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RESEARCH ARTICLE
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Evaluation of Computed Tomography Findings in Revision Endoscopic Sinus Surgery

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ABSTRACT

Objective: To investigate computerized tomography (CT) data of patients who needed revision surgery for chronic rhinosinusitis.
Material and Methods: 83 patients who underwent revision endoscopic sinus surgery by the senior author due to recurrent and/or persistent chronic rhinosinusitis were included in this study. The following data were obtained from preoperative CT scans and recorded for each side of every patient: recurrent polyposis, incomplete uncinectomy, retained agger nasi cell, lateralization of middle turbinate, recirculation phenomenon, maxillary antrostomy stenosis, incomplete anterior and posterior ethmoidectomy, scarring at the frontal recess, sphenoid ostium stenosis, or novel onset sphenoid disease.
Results: Based on our findings, septal deviation caused inadequate posterior ethmoidectomy, while incomplete uncinectomy increased the risk of frontal sinus disease.
Conclusions: We suggest that septum deviation may cause insufficient visualization, while incomplete uncinectomy may prevent adequate intervention to the frontal sinus and these subsequently play a role in ESS failure.

Keywords: Revision FESS, sinus C.T scan, Functional endoscopic sinus surgery, rhinosinusitis

INTRODUCTION

Endoscopic sinus surgery (ESS) has been widely accepted for effective treatment of chronic rhinosinusitis and other inflammatory sinus diseases for which medical management has failed. Since its initial description by Kennedy in 1985 (1), reports on surgical success have ranged from 76% (2) to 97.5% (3). Despite the high surgical success rates, 10-15% of patients need revision surgery during long-term follow-up (4). Investigation of the factors that cause recurrent or persistent symptoms after primary surgery is required for successful management of revision cases. Several authors have tried to detect anatomic and systemic factors which may play a role in primary surgery failure. It has been reported that anatomical factors that may cause failure in primary surgery include recurrent polyps, lateralization of middle turbinate, incomplete uncinectomy, inappropriate maxillary antrostomy, scarring at the frontal recess, and scarring at the middle meatal antrostomy. Systemic factors include allergic rhinitis, cystic fibrosis, Samter's Triad, ciliary abnormalities, Kartagener's syndrome and other systemic inflammatory diseases (2 ,3, 5).

The main goal of the current study is to investigate computed tomography findings of patients who need revision surgery for chronic rhinosinusitis. This article does not focus on postoperative outcomes after revision sinus surgery.

MATERIALS AND METHODS

A retrospective review of patients undergoing endoscopic sinus surgery by the senior author from January 2012 to February 2017 identified 90 patients who underwent revision endoscopic

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sinus surgery due to recurrent and/or persistent chronic rhinosinusitis. Patients with immune deficiency/suppression, cystic fibrosis, ciliary dysfunction, or history of previous Caldwell-Luc procedure and inferior meatal antrostomy were excluded from the study. Patients with incomplete information were also excluded and the remaining 83 patients were enrolled in the study.

All patients had been examined with nasal endoscopy and paranasal sinus CT scans (3-mm coronal, axial, and sagittal sections) preoperatively. Medical treatments included nasal corticosteroids, saline irrigations, decongestants, antibiotics, as well as management of allergy. Patients who have diffuse polyposis were also treated with systemic corticosteroids (1 mg/kg daily). All surgeries were performed under general anesthesia and the surgical procedure performed was that defined by Kennedy (1) and Stammberger (6, 7). During the surgical procedure the retained agger nasi cell was opened when required, residual uncinate process was removed, an incomplete anterior and/or posterior ethmoidectomy was completed, and frontal, maxillary and sphenoid ostium drainage was provided again. Absorbable packing with antibiotic ointment was put in the middle meatus at the end of surgery. Postoperatively, oral antibiotics and saline irrigations were administered for two weeks. Follow-up examinations were performed weekly during the first month after the surgery and absorbable packing remnants and crusts were removed with nasal endoscopy at the first visit.

The following data were evaluated and recorded for each side of every patient from preoperative CT scans: recurrent polyposis, incomplete uncinectomy, retained agger nasi cell, lateralization of middle turbinate, recirculation phenomenon, maxillary antrostomy stenosis, incomplete anterior and posterior ethmoidectomy, scarring at the frontal recess, sphenoid ostium stenosis, or novel onset sphenoid disease.

Ethics Committee Approval for the study was received from the Istanbul University School of Medicine Ethics Committee for Scientific Research (number 2021/415).

RESULTS

Among the 83 patients evaluated, 51 (61.4%) were male and 32 (38.6%) were female. The patients' ages ranged from 16 to 73 years, with the mean age being 45.4 (+/- 14.2) years. The mean number of previous surgeries was 1,9 (+/- 1,6) (min: 1 – max: 9). Comorbid situations of patients are shown in Table 1. All sinus diseases, anatomical structures, and residual anatomical structures were evaluated separately and are summarized in Table 2. CT findings, such as lateralization of the middle turbinate, septal deviation, incomplete uncinectomy, and incomplete anterior-posterior ethmoidectomy, were also present in preoperative physical examination and intraoperative findings.

The following results about relationship between sinus disease or residual anatomical structure with residual cells or number of previous surgeries were identified and summarized as follows:

Table 1: Comorbidities in Patients Undergoing Revision ESS (n=83).

Comorbidity	n	%
Allergy	3	3.6
Allergic Rhinitis	1	1.2
Asthma	15	18.1
Asthma + Allergy	1	1.2
Asthma + Allergy	7	8.4
Atopy	1	1.2
DM	3	3.6
Goitre	1	1.2
Goitre + HT	1	1.2
HT	3	3.6
HT + Asthma	1	1.2
HT + HI	3	3.6
Samter's Triad	2	2.4
Without Comorbidity	41	49.4

Table 2: Preoperative CT Findings in Patients Undergoing Revision ESS (n=83).

Finding	n	%
Right frontal disease	Agenesis -2	2.4
	64	77.1
Left frontal disease	Agenesis -1	1.2
	70	84.3
Right maxillary disease	72	86.7
Left maxillary disease	74	89.2
Left ethmoid disease	82	98.8
Right ethmoid disease	83	100.0
Right sphenoid disease	49	59.0
Left sphenoid disease	51	61.4
Middle turbinate lateralization - right	Resected -2	2.4
	26	31.3
Middle turbinate lateralization - left	Resected -2	2.4
	29	34.9
Incomplete uncinectomy - right	23	27.7
Incomplete uncinectomy - left	21	25.3
Unopened agger nasi - right	29	34.9
Unopened agger nasi - left	29	34.9
Stenosis of maxillary antrostomy - right	1	1.2
Stenosis of maxillary antrostomy - left	1	1.2
Frontal recess cicatrization - right	Agenesis -1	1.2
	18	21.7
Frontal recess cicatrization - left	Agenesis -1	1.2
	21	25.3
Incomplete anterior ethmoidectomy - right	32	38.6
Incomplete anterior ethmoidectomy - left	32	38.6
Incomplete posterior ethmoidectomy - right	67	80.7
Incomplete posterior ethmoidectomy - left	67	80.7
Sphenoid ostium stenosis - right	4	4.8
Sphenoid ostium stenosis - left	4	4.8
Hyperostosis	11	13.3
Septal deviation	Right -18	21.7
	Left - 29	34.9

- There was no statistically significant difference in the number of previous surgeries between patients with asthma (%28.9) and without asthma. Similar results were also found for 42 patients with comorbidity (%50.6).

- Moreover, we did not encounter a statistically significant association between the number of previous surgeries and hyperostosis (13.3%), incomplete right anterior ethmoidectomy (38.6%), incomplete left anterior ethmoidectomy (38.6%), incomplete right posterior ethmoidectomy (80.7%), incomplete left posterior ethmoidectomy (80.7%), or residual ager nasi cell (34.9%).

- There was no statistically significant difference with right frontal and maxillary disease in patients with right lateralized middle turbinate (%31.3).

- There was no statistically significant difference with left frontal, ethmoid and maxillary disease in patients with left lateralized middle turbinate (%34.9).

- There was no association between right residual agger nasi (%34.9) and right frontal disease, and no association was found on the left side either.

- No statistically significant association was found between left frontal disease and left ethmoid disease; neither did we encounter an association on the right side.

- Statistically significant association was noted between right incomplete uncinectomy and right frontal disease (p=0.037), and a significant association was also present between left incomplete uncinectomy and left frontal disease (p=0.039).

- No statistically significant associations were observed between septal deviation and both right lateralized middle turbinate and left lateralized middle turbinate.

- Finally, we encountered a statistically significant association between septal deviation and both left (p=0.002) and right (0.002) incomplete posterior ethmoidectomy. This association was not observed for right and left incomplete anterior ethmoidectomy (p=0.062).

DISCUSSION

Various studies investigating the causes of failure in ESS have been conducted before. In his study in 1992, Kennedy reported that the risk of surgical failure after ESS increased in patients with bilateral sinus disease and diffuse nasal polyposis (8). In a study published in the same year, Lazar et al. stated that the most common intraoperative findings in revision ESS cases were adhesion formation between the middle concha and lateral nasal wall, seen in 43% of patients, and nasal polyposis recurrence, seen in 22% of patients (9). Studies by Ramadan (2) and Musy and Kountakis (3) reported that the most common pathological anatomic finding in revision ESS cases was lateralized concha. Khalil et al. (10), on the other hand, evaluated computerized tomography (CT) data of 63 cases scheduled for revision ESS and reported that the most common finding was uncinate process with an incidence rate of 57.1%. They also reported residual anterior-posterior ethmoid cell on the side that requires revision in more than 90% of cases. In the study conducted by Socher et al. (11) in 2018, CT images of 28 revision ESS patients were evaluated and the most common pathological findings were reported as mucosal thickening in the maxillary sinus (89.28%) and septal deviation (75%).

Our study revealed that septal deviation caused inadequate posterior ethmoidectomy in cases requiring revision endoscopic sinus surgery and that incomplete uncinectomy increased the risk of frontal sinus disease. In addition, the relationship between lateralized middle turbinate, which is a common finding in many revision ESS cases, and the frontal, maxillary or ethmoid disease was examined, and no significant correlation was found between these conditions.

The incidence of septal deviation in revision ESS cases is highly variable, ranging from 15.9% to 75% (10,11). Septal deviation was detected in 47 (56.6%) of 83 patients who required revision ESS in our study. While there was no significant difference between septal deviation and lateralized middle turbinate or anterior ethmoidal residual cells, it was found that the risk of encountering right posterior ethmoidal residual cell in cases with right septal deviation and left posterior ethmoidal residual cell in cases with left septal deviation was statistically significant. The deviated septum may unintentionally orient the endoscope laterally, causing the surgeon to assume the skull base position to be more lateral and leave unopened posterior ethmoid cell or cells medially.

When performed poorly, uncinectomy may lead to insufficient visualization of ethmoid and frontal cells and is thought to be one of the important causes of recurrent frontal disease (1, 12). In our study, the rates of incomplete uncinectomy were 27.7% on the right and 25.3% on the left. In literature, this rate was found between 7.14% and 60.3% (10,11). Reports of such variable rates could be explained by the phenomenon that the uncinate process cannot always be distinguished in CT sections or by the differences in the extent of uncinate resection depending on the differences in surgical techniques (13). In our study, incomplete uncinectomy was found to be associated with frontal disease on both sides; however, no significant correlation was found between maxillary or ethmoid sinus disease. Based on these findings, it can be said that inadequate uncinectomy in interventions on the frontal sinus is associated with persistent or resistant disease in the frontal sinus. This may potentially be caused by further narrowing of the already restricted drainage tract due to ongoing inflammation and subsequent adverse effects on the frontal sinus drainage.

Lateralized middle turbinate is reported to be the most common finding in revision ESS cases in many studies (2, 3, 9). The possibility of occurrence increases especially in cases where mucosa is not preserved and partial middle turbinate resection is performed (9). In cases requiring revision ESS, the incidence of lateralized middle turbinate probably varies depending on the amount of conservation in different surgical techniques

(3, 10, 11). In our study, the relationship between lateralized middle turbinate and the frontal, maxillary, and ethmoid disease was examined separately, but no significant association was found. Based on these findings, it can be interpreted that lateralized middle turbinate alone may not cause ESS failure. On the other hand, each sinus being evaluated individually could lead to the difference from the literature.

Frontal sinus is a very difficult region to operate on due to its variable and complex anatomy, difficult visualization, close proximity to vital structures such as the skull base and orbit, and the need for advanced equipment and experience (12). Scarring in the frontal recess has been shown as the main cause of frontal sinus disease recurrence after ESS (14). Rates of frontal recess obliteration/scar in revision ESS cases are reported to be up to 50% in literature (3). The rate of right-sided frontal recess cicatrization was 21.7% in our study and it was 25.3% on the left side. Although the rate of frontal disease was found to be quite high (77.1% on the right and 84.3% on the left), it was found that frontal recess cicatrization did not increase the risk of frontal disease. The relationship between residual agger nasi/ethmoid cells and frontal disease was also examined and it was found that these did not increase the risk of disease occurrence in the frontal sinus. Considering the findings of our study, it can be suggested that frontal recess cicatrization and residual agger nasi/ethmoid cell presence after ESS alone do not increase the risk of frontal sinus disease.

At least one comorbid disease was found in 42 patients out of 83 enrolled in our study. The most common comorbid disease was asthma, which was present in 18.1% of patients. Similarly, in the literature, the most common comorbid factor in revision ESS cases is usually asthma, and its rate varies between 9.6% and 26% (2, 3).

As mentioned above, the reason for high variability in the findings of studies evaluating tomographic data of revision endoscopic sinus surgery cases is the use of more aggressive or more conservative resection techniques. Some authors claim that aggressive resections are necessary to prevent failure in functional ESS, while others believe that preserving normal tissues in the sinus is the key to a good clinical outcome. For instance, there are publications suggesting that the uncinate process, which is usually resected as the first step in functional endoscopic sinus surgery, protects the paranasal sinuses from allergens and should not be resected when possible (13, 15). The minimally invasive sinus technique (MIST) described in recent years has been put into practice by many surgeons (16). Preservation of the existing anatomical structure should, of course, be the main goal in every surgery; however, for endoscopic sinus surgery, which is a relatively novel surgical approach, increased preservation rates may cause an increased need for revision surgery.

In our study, unlike other studies in the literature, detailed statistics were compiled on the results of incomplete resection of some structures, such as the relationship between incomplete uncinectomy and maxillary, frontal, and ethmoid disease or the relationship between residual agger nasi and frontal sinus disease. Moreover, a comparison was made between the conditions that are thought to increase ESS failure, such as lateralized middle concha, septum deviation and frontal recess cicatrization, and the pathological conditions they may cause. For instance, the relationship between septum deviation and incomplete ethmoidectomy was evaluated. Thus, the structures and factors that may play a role in ESS failure were examined in detail and important findings were obtained, even though there was no control group in the study.

Unfortunately, there are certain limitations in our study. First, while evaluating the CT images of the patients, Lund-Mackay scoring was not used. Instead, the evaluations were made by scoring yes/no to different structures or disorders in the images. In addition, the patients included in the study were those who had various complaints that continued or just started after ESS. Since the patients who had undergone ESS but did not have residual complaints were not included in the study, there was no control group.

CONCLUSION

In our study, newly obtained CT scans of patients who required revision endoscopic sinus surgery were evaluated and it was found that septal deviation caused inadequate posterior ethmoidectomy, while incomplete uncinectomy increased the risk of frontal sinus disease. The relationship between lateralized middle turbinate and frontal, maxillary, and ethmoid disease was investigated and no significant association was found. We suggest that septum deviation may cause insufficient visualization, while incomplete uncinectomy may prevent adequate intervention to the frontal sinus and these subsequently play a role in ESS failure.

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REFERENCES

1. Kennedy DW. Functional endoscopic sinus surgery. Technique. Arch Otolaryngol 1985;111(10):643-9.
2. Ramadan HH. Surgical causes of failure in endoscopic sinus surgery. Laryngoscope 1999;109(1):27-9.

