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## Systematic Review

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# The Superficial Musculoaponeurotic System Flap in the Prevention of Frey Syndrome: A Meta-Analysis

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**Objectives/Hypothesis:** Evaluate the difference of the incidence in clinical Frey syndrome in studies comparing classical parotidectomy and parotidectomy with superficial musculoaponeurotic system (SMAS) flap elevation and suturing through meta-analysis methodology.

**Study Design:** Meta-analysis of controlled studies with and without SMAS flap.

**Methods:** Database search with the following key word combination: "Frey syndrome" and "SMAS." Inclusion criteria: parotidectomy, SMAS flap and control groups, minimal follow-up of 1 year. The outcome was the presence of clinical Frey syndrome.

**Results:** Eleven studies, mostly retrospective and not randomized. According to the fixed-effect model, SMAS technique is associated with a decrease of clinical Frey syndrome with an odds ratio (OR) of 0.42 (confidence interval [CI] 0.32–0.56). With the random-effect model, the difference remains significant ( $P = 0.006$ ) with an OR of 0.25 (CI 0.09–0.66). The heterogeneity index  $I^2$  is very high (85%).

**Conclusion:** The use of SMAS flap and suturing is associated with a decreased incidence of Frey syndrome.

**Key Words:** Parotidectomy, Frey syndrome, gustatory sweating, prevention, SMAS, meta-analysis.

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## INTRODUCTION

Frey syndrome,<sup>1</sup> or gustatory sweating and flushing, is characterized by sweating and flushing of the facial skin on the lateral aspect of the face and upper neck, usually around the parotid region, during meals. Once present, the gustatory sweating and flushing remain unchanged, that is, there is no spontaneous resolution, even after numerous years.<sup>2</sup>

The physiopathology involves denervated skin sweat glands<sup>3</sup> that have lost their sympathetic innervation, usually as a result of skin flap elevation and the aberrant re-innervation by parasympathetic sialogogue fibers from the auriculotemporal nerve, as reviewed elsewhere.<sup>4</sup> These parasympathetic fibers are normally activated in the salivation reflex during eating, and after their aberrant regeneration result in vasodilatation (flushing) and gustatory sweating.

Whereas treatment of established Frey syndrome with botulinum toxin is effective and well accepted,<sup>4–6</sup>

prevention seems a better alternative. The incidence of objective Frey syndrome (established with iodine testing) after parotidectomy without any prevention technique approaches 100%,<sup>7</sup> and thus it could be considered as an unavoidable complication of parotidectomy.<sup>7,8</sup> However only one-third of patients will consider the gustatory sweating bothersome enough to seek treatment,<sup>7</sup> the so-called clinical Frey syndrome. When questioned, the incidence increases to 50% to 60%, the so-called subjective Frey syndrome.

Techniques for Frey syndrome prevention during parotidectomy have all involved some form of barrier between the parotidectomy bed and the skin.<sup>9</sup> The different barriers include local muscle flaps such as the sternocleidomastoid or temporal muscle, free nonvascularized fascia or fat grafts, animal or cadaveric fascia-like tissue, and synthetic materials. The evidence for sternocleidomastoid flaps is inconclusive at the present time,<sup>10,11</sup> whereas meta-analysis seems to conclude for a protective effect of acellular dermis matrix grafts<sup>12,13</sup> in the prevention of Frey syndrome after parotidectomy. However, these grafts seem to be associated with a higher incidence of local wound complications such as sialoceles and salivary fistula.<sup>12,13</sup>

The superficial musculoaponeurotic system (SMAS) technique evolved from the initial attempts to improve the esthetic results of parotidectomy.<sup>14</sup> Despite the numerous publications, there is a lack of conclusive evidence for the role of SMAS flaps in Frey syndrome prevention after parotidectomy, mainly because of the limited sample groups investigated. The purpose of this

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TABLE I.  
Characteristics of Included Studies.

