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ORIGINAL ARTICLE FACIAL SURGERY

The Submandibular Gland and The Aging Neck: A Longitudinal Volumetric Study

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Abstract
Introduction The true effect of aging and other patient factors on submandibular gland (SMG) volume is unclear. We sought to evaluate the effects of age, body mass index (BMI), sex and race on SMG volume using computed tomography (CT) imaging.
Methods We conducted a retrospective longitudinal study of adult subjects with multiple CT images of the neck at least 7 years apart. Subjects with history of salivary gland pathology, neck dissection, head and neck radiation, active infection or dental artifact were excluded. Three-dimensional volumes were measured. Age, BMI, sex and race data were analyzed to track their longitudinal effect on SMG volume.
Results The study comprised 64 patients (Females n=36; Males n=28) with mean age of 47.1 and 58.5 at each respective time point (mean difference 11.4). Mean SMG volume increased from 10.1 ml to 10.5 ml ($P < 0.05$). Males had significantly greater SMG volume compared to females. Majority of growth occurred in the < 40 year age bracket (0.1 ml/year), more significantly in the male cohort. When controlling for aging and sex, a change in BMI was the only patient factor that predicted a change in SMG volume. An increase of 1.0 kg/m^2 predicted a 0.17 ml increase in gland volume. Race had no significant effect.
Conclusion Our findings suggest that the majority of SMG volume change occurs in early adulthood (< 40 years), especially in males. Among the factors we studied, a change in BMI was the only significant predictor of SMG volume change.
Level of Evidence IV This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to Table of Contents or the online Instructions to Authors www.springer.com/00266. Genital Surgery

Keywords Facelift · Rhytidectomy · Aging · Neck · Neck rejuvenation · Submandibular gland

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Introduction

Addressing the aging neck is one of the primary reasons for seeking a rhytidectomy. The major salivary glands can play a significant role in the aging face and neck. The aging changes of the salivary glands have been relatively under-investigated in the literature compared to other components such as skin, fat, muscle and bone. Knowledge of how these glands are affected by various patient factors is essential in predicting their contribution to aesthetic changes and in formulating optimal treatment plans.

The age-related microscopic and functional changes in the submandibular glands (SMG) have been consistently described in the literature. Histologic [1, 2] and radiographic [3] studies have demonstrated age-related replacement of functional parenchyma by fat and fibrovascular tissue. This occurs to a greater degree in the parotid gland compared to the SMG. Interestingly, the salivary flow remains constant despite these changes, likely due to hyperfunction of the remaining functional acinar

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cells. There is no consensus on the age-related volumetric changes of major salivary glands, with studies demonstrating conflicting correlations between age and volume [2, 4, 5]. This could be explained by the confounding effects of other factors, such as BMI and sex, not accounted for in some of these studies.

The morphologic changes that various tissues undergo with aging are the fundamental problems that rejuvenating procedures seek to solve. SMG hypertrophy can be of significant aesthetic concern, but routine management of the SMG gland can be challenging because of the distant position of the gland from the submental incision and significant neurovascular structures in and around the gland. Nevertheless, a number of interventions, including surgical resection, soft tissue suspension and chemo-denervation, have been described as means to correct for gland hypertrophy [6].

The SMG is uniquely challenging and, although the microscopic changes that occur with age are well described, to our knowledge, a detailed longitudinal volumetric analysis of the SMG has not yet been performed. A longitudinal study is ideal because it neutralizes or mitigates many of the confounding factors associated with salivary gland volume. Previous studies have demonstrated contradictory effects of various factors such as age, weight and sex on salivary gland volumes [2–5, 7]. Therefore, we sought to evaluate the effect of age, BMI, sex and race on SMG volume in a retrospective longitudinal study.

Methods

This study was approved by the Yale School of Medicine institutional review board. We identified subjects with two CT studies of the neck or face performed at least 7 years apart. A query was performed of our institution's radiology database from 2001 to 2019. Subject's age, sex, race and BMI data were collected from the hospital electronic medical record corresponding to the dates that the CT scans were performed.