3. Musy PY, Kountakis SE. Anatomic findings in patients undergoing revision endoscopic sinus surgery. Am J Otolaryngol 2004;25(6):418-22.
4. Chandra RK, Palmer JN, Tangsujarittham T, Kennedy DW. Factors associated with failure of frontal sinusotomy in the early follow-up period. Otolaryngol neck Surg Off J Am Acad Otolaryngol Neck Surg 2004;131(4):514-8.
5. Levine CG, Casiano RR. Revision Functional Endoscopic Sinus Surgery. Otolaryngol Clin North Am 2017;50(1):143-64.
6. Stammberger H. Endoscopic endonasal surgery--concepts in treatment of recurring rhinosinusitis. Part II. Surgical technique. Otolaryngol neck Surg Off J Am Acad Otolaryngol Neck Surg 1986;94(2):147-56.
7. Stammberger H. Endoscopic endonasal surgery--concepts in treatment of recurring rhinosinusitis. Part I. Anatomic and pathophysiologic considerations. Otolaryngol neck Surg Off J Am Acad Otolaryngol Neck Surg 1986;94(2):143-7.
8. Kennedy DW. Prognostic factors, outcomes and staging in ethmoid sinus surgery. Laryngoscope 1992;102(12 Pt 2 Suppl 57):1-18.
9. Lazar RH, Younis RT, Long TE, Gross CW. Revision functional endonasal sinus surgery. Ear Nose Throat J 1992;71(3):131-3.
10. Khalil HS, Eweiss AZ, Clifton N. Radiological findings in patients undergoing revision endoscopic sinus surgery: a retrospective case series study. BMC Ear Nose Throat Disord 2011;11:4.
11. Socher JA, Mello J, Baltha BB. Tomographical Findings in Adult Patients Undergoing Endoscopic Sinus Surgery Revision. Int Arch Otorhinolaryngol 2018;22(1):73-80.
12. Tajudeen BA, Adappa ND. Instrumentation in Frontal Sinus Surgery. Otolaryngol Clin North Am 2016;49(4):945-9.
13. Nayak DR, Balakrishnan R, Murty KD. Endoscopic physiologic approach to allergy-associated chronic rhinosinusitis: a preliminary study. Ear Nose Throat J 2001;80(6):390-2, 395-6, 398 passim.
14. Nakayama T, Asaka D, Kuboki A, Okushi T, Kojima H. Impact of residual frontal recess cells on frontal sinusitis after endoscopic sinus surgery. Eur Arch oto-rhino-laryngology Off J Eur Fed Oto-Rhino-Laryngological Soc Affil with Ger Soc Oto-Rhino-Laryngology - Head Neck Surg 2018;275(7):1795-801.
15. Nayak DR, Balakrishnan R, Murty KD. Functional anatomy of the uncinate process and its role in endoscopic sinus surgery. Indian J Otolaryngol head neck Surg Off Publ Assoc Otolaryngol India 2001;53(1):27-31.
16. Catalano PJ, Strouch M. The minimally invasive sinus technique: theory and practice. Otolaryngol Clin North Am 2004;37(2):401-9, viii.

RESEARCH ARTICLE
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The Role of Activin-A in the Etiopathogenesis of Nasal Polyposis

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ABSTRACT

Objective: Nasal polyposis (NP) is defined as persistent inflammation of the sinonasal mucosa intractable to medical and surgical treatment. Activin-A, is a pleiotropic cytokine in the transforming growth factor-b (TGF-β) superfamily and was shown to orchestrate the allergic inflammation in asthma via suppression of T helper-2 (Th2) cells, induction of regulatory T cells, and tissue repair. The purpose of this study was to investigate the role of the activin-A in pathophysiology of NP.
Materials and Methods: According to the European Rhinosinusitis and Nasal Polyp criteria, 50 patients and 24 healthy subjects were included in the study. There were no significant differences across age and gender between the 2 groups (p>0.05). Samples from patients with NP (n=50; 11 women, 39 men) were acquired during endoscopic sinus surgeries. Middle turbinate specimens from patients without sinus disease and who were undergoing septoplasty were collected as controls (n=24; 3 women, 21 men).
Results: Immunohistochemical staining with activin-A showed an increase in the staining intensity, number of glands and inflammatory cells in polyp specimens compared to healthy nasal mucosa. In contrast, no differences were found in fibroblasts and vascular density.
Conclusion: We evaluated the expression of activin-A in NP tissue, which showed a slightly elevated expression compared to the controls. This might support the possible role of activin-A in the pathophysiology of NP. Clearer elucidation of the roles of activin-A and other mediators in tissue remodeling in NP may ensure more accurate targets for treatment and prevention of relapse.

Keywords: Activin A, Nasal polyps, Sinusitis, TGF-β

INTRODUCTION

Nasal polyposis (NP) is a severe chronic inflammatory disease of the nasal and paranasal mucosa characterized by semitranslucent, gelatinous, pale mucosal outgrowths that typically originate from the middle meatus and major symptoms are nasal congestion, nasal obstruction and anosmia or hyposmia. It affects up to 4% of the population, is slightly more common in men and has a high recurrence rate (1). NP is frequently associated with chronic rhinosinusitis and asthma (2, 3).

Histopathologically, nasal polyps are characterized by epithelial shedding, basement membrane thickening, subepithelial edema, albumin deposition, pseudocystic formations and vascular/glandular atrophy with T helper-2 (Th2) skewed eosinophilic inflammation (4).

The belief of “one airway, one disease” is widely known and accepted all over the world. Asthma and NP have actually the same inflammatory properties, including infiltration of eosinophil, hyperplasia of goblet cell, a Th2-cell immune response, and tissue remodeling. (5). The airway epithelium can release many chemokines, cytokines and growth factors, which regulate inflammation and remodeling (6).

Among these cytokines, transforming growth factor-β1 (TGF-β1) plays a strong role in asthma pathogenesis due to its ability to inhibit airway hyperresponsiveness and promote airway remodeling (6, 7). TGF-β1 has also been shown to play

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a key role in chronic rhinosinusitis-related tissue remodeling processes in the mucosa, through promoting the differentiation of fibroblasts into myofibroblasts and increasing the production of extracellular matrix proteins (8). However, the role of TGF-β1 in NP is still controversial with increased expression in some immunohistochemical studies and lower TGF-β levels in others (5, 9).

Activin-A is a pleiotropic cytokine belonging to the inhibin activin family within the TGF superfamily of dimeric molecules and uses homologous signal transmission path as TGF-β1, including Smad-dependent and Smad-independent pathways (10). It has a regulatory role in many processes such as embryological development, immune system, hematopoiesis and cell regeneration (11). TGF-β and activin signaling pathways are activated in allergic pulmonary diseases and airway remodeling (12-14). Activin-A promotes human pulmonary fibroblasts and proliferation of airway smooth muscle cells and supplies a connection between acute allergen-specific T-cell responses and chronic TGF-β-mediated airway remodeling in asthma (13). In this study, it was aimed to evaluate the expression of activin-A in NP samples to investigate its role in the pathogenesis of the disease.

MATERIALS AND METHODS

Patients who met the European Position Paper on Rhinosinusitis and Nasal Polyps (EPOS) criteria and who agreed to participate were enrolled in the study at the department of otorhinolaryngology of a tertiary hospital (17). The study protocol was approved by the local ethics committee (Ethics committee protocol number: 2012/166). The principles of the Helsinki declaration were followed during the study and written informed consent forms were obtained from all participants. In this study, exclusion criteria were determined according to the EPOS definitions. None of the patients used a course of antibiotics or systemic/local corticosteroids in the 4 weeks prior to the surgery. Samples from patients with NP (n=50; 11 women, 39 men) were acquired while endoscopic sinus surgeries. Middle turbinate specimens of patients without sinus disease performed septoplasty were gathered as controls (n=24; 3 women, 21 men). All samples were fixed in 10% neutral buffered formalin and stored in paraffin blocks at room temperature.

Immunohistochemistry

Paraffin-embedded tissue blocks were cut into 5-µm-thick sections. Serial sections from each block were deparaffinized and hydrated to water. Dilute concentrated Diva Decloaker (Biocare, DV2005L2J) at a ratio of 1:19 (1 ml Diva to 19 ml of deionized water). The slides were placed into retrieval solution in Biocare's Decloaking Chamber at 110ºC for 40 minutes and then the slides were allowed to cool for 20 minutes. Dilute TBS tween solution (TBT999, Scytek) at a ratio of 1:19 ((50 ml TBS to 950 ml of deionized water). After washing with TBS tween 20, it was treated with 3% hydrogen peroxide (ACA125, Scytek) for 20 minutes then rewashed twice with TBS tween 20. The Super Blocks (AAA125, Scytek) were incubated for 20 minutes at room temparature. Each section was incubated with the activin-A Receptor Type IC antibody (1;100 dilution) (GTX103442, Genetex) for one hour at room temparature. The slides were washed three times with TBS tween 20 and then were visualized by diaminobenzadine (DAB). Followed by a last wash, the slides were then mounted, coverslipped, and sealed in a solution (ABF125, Scytek) for 20 minutes. The slides were washed three times with TBS tween 20, and incubated using the Sensitek Horseradish Peroxidase Solution (ABF125, Scytek) for 20 minutes. The slides were washed three times with TBS tween 2, and then were visualized by DAB. The sections were then counterstained with Mayer's hematoxylin (HMM500, Scytek) before dehydration with ethanol and xylene. The slides were then mounted with DDmount (DDKitalia, 04-102) and visualised by light microscopy.

Immunostaining intensity and density of vessels, glandular structures, inflammation and fibroblasts were evaluated using a numerical scoring system ranging from 0 to 3 defined by Muluk et al. (16).

Statistical analyses

All statistical analyses were performed using SPSS software, version 16.0 (SPSS Inc., Chicago, IL, USA). The Student's t test was used for comparison of age; Chi-Square for comparison of gender and scale between the 2 groups. Data were expressed as medians and interquartile ranges, or in box-and-whisker plots. The Mann–Whitney U 2-tailed test was used for control and NP groups. To determine correlations, the Spearman test was used, and significance was accepted where $p<0.05$.

RESULTS

The NP group consisted of 39 men (78%) and 11 women (22%), whereas the control group had 21 men (87.5%) and 3 women (12.5%). The mean age of the NP group was 42.50±15.9 years (range 16-75 years) and 35.92±13.6 years in the control group (range 18-64 years) with no statistical significant differences (p>0.05). The immunohistochemical examination presented in Table 1 showed an increased staining with activin-A antibody (p=0.003) (Figure 1), an increase in inflammatory cells and a decrease in glands (p=0.001 and p<0.001 respectively) in the polyp specimens compared to the controls (Figure 2). In contrast, no differences were found in fibroblasts and vascular density (p=0.87 and p=0.12 respectively) (Figure 3).

Table 1: Immunohistochemical examination

	Nasal polyposis	Control group	P value
Activin-A staining	3±0	2.8±0.4	0.003
Vascular density	2.5±0.6	2.7±0.7	0.12
Glandular density	1.6±1.2	2.6±0.6	0.001
Inflammation	2.6±0.6	1.75±0.6	<0.001
Fibroblast	1.6±0.6	1.58±0.6	0.87

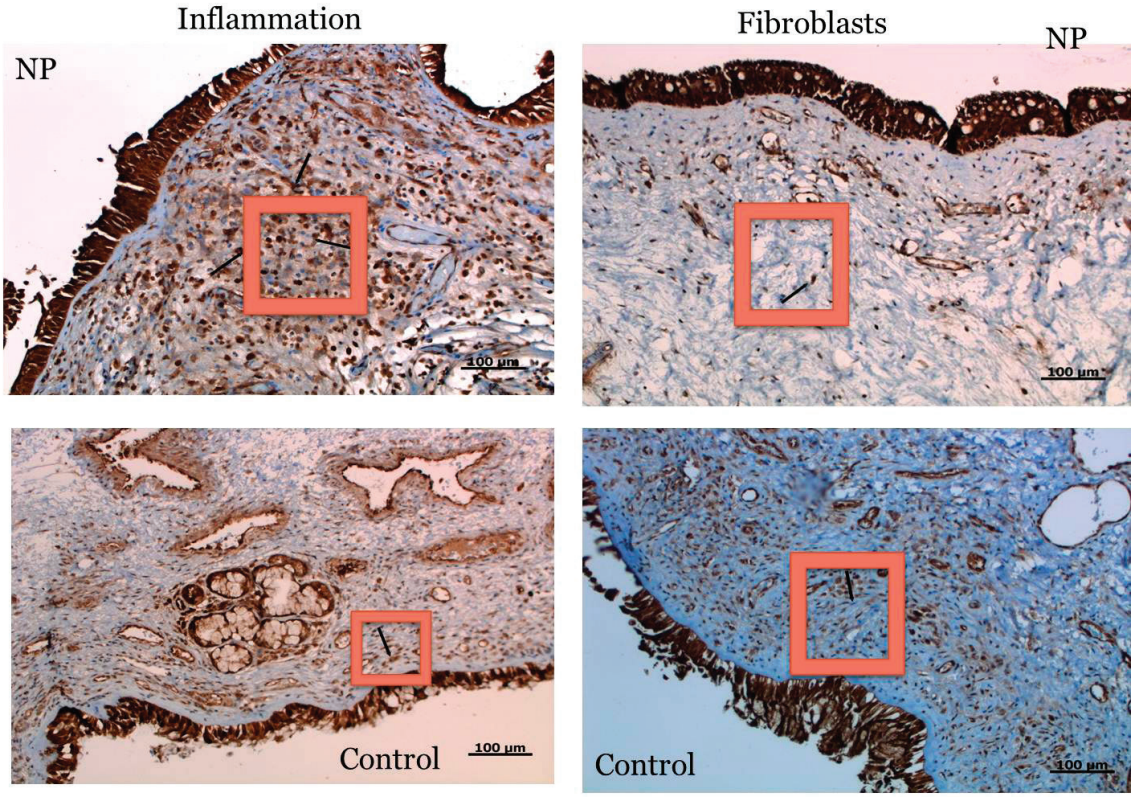

Figure 1: Increased staining with Activin-A antibody in polyp specimens [3+] compared to controls [2+].

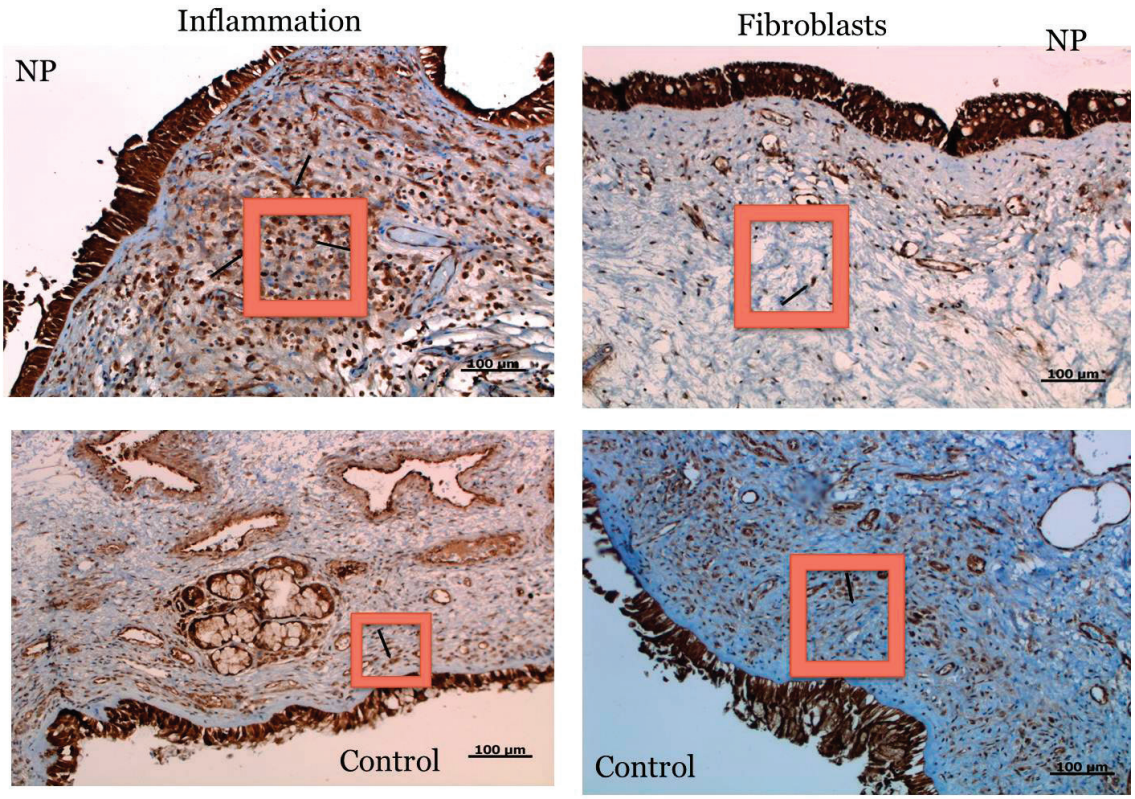

Figure 2: Increase in inflammatory cells and a decrease in glands in polyp specimens compared to controls.

