

# Risk factors associated with aspiration after partial laryngectomies

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Received 13 March 2016

Accepted 27 July 2016

The Egyptian Journal of Otolaryngology  
2016, 32:271–278

## Hypothesis

Aspiration and dysphagia still remain the most common drawbacks limiting conservation partial laryngeal surgery. Videofluoroscopic swallowing study (VFSS) has become the gold standard examination that guides the surgeon about important risk factors, helping him in technique selection and anatomical structure preservation, in balance with radical removal of laryngeal neoplasms.

## Objectives

The purpose of this study was to determine the major risk factors for postoperative aspiration using VFSS and how to overcome it following different types of partial laryngectomies.

## Study design

The authors conducted a prospective evaluation comparative study.

## Patients and methods

This study was conducted on patients with laryngeal carcinoma who underwent partial laryngectomy between October 2009 and May 2012. VFSS was carried out to evaluate postoperative swallowing and aspiration. Statistical analyses were performed using Pearson's  $\chi^2$  and Spearman's rank correlation test to detect the major risk factors associated with aspiration.

## Results

Thirty-two patients were enrolled in the present study. Six different types of partial laryngeal surgeries were carried out according to the size and extent of the primary tumor. Twenty-five (78.12%) patients suffered from various degrees of aspiration. Age, smoking, site of tumor, resection of valleculae, epiglottis, hyoid bone, ventricular folds, and true vocal folds were significantly associated with aspiration ( $P < 0.05$ ).

## Conclusion

Aspiration is common after partial laryngeal surgeries but is rarely severe or permanent. VFSS should be used before and after any partial laryngectomy to exclude silent aspiration and the risk for aspiration pneumonia. Aspiration can be minimized with careful patient selection and precise surgical technique selection and perfection.

## Keywords:

aspiration, Modified Penetration Aspiration Scale, partial laryngeal surgeries, videofluoroscopic swallowing study

Egypt J Otolaryngol 32:271–278

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1012-5574

## Introduction

Treatment of laryngeal cancer has undergone fundamental changes in the past few decades due to improvements in surgical techniques and radiotherapy. The standard treatment by total laryngectomy has increasingly been replaced by organ preservation modalities or function-conserving resection techniques. With these treatment techniques, voice preservation becomes the surgeon's priority against other complications, mainly dysphagia and aspiration [1].

Nasogastric tube removal timing and permanent gastrostomy rates were used in the past as crude indicators of persistent dysphagia and aspiration

rates [2]. Recently, videofluoroscopic swallowing study (VFSS), which could detect even minor subclinical aspiration, has been accepted as the standard radiological examination method using which functional disorders in swallowing and structural changes can be examined after partial laryngeal surgery [3]. Detection of these complications is crucial for appropriate swallowing rehabilitation.

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Knowledge of the risk factors that most influence aspiration could help the surgeon in technique selection and anatomical structure preservation, which should be accurately balanced in every patient with the objective of a radical removal of the neoplasm.

## Objectives

The purpose of this study was to determine the major risk factors for postoperative aspiration using VFSS and how to overcome it following different types of partial laryngectomies.

## Patients and methods

This prospective evaluation comparative study was conducted on laryngeal carcinoma patients who underwent open partial laryngeal surgery between October 2009 and May 2013 at the ENT Department. Approval for the study was obtained from the ethical committee. All patients signed a detailed and well-explained informed consent.

All patients underwent routine general and local head and neck examination, contrast-enhanced computed tomography of the neck, and direct laryngoscopy under general anesthesia for tumor mapping and biopsy followed by histopathology examination. Various clinical factors were documented: age, sex, smoking, comorbidities, preoperative radio-chemotherapy, tracheotomy, and site of tumor (glottis/supraglottic/subglottis). Staging was performed according to the latest American Joint Committee on Cancer TNM classification [4].

Partial laryngeal surgeries (six major partial laryngeal surgeries) were carried out for these patients according to the site, size, and extent of the primary tumor. Operative findings including type of operation, extent of resection, method of reconstruction (with special consideration for dysphagia and aspiration preventive prospective measures), and neck dissection (ND) were documented.