Name	Year	Prospective	Randomized	Pathology	Cancer	Parotidectomy procedure	Radiation therapy	Number of patients				Clinical Frey syndrome			Objective Frey syndrome		
								SMAS	Control	SMAS	Control	SMAS	Control	SMAS	Control	DIFFERENCE (p)	DIFFERENCE (p)
Allison	1993	Non	Non	Mixed	31%	Superf + Total	?	91	35	1%	83%	3%	87%	-	-	-	
Barbera	2014	Non	Non	Mixed	7%	Superf + Total	Non	26	20	38%	55%	58%	70%	0.34	0.77	-	
Belli	1996	Non	Non	Benign	0%	Superf + Total	Non	45	35	40%	57%	-	-	-	-	-	
Curry	2008	Non	Non	Benign	0%	Superficial	Non	50	35	6%	31%	-	-	-	-	-	
De Ru	2007	Non	Non	Mixed	0%	Superf + Total	18%	32	29	0%	14%	-	-	-	-	-	
Durgut	2013	Yes	Yes	Benign	0%	Superficial	Non	15	15	0%	13%	80%	87%	0.48	1.00	-	
Hsu	1994	Non	Non	Benign	0%	Superf + Total	Non	76	20	4%	25%	-	-	0.01	-	-	
Lafont	2015	Non	Non	Mixed	10%	Superf + Total	Yes	112	222	62%	38%	-	-	0.028	-	-	
Taylor	2003	Yes	Non	Benign	0%	Superficial	Non	21	24	52%	42%	73%	54%	0.33	0.14	-	
Wille-Bischofberger	2007	Yes	Non	Benign	0%	Superficial	Non	25	23	41%	43%	86%	100%	0.42	0.42	-	
Zhao	2008	Non	Non	Benign	0%	Total	Non	136	90	5%	50%	26%	54%	0.001	0.02	-	

SMAS = superficial musculoaponeurotic system.

study is to evaluate this question through meta-analysis methodology.

## MATERIALS AND METHODS

The existence of previous meta-analysis on the subject was searched for on PubMed and Embase databases with the terms “Frey syndrome” and “meta-analysis” and “prevention.” Of the seven articles found, one did not deal with parotidectomy, two evaluated sequels <http://www.oxforddictionaries.com/definition/english/sequel> of parotidectomy in general, and four articles evaluated the potential benefits for Frey syndrome prevention by the use of a sternocleidomastoid muscle rotation flap<sup>10</sup> or different graft materials.<sup>12,13,15</sup> Thus, no previous meta-analysis addressed the use of a SMAS flap for Frey syndrome prevention.

For this study, the PubMed and Embase databases were searched in April 2015 with the following key word combination: “Frey syndrome” and “SMAS.” No language restriction was imposed, and unpublished abstracts were not searched for. Overall, 44 articles were found: 27 in Pub Med and 17 in Embase. To be included, studies needed to: 1) deal with parotidectomy, irrespective of its extent (superficial, or total); 2) include a SMAS flap elevation group; 3) include a control group where a traditional surgical parotidectomy technique was employed; 4) lack additional Frey prevention technique usage; 5) have a minimal follow-up of 1 year; and 6) specify the incidence of Frey syndrome in both groups. The etiology of the underlying pathology motivating the procedure was not taken into account. The outcome used was the presence of clinical Frey syndrome at the last follow-up visit.

Among the identified articles, 33 were excluded because of the lack of control group (18), using fascia and SMAS (1), unclear incidence in the control group (1), duplicate publication in a different language (1), and dealing with Frey treatment (1), thus leaving 11 studies.<sup>8,14,16-24</sup>

Articles search and selection, as well as data extraction, was performed independently by two authors (A.M., P.D.). The following variables were extracted: prospective versus retrospective study, the number of patients by study arm, the type of parotidectomy, the duration of follow-up, the surgical procedure in the control group, the incidence of Frey syndrome in both groups, and the Frey syndrome evaluation technique.

Statistical analysis was carried out with RevMan v5.3 (Cochrane.org). Odds ratio (OR) and confidence intervals (CI) were calculated and an estimate for significance was computed, taking  $P < 0.05$  as significant. Heterogeneity of studies was carried out with  $\chi^2$  and  $I^2$  and visualized with funnel plots. Fixed-effect and random-effect models were used.

## RESULTS

In the 11 studies,<sup>8,14,16-24</sup> 550 patients underwent the SMAS technique, whereas the control parotidectomy group included 495 patients (Table I). The majority of studies were retrospective and not randomized,<sup>14,16-19,21,22,24</sup> some prospective and not randomized,<sup>8,23</sup> and only exceptionally prospective and randomized.<sup>20</sup> Only one study used a blinded evaluation.<sup>16</sup>

A decrease in clinical Frey syndrome incidence was observed in nine studies,<sup>8,14,16-21,24</sup> whereas two found an increased incidence.<sup>22,23</sup> The differences were statistically significant in three studies,<sup>8,21,24</sup> not significant in five,<sup>16,18,20,22,23</sup> and three publications did not perform any statistical evaluation.<sup>14,17,19</sup>

The meta-analysis with the fixed-effect model favors the SMAS technique with an OR of 0.42 (CI 0.32–0.56)