A total of 64 subjects (Table 1) were identified. Subjects with history of salivary gland pathology, neck dissection, head and neck radiation, active infection or dental artifact were excluded. CT studies with a maximum slice thickness of 2.5 mm were selected for use. Visage Image viewer (Visage Imaging Inc., San Diego, CA, USA) was used to calculate 3D volumes by tracing the two-dimensional surface area of each consecutive 2.5 mm axial CT slice (Fig. 1)—volume was automatically computed by the imaging software. The right and left submandibular glands were measured at time point 1 (T1) and time point 2 (T2) and averaged for each individual.

Table 1 Subject demographics

		N	%Total
Sex	Total	64	100
	Female	36	56.3
	Male	28	43.7
Age			
	< 40	20	31.3
	40–49	22	34.4
	50–59	10	15.6
	60+	12	18.7
BMI			
	< 20	2	3.1
	20–29	18	28.1
	30–39	30	46.9
	40–49	9	14.1
	50+	2	3.1
	Unknown	3	4.7
Race/Ethnicity			
	White	30	46.9
	Black	19	29.6
	Hispanic or Latino	14	21.9
	Asian	1	1.6

Statistical analysis was performed using SPSS (IBM Corp., Armonk, N.Y., USA). The mean, range and standard deviation were calculated for age, BMI and SMG volume measurements. Paired t-tests were performed to evaluate longitudinal differences of submandibular gland volume in males, females, different age subgroups (< 40, 40–49, 50–59 and > 60 years old) and the total cohort. Unpaired *t*-tests were performed to evaluate the mean differences between males and females. Sex was coded as '0' for females and '1' for males to aid with statistical analysis. Race was similarly numerically coded and analyzed using ANOVA test to assess for relationship between race and SMG volume. Multiple linear regression analysis was performed to analyze the relationship between SMG volume (dependent variable), age, sex, BMI and race (independent variables). Statistical significance was determined at $P < 0.05$.

Results

Among the 64 subjects in our study (Table 1), 36 were female and 28 were male. Mean (SD) ages at the two image time points were 47.1 (13.0) years and 58.5 (12.7) years, respectively. Distribution of age was similar in males and females. An average of 11.4 years (range 7.4–18.1 years;

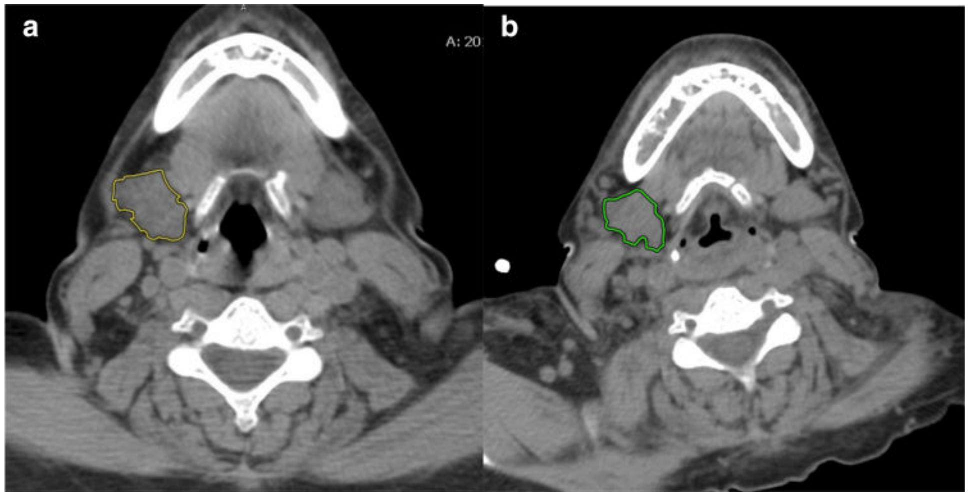

Fig. 1 Comparison between axial CT neck images of the same man at two time points. **a** Subject at age 37 years old (BMI 27.8) **b** Subject at age 46 years old (BMI 17.7). The right SMG is outlined

SD 2.7) elapsed between the two imaging time points (T1 and T2) in both males and females.