Swallowing analysis by using preoperative and postoperative VFSS was conducted 4 weeks after starting oral feeding. VFSS was carried out by oral administration of liquid and semiliquid contrast media (gastrograffin) in the lateral and anteroposterior projections [5] with rapid digital registration of swallowing (30 frames per second) using a Siregraph CF (Siemens, Forchheim, Germany).

Grading of postoperative aspiration was performed in accordance with the Modified Penetration Aspiration

Scale (MPAS) (inclusion criteria are presented in Table 6) [6]. Scoring was given by both a surgeon and a phoniatician subspecialized in swallowing rehabilitation after partial laryngectomies. In this study, scores 1 and 2 were considered as low-risk group, scores 3 and 4 as moderate-risk group and scores 5 and 6 as high-risk group.

Statistical analyses were carried out using Pearson's  $\chi^2$ -test and Spearman's rank correlation test as appropriate, to analyze the potential statistical relationships among the risk factors in relation to postoperative aspiration (MPAS). All reported *P* values were two-tailed. A *P* value of less than 0.05 was considered statistically significant. All statistical data were analyzed with SPSS, version 20 software for Windows (SPSS Inc., Chicago, Illinois, USA).

## Results

### Patient demographics

A total of 32 patients who fulfilled the required criteria of data availability and follow-up were included. All the patients were males (age range, 36–78 years). Twenty-one patients (65.62%) were smokers. Six patients were diabetic, four patients were hypertensive, and three patients were diabetic and hypertensive (Table 1).

The correlation of age to the different aspiration risk groups are shown in Table 2.

### Surgical findings and techniques

The preoperative variables and its relation with preoperative aspiration are shown collectively in

**Table 1** General subject characteristics and its association with postoperative aspiration

| Characteristics | Number of patients (%) | <i>P</i> value      |
|-----------------|------------------------|---------------------|
| Age (years)     |                        |                     |
| Median          | 57.5                   | $\rho=-0.387$       |
| Range           | 36–78                  | 0.029 <sup>*†</sup> |
| Sex             |                        |                     |
| Male            | 32 (100)               |                     |
| Female          | 0 (0)                  |                     |
| Smoking         |                        |                     |
| Smoker          | 21 (65.62)             | 0.010 <sup>§</sup>  |
| Nonsmoker       | 11 (34.38)             |                     |
| Comorbidities   |                        |                     |
| Diabetic        | 6 (18.8)               | 0.107 <sup>§</sup>  |
| Hypertensive    | 4 (12.5)               |                     |
| Both            | 3 (9.4)                |                     |
| Free            | 19 (59.4)              |                     |

<sup>†</sup>Spearman's correlation test. <sup>§</sup>Pearson's  $\chi^2$ . \**P*<0.05 significant; statistical positive value of our findings.

Table 3. There was a statistically significant association between the site of tumor ( $P=0.002$ ) and postoperative aspiration. On the other hand, the severity of aspiration increased with rise of tumor stage (from MPAS 2 with T1 to 3 with T2 to 4 with T3), rise of nodal stage (from MPAS: 3 with N0 to 4 with N1) and presence of preoperative radiochemotherapy (from MPAS: 3 in absence to 4 with presence of preoperative radiochemotherapy). However, these relations did not achieve statistical significance (Table 3).

**Table 2 Correlation of age to the different aspiration risk groups**

| Variable    | Groups              | N  | Mean age          | SD    |
|-------------|---------------------|----|-------------------|-------|
| Age (years) | Low-risk group      | 15 | 58.73             | 8.242 |
|             | Moderate-risk group | 7  | 62.00             | 8.602 |
|             | High-risk group     | 10 | 48.4 <sup>*</sup> | 7.214 |
|             | Total               | 32 | 56.22             | 9.510 |

<sup>\*</sup> $P=0.003$ .

