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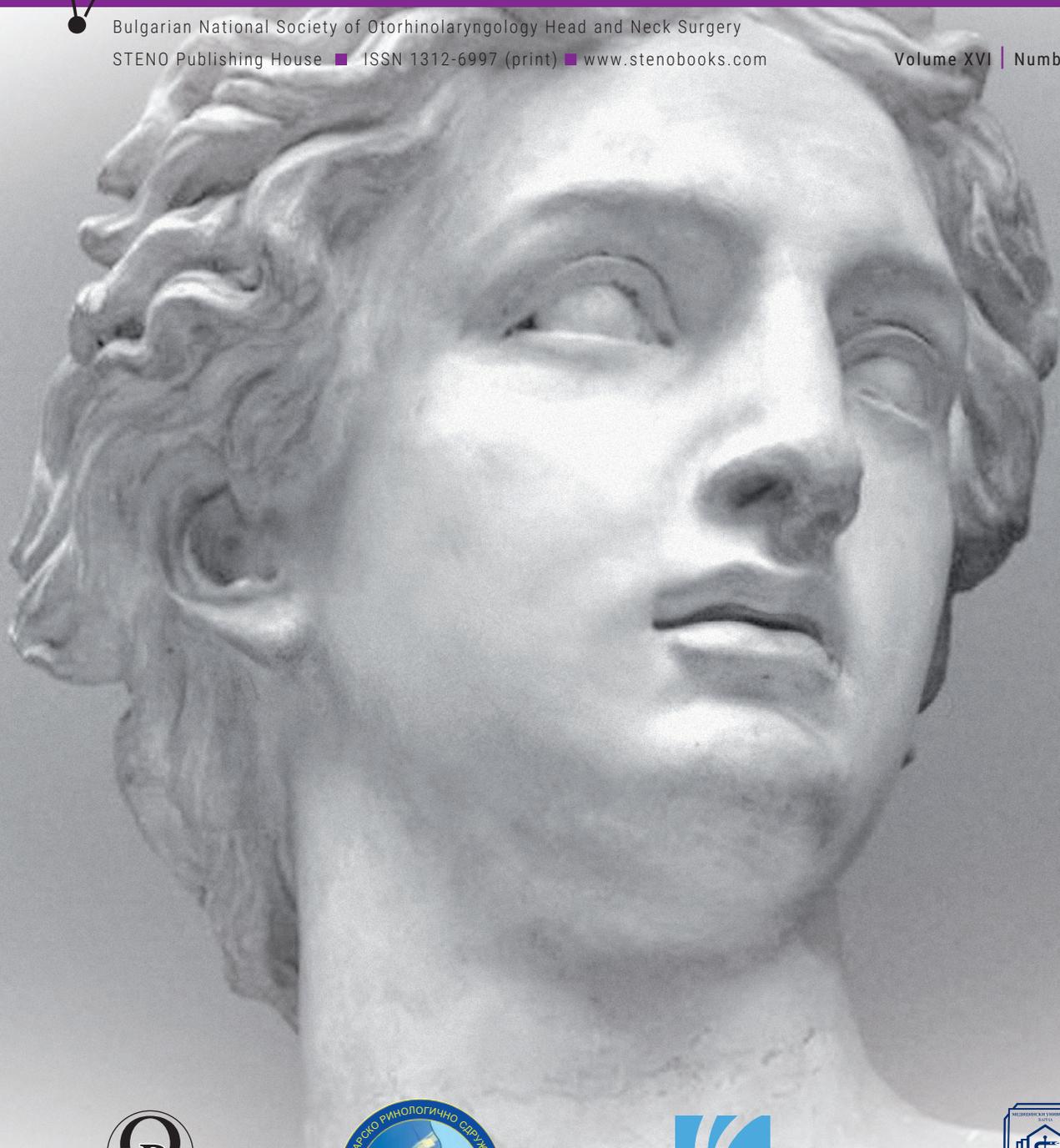
OTORHINOLARYNGOLOGY

Международен бюлетин по оториноларингология

Bulgarian National Society of Otorhinolaryngology Head and Neck Surgery

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international bulletin



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These guidelines are in accordance with the „Uniform Requirements for Manuscripts submitted to Biomedical Journals“ published in *N Engl J Med* 1997; 336: 309-315

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Submit an original manuscript with one set of original figures and two copies of the complete manuscript. Address all submissions to the Editor/M. Milkov, Journal Steno, street, №, Varna, Bulgaria.

The manuscripts should be on standard-sized A4 paper in double-spaced typewriting on one side of the paper only. Manuscripts must be prepared in accordance with the „Uniform Requirements for Manuscript submitted to Biomedical Journals“. Manuscripts improperly prepared will be returned to the author without review. A separate covering letter signed by the authors must state that the data have not published elsewhere and identify the author to whom the correspondence must be submitted. All original manuscripts will be submitted to reviewers, known personalities in the field.

Manuscript preparation

Arrange manuscript as follows, each component (1-9) beginning on a separate page: (1) title page, (2) abstract, (3) introduction/background, (4) material and methods, (5) results, (6) discussion, (7) references, (8) figure legends, (9) tables.

Place page number and first author's last name at top of each page.