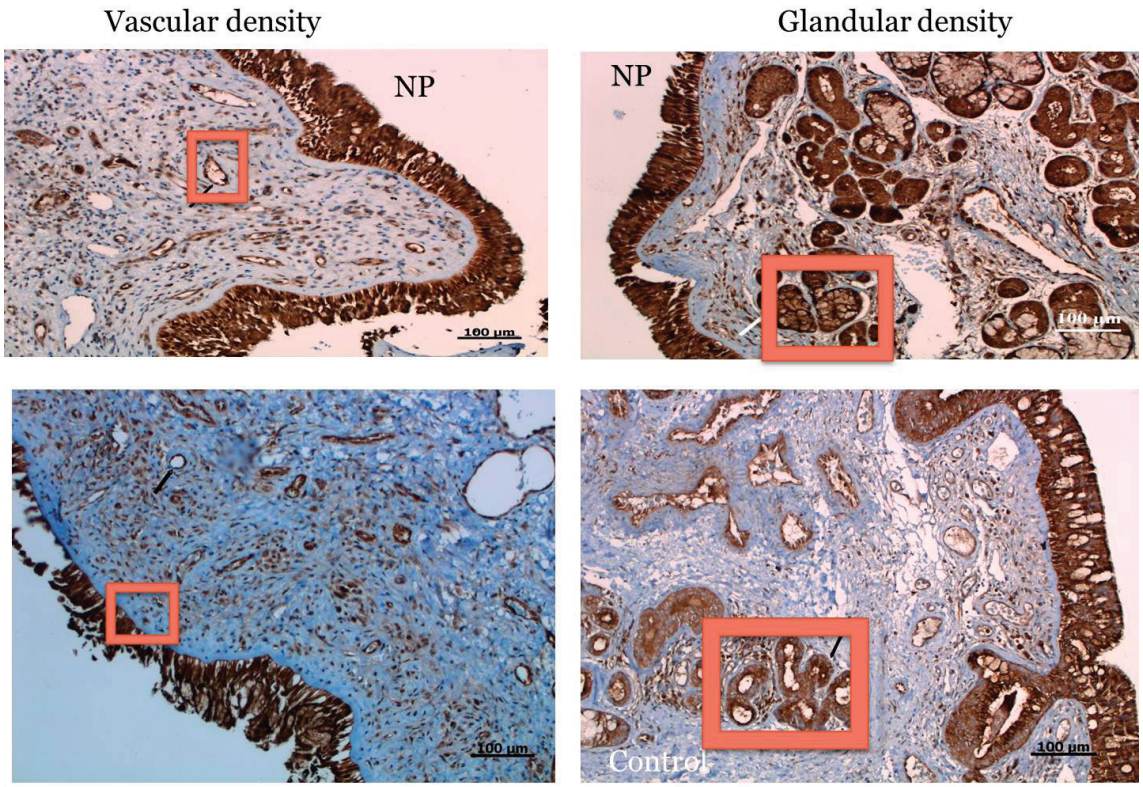

Figure 3: No differences were found in fibroblasts and vascular density in polyp specimens compared to controls

DISCUSSION

Nasal epithelial repair and remodeling has a remodeling phenomenon similar to the lower airway changes in asthma; It includes inflammation, differentiation, proliferation, and matrix accumulation and regulated by many different growth factors and cytokines (17). Chronic rhinosinusitis is classified into two main subgroups: with and without nasal polyps, which are different clinical conditions depend on different inflammatory mediator and remodeling profiles.

Chronic rhinosinusitis with NP is defined by a predominant Th2-skewed eosinophilic inflammation with high levels of IL-5, eosinophilic cationic protein and eotaxin, and high local IgE concentration in Caucasians and a Th1/Th17 skewed neutrophilic inflammation in Asians (4, 18). Huvenne et al. conducted a study in which patients with chronic rhinosinusitis with NP were investigated for inflammatory cytokines simultaneously in samples of the upper and lower airways compared to the control group, and they met higher Th2 levels nasal polyps compared to bronchial samples , there was a strong correlation between upper and lower airway inflammation characteristic (19). Inflammation leads to remodeling in the airway epithelium and several factors such as TGF-β, matrix metalloproteinases [MMPs], platelet derived growth factor [PDGF] and fibrinolytic components have been implicated in remodeling (10, 20). TGF-β1 appears to play a key role in tissue remodeling processes in chronic rhinosinusitis in sinus mucosa, through promoting the differentiation of fibroblasts into myofibroblasts, which synthesize extracellular matrix proteins (8). It also influences the balance between MMPs and tissue inhibitors of metalloproteinase (TIMP), which possibly leads to the pathologic tissue remodeling in chronic rhinosinusitis. Wang et al. showed higher expression of TGF-β1 and collagen deposition in chronic rhinosinusitis without NP than with NP, in accordance with the former studies (21). There was more severe basement membrane thickening in chronic rhinosinusitis without NP which also confirms the influence of TGF-β1 for extracellular matrix production production.

Activin-A, which belongs to the TGF-β family, phosphorylates Smad2 and Smad3 from Smad R-Smad) proteins when activated, and this complex translocates into nucleus to activate gene transcription (22).

There is a wealth of data showing that Activin-A promotes inflammation and remodeling in allergic asthma. In an experimental asthma model, mast cells and lymphocytes were shown to secrete activin-A after stimulation by IgE receptor cross-linking or intranasal ovalbumin challenge (23). In another study, its overexpression was shown to induce severe pulmonary inflammation, which was reversed by Activin-A neutralization (24). Smad2 overexpression was found to enhance airway hyperreactivity after intranasal allergen exposure to house

dust mite extract concomitant with the changes in airway remodeling, such as subepithelial collagen accumulation and hyperplasia of smooth muscle, whereas mice lacking Smad 3 were shown to have decreased peribronchial fibrosis and smooth muscle deposition (13). Interestingly, in some studies, activin-A was shown to be a critical immunoregulator in asthma (25). It induces Foxp3+ regulatory T cells, which suppress T helper cell activity, maintains immune tolerance in the stable situation and inhibits asthma attack (26). The expression and secretion of activin-A in the upper airways are not well known yet. Yang et al. evaluated the level of activin-A and its inhibitor, follistatin, in nasal tissue specimens from chronic rhinosinusitis cases with and without NP, and monitored the spontaneous secretion of these cytokines in a human mucosal model (27). By means of ELISA kits, activin-A, follistatin, TGF-β1, and IFN-γ concentrations were found to be higher in tissue homogenates from subjects with chronic rhinosinusitis without NP compared to those with NP, while the levels of IL-5 and eosinophilic cationic protein were remarkably lower.

Similar to our study, Chaker et al. collected nasal samples from control turbinate nasal tissue from 48 patients with CRSsNP, during endonasal functional endoscopic sinus surgery as well as from 31 patients without a history of chronic rhinosinusitis during turbinoplasty and septoplasty. They reported a dramatic (48-fold) increase in the frequency of activin-A-producing cells in patients suffering from CRS with NP compared with controls without sinusitis (28). Also Yamin et al. examined the expression of the profibrotic cytokines TGF-β1 and activin-A in chronic rhinosinusitis with NP compared to healthy controls and chronic rhinosinusitis without NP sinus or middle turbinate tissue. They showed that TGF-β1 and activin-A increased in CRSwNP by immunostaining method (29).

The fact that we did not include cases of chronic rhinosinusitis without NP and did not examine the expression of TGF-β1 and activin-A antagonist follistatin, which can provide more information about the inflammatory and fibrotic process in NP, might be considered as a limitation of our study.

CONCLUSIONS

In this study, we evaluated the expression of activin-A in NP tissue and showed a slightly more elevated expression compared to the controls. While activin-A can't be defined as a specific molecule playing a role in the pathophysiology of nasal polyps, it does seem to be commonly expressed in nasal tissue with inflammation. Clearer elucidation of the roles of activin-A and other mediators in the etiology of NP may provide more effective solutions for treatment and prevention of relapse.

Ethics Committee Approval: The study protocol was approved by Selcuk University Ethics Committee (Ethics committee protocol number: 2012/166), and conducted in accordance with the ethical principles for medical research formulated in the WMA declaration of Helsinki.

Informed Consent: Written informed consent was obtained.

Peer-Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- H.D., M.K.B., Ç.E., P.K.; Data Acquisition- H.D., Ç.E.; Data Analysis/Interpretation- H.D., M.K.B., P.K.; Drafting Manuscript- H.D., M.K.B., Ç.E., P.K.; Critical Revision of Manuscript- H.D., M.K.B., P.K.; Final Approval and Accountability- H.D., M.K.B., Ç.E., P.K.;Conflict of Interest: Authors declared no conflict of interest.

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REFERENCES

1. Stevens WW, Schleimer RP, Kern RC. Chronic Rhinosinusitis with Nasal Polyps. J Allergy Clin Immunol Pract 2016;4(4):565-72.
2. Rajguru R. Nasal polyposis: current trends. Indian Journal of Otolaryngology and Head & Neck Surgery, 2014;66:16-21.
3. Gelardi M, Iannuzzi L, Tafuri S, Passalacqua G, Quaranta N. Allergic and non-allergic rhinitis: relationship with nasal polyposis, asthma and family history. Acta Otorhinolaryngol Ital 2014;34(1):36-41.
4. Cao PP, Li HB, Wang BF, Wang SB, You XJ, Cui YH, et al. Distinct immunopathologic characteristics of various types of chronic rhinosinusitis in adult Chinese. J Allergy Clin Immunol 2009;124(3):478-84.
5. Bachert C, Gevaert P, Holtappels G, Cuvelier C, van Cauwenberge P: Nasal polyposis: from cytokines to growth. Am J Rhinol 2000;14(5):279-90.
6. Hammad H, Lambrecht BN. Dendritic cells and epithelial cells: linking innate and adaptive immunity in asthma. Nat Rev Immunol 2008;8(3):193-204.
7. Alcorn JF, Rinaldi LM, Jaffe EF, van Loon M, Bates JH, Janssen-Heininger YM, et al. Transforming growth factor-beta1 suppresses airway hyperresponsiveness in allergic airway disease. Am J Respir Crit Care Med 2007;176(10):974-82.
8. Kou W, Guo-Hua H, Yao H-B, Wang X, Shen Y, Kang H-Y, et al. Regulation of transforming growth factor-1 activation and expression in the tissue remodeling involved in chronic rhinosinusitis. ORL J Otorhinolaryngol Relat Spec 2012;74(3):172-8.
9. Hirschberg A, Jokuti A, Darvas Z, Almay K, Repassy G, Falus A. Pathogenesis of nasal polyposis by immunoglobulin E and interleukin-5 is complete by transforming growth factor-β1. Laryngoscope 2003;113(1):120-4.
10. Yang Y, Zhang N, Lan F, Van Crombruggen K, Fang L, Hu G, et al. Transforming growth factorbeta1 pathways in inflammatory airway diseases. Allergy 2014;69(6):699-707.
11. Hedger MP, Kretser de DM. The activins and their binding protein, follistatin-Diagnostic and therapeutic targets in inflammatory disease and fibrosis. Cytokine Growth Factor Rev 2013;24(3):285-95.
12. Gregory LG, Mathie SA, Walker SA, Pegorier S, Jones CP, Lloyd CM. Overexpression of Smad2 drives house dust mite-mediated airway remodeling and airway hyperresponsiveness via activin and IL-25. Am J Respir Crit Care Med 2010;182(2):143-54.
13. Karagiannidis C, Hense G, Martin C, Epstein M, Ruckert B, Mantel PY et al. Activin A is an acute allergen-responsive cytokine and provides a link to TGF-beta-mediated airway remodeling in asthma. J Allergy Clin Immunol 2006;117(1):111-8.
14. Kariyawasam HH, Pegorier S, Barkans J, Xanthou G, Aizen M, Ying S, et al. Activin and transforming growth factor-beta signaling

pathways are activated after allergen challenge in mild asthma. J Allergy Clin Immunol 2009;124(3):454-62.
15. Fokkens WJ, Lund VJ, Mullol J, Bachert C, Alobid I, Baroody F, et al. EPOS 2012: European position paper on rhinosinusitis and nasal polyps. A summary for otorhinolaryngologists. Rhinology 2012;50(Suppl S23):1-12.
16. Muluk NB, Arikan OK, Atasoy P, Kiliç R, Yalçinozan ET. The role of endothelial nitric oxide synthase (eNOS) in the pathogenesis of sinonasal polyps. Eur Rev Med Pharmacol Sci 2014;18(6):918-29.
17. Yan Y, Gordon WM, Wang DY. Nasal epithelial repair and remodeling in physical injury, infection, and inflammatory diseases. Curr Opin Otolaryngol Head Neck Surg 2013;21(3):263-70.
18. Huvenne W, Van Bruaene N, Zhang N, van Zele T, Patou J, Gevaert P, et al. Chronic rhinosinusitis with and without nasal polyps: what is the difference? Curr Allergy Asthma Rep 2009;9(3):213-20.
19. Håkansson K, Bachert C, Konge L, Thomsen SF, Pedersen AE, Poulsen SS, et al. Airway Inflammation in Chronic Rhinosinusitis with Nasal Polyps and Asthma: The United Airways Concept Further Supported. PLoS One. 2015;10(7):e0127228
20. Van Bruaene N, Bachert C. Tissue remodeling in chronic rhinosinusitis. Curr Opin Allergy Clin Immunol 2011;11(1):8-11.
21. Wang X, Zhao C, Ji W, Xu Y, Guo H. Relationship of TLR2, TLR4 and tissue remodeling in chronic rhinosinusitis. Int J Clin Exp Pathol 2015;8(2):1199-212.
22. Tsuchida K, Nakatani M, Hitachi K, Uezumi A, Sunada Y, Ageta H, et al. Activin signaling as an emerging target for therapeutic interventions. Cell Commun Signal 2009;7:1-11.
23. Cho SH, Yao Z, Wang SW, Alban RF, Barbers RG, French SW, Oh CK. Regulation of activin A expression in mast cells and asthma: its effect on the proliferation of human airway smooth muscle cells. J Immunol 2003;170(8):4045-52.
24. Apostolou E, Stavropoulos A, Sountoulidis A, Xirakia C, Giaglis S, Protopapadakis E, et al. Activin-A overexpression in the murine lung causes pathology that simulates acute respiratory distress syndrome. A m J Respir Crit Care Med 2012;185(4):382-91.
25. Hardy CL, Rolland JM, O'Hehir RE. The immunoregulatory and fibrotic roles of activin A in allergic asthma. Clin Exp Allergy 2015;45(10):1510-22.
26. Kariyawasam HH, Semitekolou M, Robinson DS, Xanthou G. Activin-A: a novel critical regulator of allergic asthma. Clin Exp Allergy 2011;41(11):1505-14.
27. Yang Y, Zhang N, Crombruggen KV, Lan F, Hu G, Hong S, Bachert C. Differential expression and release of Activin A and follistatin in chronic rhinosinusitis with and without nasal polyps. PLoS One 2015;10(6):e0128564.
28. Chaker AM, Zissler UM, Poulos N, Wagenmann M, Bas M, Gürth F, Xanthou G, Schmidt-Weber C. Activin-A Is a Pro-Inflammatory regulator in type-2-driven upper airway disease. Int Arch Allergy Immunol 2018;176:15-25.
29. Yamin M, Holbrook EH, Gray ST, Busaba NY, Lovett B, Hamilos DL. Profibrotic transforming growth factor beta 1 and activin A are increased in nasal polyp tissue and induced in nasal polyp epithelium by cigarette smoke and Toll-like receptor 3 ligation. Int Forum Allergy Rhinol 2015;5(7):573-82.