**Table 3 Preoperative variables and its association with postoperative aspiration**

| Characteristics                | Number of patients (%) | MPAS median value | P value <sup>§</sup> |
|--------------------------------|------------------------|-------------------|----------------------|
| Site of tumor                  |                        |                   |                      |
| Glottic                        | 18 (56.3)              | 2                 | 0.002 <sup>*</sup>   |
| Supraglottic                   | 10 (31.3)              | 3                 |                      |
| Transglottic                   | 4 (12.5)               | 5                 |                      |
| Tumor stage                    |                        |                   |                      |
| T1                             | 7 (21.9)               | 2                 | 0.298                |
| T2                             | 20 (62.5)              | 3                 |                      |
| T3                             | 5 (15.6)               | 4                 |                      |
| Nodal stage                    |                        |                   |                      |
| N0                             | 28 (87.5)              | 3                 | 0.891                |
| N1                             | 4 (12.5)               | 4                 |                      |
| Preoperative tracheostomy      |                        |                   |                      |
| Yes                            | 7 (30.4)               | 2                 | 0.138                |
| No                             | 25 (69.6)              | 5                 |                      |
| Preoperative radiochemotherapy |                        |                   |                      |
| Yes                            | 2 (6.3)                | 4                 | 0.512                |
| No                             | 30 (93.7)              | 3                 |                      |

MPAS, Modified Penetration Aspiration Scale. <sup>§</sup>Pearson's  $\chi^2$ -test. <sup>\*</sup> $P<0.05$  was considered statistically significant (two-tailed); statistical positive value of our findings.

**Table 4 Site of tumor and type of operation in the study group**

| Site of tumor | Operation |   |                                    |                                |                           |                           | Total |
|---------------|-----------|---|------------------------------------|--------------------------------|---------------------------|---------------------------|-------|
|               | CHEP      | Extended frontolateral hemilaryngectomy | Extended supraglottic laryngectomy | Frontolateral hemilaryngectomy | Supraglottic laryngectomy | Vertical hemilaryngectomy |       |
| Glottic       | 2         | 2                                       | 0                                  | 3                              | 0                         | 11                        | 18    |
| Supraglottic  | 0         | 0                                       | 1                                  | 0                              | 9                         | 0                         | 10    |
| Transglottic  | 0         | 1                                       | 0                                  | 3                              | 0                         | 0                         | 4     |
| Total [n (%)] | 2 (6.3)   | 3 (9.4)                                 | 1 (3.1)                            | 6 (18.8)                       | 9 (28.1)                  | 11 (34.4)                 | 32    |

CHEP, cricohyoidoepiglottopexy.

Six different types of partial laryngeal surgeries were included in this study, according to the size and extent of the primary tumor (Table 4).

Operative variables and their relation to MPAS are summarized in Table 5. Only one patient underwent partial tongue base resection (MPAS: 5).

Postoperatively, seven patients (21.9%) had radiochemotherapy, whereas 25 patients (78.1%) did not.

**Videofluoroscopic swallowing study results**

Twenty-five (78.12%) patients (out of 32) suffered from different degrees of penetration and aspiration (Figs 1 and 2), whereas the remaining seven patients (21.9%) did not (Table 6).

**Correlation between the risk factors and postoperative aspiration**

Among the general subject characteristics, there were significant associations between age ( $\rho=-0.387$  and  $P=0.029$ ) and smoking ( $P=0.010$ ) in relation to postoperative aspiration (Table 1).

The severity of aspiration was inversely associated with age ( $P=0.003$ ). The high-risk group (MPAS: 5 and 6) was found in patients with a mean age 48.4 years, whereas the low-risk group (MPAS: 1 and 2) was found in patients with a mean age 58.73 years (Table 2).