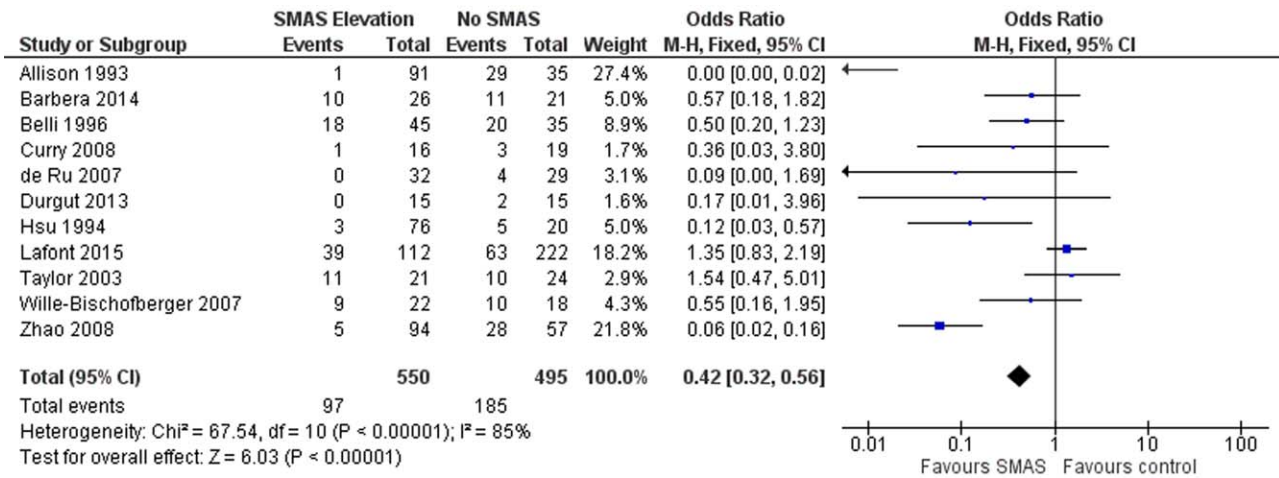


Fig. 1. Fixed-model analysis. CI = confidence interval; SMAS = superficial musculoaponeurotic system; M-H = Mantel-Haenszel. Color figure can be viewed in the online issue, which is available at [www.laryngoscope.com](http://www.laryngoscope.com).]

with the fixed model, a statistically significant difference ( $P < 0.00001$ ) as shown in Figure 1. Because the heterogeneity ( $I^2 = 85\%$ ) is very high, a random-effect model is probably more adequate. Again, the difference is significant with an OR of 0.25 (CI 0.09–0.66) and a  $P = 0.006$  (Fig. 2). Despite the large heterogeneity, the funnel plot (Fig. 3) is rather symmetric and does not favor publication bias.

The majority of parotidectomies performed were superficial, either because of the inclusion criteria of the studies<sup>8,18,20,23</sup> or because of the clinical decision in most patients<sup>14,16,17,19,21,22</sup>—Zhao et al.<sup>24</sup> including only patients with total parotidectomy. The majority (92%) of patients included had benign pathology due to the studies' inclusion criteria.<sup>8,17,18,20,21,23,24</sup> Only a few (< 5%) of the included patients had radiation therapy, a treatment supposedly reducing the incidence of Frey syndrome.

## DISCUSSION

A relationship between the thickness of the parotid skin flap was postulated 35 years ago,<sup>25</sup> when the SMAS

was not yet an established entity.<sup>26</sup> Despite conflicting results in the individual studies analyzed here, the meta-analysis seems to confirm these findings. Superficial musculoaponeurotic system flap coverage results in significantly less clinical Frey syndrome than simple skin elevation. Because the surgical technique is simple and adds only limited amount of time to regular parotidectomy,<sup>24</sup> we recommend its general use in routine parotidectomy.

This conclusion is, however, to be tampered by the results of two of the publications analyzed. The only prospective randomized study by Durgut et al. did not find a statistical difference in clinical Frey syndrome with SMAS elevation.<sup>20</sup> However, there was no clinical Frey syndrome in the SMAS group; the number of patients included was small; and the follow-up was rather short. Although this study did not find a statistically significant difference of objective Frey syndrome by the Minor test, the intensity and surface of gustatory sweating was more important without SMAS flap. Wille-Bischofberger