The SMG volumes averaged 10.1 (3.1) ml and 10.5 (3.6) ml at T1 and T2, respectively. There was no significant difference between volumes of the right and left glands (*P*=0.82 and *P*=0.38 at T1 and T2, respectively). When controlling for BMI and age, males had a mean 1.2 ml greater volume at T1 and 2.4 ml at T2 compared to females. Over an average of 11.4 years, males had a mean volume increase by 1.1 ml ($P < 0.05$) compared to a mean loss of 0.1 ml in females (*P*=0.66). When dividing our cohort into different age groups at T1 (Table 2), individuals < 40 years experienced a mean increase of 1.2 ml over a 12.1 year period ($P < 0.05$), representing a 0.1 ml/year growth rate. Individuals aged >40 years had no statistically significant changes in gland volume. When analyzing age groups by gender, males aged < 40 years (*n*=9) had the only significant increase in gland volume at a rate of 0.2 ml/year ($P < 0.05$) vs. 0.02 ml/year (*P*=0.88) in females of the same age bracket. Interestingly, females >40 years (*n*=25) had a decrease in volume by 0.04 ml/year versus increase in volume by 0.4ml/year in males, although these did not reach statistical significance (*P*=0.66 and *P*=0.36, respectively). An ANOVA test demonstrated that race was not a statistically significant predictor of SMG volume (*P*= 0.64).

Our analysis demonstrated no direct correlation of SMG volumes with BMI (*r*=0.12; *P*=0.38) or age (*r*=0.08; *P*=0.51; Fig. 2). To control for confounding effects, a multiple regression analysis was performed to determine the effects of age, BMI and sex on gland volume at T2. This again showed no correlation of these factors to volumes (Table 3).

Longitudinal BMI data (i.e., data for both time points T1 and T2) were available for 18 of the 64 subjects. Age *change* and BMI *change* were scatter-plotted against SMG volume *change* (Figs. 3 and 4, respectively). This showed a linear correlation of BMI *change* with volume *change* (*r*=0.75; $P < 0.05$), while age *change* had no significant correlation (*r*=0.13; *P*=0.34). A linear regression analysis was performed in this subcohort (Table 4). We observed that, when controlling for age changes and sex, a *change* in BMI in an individual was the only significant predictor of volume change ($P < 0.05$). A 1 unit increase in BMI predicted a 0.17 ml SMG volume increase.

Table 2. Longitudinal change in submandibular gland volume by age group

Age	N	Vol.1 (cc)	Vol.2 (cc)	Diff (cc)	*T* Test (*P* value)	Age1	Age2	Diff (yr)	Rate of change (cc/yr)	BMI* kg/m^2
< 40	20	10.2	11.4	1.2	< 0.05	33.5	45.6	12.1	0.10	33.4
40–49	22	9.2	9.1	0.1	0.85	45.1	56.2	11.1	0.01	33.5
50–59	10	12.2	12.4	0.2	0.70	54.4	66.0	11.6	0.02	35.9
60 +	12	10.2	9.8	0.4	0.74	67.6	77.8	10.2	0.04	30.9
Total	64	10.1	10.5	0.4	0.03	47.1	58.5	11.4	0.04	33.4
Male	28	10.7	11.8	1.1	< 0.05	47.3	58.6	11.4	0.1	31.6
Female	36	9.8	9.6	0.2	0.66	47.0	58.4	11.4	0.02	34.6