The severity of aspiration showed a statistically significant association in patients who underwent resection of valleculae ( $P=0.025$ ), epiglottis ( $P=0.037$ ), hyoid bone ( $P=0.005$ ), ventricular folds ( $P=0.022$ ), and vocal folds ( $P=0.039$ ). On the other hand, the severity of aspiration increased in patients who underwent resection of aryepiglottic folds (MPAS: 2 when both are preserved and 3 when both are resected), resection of thyroid cartilage (MPAS: 2 with preservation of one thyroid ala and MPAS: 4 with total thyroid

**Table 5 Operative variables and their association with postoperative aspiration**

| Operative variables                                | Number of patients (%) | MPAS median value | P value <sup>§</sup> |
|--|------------------------|-------------------|----------------------|
| Valleculae resection                               |                        |                   |                      |
| Yes  | 6 (18.8)               | 5                 | 0.025*               |
| No   | 26 (81.25)             | 2                 |                      |
| Epiglottis   |                        |                   |                      |
| Removed  | 10 (31.25)             | 3                 | 0.037*               |
| Preserved  | 18 (56.25)             | 2                 |                      |
| Epiglottopexy                                      | 4 (12.5)               | 4                 |                      |
| Hyoid bone resection                               |                        |                   |                      |
| Yes  | 10 (31.3)              | 3                 | 0.005*               |
| No   | 22 (68.7)              | 2                 |                      |
| Aryepiglottic folds                                |                        |                   |                      |
| Both removed                                       | 12 (37.5)              | 3                 | 0.107                |
| One preserved                                      | 12 (37.5)              | 2                 |                      |
| Both preserved                                     | 8 (25)                 | 2                 |                      |
| Arytenoids   |                        |                   |                      |
| Only one preserved                                 | 15 (46.87)             | 2                 | 0.321                |
| Both preserved                                     | 17 (53.12)             | 3                 |                      |
| Ventricular folds                                  |                        |                   |                      |
| Both removed                                       | 20 (62.5)              | 3                 | 0.022*               |
| One removed  | 12(37.5)               | 2                 |                      |
| Vocal folds  |                        |                   |                      |
| Both removed                                       | 2 (6.25)               | 4                 | 0.039*               |
| One removed  | 20 (62.5)              | 2                 |                      |
| Both preserved                                     | 10 (31.25)             | 3                 |                      |
| Anterior commissure                                |                        |                   |                      |
| Removed  | 10 (31.25)             | 2                 | 0.629                |
| Preserved  | 22 (68.75)             | 3                 |                      |
| Thyroid cartilage                                  |                        |                   |                      |
| Totally removed                                    | 2 (6.25)               | 4                 | 0.142                |
| Leaving lower part                                 | 10 (31.25)             | 3                 |                      |
| Leaving 2/3 of one ala                             | 3 (9.3)                | 5                 |                      |
| Leaving 2/3 of ala and posterior part of other ala | 7 (21.87)              | 2                 |                      |
| Leaving one ala                                    | 10 (31.25)             | 2                 |                      |
| SLN  |                        |                   |                      |
| Both resected                                      | 2 (6.3)                | 4                 | 0.144                |
| One preserved                                      | 3 (9.4)                | 3                 |                      |
| Both preserved                                     | 27 (84.4)              | 3                 |                      |
| Neck dissection                                    |                        |                   |                      |
| No   | 25 (78.1)              | 2                 |                      |
| Unilateral ND                                      | 4 (12.5)               | 3                 | 0.302                |
| Bilateral ND                                       | 3 (9.4)                | 5                 |                      |

MPAS, Modified Penetration Aspiration Scale; ND, neck dissection; SLN, superior laryngeal nerve. <sup>§</sup>Pearson's  $\chi^2$ -test. \* $P < 0.05$  was considered statistically significant (two-tailed); statistical positive value of our findings.

cartilage removal), affection of superior laryngeal nerve (SLN) (MPAS: 3 with preservation of both SLN and MPAS: 4 with resection of both SLN), and performance of ND (MPAS: 2 with no ND, MPAS: 3 with unilateral ND and MPAS: 5 with bilateral ND). However, these relations did not achieve statistical significance (Table 5).

## Discussion

When considering patients operated by partial open laryngectomy, the anatomy was completely changed and could react to the surgical modifications in various ways, therefore affecting postoperative outcome, which could be influenced also by the mode of investigation [7].