RESEARCH ARTICLE
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Pediatric Tracheotomy: 5-years of Experiences at a Tertiary Care Center

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ABSTRACT

Objective: To describe specific indications and complications of pediatric tracheostomies performed in our tertiary care children's hospital between 2015 and 2020.
Materials and Methods: A retrospective study analyzing charts of pediatric tracheostomies utilizing the maturation suture technique was conducted. The review included patient data covering a 5-year period, commencing on the 1st of January 2015 through the 31st of May 2020.
Results: Fifty-five patients (33 females, 22 male) were included in the study. A tracheostomy was performed to address complications arising from prolonged ventilation in 48 children (87%) or upper airway obstruction in 7 children (13%).
There was one intraoperative complication that resulted in death. There was one early postoperative complication (2%) (one child suffered accidental decannulation and the cannula was replaced without further incident). There were 7 late postoperative complications all featuring peristomal granulation tissue (13%). There were 16 deaths; however, only one resulted from the tracheostomy as outlined above. Eight patients (15%) were successfully decannulated. In 6 cases, the tracheostomy was spontaneously closed. Repair of tracheoesophageal fistula was required in two patients.
Conclusion: Currently, the tracheostomy is the preferred course of treatment. Though it can potentially lead to severe complications in children, instances of this occurring are rare. Therefore, a tracheostomy should be performed by a multidisciplinary team following predetermined rules in a specialized center.

Keywords: Pediatric tracheotomy, maturation suture technique, upper airway obstruction

INTRODUCTION

The last 30 years has seen alterations in indications of tracheostomy in children (1, 2). In the past, the most common indications were acute inflammatory airway obstructions such as diphtheria or acute epiglottitis. The two pronged approach of vaccine development against Corynebacterium diphtheriae and Haemophilus influenzae as well as modern neonatal intensive care units have served to reduce the totality of infection based indications for a tracheostomy (3). Recent series have shown that prolonged ventilation or upper airway obstruction due to larygotracheal anomalies have become the most prevalent indications of pediatric tracheostomy (4).

The tracheostomy has many advantages, it is comfortable for patients, it requires less sedation, breathing is easier, long-term laryngeal function is improved, there is less need for mechanical ventilation, there is a lower risk of ventilator-associated pneumonia, it results in earlier discharging from PICU and improved oral hygiene (5, 6).

Tracheostomy complications include subcutaneous emphysema, hemorrhage, accidental decannulation, pneumothorax, pneumomediastinum, intratracheal mucosal plugs, occlusion of the tracheostomy tube with mucus, granuloma around the tracheostomy and infections such as tracheitis (3, 7).

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The purpose of the study is to describe primary indication and complications of tracheostomy utilizing the maturation suture technique performed in children between 2015- 2020, in our tertiary care children's hospital.

MATERIALS AND METHODS

A retrospective study analyzing charts of patients that underwent pediatric tracheostomy utilizing the maturation suture technique was conducted at the tertiary care children's hospital. In this study, we reviewed the patient data of a 5-year period, from January 1 2015, through May 31 2020. The hospital ethics committee approved the study.

Charts were reviewed for demographic data such as gender and age at tracheostomy, indication of tracheostomy, date of tracheostomy, last clinical examination, mortality and comorbidities such as preterm birth, congenital heart disease, bronchopulmonary dysplasia, neurologic, neuromuscular or neoplastic disease, known syndrome, severe systemic infection. Tracheostomy indications were separated into 2 groups: 1) long intubation, and 2) upper airway obstruction. Patients with incomplete medical records or age>18 years at the time of tracheostomy were excluded from this study.

Surgical procedure

The same technique was used in all patients. During the tracheostomy, general anesthesia was applied to all childrens.. The patient was placed in a supine position and extension of the neck was supported by a shoulder roll. A horizontal skin incision was performed on the midpoint between the cricoid cartilage and the sternal notch. Cervical lipectomy was performed. The platysma was divided, midline raphe between the strap muscles was encountered, strap muscles were retracted laterally with regular finger palpation to secure the medial positioning of the trachea. After division of the thyroid gland, the pretracheal fascia was identified. The cricoid cartilage was palpated superiorly after loose fascia was excised bluntly from the anterior trachea. Two traction sutures with 4-0 vicryl were placed at the 3rd or 4th tracheal rings on either side of the. The tracheal incision was made vertically between the sutures. We placed four maturity sutures (with 4-0 PDS) between the trachea and the skin. The tracheostomy cannula was inserted and secured by a twine and tightened around the neck.

After surgery, the patient was promptly admitted to the intensive care unit (ICU). An AP thoracic X-ray was performed to establish the place of the cannula and the absence of pneumothorax or pneumomediastinum.

Patients were decannulated when they no longer required mechanical ventilation, nasal oxygen and no longer suffered from airway obstruction. Our decannulation protocol mandates the following: direct laryngoscopy and bronchoscopy are preformed to rule out airway stenosis, suprastomal collapse and granulation. Afterwards, a one size smaller cannula is placed, plugged and the patient is observed in the ward for 2 days before being discharged. If the patient can tolerate the plugged cannula for 3 weeks, the patient is then readmitted before undergoing direct laryngoscopy and tracheoscopy again. If no airway obstruction is present, the same cannula is placed after which the patient can return to the ward. Decannulation is then performed and the patient is observed for three days before being discharged. The final direct laryngoscopy and tracheoscopy is performed six weeks thereafter.

RESULTS

Fifty-five patients (33 female, 22 male) were included in the study. The median age at tracheostomy was 24, 2 months (range 1 month to 11 years). Thirty-six patients underwent tracheostomies within the first year of life (Graphic 1).

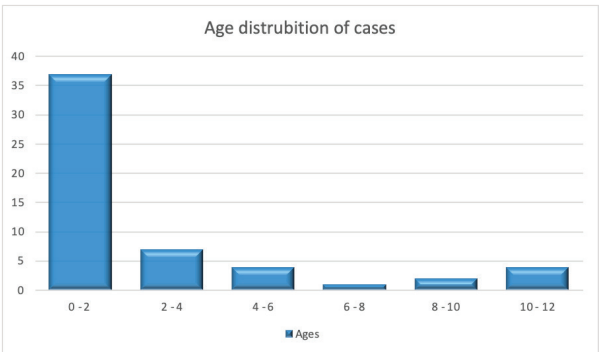

Figure 1: Age distribution of cases.

There were two main indications for tracheostomy: prolonged intubation and airway obstruction. Primary indications in 48 patients with prolonged intubation were cardiopulmonary disease (n=23), neuromuscular disease (n=24) and chronic aspirations (n=1). In patients with airway obstruction, 4 resulted from subglottic stenosis, 2 from Pierre-Robin's syndrome and 1 from bilateral vocal cord paralysis.

There was one intraoperative complication that resulted in death. The child had a tracheoesophageal fistula due to long intubation. The tracheoesophageal fistula was not noticeable prior to the tracheostomy. After the tracheostomy was performed, uninterrupted air flow into the patient's stomach lead to the spotting of the fistula. However, the patient was lost because he was unable to respirate sufficiently. There was one early postoperative complication (2%) where one child suffered accidental decannulation and the cannula was replaced without complications. There were 7 late postoperative complications all featuring peristomal granulation tissue (13%).

There were 16 deaths; with only one being directly related to the tracheostomy as already outlined above. 15 patients suffered from cardiopulmonary arrest due to complications related to their disease.

We decannulated 8 patients (15%) successfully. Mean duration from tracheotomy to decannulation was 176 days (range, 30 days to 455 days). In 6 of the cases, the tracheostomy closed spontaneously. Repair of the tracheoesophageal fistula was required in two patients.

DISCUSSION

In our study, we retrospectively analyzed 55 patients who underwent tracheotomy between January 2015 and May 2020 using a maturation suture. 16 patients died, and of these patients, one death arose due to the complications related to the tracheostomy. 8 patients were decannulated successfully.

In our study, the ages of the patients spanned ranged from 0 to 11 years, with 62% of the pediatric patients being younger than 12 months old and of those, 53% were younger than 6 months of age. Previous studies noted similar trends with patients in this lower age bracket featuring predominately in tracheostomies (3, 8, 9). This study found the mean age of patients undergoing tracheostomy for both airway obstruction and prolonged ventilation to be similar. In support of this thesis a study by Nasif et al involving 57 pediatric tracheostomies performed between 2004-2014, reported no difference in the mean age of patients receiving tracheostomies for either airway obstruction or prolonged intubation (3). Conversely, another study which includes 122 pediatric tracheotomies between the years 1987-2003, Mahadevan et al. noted a mean age of 4.5 months for airway obstruction surgeries, versus 16 months for prolonged intubation (10).

Due to improvements in diagnosis and treatment, the survival rates of pediatric patients with chronic diseases have increased and these patients are managed in intensive care units under endotracheal intubation for a long period. Therefore prolonged intubation remains the leading indication necessitating tracheostomy (11-13). Tracheostomy, which is a part of palliative treatment in children with chronic diseases, enables patients to spend more time with their families whilst allowing them to be more comfortable (14). As in the literature, and confirmed by our study, the most common indication was prolonged intubation caused by cardiopulmonary diseases, neurological diseases, upper airway obstruction and craniofacial anomalies (15). Our series did not feature cases of tracheotomy for laryngeal trauma similar to studies that have taken place within the last decade, unlike studies that took place over 10 years ago (3, 13, 16). This reduction is mostly likely due to increased car seat belt use. There were no indications for laryngeal infection or inflammation owing largely to vaccinations against H. influenzae type B and diphtheria. In a series of 282 pediatric tracheostomies between 1968 and 2005, infection led to airway obstruction in 101 patients (16). Endotracheal tube improvements, notably in the selection of appropriate diameters, have resulted in fewer laryngeal complications, particularly in neonates (6, 17). Indications of tracheotomy for severe laryngomalacia, recurrent laryngeal papillomatosis and certain cases of subglottic stenosis have reduced arising from improvements in surgical techniques (18, 19). Lastly, propranolol is currently the preferred treatment for laryngeal hemangioma, after surmounting the preference for surgeries that used to be in favor (20, 21). After enhancements in non-invasive ventilation, the need for intubation and tracheostomy in some airway obstruction diagnoses, such as severe laryngomalacia or Pierre Robin sequence has relegated (23). Prolonged inbutation in immature children with bronchodysplasia, as well as airway obstruction caused by congenital or acquired bilateral vocal fold palsy, deformity, or malignancy, are currently the main indications (9, 13).

Although the frequency of pediatric tracheostomy has increased, death resulting from tracheostomy is extremely rare (5, 13, 22). In a study which includes 420 pediatric tracheostomies, Wetmore et al. reported that the mortality rate was 28% in 1982 (1). Case mortalities are on the decline, there were 2 instances out of 57 for Nassif et al. (3), 2 out of 122 for Mahadevan et al.(10), 3 out of 282 for Ozmen et al. (16), 1 out of 112 for Trey et al. (9), and zero for Ang et al. (48 children) (8). Risks are not totally eradicated even with the presence of contemporary surveillance protocols such as cardiac and oxygen monitoring. In our series, one death occurred as a result of tracheoesophageal fistula.

In this case series, the early complication rate was 2%. Where one child suffered accidental decannulation and the cannula was replaced without further incident. Early accidental decannulation was reported as 2.5%-3.7% in many studies (10, 23). Recannulation is prevented by tracheal suture tension on both sides of the incision. The maturation suture technique that secures the trachea to the skin, creating a formal, safe stoma, also helps recannulation (24).

Accidental decannulation, intratracheal mucosal plugs, and granuloma surrounding the tracheotomy and in the trachea, subglottic or tracheal stenosis occurring occasionally are late complications of pediatric tracheostomy. Our study returned a late complication rate of 13% (only granulation tissue), in contrast to other reports which had a complication rate of 31-51% (3, 8, 10, 25).

The literature noted a decannulation rate that ranged between 17% and 78% depending on the variety of tracheotomy indications and associated comorbid diseases (25-28). In this study, 8 patients (15%) were successfully decannulated a figure similar to that presented by the literature (3, 4, 27-29).

CONCLUSION

Tracheostomy is performed in cases of prolonged ventilation and for airway obstruction. Currently tracheostomy is the preferred option, however, it can potentially lead to severe complications in children albeit rarely, therefore, it must be carried out by a multidisciplinary team following predetermined rules in a specialized center.

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REFERENCES

1. Wetmore RF, Handler SD. Pediatric Tracheostomy Experience During the Past Decade. Ann Otol Rhinol Laryngol 1982;91(6 Pt 1):628-32.
2. Line WS, Hawkins DB, Kahlstrom EJ, MacLaughlin EF, Ensley JL. Tracheotomy in infants and young children: The changing perspective 1970-1985. Laryngoscope 1986;96(5):510-5.
3. Nassif C, Zielinski M, Francois M, Van Den Abbeele T. Tracheotomy in children: A series of 57 consecutive cases. Eur Ann Otorhinolaryngol Head Neck Dis 2015;132(6):321-5.
4. Can FK, Anıl AB, Anıl M, Gümüşsoy M, Çitlenbik H, Kandoğan T, et al. The outcomes of children with tracheostomy in a tertiary care pediatric intensive care unit in Turkey. Turk Pediatr Ars 2018;53(3):177-84.
5. Berry JG, Graham RJ, Roberson DW, Rhein L, Graham DA, Zhou J, et al. Patient characteristics associated with in-hospital mortality in children following tracheotomy. Arch Dis Child 2010;95(9):703-10.
6. Kremer B, Botos-Kremer AI, Eckel HE, Schlöndorff G. Indications, complications, and surgical techniques for pediatric tracheostomies - An update. J Pediatr Surg 2002;37(11):1556-62.
7. Gaudreau PA, Greenlick H, Dong T, Levy M, Hackett A, Preciado D, et al. Preventing complications of pediatric tracheostomy through standardized wound care and parent education. JAMA Otolaryngol Head Neck Surg 2016;142(10):966-71.
8. Ang AHC, Chua DYK, Pang KP, Tan HKK. Pediatric tracheotomies in an Asian population: The Singapore experience. Otolaryngol Head Neck Surg 2005;133(2):246-50.
9. De Trey L, Niedermann E, Ghelfi D, Gerber A, Gysin C. Pediatric tracheotomy: A 30-year experience. J Pediatr Surg 2013;48(7):1470-5.
10. Mahadevan M, Barber C, Salkeld L, Douglas G, Mills N. Pediatric tracheotomy: 17 year review. Int J Pediatr Otorhinolaryngol 2007;71(12):1829-35.
11. Hadfield PJ, Lloyd-Faulconbridge RV, Almeyda J, Albert DM, Martin Bailey C. The changing indications for paediatric tracheostomy. Int J Pediatr Otorhinolaryngol 2003;67(1):7-10.
12. Parrilla C, Scarano E, Guidi ML, Galli J, Paludetti G. Current trends in paediatric tracheostomies. Int J Pediatr Otorhinolaryngol 2007;71(10):1563-7.
13. Zenk J, Fyrmpas G, Zimmermann T, Koch M, Constantinidis J, Iro H. Tracheostomy in young patients: Indications and long-term outcome. Eur Arch Oto-Rhino-Laryngology 2009;266(5):705-11.
14. Chan T, Devaiah AK. Tracheostomy in Palliative Care. Otolaryngol Clin North Am 2009;42(1):133-41.
15. Gergin O, Adil EA, Kawai K, Watters K, Moritz E, Rahbar R. Indications of pediatric tracheostomy over the last 30 years: Has anything changed? Int J Pediatr Otorhinolaryngol 2016;87:144-7.
16. Özmen S, Özmen ÖA, Ünal ÖF. Pediatric tracheotomies: A 37-year experience in 282 children. Int J Pediatr Otorhinolaryngol 2009;73(7):959-61.
17. Walner DL, Loewen MS, Kimura RE. Neonatal subglottic stenosis - Incidence and trends. Laryngoscope 2001;111(1):48-51.
18. Mirabile L, Serio PP, Baggi RR, Couloigner VV. Endoscopic anterior cricoid split and balloon dilation in pediatric subglottic stenosis. Int J Pediatr Otorhinolaryngol 2010;74(12):1409-14.
19. Blanchard M, Leboulanger N, Thierry B, Blancal JP, Glynn F, Denoyelle F, et al. Management specificities of congenital laryngeal stenosis: External and endoscopic approaches. Laryngoscope 2014;124(4):1013-8.
20. Léauté-Labrèze C, De La Roque ED, Hubiche T, Boralevi F, Thambo JB, Taïeb A. Propranolol for severe hemangiomas of infancy. N Engl J Med 2008;358(24):2649-51.
21. Fauroux B, Leboulanger N, Roger G, Denoyelle F, Picard A, Garabedian EN, et al. Noninvasive positive-pressure ventilation avoids recannulation and facilitates early weaning from tracheotomy in children. Pediatr Crit Care Med 2010;11(1):31-7.
22. Carr MM, Poje CP, Kingston L, Kielma D, Heard C. Complications in Pediatric Tracheostomies. Laryngoscope 2001;111(11):1925-8.
23. Atmaca S, Bayraktar C, Aşilioğlu N, Kalkan G, Özsoy Z. Pediatric tracheotomy: 3-year experience at a tertiary care center with 54 children. Turk J Pediatr 2011;53(5):537-40.
24. Colman KL, Mandell DL, Simons JP. Impact of stoma maturation on pediatric tracheostomy-related complications. Arch Otolaryngol - Head Neck Surg 2010;136(5):471-4.
25. Carron JD, Derkay CS, Strope GL, Nosonchuk JE, Darrow DH. Pediatric Tracheotomies: Changing Indications and Outcomes. Laryngoscope 2000;110(7):1099-104.
26. Simma B, Spehler D, Burger R, Uehlinger J, Ghelfi D, Dangel P, et al. Tracheostomy in children. Eur J Pediatr 1994;153(4):291-6.
27. Dursun O, Ozel D. Early and long-term outcome after tracheostomy in children. Pediatr Int 2011;53(2):202-6.
28. Zia S, Arshad M, Nazir Z, Awan S. Pediatric tracheostomy: Complications and role of home care in a developing country. Pediatr Surg Int 2010;26(3):269-73.
29. Karapinar B, Arslan MT, Ozcan C. Pediatric bedside tracheostomy in the pediatric intensive care unit: six-year experience. Turk J Pediatr 2008;50(4):366-72.