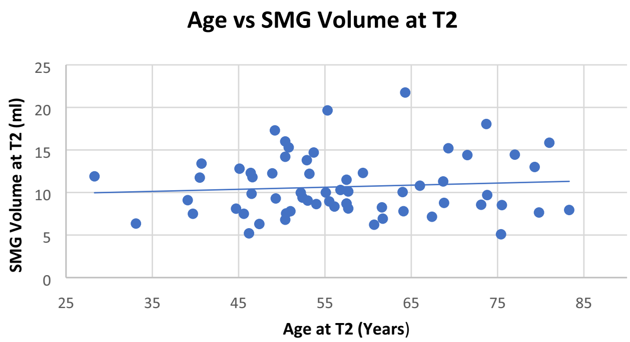

Fig. 2 Age versus SMG volume at timepoint 2 (r=0.08; P=0.513)

Table 3. Multiple linear regression analysis at time point 2

	Coefficients	P-value	Lower 95%	Upper 95%
Intercept	5.89	0.06	0.31	12.10
Age	0.01	0.74	0.60	0.09
BMI	0.08	0.06	0.03	0.19
Sex	2.40	0.01	0.60	4.20

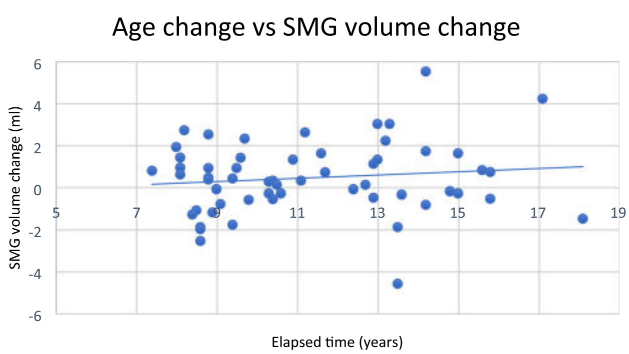

Fig. 3 Longitudinal age change versus SMG volume change (r=0.13; P=0.34)

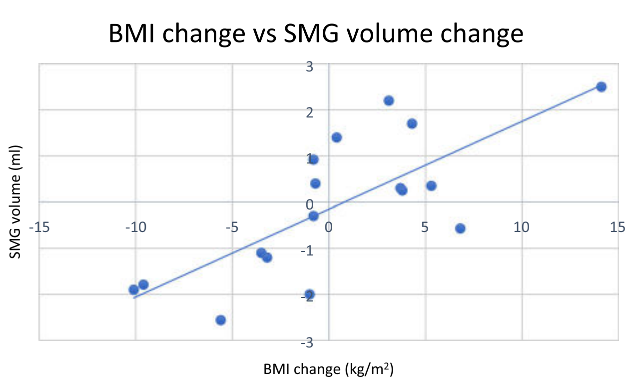

Fig. 4 BMI change versus SMG volume change (r=0.75; $P < 0.05$)

Table 4. Multiple linear regression analysis of longitudinal cohort.

	Coefficients	P-value	Lower 95%	Upper 95%
Intercept	2.19	0.18	5.49	1.11
Age change	0.21	0.20	0.13	0.55
BMI change	0.17	< 0.05	0.08	0.27

Discussion

Aging of the neck is a multifactorial process involving changes to the skin, fat compartments, salivary glands, muscle and skeletal framework. The submandibular gland is the main occupant of the submandibular triangle and, with the lateral subplatysmal fat pad, contributes to the majority of the volume within the triangle which can result in undesirable fullness and bulging in the neck. The existing literature has not been conclusive as to the true effect of age on SMG volume [2, 4, 5]. To our knowledge, this study is the first to analyze the longitudinal effects of age, sex and BMI on SMG volume in the same individuals at two serial time points. The evidence presented in this study shows that, in adults, the majority of gland volume increase occurs in early adulthood, specifically in males. This is followed by a non-significant volume gain in males and volume loss in females. Changes in BMI in an individual would predict SMG volume changes.