In our study, we investigated the laryngeal aspiration of each patient with the VFSS to determine the MPAS so that to evaluate the potential risk factors for aspiration.

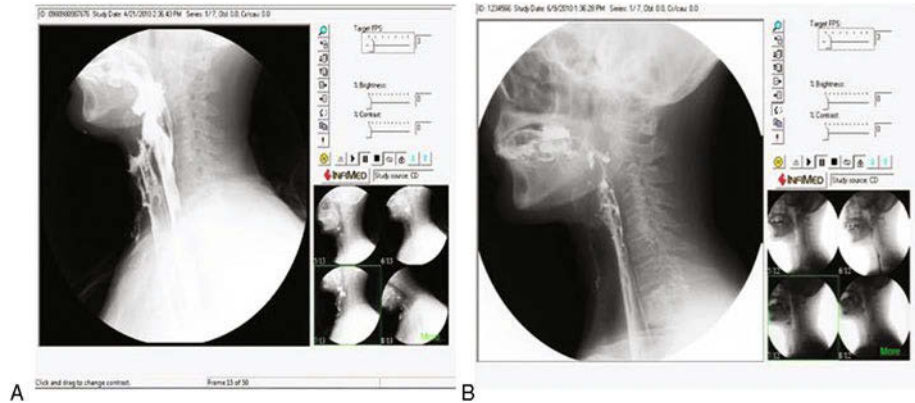
The overall aspiration in the present study occurred in 78.12% (25/32) of patients. However, Kreuzer *et al.* [2] reported overall aspiration in 93% (61/65) of the patients in their study. This discrepancy might be attributed to the fact that their patient group was selected to include only patients with the clinical symptoms of dysphagia.

Patients' advanced age in many studies was considered one of the risk factors for aspiration, as reported by Caudell *et al.* [8]. Advanced age is associated with impaired oropharyngeal motor commands, laryngopharyngeal sensitivity, and comorbidities that can affect the swallowing function. In their study, Laccourreye *et al.* [9] stated that age by itself should not be considered as a deterrent for supraglottic partial laryngeal surgery completion. However, many authors think that the biological age and overall medical condition of the patient (including the comorbidities) are more important than the chronologic age.

In our study, age was inversely correlated with postoperative aspiration ( $\rho = -0.387$  and  $P = 0.003$ ). This means that the younger the patient, more the increase in the incidence of aspiration (Tables 1 and 2). This discrepancy might be explained in our study by the fact that the older patients underwent a less aggressive surgery, whereas the younger patients underwent more aggressive surgery (different tumor stage).

In the present study, there was a significant correlation between smoking and postoperative aspiration ( $=0.010$ ), which is in agreement with the findings of McCulloch *et al.* [10], who identified smoking as a significant risk factor associated with postoperative pulmonary complications after head and neck surgery. In their study conducted on patients who underwent supracricoid partial laryngectomies, Joo *et al.* [11], using the univariate analysis, reported that 14 nonsmokers had nearly no permanent complications,

Figure 1



(a) VFSS after right vertical partial laryngectomy (VPL), showing severe aspiration to thin fluids 4 weeks after starting oral feeding. (b) Very minimal aspiration when repeated 4 weeks later. VFSS, videofluoroscopic swallowing study.

Figure 2



(a) VFSS after fronto-lateral hemi-laryngectomy (FLHL) and ND showed moderate aspiration to 10 ml thin fluids. (b) Aspiration was eliminated when VFSS was repeated 4 weeks later. ND, neck dissection; VFSS, videofluoroscopic swallowing study.

