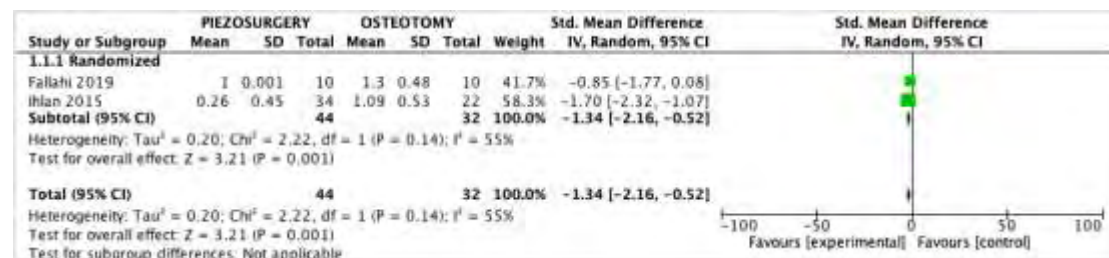


Figure 13 Forest plot of standardized mean differences for the assessment of eyelid edema on postoperative Day 7 (sensitivity analysis)

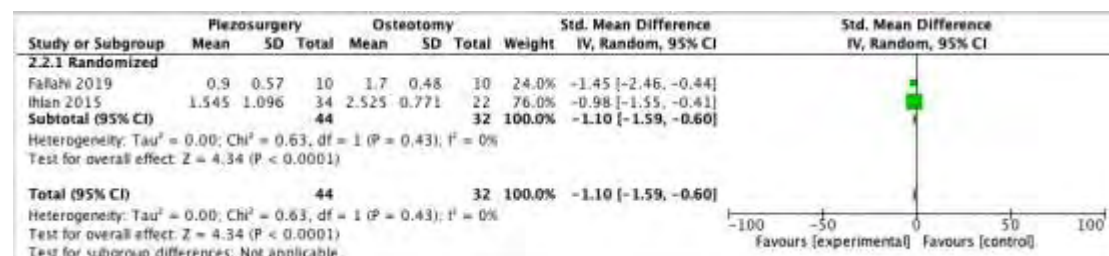


Figure 14 Forest plot of standardized mean differences for the assessment of periorbital ecchymosis within the first three postoperative days (sensitivity analysis)

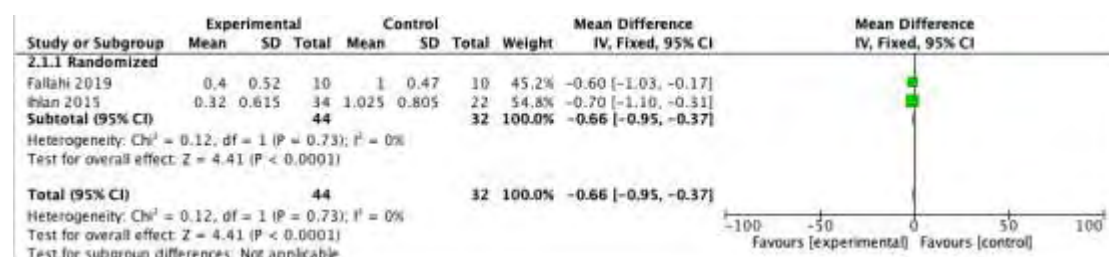


Figure 15 Forest plot of standardized mean differences for the assessment of periorbital ecchymosis on postoperative Day 7 (sensitivity analysis)

Discussion

Various studies show that soft-tissue injury during osteotomies lead to postsurgical edema and ecchymosis (6,7,9,30,32,41, 43 -54). During rhinoplasty, the surgeon must sculpt the bony pyramid while preserving the soft-tissue envelope, through a series of procedures that may include narrowing the lateral nasal walls, reducing the dorsal hump, closing an open-roof deformity, and straightening the bony framework of the nose. (44-45,57) These actions often lead to complications and require great precision. Surgical techniques and devices might have a role in these morbidities. Therefore, the ideal method and approach for lateral osteotomy is still unclear (59) and there is a great interest in potential osteotomy techniques and instruments to prevent soft-tissue injury (55-56).

Traditionally, osteotomies in rhinoplasty are conducted with osteotomes (e.g. Alexander, McIndoe, or Walter chisel) that apply a significant amount of mechanical force on the bone and on soft tissue (58). For this reason, they are highly susceptible to disrupting major blood vessels in the soft tissues around the nasal bone. As a result, ecchymosis and edema may develop perioperatively and may persist until the ninth postoperative day (60). On the contrary, Piezotome is an instrument that converts electric current to ultrasonic waves and transmits them to a chisel located at the tip of the instrument, providing a gentle and easy way of osteotomy with minimal external pressure, suitable especially for complex anatomic areas. (21, 22) The rhythmic microscopic pressure waves enable more precise separation of soft tissue layers and detachment of the periosteum (64,64) and fact that leads therefore to less intraoperative and postsurgical bleeding from disrupted intra-periosteal blood vessels in comparison with the traditional periosteal elevators (61,62,63).

In this systematic review and meta-analysis, we compared the intra-surgical and post-surgical morbidities of piezoelectric and conventional lateral osteotomy in rhinoplasty. Piezoelectric osteotomies were indeed associated with statistically less periorbital ecchymosis and eyelid edema, not only during the first three postsurgical days but also on the postsurgical Day 7. For eyelid edema, the Standardized Mean Difference between the control and the intervention group was quite similar and was characterized as moderate on both the first three postoperative days and on postoperative Day 7. Thus, eyelid edema was moderately and almost equally decreased in piezoelectric osteotomies through the first postoperative week in comparison with conventional osteotomies. For periorbital ecchymosis the Standardized Mean Difference was higher within the first three postoperative days than on post-operative Day 7 and was characterized as large for the first three post-operative days and as moderate on postoperative Day 7. Thus, we conclude that especially regarding the first three postoperative days, lateral osteotomies in rhinoplasty which are conducted with Piezotomes are connected with significantly less periorbital ecchymosis compared to conventional osteotomies.