Our study of submandibular gland volume complements some existing research. A study by Saito et al. [3] utilizing MRIs reported a logarithmic increase in major salivary gland volumes from childhood to early adulthood. This was followed by varied growth patterns into late adulthood. The effect of weight or sex was not taken into account in their study. They also reported radiographic findings suggestive of age-related increase in proportion of fatty tissue in all major salivary glands. Another radiographic study [4] utilizing MRIs and CT PET images reported mixed results, with the MRI cohort demonstrating no significant volumetric changes with age while a separate CT/PET cohort demonstrated a positive correlation with age (r=0.5; $P < 0.05$). This discrepancy in findings was also seen when they analyzed the effect of gender, with males demonstrating significantly greater volumes in the MRI cohort but not in the CT cohort. BMI was not accounted for in their study and they utilized images with slice thickness of at least 5 mm, thus limiting accurate volume measurements. In another study focusing on the Korean population [7], a significant decrease in SMG maximum cross-sectional area (MCSA) was seen in the >60 year population, with no significant changes reported in the < 60 years population. As the submandibular is not spherical, the use of MCSA as an indicator of size may result in inaccurate volume measurements. MCSA was significantly greater in their male population. Our male cohort did also demonstrate significantly larger SMG glands as well as propensity to gain volume at a faster rate compared to females, but this was primarily seen in early adulthood. Our findings could represent a true effect of gender on SMG volume or a confounding effect of BMI (i.e., our younger male cohort had greater BMI gain compared to the remaining subjects). Finally, they reported no correlation between BMI and MSCA in their cohort. This is similar to our findings where we demonstrated no correlation between BMI and volumes at T2. For example, 2 subjects in our study had similar SMG volumes (9.1 ml) at T2 but widely different BMIs of 16.7 and 65.2 kg/m2. When looking at our longitudinal data, we could see that a BMI *change,* as opposed to an absolute value of BMI, significantly correlates with volumes changes. The longitudinal sub-cohort in our study is advantageous as it allows more precise evaluations of the cause-and-effect relationships, particularly with regard to patient BMI. A comparison of male versus female longitudinal BMI gain/loss was limited by low statistical power.

Our study has limitations that are important to consider. First, some degree of measurement error is expected with any anatomic study. We maintained a consistent measuring methodology and excluded images with significant artifact that would prevent us from accurately measuring volume. We attempted to minimize observer bias by measuring the right and left SMG volumes separately and using the average values. Second, the retrospective nature of this study prohibits us from fully controlling for factors not available in the electronic medical record, such as certain medical conditions, undocumented surgical procedures and radiation, or lifestyle elements such as smoking and alcohol use. The longitudinal portion of our study helps neutralize or mitigate some of these limitations. Third, although we included a relatively large diverse patient cohort, longitudinal BMI data were only available in 18 out of the 64 subjects, thus reducing the statistical power for the longitudinal BMI analysis, especially when looking for differences between genders. Finally, with our study's methodology, we are unable to determine where a volume change would be concentrated (i.e., in the superficial vs deep aspect of the gland).This is of clinical relevance as an aesthetically apparent SMG is usually located below the inferior border of the mandible. Although we do demonstrate some statistically significant volume changes, we believe that in most instances this will not translate into clinically significant cosmetic changes (i.e., does a 1 ml change in gland volume really result cosmetically apparent changes?).

As the majority of patients presenting for rhytidectomy typically report noticing accelerated 'aging' changes in their 6th and 7th decades, we hypothesize that factors other than SMG volume changes, which have primarily occurred earlier in life, have a greater contribution to a prominent and ptotic submandibular triangle. This can include changes in the subplatysmal fat, digastric muscle, mandible and/or laxity of the soft tissue envelope. Further analyzing the effect of volume changes on degree of submandibular ptosis and how it relates to the aforementioned components of the submandibular triangle will be of clinical relevance for the aesthetic surgeon.

Conclusion

Our findings suggest that the majority of gland volume change occurs in early adulthood (< 40 years), more significantly in the male population. BMI change is the only patient factor that had a significant effect on change in SMG volume.

Compliance with Ethical Standards

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

Standard of Human and Animal Rights This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent For this type of study, informed consent is not required.

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