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An Epidemiological Analysis of Maxillofacial Fractures in the Inner Aegean Region: A Retrospective Evaluation of 343 Cases

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ABSTRACT

Objective: The focus of this study was the sociocultural, economic, educational, and geographical factors that influence the incidence and types of fractures in maxillofacial trauma (MFT). The aim of this study was to identify the etiology and demographic characteristics of MFT cases in the inner (eastern) Aegean region.
Materials and Methods: The records of patients treated at the Kütahya Health Sciences University Evliya Çelebi Education and Research Hospital for MFT from January 1, 2017 to March 1, 2020 were analyzed retrospectively.
Results: A total of 476 bone fractures in 343 patients were analyzed. The sample comprised 239 male patients and 104 female patients. The average age was 35.19±17.79 years. Traffic accidents were found to be the most common cause (42%) of MFT. Of the isolated non-nasal bone fractures, 19 were in the maxilla, 17 in the zygoma, 14 in the mandible, and 7 in the frontal sinus. Nasal fractures (42.6%) were found to be the most frequently occurring breakages. Surgery was performed in 35.27% of the patients who agreed to have surgery for MFT.
Conclusion: The etiology and incidence of MFT can vary not only by country but also by geographical region within countries. The results of this study support this view. A review of the literature indicated that MFT in the inner (eastern) Aegean region in Turkey has not yet been studied. Societal differences must be considered in the recommendation of measures to reduce the incidence of MFT and thus morbidity and mortality.

Keywords: Maxillofacial fracture, trauma, etiology

INTRODUCTION

In emergency medicine, maxillofacial trauma (MFT) is an important and frequently encountered health problem that usually requires a multidisciplinary approach. According to the World Health Organization, one person dies every 9 seconds because of severe MFT and the related complications (1). Nasal fractures are the most common facial fractures resulting from MFT, and mandible fractures are the second most common (2). The causes of MFT are, in descending order, traffic accidents, assaults, and falls. The ranking of these three etiologies is associated with sociocultural and socioeconomic factors. Assault was found to be the most common reason for MFT in developed societies, and traffic accidents were the most common reason in developing societies (3). In a Toronto-based study, assault was identified as the most common reason independent of gender. Traffic accidents were found to be the most common reason in a Tehran-based study (2, 3).

Anamnesis, physical examinations, and tomography (direct radiography and computed tomography) are the three main steps in diagnosis and treatment. The indications for surgery to treat trauma are based on these findings (4, 5). Besides having cosmetic problems, most of these patients have functional disorders, such as long-term eye and smell impairments, chewing problems, and breathing difficulties (6, 7). Therefore, the treatment of MFT patients should include the correction of not only potential functional defects but also cosmetic defects because deformities can cause severe psychological problems.

The study aimed to analyze the diagnosis and follow-up processes for patients with MFT. The demographic and clinical features of patients treated at the Kütahya Health Sciences

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University Evliya Çelebi Education and Research Hospital from January 1, 2017 to March 1, 2020 were evaluated.

MATERIALS AND METHODS

This study was conducted with the permission of the Kütahya University of Health Sciences ethics committee dated 26/06/2020 (2020/10-20). In this investigation, the Helsinki Declaration guidelines were followed.

The files of patients who were treated for MFT at the Kütahya Health Sciences University Evliya Çelebi Education and Research Hospital from January 1, 2017 to March 1, 2020 were analyzed retrospectively. The following patient data were considered: demographics (e.g., age, gender, and etiology), diagnosis, diagnostic radiological evaluations of bone fractures and the localization of traumatic fractures, treatment methods, and complications.

MFT patients with only superficial skin lacerations or with no pathology other than soft tissue injury were excluded from the study. In addition, patients whose essential data could not be obtained from the records were not included. The data were evaluated and descriptive statistics (means, minimum–maximum values, and standard deviations) were used for the continuous variables. Frequencies and percentages were used for the categorical variables. The chi-square test was used to determine the relationships between the groups and categorical variables. A value of $p<0.05$ was considered statistically significant.

RESULTS

The study evaluated 343 patients with an MFT diagnosis, there were 239 male and 104 female patients. The average age was 35.19±17.79 years, and the period reviewed was January 1, 2017 to March 1, 2020. Traffic accidents (42%) were found to be the most common cause of MFT. The etiological distribution is summarized in Table 1.

Table 1: Etiological distribution of maxillofacial trauma

	Number of patients (*n*)	Percentage (%)
Traffic accident	144	42
Fall	85	24.7
Assault	52	15.2
Work accident	37	10.8
Non-car traffic accident (bicycle/motorcycle)	16	4.7
Animal kick	5	1.5
Firearm injury	4	1.1
Total	343	100

A total of 476 bone fractures were evaluated in 343 patients. When we examine the distribution of bone fractures, nasal fractures (42.6%) were most frequent. Zygoma (25%) and maxillary fractures (16%) were highest in the distribution of bone fractures due to MFT without isolated nasal fracture.

Table 2 summarizes the distribution of bone fractures in MFT.

Table 2: Distribution of bone fractures caused by maxillofacial trauma

	Number of patients (*n*)	Percentage (%)
Nasal bone	**203**	**42.6**
Zygoma	**119**	**25**
Inferior orbital rim	44	37
Zygomatic arc	53	44.5
Orbital base	19	16
Tripod	3	2.5
Maxilla	**76**	**16**
Maxilla front wall	69	90.7
Alveolus	5	6.5
Le Fort I	2	2.8
Mandibula	**68**	**14.3**
Angulus	17	25
Parasymphysis	12	17.6
Corpus	10	14.8
Subcondyle	6	8.7
Alveolus	6	8.7
Condyle	5	7.4
Ramus	5	7.4
Symphysis	5	7.4
Coronoid process	2	3
Frontal sinus front wall	**10**	**2.1**
Total	476	100

Some patients had multiple fractures.

Of the patients with isolated non-nasal fracture MFT, 57 had a fracture on the right side of the face, and 62 had a fracture on the left side. Twenty-one patients had fractures on both sides of the face. Of the fractures classified as both isolated and multiple, 57 patients were observed to have only one bone fracture. Of the isolated bone fractures, 19 were in the maxilla, 17 in the zygoma, 14 in the mandible, and 7 in the frontal sinus.

When we examine the fractures according to their etiology, it was observed that the patients who had been involved in a traffic accident had a zygoma and mandible fracture, and patients who had been involved in a work accident mostly had a fracture in the mandible. Parasymphysis is the localization of the mandible fracture, which is seen most after a traffic accident and the corpus is seen most after a work accident. Zygoma fractures are seen as a result of assault and falling, and maxillary bone fracture in cases of gunshot injury.

The distribution of zygoma fractures showed that the zygomatic arch was the most common site (44.5%), and the orbital rim was the second most common (Table 2). Maxillary bone fracture (38 patients) was the most common with zygoma fracture. In the zygomatic arch, non-displaced and displaced fractures without the collapse of the malar region and displaced fractures with the collapse of the malar region were seen. In two patients with

an isolated collapse of the zygomatic arch, the Gillies approach was used for reduction. The transoral Keen approach was used in zygomatic arch reduction in five patients with combined fractures.

The maxilla fractures were primarily anterior maxillary sinus fractures. Five patients had alveolar process fractures, and two had Le Fort I fractures. Isolated maxillary bone fractures were diagnosed in 20 patients. In addition, maxillary bone fractures were seen in 38 patients, and coexisting zygomatic bone fractures were also detected. In 10 patients, the fracture line had passed through the infraorbital foramen and damaged the infraorbital nerve. In these patients, the nerve was relieved by the administration of neurolysis to the infraorbital nerve.

In this series, 68 mandible fractures were diagnosed in 41 patients. Twenty-seven of the patients had fractures in only the mandibular bone, and 14 had fractures in the mandibular and other facial bones. In 14 of the cases with isolated mandible fractures (Figure 1), a single fracture line was seen in the mandible; 13 had complex mandible fractures. The ranking on the basis of the localization of the mandible fractures indicated that the angulus (25%) was the most common site (Table 2). Fractures of the mandibular condyle were treated with intermaxillary fixation. For the reduction of displaced segments of the mandibula and the achievement of precise occlusion in multiple fractures, an arch bar and cerclage wire were applied before rigid fixation was performed. The patients with mandibular fractures were required to wear face-lifting masks to provide external support for the bone and to restrict movement. Five patients who underwent surgery developed occlusion disorders. In one patient, an orocutaneous fistula developed, and in another, plate screw exposure in the parasymphysis occurred. None of the patients had facial nerve parasites. The damaged mandibular nerve in two patients, mental nerve in one patient, and marginal mandibular nerve in one patient were repaired.

Figure 1: Patient's isolated mandibular corpus fracture

In this study, seven of the 10 frontal sinus fractures were isolated fractures. Surgical interventions were not carried out in the cases where the patients had not been affected aesthetically. Reduction and microplate and screw fixation were used in the open frontal sinus and anterior wall fractures. They were also used in clean lacerations on the forehead. Alloplastic materials were not used in dirty injuries. The temporal muscle or dermo-fascial flap from the area adjacent to the collapsed area was transposed onto the collapsed area for aesthetic alignment, and the flap was used as an awning.

Surgical intervention was performed under general anesthesia in 121 patients in our cases. Of these, 76 were due to nasal bone fracture, while 45 patients were due to other MFT. The reduction was performed under local anesthesia due to isolated nasal fracture in 44 patients. While 46 patients did not agree to surgical intervention, 132 patients were not planned for surgery.

DISCUSSION

Patient age and gender, the incidence of MFT, the etiology and distribution of the fractures by bone have been associated with socioeconomic, cultural, educational, and geographical factors (9). A review of the literature indicated that the most common etiologies were traffic accidents, assaults, and falls (9). Traffic accidents were the most frequent cause of MFT in developing countries, and assaults were the most common reason in developed countries. However, sports injuries were also a frequent cause of MFT in societies in which sports such as rugby were popular (10). In Şanlıurfa, traffic accidents were the most frequent reason for falls (3, 9, 11). In this study, traffic accidents accounted for almost half (42%) of the MFT cases. Falls were the next most frequently occurring reason, followed by violence.

MFT can occur at any age; however, in our study 50% of the patients were aged 15 to 45 years (12). Similar rates (60.7%) were found in previous studies. The incidence of MFT in the pediatric age group has been reported to be 5% (13), Bamjee et al. (14) reported this rate as 8%. The most frequent causes were attacks and firearm injuries. Unlike the findings of studies in other countries, those from the studies conducted in Turkey (Gönüllü et al.) indicated rates of pediatric cases as high as 33.7% (9). These patients had most frequently reported falls and traffic accidents. In this study, the rate of pediatric patients was found to be 13.1%, and the etiological distribution of the patients was found to be traffic accidents and assaults. Twenty-eight patients were over the age of 65. As was found in previous studies, falls were the most common etiology in geriatric patients.

The incidence of MFT is higher in men than in women. In a study conducted at Osaka University in 2001, Iida et al. reported the male–female ratio as 2.8:1 (15). In their study based in Van in 2009, Kırış et al. found that 73.9% of the MFT patients were male (16). In their 2008 study in Ankara, Demir et al. found that the male–female ratio was 2.8:1 (3). The findings of this study were similar to those of previous studies. The male–female ratio was 2.3:1. This was slightly lower than the previously reported rate. This difference was attributed to higher numbers of female drivers and increased participation in business and social life.

As Topuz (17) and Hwang et al. (18) stated, due to its anatomical structure and protruding location, the most common facial fractures in this study were found to be nasal fractures (42.6%). The most common causes of nasal bone fractures are: traffic accidents, falls, exposure to physical violence, work accidents, and sports injuries (17). In this study, the most common causes were traffic accidents (46.2%). When isolated nasal fractures were not considered, there were differences in the most commonly reported facial bone fracture associated with MFT. Schaftenaar et al. (19) and Bamjee et al. (14) reported that the most common fractures were in the mandibular. Afzelius et al. (20) and Bernstein (21) reported that zygoma and maxilla fractures were the most common. An examination of studies conducted in Turkey indicated that the most common types of mandibular fractures found in the 2,901 disease series in Diyarbakır, the Elazig-Sivas- and Sanliurfa-based studies, and the Van (province)-centered study were maxilla fractures (9-11, 22, 23).

In the present study, which was based in Kütahya, the zygomatic bone was the most common site in multiple fracture cases, and in isolated non-nasal fractures, single bone fractures were found in the maxillary bone. The zygoma fractures were caused primarily by trauma. The zygoma is a strong bone, however, its protruding structure and the relative weakness of the adjacent bones make it vulnerable to trauma.

Although most studies have found the mandibular to be the most common site of facial bone fractures, these injuries were the fourth most frequent type in this study. Mandibular fractures can have multiple etiologies, however, they develop especially after been struck. In the present study, the rates of mandibular fractures were lower than those in previous studies because only a relatively small number of MFT patients had experienced assaults. The mandible, which is U-shaped, can be divided into nine anatomical regions. Frontal impacts can cause fractures in the symphysis, condyle, and angulus. Impacts to the mental or corpus region can cause subcondylar fractures (24). In addition, there is an anatomical weakness in the third molar tooth-bound angulus region (24). Fractures have most frequently been observed in the condyle, corpus, and angulus (24) Kırış et al. (16) found that the parasymphysis was the most common fracture site. The findings of the present study confirmed those of previous studies regarding the angulus as the most common fracture area.

Frontal sinus fractures constitute 5% to 12% of all facial bone fractures (25). Because of trauma-related edema, the fracture can be detected only by examination and tomography. Rodriguez et al. (26) found frontal sinus fractures, fractures, brain injuries, shock, and comas in 75% of high-energy trauma cases. Schults et al. (25) treated frontal sinus anterior wall contour disorders and moderate collapse fractures with fillers. They reported that interventions were not required because the frontal sinus in pediatric patients is not well developed. Kim et al. (27) discussed the potentially fatal complications that can result from frontal sinus fractures. They asserted that moderate and advanced aesthetic appearance disorders that occur after a fracture can be treated with local or free flaps and alloplastic materials.