Also, patients that underwent piezoelectric osteotomy suffered from fewer intraoperative mucosal injuries. In particular the control group had 16,67 higher relative odd of mucosal injury during the conventional osteotomies compared to intervention group. These results verify that piezoelectric osteotomies are much safer regarding intraoperative mucosal injuries and soft tissue damage in general compared to conventional osteotomies.

Additionally, patients that underwent piezoelectric lateral osteotomy during rhinoplasty experienced less postoperative pain within the first three postsurgical

days in comparison with patients that underwent conventional osteotomies. The Standardized Mean Difference between those groups of patients was quite high and was characterized as large. This proves as a result, that Piezosurgery causes less nerve damage and consequently less pain compared with conventional osteotomies.

Furthermore, in an attempt to minimize bias in our results we conducted a pre-determined sensitivity analysis in which trials of an unclear or high risk of bias were excluded. Statistical differences were detected between primary and sensitivity analysis when we accounted for periorbital ecchymosis and eyelid edema as the Standard Mean Differences calculated after sensitivity analysis were higher in all outcomes in comparison with the primary analysis. Thus, the sensitivity analysis further verified the differences in postoperative eyelid edema and periorbital ecchymosis between control and intervention groups and the benefits of executing lateral osteotomies in rhinoplasty with a Piezotome.

Undoubtedly, all those findings of the quantitative synthesis prove that Piezosurgery could be the surgical method of choice for lateral osteotomies in rhinoplasties, either open or close. However, the total number of cases in the quantitative analysis (n=246) even though adequate could be further enriched in the future with more Randomized Controlled Trials on this topic in order to further generalize the results of this study.

One major issue we faced during the quantitative analysis was the significant heterogeneity of the outcomes regarding postoperative eyelid edema and ecchymosis. Therefore, we attempted a subgroup analysis taking into consideration differences in surgical approach, in order to minimize as possible heterogeneity of the outcomes. Generally, there has been great ambiguity regarding the favorable surgical approach (percutaneous or intranasal) of lateral osteotomy in rhinoplasty, depending not only on the aesthetic results but also on the intraoperative and postoperative morbidities. Various studies have attempted to compare those approaches without a clear result (21). In our review we included studies where both approaches were executed, but data exploitable for analysis came only from studies with internal osteotomies. Thus, the post-surgical results of the surgical approach performed (external or intranasal approach) could not be assessed. However, in our review we incorporated studies where lateral osteotomies were executed either with a wide surgical incision and thus under direct visualization of the procedure, or with a narrow surgical incision. Totally 110 patients were subjected to lateral osteotomies with a wide surgical incision in both the control and the intervention groups and presented an undoubted lower difference regarding postoperative edema and ecchymosis for piezoelectric osteotomy under direct vision in comparison with the patients subjected to blind lateral osteotomies that were executed with a narrow surgical incision.

Overall, those results indicate that piezoelectric lateral osteotomy in rhinoplasty is especially effective for osteotomies that are not executed under direct vision.

Finally, for a more spherical assessment of Piezosurgery, some limitations regarding piezoelectric osteotomy must be underlined. First of all, the cost of the piezoelectric devices is quite expensive, without taking consideration as well the cost of the ultrasonic tips that are applied for each operation. (3) Additionally, a considerable learning curve for potential surgeons is needed in order to intergrade Piezo-surgery as method of choice for their rhinoplasties. Thus, especially during the learning period, the absence of adequate experience in addition to the slower cutting action of the piezoelectric device, leads to longer surgical time (34,66). Finally, the piezoelectric tools due to the thermic energy

they produce intraoperatively, need continuous saline irrigation in order skin burns to be avoided. (33) Hopefully these drawbacks are expected to get minimized with the further evolution of piezoelectric instruments and the greater familiarization of surgeons with them.

Dealing with clinical diversity

In the present study, we performed a comparison of postsurgical morbidities linked to the surgical technique chosen (piezoelectric or conventional osteotomy) using a pair-wise meta-analysis study design. After analyzing data, we observed significant heterogeneity indicating that the intervention effects were significant by factors that varied across studies. (67). Taking into consideration that the optimal surgical approach (intranasal or percutaneous osteotomy / blind or under direct vision osteotomy) is yet to be defined, this heterogeneity could be attributed to the different surgical approaches with which each surgeon applies the piezoelectric instrument for the lateral osteotomy.

Strengths and limitations of the present systematic review

In this systematic review, the sample size was adequate enough to allow us for testing our hypothesis, whether piezoelectric osteotomy is connected with fewer postoperative morbidities than conventional osteotomy in rhinoplasty. However, for the assessment of the outcomes, not all of the studies provided their data in a way exploitable in our analysis, fact that resulted in a final less adequate number of cases analyzed. Additionally, almost half of the studies were characterized to be of unclear risk of bias. Finally, we detected that mid-term and long-term postsurgical results were absent from the majority of the studies.

Implications for future research

More randomized control trials comparing the piezoelectric with the conventional osteotomy should be conducted so that a more adequate sample of patients would be available for future analysis. Additionally, emphasis should be placed not only on the short-term results of each surgical method but also on mid-term or long-term results, such as aesthetic results and the patient's satisfaction.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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