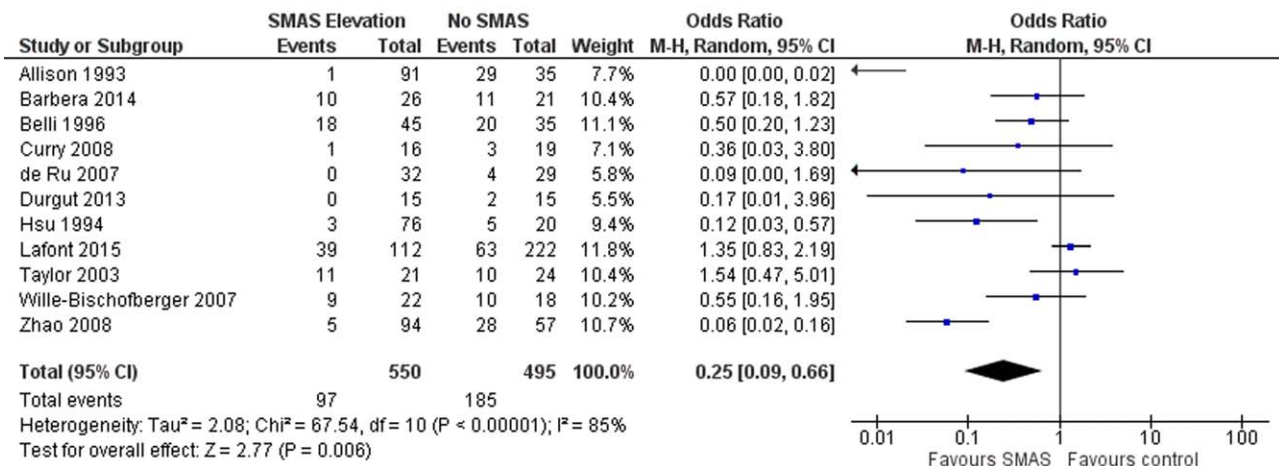


Fig. 2. Random-model analysis. CI = confidence interval; SMAS = superficial musculoaponeurotic system; M-H = Mantel-Haenszel. Color figure can be viewed in the online issue, which is available at [www.laryngoscope.com](http://www.laryngoscope.com).]

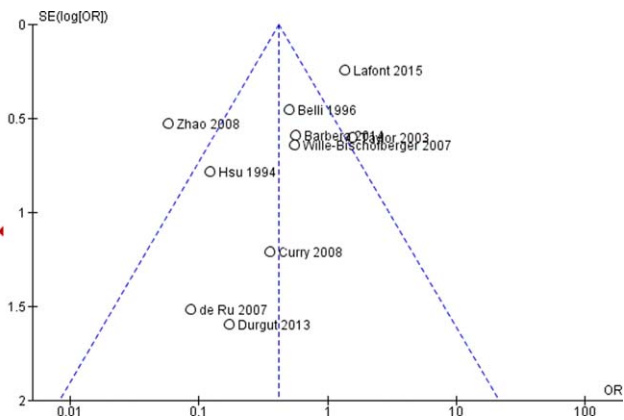


Fig. 3. Random-model funnel plot. OR = odds ratio; SE = standard error. Color figure can be viewed in the online issue, which is available at [www.laryngoscope.com](http://www.laryngoscope.com).]

et al.<sup>8</sup> evaluated the two groups at 2 and 6.5 years after parotidectomy: the results were significant at 2 years and not at 5 years; furthermore, objective Frey syndrome reached almost 100% in both groups with the longer follow-up. When clinical complaints are missing, although the exact importance of an objective Frey syndrome on the patient well-being remains to be determined, the role of the SMAS might be seen as reducing the intensity of gustatory sweating rather than completely preventing it.

The main shortcoming of this study is due to the quality of the publications included, with few prospective and only one randomized study. Even with randomized prospective studies, the exact definition of SMAS flap elevation and redraping probably varies not only among surgeons but with each clinical situation. Sometimes “holes” can occur during SMAS elevation, and if not sutured can be responsible for some Frey syndrome cases. Sometimes the tumor is very superficial or too big, and SMAS preservation is unjustified even in benign tumors and, despite adequate suturing of the SMAS excision edges, could result in gustatory sweating. Other sources of variability include the extent of parotidectomy, the inclusion of few malignancies, and the possible role of radiotherapy in few cases. Ideally, homogenous series of patients with the same extent of parotidectomy, performed for benign disease and without postoperative radiation, should have been included. However, this would have required the rejection of several studies for few patients (Table I). Furthermore, despite the impression of an increased incidence of Frey syndrome with larger extents of parotidectomy in the literature, there is no clear consensus.<sup>27</sup> The final and probably most important source of bias is the lack of standardized questionnaire evaluation of subjective Frey syndrome and the nonblinded evaluation in most studies. All of these parameters result in a very elevated heterogeneity among the included studies.

## CONCLUSION

The use of SMAS flap elevation and suturing is associated with a decreased incidence of Frey syndrome.

However, variability between studies is responsible for a very high heterogeneity, and the single randomized of the subject was not conclusive. Further prospective randomized studies with standardized and blinded Frey syndrome evaluation are necessary to definitively answer the question.

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