Table 6 Results of MPAS in the study group

| Grades | MPAS  | Frequency in study group | Percentage |
|--------|---|--------------------------|------------|
| 1      | Material does not enter airway (no aspiration)  | 7                        | 21.9       |
| 2      | Material enters airway, contact epiglottis, stimulate cough reflex, and is ejected completely     | 8                        | 25.0       |
| 3      | Material enters airway, contact epiglottis, stimulate cough reflex, and not completely ejected    | 6                        | 18.8       |
| 4      | Material enters airway, pass below glottis, stimulate cough reflex, and is ejected completely     | 1                        | 3.1        |
| 5      | Material enters airway, pass below glottis, stimulate cough reflex, and is not completely ejected | 4                        | 12.5       |
| 6      | Material enters airway, pass below glottis, and no effort made to reject (silent aspiration)      | 6                        | 18.8       |
| Total  |   | 32                       | 100        |

MPAS, Modified Penetration Aspiration Scale.

10 ex-smokers had a 30% complication rate, whereas 87 current smokers had a 37.9% complication rate.

This study revealed no correlation between preoperative tracheostomy and postoperative aspiration ( $P=0.138$ ). This was in agreement with the findings of Leder and Ross [12] who found no causal relationship between tracheostomy and aspiration status. They reported that patients with tracheostomy tubes often have other risk factors than the presence of a tracheostomy tube that predisposes them to aspiration (e.g. chronic obstructive pulmonary disease), and that the presence of dysphagia is likely to be due to the medical condition and not to the mere presence of the tracheostomy tube.

Interestingly, tumor location achieved a significant statistical correlation with aspiration in this study ( $P=0.002$ ), which is in agreement with the findings Stenson *et al.* [13], who reported aspiration incidence rate reaching 30% in oral tumors, 67% with laryngeal, and 80% in patients with pharyngeal head and neck cancer (HNC). In addition, Starmer *et al.* [14] reported that HNC extending into the larynx or the hypopharynx is a principal risk factor for aspiration. On the other hand, Campbell *et al.* [15] postulated no significant correlation between tumor location and aspiration in patients who survived 5 years or longer after active treatment. They explained that aspiration in patients with HNC is affected by treatment modality

and its extent (radiotherapy, chemotherapy, or surgery) rather than by tumor location.

We found that the severity of aspiration increases with the rise of tumor stage and nodal stage. This was consistent with Jung *et al.* [16] who mentioned that a higher American Joint Committee on Cancer stage was the principal predictive factor, as these patients need more aggressive therapies.

Radiotherapy heightens the risk for aspiration by 35%, which is mostly related to fibrosis and decreases muscle activity of swallowing and related structures [17]. Chemotherapy has been shown to increase the aspiration incidence from 17 to 59%, and this could be correlated to odynophagia, mucositis, glossitis, fibrosis, and lymphedema resulting from apoptosis caused by cytotoxic drugs [18]. This was in line with our results but failed to achieve statistical significance (Table 5).

This study also documented that resection of valleculae ( $P=0.025$ ), epiglottis ( $P=0.037$ ), the ventricular folds ( $P=0.022$ ), and aryepiglottic folds were statistically correlated with postoperative aspiration as these structures are involved in airway protection during the pharyngeal phase of swallowing and usually removed in open supraglottic laryngectomies. Such operations remove not only tumors but also normal muscles, cartilage, and bones (which constitute important barriers of aspiration) for the purposes of safe marginal security, and, as a result, swallowing-related organs malfunction. However, this was in contrast to the findings of Schweinfurth and Silver [19], who reported that epiglottectomy plays a relatively minor role in protecting the airway and therefore epiglottectomy usually does not result in aspiration.

Adduction is the most important barrier against aspiration. Airway closure is maintained only for the fraction of a second (0.03–0.06 s) that the bolus is passing the airway [20]. In this study, and in agreement with Hirano *et al.* [21], resection of true vocal folds was statistically correlated with aspiration ( $P=0.039$ ).

Arytenoid resection during cricohyoidopexy or cricohyoidoepiglottopexy did not significantly increase aspiration incidence, but the extent of arytenoid resection may have an effect on the timing of swallowing recovery [22]. Yüce *et al.* [23] were of the view that arytenoid resection in cricohyoidopexy may affect the swallowing function in the early postoperative period, and even bilateral arytenoids resection is not significantly different from unilateral as regards long-term results.