The treatment protocol for MFT is the reduction of bone fragments, correction of occlusions, stabilization of broken bones, and achievement of functional and aesthetically acceptable improvements. Dimitroulis et al. (28) reported that 57% of MFT cases received treatment. Gönüllü et al. (9) performed surgery on 25% of maxilla fractures, 44.3% of zygoma fractures, and 64.5% of mandible fractures. Forty-five patients in the present study underwent surgical interventions; 10 patients did not agree to this treatment. Surgery was not planned for 85 patients. Of the patients who accepted surgery as an MFT treatment option, 35% received surgical interventions.

MFT has a multifaceted etiology that is influenced by socioeconomic, cultural, and geographical factors. A review of the literature revealed epidemiological differences not only by country but also by region within countries. The first study examining MFT patients in the Aegean region, which we can find in the literature, was the study Aydın-based 63 diseases İlkören et al. (29). However, this study examined only patients with mandible fractures. The present study is very valuable because of the high frequency and epidemiological distribution of MFT cases in the Aegean region.

The most important limitation of our study is that patients with isolated non-displaced nasal fractures and patients who do not want to undergo intervention despite having a displaced fracture generally do not apply to ENT/Plastic surgeons after admission to the emergency department. Therefore, nasal fracture rates were lower than we expected. It is thought that the number of patients with isolated alveolar fractures is relatively low due to the fact that patients with isolated alveolar fractures are referred to dentists for treatment.

Most had received dental referrals. MFT is often seen in multi trauma, such as that caused by traffic accidents. The primary evaluation of vital functions is a more accurate approach to the treatment of severe trauma. Unfortunately, some of these patients died at the time of trauma during the first intervention or even without intervention; thus, MFT-related departments cannot be consulted. Therefore, these patients could not be included in the study.

CONCLUSION

A majority of MFT cases require hospital admission. Epidemiological studies can contribute to the identification of measures to reduce the incidence of trauma in geographically and socioeconomically diverse regions.

Ethics Committee Approval: This study was conducted with the permission of the Kütahya University of Health Sciences ethics committee dated 26/06/2020 (2020/10-20). In this investigation, the Helsinki Declaration guidelines were followed.

Informed Consent: Written informed consent was obtained.

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REFERENCES

1. Tokat T. Maxillofacial trauma. IN: Müderris T, Muz SE, Kesici GG, İslamoğlu Y editors. Basic approach and management of otorhinolaryngology. Academician bookstore 2019; Chapter 103, pp 889-901.
2. Zargar M, Khaji A, Karbakhsh M, Zarei MR. Epidemiology study of facial injuries during a 13 month of trauma registry in Tehran. Indian J Med Sci 2004;58(3):109-14.
3. Demir Z, Öktem F, Velidedeoglu H, Çelebioğlu S. Evaluation of 121 cases with maxillofacial fracture and comparison with the literature. KBB – Forum 2008;7(3):85-90.
4. Sojot AJ, Meisami T, Sandor GK, Clokie CM. The epidemiology of mandibular fractures treated at the Toronto general hospital: A review of 246 cases. J Can Dent Assoc 2001;67(11):640-4.
5. Carlin CB, Ruff G, Mansfeld CP, Clinton MS. Facial fractures and related injuries: a ten-year retrospective analysis. J Craniomaxillofac Trauma 1998;4(2):44-3.
6. Kırış M, Yuca K, Çelebi S, Kıroğlu F, Çankaya H. Our treatment approach in maxillofacial fractures: retrospective review. Türkiye Klinikleri J Med Sci 2009;29(3):696-701.
7. Gassner R, Tuli T, Hächl O, Rudisch A, Ulmer H. Cranio-maxillofacialtrauma: a 10 year review of 9,543 cases with 21,067 injuries. J Craniomaxillofac Surg 2003;31(1):51-61.
8. Kim JJ, Huoh K. Maxillofacial (midface) fractures. Neuroimaging Clin N Am 2010;20(4):581-96.
9. Gönüllü H, Karadaş S, Işık D, Kocak ÖF, Tekin H. Maxillofacial Trauma Cases Applying To An Emergency Service: A Retrospective Study. Turk Plast Surg 2011;19(3):121-4.
10. Esen A, Isık K. Etiology of Maxillofacial Injuries Observed in Our Country and Report of Two Cases. ADO Journal of Clinical Sciences 2013;6(4):1329-35.
11. Gürger M., Ateşçelik M. Epidemiological features of maxillofacial traumas presenting to the emergency department. JAEM 2012;11:98-101.
12. O'Connor RC, Shakib K, Brennan PA. Recent advances in the management of oral and maxillofacial trauma. Br J Oral Maxillofac Surg 2015;53(10):913-21.
13. Lee WT, Koltai PJ. Nasal deformity in neonates and young children. Pediatr Clin North Am 2003;50(2):459-67.
14. Bamjee Y, Lownie JF, Cleaton-Jones PE, Lownie MA. Maxillofacial injuries in a group of South Africans under 18 years of age. Br J Oral Maxillofac Surg 1996;34(4):298-302.
15. Iida S, Kogo M, Sugiura T, Mima T, Matsuya T. Retrospective analysis of 1502 patients with facial fractures. Int J Oral Maxillofac Surg 2001;30(4):286-90.
16. Kırış M, Yuca K, Çelebi S, Kıroğlu F, Çankaya H. Treatment Modalities in Maxillofacial Fractures: Retrospective Analysis. Türkiye Klinikleri J Med Sci 2009;29(3):696-701.
17. Topuz MF, Tok Umay S, Oghan F, Musmul A, Erdogan O, Kutuk SG. Investigation of the effectiveness of physical examination and radiologıcal imaging methods in the diagnosis of nasal bone fractures. Annals of Medical Research 2021;27(7):1913-7.
18. Hwang K, You SH. Analysis of facial bone fractures: An 11-year study of 2,094 patients. Indian J Plast Surg 2010;43(1):42-8.
19. Schaftenaar E, Bastiaens GJ, Simon EN, Merkx MA. Presentation and management of maxillofacial trauma in Dar es Salaam, Tanzania. East Afr Med J 2009;86(6):254-8.
20. Afzelius LE, Rosén C. Facial fractures. A review of 368 cases. Int J Oral Surg 1980;9(1):25-32.
21. Bernstein MP. The Imaging of Maxillofacial Trauma 2017. Neuroimaging Clin N Am 2018;28(3):509-24.
22. Erol B, Tanrikulu R, Görgün B. Maxillofacial fractures. Analysis of demographic distribution and treatment in 2901 patients (25-year experience). J Craniomaxillofac Surg 2004;32(5):308-13.
23. Bozkuş F, İynen İ, Şan İ. Retrospective analysis of the patients with maxillofacial traumas. Journal of Medical Research 2011;9(1):10-6.
24. Demirdöver C, Şahin B, Ataseven M, Özkan HS, Öztan HY. Retrospective Analysis of 124 Mandible Fracture Cases who have been operated ın one year. Turk Plast Surg 2009;17(3):145-8.
25. Schultz K, Braun TL, Truong TA. Frontal Sinus Fractures. Seminars Plast Surg 2017;31(2):80-4.
26. Rodriguez ED, Stanwix MG, Nam AJ, et al. Twenty-six-year experience treating frontal sinüs fractures: a novel algorithm based on anatomical fracture pattern and failure of conventional techniques. Plast Reconstr Surg 2008;122(6):1850-66.
27. Kim YW, Lee DH, Cheon YW. Secondary Reconstruction of Frontal Sinus Fracture. Arch Craniofac Surg 2016;17(3):103-10.
28. Dimitroulis G, Eyre J. A 7-year review of maxillofacial trauma in a central London hospital. Br Dent J 1991;170(8):300-2.
29. İlkören Sahin NS, Bulut B, Sonel AM, Ceyan E. Retrospective analysis of 63 mandible fracture cases operated within three years. Journal of ADÜ Faculty of Medicine 2011;12:1-4.

RESEARCH ARTICLE
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Oncological and Functional Outcomes of Supracricoid Partial Laryngectomy

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ABSTRACT

Objective: The aim of this study is to review the oncological outcomes of T1-T4 glottic or supraglottic tumor patients who underwent supracricoid partial laryngectomy in our clinic.
Material and Methods: A total of 43 patients with laryngeal squamous cell carcinoma who underwent supracricoid partial laryngectomy between January 2014 and December 2016 in the Otorhinolaryngology Department of Istinye University Hospital were retrospectively analyzed. Postoperative data of these patients regarding surgical margin, nasogastric feeding tube removal time, decannulation time, postoperative radiotherapy, local regional recurrence, and distant metastases were recorded.
Results: Cricohyoidoepiglotopexy was applied to 16 patients by preserving both arytenoids and applied to 7 patients with a single arytenoid; Cricohyoidopexy was applied to 14 patients with both arytenoids preserved, and 6 patients were treated with a single arytenoid.
The five-year survival was compared for Cricohyoidopexy/Cricohyoidoepiglotopexy with single arytenoid to double arytenoid preservation and found to be 80%-76% (p=0.56). The mean 5-year survival was 88% in the post-operative radiotherapy group, and 86% in the non- radiotherapy group. The study compared patients with Cricohyoidopexy/Cricohyoidoepiglotopexy with a single arytenoid to those with double arytenoid preservation; the mean decannulation time was 54.23±34.12 to 35.62±27.08 (p=0.05). Postoperative radiotherapy prolonged the decannulation time (51.16±38.5 versus 32.68±20.1; p=0.043). The duration of nasogastric tube placement in the Cricohyoidopexy/Cricohyoidoepiglotopexy with a single arytenoid group was 50.3±14.3 and double arytenoid preservation was 35.17±32.9 (p=0.088). Nasogastric tube removal time was 53.29±50.2 in the post-operative radiotherapy group and was 30.24±16.8 in patients who did not receive post-operative radiotherapy (p=0.040).
Conclusion: Supracricoid partial laryngectomy with Cricohyoidoepiglotopexy and Cricohyoidopexy had satisfactory oncological outcomes, and laryngeal function was preserved by rebuilding the neolarynx.

Keywords: Partial laryngectomy, Head and neck carcinoma, Cricohyoidopexy, Cricohyoidoepiglotopexy, Supracricoid laryngectomy

INTRODUCTION

The larynx is an important organ in the upper airway with three main functions: speaking, breathing and swallowing. Anatomically, it is divided into three regions: the supraglottic larynx, the glottis, and the subglottic region (1).

Laryngeal cancers are the most common malignant tumors of the upper airway and most commonly originate from the glottic region (1, 2). More than 98% of laryngeal malignancies are well-differentiated squamous cell carcinomas; only 2% are chondrosarcomas, leiomyosarcomas, and melanomas (3).

There are various surgical and nonsurgical oncological options in the treatment of laryngeal cancers (4). It has been reported that organ preservation strategies based on the combination of chemotherapy and radiotherapy (RT) achieve oncological results similar to surgery, but they cause significant toxic effects (4, 5). In addition, the oncological results of chemoradiation protocols are not as good as surgery, and the functional results are poor in cases of invasion of the cartilage of the larynx or in bulky tumors (6).

In recent years, surgical treatment of laryngeal cancer has shifted from radical (total laryngectomy [TL]) to more

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conservative surgical techniques (partial laryngectomies) in selected patients (7). Local control and survival rates are similar (1, 7). The most important advantage of partial laryngectomy is the preservation of the functions of the larynx, which provides a better quality of life (normal speech and swallowing and the absence of a permanent tracheostomy) (8, 9).

One of these conservative procedures, supracricoid partial laryngectomy (SCPL), was first described by Majer and Rieder in 1951 (10). Resection includes both true and false vocal cords, the paraglottic space, and the entire thyroid cartilage. If necessary, the epiglottis and pre-epiglottic space and a complete arytenoid cartilage can be included in the resection. The reconstruction is called cricohyoidopexy (CHP) if it is performed with 5 sutures that firmly join the cricoid to the hyoid bone, or cricohyoidoepiglottopexy (CHEP) if it is sutured with the epiglottis preserved (10).

SCPL is a partial laryngectomy technique that allows safe resection of selected T1-T4 glottic or supraglottic tumors. The aim of this study is to review the oncological outcomes of patients who underwent SCPL in our clinic.

MATERIAL AND METHODS

A total of 43 patients with laryngeal squamous cell carcinoma (LSCC) who underwent SCPL between January 2014 and December 2016 in the Otorhinolaryngology Department of Istinye University Hospital were retrospectively analyzed.

Pathological diagnosis was confirmed by preoperative biopsy in all patients.

Once LSCC was diagnosed, a multidisciplinary team of ENT, oncologists, radiotherapists, and radiologists discussed the diagnosis and treatment alternatives with patients and their families to make a decision. Tumor location and size, extent of tumor invasion, and regional lymph node metastases were assessed by preoperative examinations including contrast-enhanced magnetic resonance imaging and laryngoscopy. Age, gender, smoking, alcohol consumption, TNM stages, and pathology type were documented. Postoperative data of these patients regarding surgical margin, nasogastric feeding tube removal time, decannulation time, postoperative radiotherapy, local regional recurrence, and distant metastases were recorded. Tumor stages were determined according to TNM classification, which was determined according to the 8th edition of the American Joint Committee on Cancer (AJCC) (11).

This research was conducted according to the Declaration of Helsinki for Biomedical Research Involving Human Subjects (WMA; 1997) and was approved by the ethics committee of Istinye University Hospital (2017-KAEK-120)/ 2/2021.G-70). All participants gave written consent after being informed about the procedures and purpose of the study.

Operations

All patients were treated with CHEP and CHP based on their preoperative assessment, and operated on by the same surgical team according to the technique previously described. Surgical margins of all laryngeal specimens were examined by pathologists.

Postoperative care

Nasogastric feeding tube (NGT) and temporary tracheostomy were applied to all patients at surgery. Air humidification was provided with a tracheostomy cannula in all patients and the cannula was cleaned daily. Nutrition of the patients was started with NGT on the first postoperative day. Swallowing exercises were performed first with solid foods, then with liquids on the 20th day after surgery. The feeding tube was removed when normal oral feeding was deemed satisfactory. When normal breathing without shortness of breath was maintained for at least 48 hours, the tracheostomy was closed. Postoperative complications were recorded, and related treatments were applied to these patients. Local recurrence, regional recurrence, locoregional recurrence, and distant metastases were recorded and necessary treatments were conducted for these patients.

Statistical analyses

For statistical analysis, the IBM SPSS Statistics version 21 software package was used. Data are presented as median and range or interquartile range (IQR). The Mann-Whitney test was used to compare continuous variables. The Kaplan-Meier Method (log rank test) was used to calculate the unadjusted survival rate. A p value of less than 0.05 was considered the threshold for statistical significance.

RESULTS

Our study included 43 patients. CHEP was applied to 16 patients by preserving both arytenoids and applied to 7 patients with a single arytenoid; CHP was applied to 14 patients with both arytenoids preserved, and 6 patients were treated with a single arytenoid. The youngest patient was 32 years old; the oldest patient was 94 years old (32-94/mean 62.4±11.69). 39 patients were male and 4 were female. Simultaneous neck dissection was performed in 38 of the patients. Post-operative radiotherapy (RT)/chemotherapy was applied to 18 patients. The number of patients and adjuvant treatment status (CT/RT) are given in Table 1, and the demographic and clinical data of the patients are given in Table 2.

Table 1. Number of patients and adjuvant treatment status (KT/RT)

	RT/KT +	RT/KT -	Total
CHP	9	5	14
CHEP	5	11	16
A-CHP	3	3	6
A-CHeP	1	7	7
Total	17	26	43

CHP: Cricohyoidopexy; CHEP: cricohyoidoepiglottopexy; A-CHP: cricohyoidopexy with preservation of one arytenoid; A-CHEP: cricohyoidoepiglottopexy cricohyoidopexy with preservation of one arytenoid

Table 2. Demographics and clinical characteristics of 43 patients.

	Mean	Range
Age	62,4	32-94
	n	**%**
Sex		
Male	39	90,7
Famale	4	9,3
Drinking		
+	10	23,3
-	33	76,7
Smoking		
+	41	95,3
-	2	4,7
Stage		
Early	14	32,5
T2N0	14	32,5
Advanced	29	67,5
T2N1	3	7
T2N2b	3	7
T3N0	7	16,3
T3N1	4	9,3
T3N2b	6	14
T4N0	5	11,6
T4N2a	1	2,3
Neck Dissection		
+	38	88,4
-	5	11,6

When the five-year survival rate was examined, no significant difference was observed between the patients who underwent CHP/CHEP with single arytenoid and patients with double arytenoid preservation (80%-76%; p=0.56) (Figure 1). The mean 5-year survival rate was 88% in the post-operative RT group, and 86% in the non-RT group (Figure 2).

All patients were decannulated, except for one patient who underwent CHP. The earliest postoperative decannulation time was 20 days and the latest was 140 days (mean 41 days). In patients who underwent CHP/CHEP with a single arytenoid compared to those with double arytenoid preservation, the mean decannulation time was 54.23±34.12 to 35.62±27.08 (p=0.05) (Figure 3). Postoperative radiotherapy prolonged the decannulation time (51.16±38.5 versus 32.68±20.1; p=0.043) (Figure 4).

All patients started oral feeding, except for 2 patients, and PEG was opened. NGT removal time was 19 days at the earliest and 110 days at the latest (mean 32). The duration of nasogastric

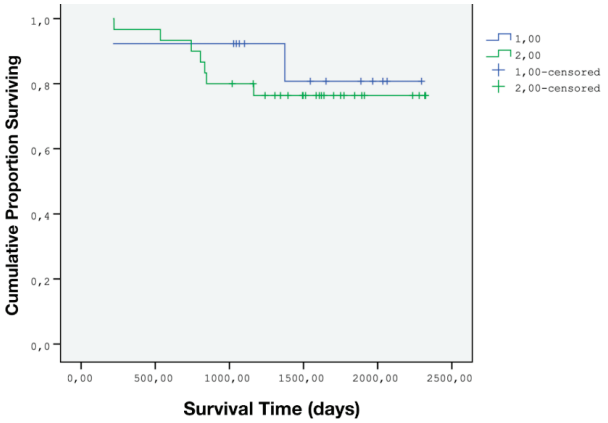

Figure 1. Kaplan-Meier analysis of disease-specific survival in patients with single arytenoid to double arytenoid preservation. (1- Single arytenoid, 2- Double arytenoid)

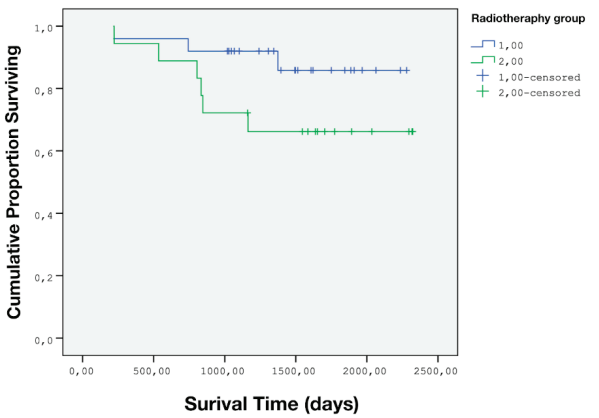

Figure 2. Kaplan-Meier analysis of disease-specific survival in patients with single arytenoid to double arytenoid preservation. (1- Radiotherapy group, 2- Non-Radiotherapy group)

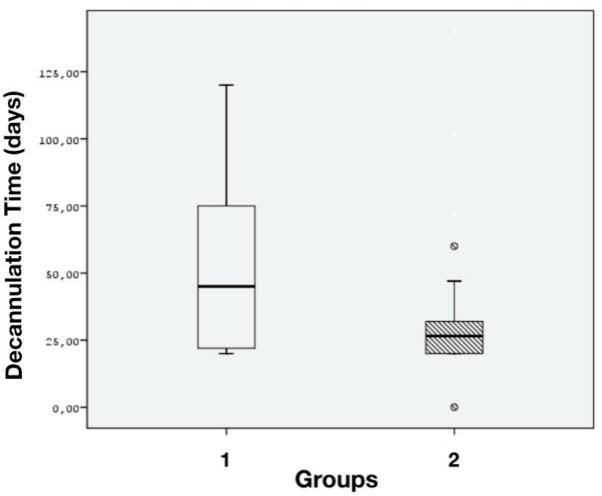

Figure 3. Comparison of decannulation time between single arytenoid to double arytenoid preservation (1- Single arytenoid, 2- Double arytenoid)

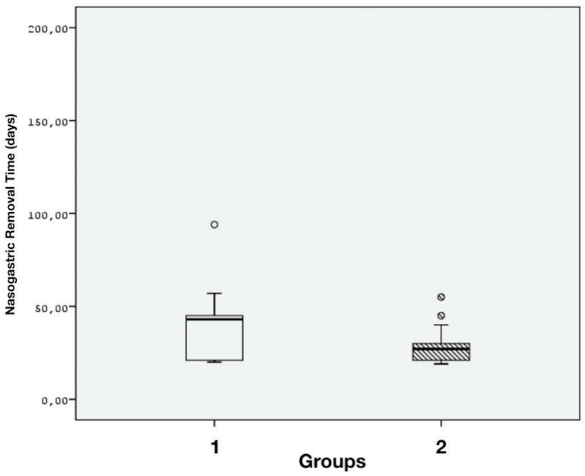

Figure 4. Comparison of nasogastric removal time between single arytenoid to double arytenoid preservation (1- Single arytenoid, 2- Double arytenoid)

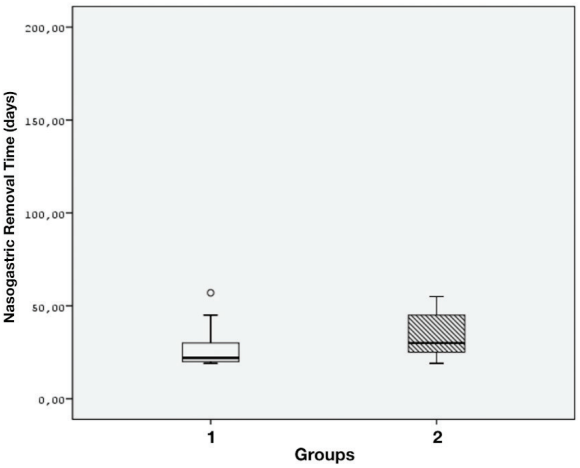

Figure 6. Comparison of nasogastric removal time between post-operative radiotherapy group to non-radiotherapy group. (1- Non-radiotherapy group, 2- Radiotherapy group)

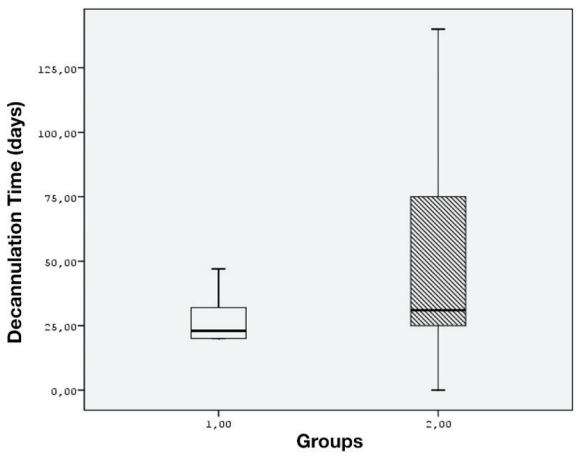

Figure 5. Comparison of decannulation time between post-operative radiotherapy group to non-radiotherapy group. (1- Non-radiotherapy group, 2- Radiotherapy group)

tube placement was relatively longer in the CHP/CHEP with a single arytenoid group than double arytenoid preservation (50.3±14.3 versus 35.17±32.9, p=0.088) (Figure 5).

NGT removal time was 53.29±50.2 in the post-operative radiotherapy group and 30.24±16.8 in patients who did not receive post-operative RT (p=0.040) (Figure 6).

Of the patients who were operated on, 14 were in the early stage (I-II) and 29 were in the late stage (III-IV).

The mean follow-up period was 62.9 months; 9 patients died during this period. Of these, 3 died due to lung carcinoma, 2 due to myocardial infarction, 3 due to locoregional recurrence, and 1 due to distant organ metastasis.

DISCUSSION

The treatment of laryngeal cancer aims to increase survival while maintaining quality of life as much as possible. While total laryngectomy offers the best results in terms of oncological safety, there are aspects that negatively affect the quality of life such as the presence of permanent tracheotomy and loss of voice. Therefore, it is important to apply larynx-sparing procedures in locally advanced cases (10, 12, 13). Radiation therapy alone, concomitant chemoradiotherapy, transoral laser surgery, and supracricoid laryngectomy are generally used in the treatment of early and selected locally-advanced laryngeal cancers with the advantage of preserving laryngeal function (14-17). Appropriate patient selection seems to be the most important factor for the technique to have good oncological and functional results. The functional capacity of the patient and the lesion should be examined in detail.

SCPL is one of the organ-preserving treatment options commonly used in the treatment of glottic and supraglottic laryngeal cancer. It has been shown to have reliable oncological results in many studies in the literature (18-21). In the literature, the 5-year local control rates vary between 71% and 95.7%. Five-year overall survival is 65%-95% (19, 21-30). Larynx preservation rate after SCPL is approximately 85%, and TL is applied in approximately 10% of patients for functional or oncological reasons (24, 26). In the follow-up of the patients in the study, TL operation was not needed in any of the patients. However, 3 patients died due to lung carcinoma, 2 patients due to myocardial infarction, 3 patients due to locoregional recurrence, and 1 patient due to distant organ metastasis.

Wang et al. found that in their series, the mean decannulation time was 41 days and the decannulation rate was 97.6%. Decannulation was achieved in nearly all patients, with the average time to decannulation being 20±11.52 days in CHEP patients and 28±8.92 days in CHP (21). In the series of Pelini et al. the tracheostomy tube was removed in 75 (91%) of 82 patients between 6 and 180 days (mean 19.3 days) after surgery (30). In our series, all patients were decannulated, except for one patient who underwent CHP. The earliest postoperative decannulation time was 20 days and the latest was 140 days (mean 41 days).

NGT removal time varies between 15 and 70 days, according to the literature (17, 31-33). Wang et al. reported the mean nasogastric tube removal time as 18 days in CHEP patients and 25 days in CHP patients (21). Although this is compatible with the literature, the factors affecting NGT run time include the fact that the patients in our series are in the late stages of disease and that the frequency of postoperative RT is high.

Early or late complications can be seen in the follow-up after SCPL operation. In the early period, local complications such as abscess, wound infection, hematoma, bleeding, opening of pexial sutures and related laryngocutaneous fistula formation, respiratory complications due to bronchopulmonary infection, and laryngeal stenosis are seen. Pneumonia due to aspiration can be seen because of swallowing disorders. In the late period, stenosis and airway problems may occur due to laryngeal membrane, residual false cord or arytenoid edema. In laryngeal membrane formation, laser resection is useful in opening the obstruction. Severe stenosis due to granulation tissue may be seen in some patients. Other late complications are subglottic stenosis due to tracheostomy and anterior synechia due to pexial opening (34). One patient in our series had diffuse subcutaneous emphysema in the early postoperative period and was treated. No late complications were observed in any of the patients.

In conclusion, this study comprehensively analyzed 43 glottic and supraglottic laryngeal carcinoma patients and demonstrated that patients treated with CHEP and CHP had satisfactory oncological outcomes, and laryngeal function was preserved by rebuilding the neolarynx. Laryngeal carcinoma should be treated with the intent of organ-sparing, and our reliable data indicate that the SCPL can serve as a standard procedure for adequate tumor resection and function preservation for selected patients with T1-T4 glottic and supraglottic carcinomas.

Ethics Committee Approval: This research was conducted according to the Declaration of Helsinki for Biomedical Research Involving Human Subjects (WMA; 1997) and was approved by the ethics committee of Istinye University Hospital (2017-KAEK-120)/ 2/2021.G-70).

Informed Consent: All participants gave written consent after being informed about the procedures and purpose of the study.

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Author Contributions: Conception/Design of Study- C.K., E.Y., İ.Y.; Data Acquisition- E.Y.; Data Analysis/Interpretation- C.K.; Drafting Manuscript- C.K., E.Y., İ.Y.; Critical Revision of Manuscript- İ.A.; Final Approval and Accountability- C.K., E.Y., İ.Y., İ.A.

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REFERENCES

1. Steuer CE, El-Deiry M, Parks JR, Higgins KA, Saba NF. An update on larynx cancer. CA Cancer J Clin 2017;67(1):31-50.
2. American Cancer Society. Facts & Figures 2019: US Cancer Death Rate has Dropped 27% in 25 Years. Am Cancer Soc 2019;2019:2015-7.
3. Ciolofan MS, Vlăescu AN, Mogoantă CA, Ioniță E, Ioniță I, Căpitănescu AN, et al. Clinical, Histological and Immunohistochemical Evaluation of Larynx Cancer. Curr Health Sci J 2017;43(4):367-375.
4. Gallo A, Manciocco V, Simonelli M, Pagliuca G, D'Arcangelo E, De Vincentiis M. Supracricoid partial laryngectomy in the treatment of laryngeal cancer: univariate and multivariate analysis of prognostic factors. Arch Otolaryngol Neck Surg 2005;131(7):620-5.
5. Lefebvre JL. Laryngeal preservation in head and neck cancer: multidisciplinary approach. Lancet Oncol 2006;7(9):747-55.
6. Pfister DG, Laurie SA, Weinstein GS, Mendenhall WM, Adelstein DJ, Ang KK, et al. American Society of Clinical Oncology clinical practice guideline for the use of larynx-preservation strategies in the treatment of laryngeal cancer. J Clin Oncol 2006;24(22):3693-704.
7. Weinstein GS, El-Sawy MM, Ruiz C, Dooley P, Chalian A, El-Sayed MM, et al. Laryngeal preservation with supracricoid partial laryngectomy results in improved quality of life when compared with total laryngectomy. Laryngoscope 2001;111(2):191-9.
8. Schindler A, Favero E, Nudo S, Albera R, Schindler O, Cavalot AL. Long-term voice and swallowing modifications after supracricoid laryngectomy: objective, subjective, and self-assessment data. Am J Otolaryngol 2006;27(6):378-83.
9. Gillespie MB, Brodsky MB, Day TA, Lee F, Martin-Harris B. Swallowing-related quality of life after head and neck cancer treatment. Laryngoscope 2004;114(8):1362-7.
10. Majer H, Rieder W. Technique de laryngectomie permettant de conserver la permeabilite'respiratoire la cricohyoido-pexie. Ann Otolaryngol Chir Cervicofac 1959;76:677-83.
11. Edge SB, Edge SB. AJCC Cancer Staging Manual 8th Ed. Springer; 2017.
12. Nakayama M, Laccourreye O, Holsinger FC, Okamoto M, Hayakawa K. Functional organ preservation for laryngeal cancer: past, present and future. Jpn J Clin Oncol 2012;42(3):155-60.
13. Pfister DG, Ang KK, Brizel DM, Burtness BA, Busse PM, Caudell JJ, et al. National Comprehensive Cancer Network. Head and neck cancers, version 2.2013. Featured updates to the NCCN guidelines. J Natl Compr Canc Netw. 2013;11(8):917-23. doi: 10.6004/jnccn.2013.0113. Erratum in: J Natl Compr Canc Netw 2013;11(12):1458.
14. Caicedo-Granados E, Beswick DM, Christopoulos A, Cunningham DE, Razfar A, Ohr JP et al. Oncologic and functional outcomes of partial laryngeal surgery for intermediate-stage laryngeal cancer. Otolaryngol Head Neck Surg 2013;148(2):235-42.
15. Forastiere AA, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. N Engl J Med 2003;349(22):2091-8.
16. Department of Veterans Affairs Laryngeal Cancer Study Group. Induction Chemotherapy plus Radiation Compared with Surgery plus Radiation in Patients with Advanced Laryngeal Cancer. N Engl J Med 1991;324(24):1685-90.
17. Ambrosch P. The role of laser microsurgery in the treatment of laryngeal cancer. Curr Opin Otolaryngol Head Neck Surg 2007;15(2):82-8.