In this study, and in agreement with Lewin *et al.* [22], arytenoid resection was not correlated with aspiration. Our results were in contrast to those of Hirano *et al.* [21], who mentioned that resection of an arytenoid cartilage is one of the risk factors that has been shown to correlate statistically with adverse operative outcome following supraglottic horizontal laryngectomy. In this special situation, arytenoid resection causes incomplete adduction capability and incompetent glottis, and the likelihood of aspiration is greatly increased. When the arytenoid cartilage is removed, it should be reconstructed to prevent severe aspiration.

In the present study, resection of the hyoid bone ( $P=0.005$ ) and total resection of the thyroid cartilage (MPAS: 4) were found to increase the severity of aspiration. Forward and upward displacement of the hyoid bone during swallowing contributes to airway protection and transport of the bolus to the esophagus [24], whereas thyroid cartilage removal entails resection of all sphincters that guard against aspiration. This was in agreement with Strek *et al.* [25], who reported that resection of the hyoid bone is one of the factors that causes intensified difficulty during swallowing and increase in the frequency of the occurrence of aspiration after partial laryngectomy.

Aspiration was found to be associated with injury of SLN and ND in the present study. In healthy individuals, it has been shown that selective anesthesia of the internal branch of the SLN causes laryngeal penetration during swallowing [26]. Bilateral preservation of the SLN in partial laryngeal surgeries has been considered critical for successful swallowing rehabilitation [27]. Patients who have undergone ND often complain about dysphagia because of surgical interruption of the pharyngeal plexus or injury to the recurrent laryngeal nerve [28] and sometimes associated with resection of the suprahyoid muscles, resulting in a change in the hyoid bone position. However, this effect did not achieve statistical significance, which could be attributed to the small sample size.

We specially designed this study to overcome the shortcomings of noneffective, nonavailable modern radiotherapy techniques in many areas of country because of a lack financial resources and social problems, and this was also applied to laser partial laryngeal surgery. Still, the partial open laryngeal surgeries are the ideal choice for early-stage laryngeal carcinomas, where function and organ preservation strategy could be conducted, with having salvage total laryngectomy and postoperative radiotherapy as a reserve

in hand. We had analyzed aspiration, which was the commonest problem with the partial laryngeal surgeries whatever its type and modifications, and applied VFSS and MPAS as an objective preoperative and postoperative tool for its analysis and guidance for surgical technique selection, modification, and perfection.

One of the limitations of this study was the small number of patients, which may render the statistical analysis to be nonsignificant for some variables. Moreover, additional limitations include heterogeneous treatment modalities, which varied depending on tumor stage and the philosophy of the attending surgeon. Accordingly, a large-scale prospective study including partial laryngeal surgeries with preoperative and postoperative VFSS should be conducted on patients with HNC.

## Conclusion

Aspiration is a common complication after partial laryngeal surgeries, which is usually mild but could be severe or permanent. Among the variables tested for the entire cohort of patients, age, smoking, site of tumor, resection of valleculae, epiglottis, hyoid bone, ventricular fold, and true vocal fold had a statistically significant impact on aspiration after partial laryngectomy. With the application of VFSS and MPAS as an objective tool for aspiration analysis, we reported that it had a good impact on surgical technique selection, modification, and perfection for improving the patient's quality of life.

## Acknowledgements

The authors greatly thank and acknowledge Professor, Dr Bader El-Din Mostafa, for his substantial help in this research. He provided with a lot of cases of partial laryngectomies from his series where the authors were short of time and cases. He agreed to conduct or protocol and to share the results with the authors. As usual, the authors had a lot of scientific and practical help from him.

All authors had equal and substantial contributions to conception and design, acquisition of data, analysis and interpretation; drafting the article and revising it critically for important intellectual content; and final approval of the version to be published. All surgical cases were either done by the senior two authors or under their direct supervision. The swallowing analysis was carried out by or under the supervision of Dr Samia Bassiouny. This study was based on the thesis of Dr Ahmed Nabil in his preparation for the

MD degree in otolaryngology. The final stage of editing and publishing was done by Dr Hossam Rabie.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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