18. Laccourreye H, Laccourreye O, Weinstein G, Menard M, Brasnu D. Supracricoid laryngectomy with cricohyoidopexy: a partial laryngeal procedure for selected supraglottic and transglottic carcinomas. Laryngoscope 1990;100(7):735-41.
19. Pinar E, Imre A, Calli C, Oncel S, Katilmis H. Supracricoid partial laryngectomy: analyses of oncologic and functional outcomes. Otolaryngol Neck Surg 2012;147(6):1093-8.
20. Wang PW, Abedini MR, Yang LX, Ding AA, Figeys D, Chang JY, et al. Gelsolin regulates cisplatin sensitivity in human head-and-neck cancer. Int J Cancer 2014;135(12):2760-9.
21. Wang Y, Li X, Pan Z. Analyses of functional and oncologic outcomes following supracricoid partial laryngectomy. Eur Arch Oto-Rhino-Laryngology 2015;272(11):3463-8.
22. Soudry E, Marmor Y, Hazan A, Marx S, Sadov R, Feinmesser R. Supracricoid partial laryngectomy: an alternative to total laryngectomy for locally advanced laryngeal cancers. J Laryngol Otol 2008;122(11):1219-23.
23. Enver N, Şahin A, Yumusakhuylu A, Sahin-Yilmaz A, Oysu C. Oncologic Results of Supracricoid Laryngectomy: Results From Two Tertitory Centers. Acta Oncol Turc 53(3):504-10.
24. Sánchez-Cuadrado I, Castro A, Bernáldez R, Del Palacio A, Gavilán J. Oncologic outcomes after supracricoid partial laryngectomy. Otolaryngol Neck Surg 2011;144(6):910-4.
25. Scola B, Fernández-Vega M, MartÍNez T, Fernández-Vega S, Ramirez C. Management of cancer of the supraglottis. Otolaryngol Neck Surg 2001;124(2):195-8.
26. Gonçalves AJ, Bertelli AAT, Malavasi TR, Kikuchi W, Rodrigues AN, Menezes MB. Results after supracricoid horizontal partial laryngectomy. Auris Nasus Larynx 2010;37(1):84-8.
27. Deganello A, Gallo O, De Cesare JM, Ninu MB, Gitti G, de' Campora L, et al. Supracricoid partial laryngectomy as salvage surgery for radiation therapy failure. Head Neck 2008;30(8):1064-71.
28. Lewin JS, Hutcheson KA, Barringer DA, May AH, Roberts DB, Holsinger FC, et al. Functional analysis of swallowing outcomes after supracricoid partial laryngectomy. Head Neck 2008;30(5):559-66.
29. Park J-O, Joo Y-H, Cho K-J, Kim N-G, Kim M-S. Functional and oncologic results of extended supracricoid partial laryngectomy. Arch Otolaryngol Neck Surg 2011;137(11):1124-9.
30. Pellini R, Manciocco V, Spriano G. Functional outcome of supracricoid partial laryngectomy with cricohyoidopexy: radiation failure vs previously untreated cases. Arch Otolaryngol Neck Surg 2006;132(11):1221-5.
31. Cho KJ, Joo YH, Sun D Il, Kim MS. Supracricoid laryngectomy: oncologic validity and functional safety. Eur Arch oto-rhino-laryngology 2010;267(12):1919-25.
32. Szyfter W, Leszczyńska M, Wierzbicka M. Outcome after supracricoid laryngectomies in the material of ENT Department, Poznan University of Medical Sciences. Eur Arch oto-rhino-laryngology 2011;268(6):879-83.
33. Saito K, Araki K, Ogawa K, Shiotani A. Laryngeal function after supracricoid laryngectomy. Otolaryngol Neck Surg 2009;140(4):487-92.
34. Decotte A, Woisard V, Percodani J, Pessey J-J, Serrano E, Vergez S. Respiratory complications after supracricoid partial laryngectomy. Eur Arch oto-rhino-laryngology 2010;267(9):1415-21.

AIM AND SCOPE

The Turkish Journal of Ear Nose and Throat (Tr-ENT) aims to contribute to the literature by publishing high quality original articles, case clinical reports, surgical techniques and invited reviews focusing on key subjects and contemporary developments in the field. The scope of the journal includes otology, neurootology, rhinology, head and neck, general ORL, facial plastic surgery and laryngology. The journal welcomes articles from other disciplines as well, provided that these are related to the major subject area. The target audience of the journal consists of academicians, researchers, professionals, students, related professional and academic bodies and institutions.

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INSTRUCTION TO AUTHORS

The Turkish Journal of Ear Nose and Throat (Tr-ENT) is an international, scientific, open acces and peer-reviewed publication of Istanbul University. It is published quarterly in March, June, September and December. The publication language of the journal is English. The journal started off in 1990 under the editorship of Professor Behbut Cevanşir. Since then it has been a significant source of knowledge in the field of otorhinolaryngology for researchers, residents and specialists. As of year 2018 Volume 28 Issue 1, the title of the journal was changed from “Kulak Burun Boğaz İhtisas Dergisi” (ISSN: 1300-7475, E-ISNN: 2147-67569) to “The Turkish Journal of Ear Nose and Throat” and the journal decided to publish articles only in English with a frequency of four issues per year. The Turkish Journal of Ear Nose and Throat aims to contribute to the literature by publishing high quality original articles, case reports, surgical techniques and invited reviews focusing on key subjects and contemporary developments in the field. The scope of the journal includes otology, neurootology, rhinology, head and neck, general ORL, facial plastic surgery and laryngology. The journal welcomes articles from other disciplines as well, provided that these are related to the major subject area. The target audience of the journal consists of academicians, researchers, professionals, students, related professional and academic bodies and institutions. Former title of the journal: Kulak Burun Boğaz İhtisas Dergisi (P-ISNN: 1300-7475 / E-ISNN: 2147-6756)

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The journal is committed to upholding the highest standards of publication ethics and pays regard to Principles of Transparency and Best Practice in Scholarly Publishing published by the Committee on Publication Ethics (COPE), the Directory of Open Access Journals (DOAJ), the Open Access Scholarly Publishers Association (OASPA), and the World Association of Medical Editors (WAME) on https://publicationethics.org/resources/guidelines-new/principles-transparency-and-best-practice-scholarly-publishing

The subjects covered in the manuscripts submitted to the Journal for publication must be in accordance with the aim and scope of the Journal. Only those manuscripts approved by every individual author and that were not published before in or sent to another journal, are accepted for evaluation.

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All parties involved in the publishing process (Editors, Reviewers, Authors and Publishers) are expected to agree on the following ethical principles.

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Each manuscript is reviewed by at least two referees under double-blind peer review process. Plagiarism, duplication, fraud authorship/denied authorship, research/data fabrication, salami slicing/salami publication, breaching of copyrights, prevailing conflict of interest are unethical behaviors.

All manuscripts not in accordance with the accepted ethical standards will be removed from the publication. This also contains any possible malpractice discovered after the publication.

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The journal adheres to the highest standards in research ethics and follows the principles of international research ethics as defined below. The authors are responsible for the compliance of the manuscripts with the ethical rules.

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- The research team and participants should be fully informed about the aim, methods, possible uses and requirements of the research and risks of participation in research.
- The confidentiality of the information provided by the research participants and the confidentiality of the respondents should be ensured. The research should be designed to protect the autonomy and dignity of the participants.
- Research participants should participate in the research voluntarily, not under any coercion.
- Any possible harm to participants must be avoided. The research should be planned in such a way that the participants are not at risk.
- The independence of research must be clear; and any conflict of interest or must be disclosed.
- In experimental studies with human subjects, written informed consent of the participants who decide to participate in the research must be obtained. In the case of children and those under wardship or with confirmed insanity, legal custodian's assent must be obtained.
- If the study is to be carried out in any institution or organization, approval must be obtained from this institution or organization.
- In studies with human subject, it must be noted in the method's section of the manuscript that the informed consent of the participants and ethics committee approval from the institution where the study has been conducted have been obtained.

Ethics Committee Approval and Informed Consent

The Turkish Journal of Ear Nose and Throat (Tr-ENT) takes as principle to comply with the ethical standards of World Medical Association (WMA) Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects revised in 2003 and WMA Statement on Animal Use in Biomedical Research revised in 2016.

An approval of research protocols by the Ethics Committee in accordance with international standards mentioned above is required for experimental, clinical, and drug studies and for some case reports. If required, ethics committee reports or an equivalent official document will be requested from the authors. For manuscripts concerning experimental research on humans, a statement should be included that shows that written informed consent of patients and volunteers was obtained following a detailed explanation of the procedures that they may undergo. For studies carried out on animals, the measures taken to prevent pain and suffering of the animals should be stated clearly. Information on patient consent, the name of the ethics committee, and the ethics committee approval number should also be stated in the Materials and Methods section of the manuscript. It is the authors' responsibility to carefully protect the patients' anonymity. For photographs that may reveal the identity of the patients, signed releases of the patient or of their legal representative should be enclosed.

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All the authors of a submitted manuscript must have direct scientific and academic contribution to the manuscript. The author(s) of the original research articles is defined as a person who is significantly involved in "conceptualization and design of the study", "collecting the data", "analyzing the data", "writing the manuscript", "reviewing the manuscript with a critical perspective" and "planning/conducting the study of the manuscript and/or revising it". Fund raising, data collection or supervision of the research group are not sufficient roles to be accepted as an author. The author(s) must meet all these criteria described above. The order of names in the author list of an article must be a co-decision and it must be indicated in the Copyright Agreement Form. The individuals who do not meet the authorship criteria but contributed to the study must take place in the acknowledgement section. Individuals providing technical support, assisting writing, providing a general support, providing material or financial support are examples to be indicated in acknowledgement section.

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Editor-in-Chief evaluates manuscripts for their scientific content without regard to ethnic origin, gender, sexual orientation, citizenship, religious belief or political philosophy of the authors. He/She provides a fair double-blind peer review of the submitted articles for publication and ensures that all the information related to submitted manuscripts is kept as confidential before publishing.

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Reviewers must have no conflict of interest with respect to the research, the authors and/or the research funders. Their judgments must be objective.

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A reviewer who feels unqualified to review the topic of a manuscript or knows that its prompt review will be impossible should notify the editor and excuse himself from the review process.

The editor informs the reviewers that the manuscripts are confidential information and that this is a privileged interaction. The reviewers and editorial board cannot discuss the manuscripts with other persons. The anonymity of the referees must be ensured. In particular situations, the editor may share the review of one reviewer with other reviewers to clarify a particular point.

PEER REVIEW

Peer Review Policies
Only those manuscripts approved by its every individual author and that were not published before in or sent to another journal, are accepted for evaluation.

Submitted manuscripts that pass preliminary control are scanned for plagiarism using iThenticate software. After plagiarism check, the eligible ones are evaluated by editor-in-chief for their originality, methodology, the importance of the subject covered and compliance with the journal scope.

The editor hands over the papers matching the formal rules to at least two national/international referees for double-blind peer review evaluation and gives green light for publication upon modification by the authors in accordance with the referees' claims.

Responsibility for the Editor and Reviewers
Editor-in-Chief evaluates manuscripts for their scientific content without regard to ethnic origin, gender, citizenship, religious belief or political philosophy of the authors. Editor-in-Chief provides a fair double-blind peer review of the submitted articles for publication and ensures that all the information related to submitted manuscripts is kept as confidential before publishing.

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- Does the abstract clearly and accurately describe the content of the manuscript?
- Is the problem significant and concisely stated?
- Are the methods described comprehensively?
- Are the interpretations and consclusions justified by the results?
- Is adequate references made to other Works in the field?
- Is the language acceptable?

Reviewers must ensure that all the information related to submitted manuscripts is kept as confidential and must report to the editor if they are aware of copyright infringement and plagiarism on the author's side.

A reviewer who feels unqualified to review the topic of a manuscript or knows that its prompt review will be impossible should notify the editor and excuse himself from the review process.

The editor informs the reviewers that the manuscripts are confidential information and that this is a privileged interaction. The reviewers and editorial board cannot discuss the manuscripts with other persons. The anonymity of the referees is important.

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Manuscripts submitted to the journal will first go through a technical evaluation process where the editorial office staff will ensure that the manuscript has been prepared and submitted in accordance with the journal's guidelines. Submissions that do not conform to the journal's guidelines will be returned to the submitting author with technical correction requests.

Author(s) are required to submit the following documents together with the manuscript and must ensure that the abstract and keywords are in line with the standards explained in below.

- **Copyright Agreement Form**
- **Author Form and ICMJE Potential Conflict of Interest Disclosure Form**
- **Ethics Committee Approval**
- **Cover Letter to the Editor**
- **Title Page**: A separate title page should be submitted with all submissions and this page should include:

- The full title of the manuscript as well as a short title (running head) of no more than 50 characters,
- Name(s), affiliations, academic degree(s) and ORCID ID(s) of the author(s),
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- Name, address, telephone (including the mobile phone number) and fax numbers, and email address of the corresponding author,
- Acknowledgment of the individuals who contributed to the preparation of the manuscript but who do not fulfil the authorship criteria.

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Manuscript Types

Original Articles: This is the most important type of article since it provides new information based on original research. The main text of original articles should be structured with Introduction, Material and Method, Results, Discussion, and Conclusion subheadings..

Statistical analysis to support conclusions is usually necessary. Statistical analyses must be conducted in accordance with international statistical reporting standards (Altman DG, Gore SM, Gardner MJ, Pocock SJ. Statistical guidelines for contributors to medical journals. Br Med J 1983: 7; 1489-93). Information on statistical analyses should be provided with a separate subheading under the Materials and Methods section and the statistical software that was used during the process must be specified.

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Tables should be included in the main document, presented after the reference list, and they should be numbered consecutively in the order they are referred to within the main text. A descriptive title must be placed above the tables. Abbreviations used in the tables should be defined below the tables by footnotes (even if they are defined within the main text). Tables should be created using the "insert table" command of the word processing software and they should be arranged clearly to provide easy reading. Data presented in the tables should not be a repetition of the data presented within the main text but should be supporting the main text.

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Figures, graphics, and photographs should be submitted as separate files (in TIFF or JPEG format) through the submission system. The files should not be embedded in a Word document or the main document. When there are figure subunits, the subunits should not be merged to form a single image. Each subunit should be submitted separately through the submission system. Images should not be labeled (a, b, c, etc.) to indicate figure subunits. Thick and thin arrows, arrowheads, stars, asterisks, and similar marks can be used on the images to support figure legends. Like the rest of the submission, the figures too should be blind. Any information within the images that may indicate an individual or institution should be blinded. The minimum resolution of each submitted figure should be 300 DPI. To prevent delays in the evaluation process, all submitted figures should be clear in resolution and large in size (minimum dimensions: 100 × 100 mm). Figure legends should be listed at the end of the main document.

All acronyms and abbreviations used in the manuscript should be defined at first use, both in the abstract and in the main text. The abbreviation should be provided in parentheses following the definition.

When a drug, product, hardware, or software program is mentioned within the main text, product information, including the name of the product, the producer of the product, and city and the country of the company (including the state if in USA), should be provided in parentheses in the following format: "Discovery St PET/CT scanner (General Electric, Milwaukee, WI, USA)"

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Limitations, drawbacks, and the shortcomings of original articles should be mentioned in the Discussion section before the conclusion paragraph.

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Example: AB Author, CD Author. Title of document. Retrieved from http://Web address (Accession date: aa/bb/2016).

Congress papers:

Thesis: Maden KL. Experimental investigation of the ..... Master Thesis, Health Science Institute of Ankara University, Ankara, 2005.

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- Cover letter to the editor
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  - Including disclosure of any commercial or financial involvement.
  - Confirming that the statistical design of the research article is reviewed.
  - Confirming that last control for fluent English was done.
  - Confirming that journal policies detailed in Information for Authors have been reviewed.
  - Confirming that the references cited in the text and listed in the references section are in line with NLM.
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- Acknowledgement of the study "in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration.
- Statement that informed consent was obtained after the procedure(s) had been fully explained. Indicating whether the institutional and national guide for the care and use of laboratory animals was followed as in "Guide for the Care and Use of Laboratory Animals".
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  - Abstract 200-250 words
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