Cite references, figures and tables consecutively as they appear in the text.

(1) Title page

Title should be concise and descriptive. The title page should include the name of the author with initials or distinguishing first name, and the name and address of the hospital or institution where the work was performed.

List grant support and other assistance.

List alphabetically abbreviations used and three to ten keywords.

Provide name, complete address, telephone number and fax number of corresponding author.

Title page should include also a short (fewer than 45 characters) running head.

(2) Abstract

Provide on a separate page an abstract of not more than 250 words, consisting of four paragraphs, labeled: Background, Methods, Results and Conclusions. Do not use abbreviations, footnotes, or references. For original articles, if the paper is published in French, an English abstract should be added to the manuscript, and conversely.

(3) Body of paper

The paper must be conventionally structured in the following chapters: Introduction/

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Approval of institutional human research review committees or animal welfare committees should be cited. Outline statistical

methods used. Identify drugs and chemicals used by generic name (if trademarks are mentioned, manufacturer name and city are given).

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Cite references in order of appearance in text using arabic numerals in parentheses. Cite personal communications and unpublished data directly in text without being numbered. Conform abbreviation to those used in Index Medicus. List of all authors when there are six or fewer; when there are seven or more, list the first three, than et al.

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23. Kimura K, Ohto M, Matsutani S, Furuse J, Hoshino K, Okuda K. Relative frequencies of portosystemic pathways and renal shunt formation through the „posterior“ gastric vein: portographic study in 460 patients. *Hepatology* 1990; 12: 725-728

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The Editorial Team Steno



Acquired hearing loss

Dobriyanova V.

Throat Diseases Department, Faculty of Medicine at Sofia Medical University

SNHL – Sensorineural Hearing Loss

BAEP – Brainstem Auditory Evoked Potentials

Identifying the causes for deafness can provide prognostic information, help in developing a rehabilitation plan and contribute to treatment or a patient's prognosis. Depending on the onset of hearing loss as concerning speech development it can be classified as prelingual, occurring before speech is developed and usually involving severe deafness (hearing thresholds from 61 to 90dB for speech frequencies) and profound deafness (tone thresholds above 91dB), and postlingual – occurring gradually after normal speech has developed. In cases of postlingual deafness communication ability is not necessarily affected after loss of hearing.

Acquired hearing loss is a complex problem due to various reasons. The majority of cases are caused by external factors such as infections, diseases and trauma or can be age-related.

Infectious causes leading to deafness can occur before and after birth.

Neurotropic viruses such as herpes simplex, cytomegalovirus and rubella are well-known aetiological reasons for congenital sensorineural hearing loss and presumed causes for acquired hearing loss in acute viral infection. Mechanisms of action include direct viral invasion of the cochlea or the cochlear nerve, reactivation of a latent virus in the spiral ganglion and immune-mediated mechanisms such as mimicry, after an infection becomes systemic [1].

HSV-1 and HSV-2 can also cause both congenital and acquired SNHL. These are encapsulated, double-stranded DNA viruses from the Herpes virus

family. The infection results from contact between secretions containing the virus and mucous membranes or damaged skin. The initial infection can be asymptomatic. HSV-1 infections are associated with a post-infection hearing loss or reactivation of the infection in early childhood. SNHL caused by HSV-1 infection is more common than an HSV-2 one. If a herpes simplex infection is confirmed in young children, an audiometry is recommended.

Audiological and vestibular symptoms can also occur in people infected with *Human immunodeficiency virus (HIV)*. It includes conductive hearing loss (often due to acute otitis media), sensorineural hearing loss, tinnitus, vertigo, ataxia [2, 3, 4]. Deafness can appear as the result of direct infection of the inner ear with HIV or indirectly after developing an opportunistic infection (For example: with CMV, syphilis, tuberculosis, cryptococcal meningitis) or ototoxic drug therapy.

HIV can also affect the central and peripheral part of the auditory system and the virus is detected in auditory and vestibular sensory cells, in strial cells and in the tectorial membrane [5]. Patients with HIV infection have abnormal BAEP, which implies engagement of the auditory nerve [6].

Epidemic parotitis caused by a virus belonging to *Paramyxoviridae* family, is characterised by unilateral or bilateral affecting of the parotid glands and complications, one of which can be sensorineural hearing loss. According to a study performed in Japan in 2009, cases of deafness after epidemic parotitis indicates 0.1% cases with unilateral hearing loss, severe hearing loss to deafness. The Centers for Control and Prevention of Diseases in the USA state that incidents are below 1% [7]. Hearing loss associated with epidemic parotitis can appear before or after the infection in asymp-

tomatic patients as well. Deafness associated with measles, mumps and rubella has decreased after the widespread use of the live attenuated vaccine.

The measles virus belongs to the family of the Paramyxovirus family. Hearing loss is a frequent complication of the measles infection. Before the widespread use of vaccination, measles accounted for 5 to 10% of the cases of deafness in the United States [8]. At present, it continues to be a common cause for profound hearing loss in areas where vaccination is rare [9].

Hearing loss resulting from measles is typically bilateral, moderate to severe and can follow measles encephalitis [8]. Measles is related to a high rate of otitis media (in 8.5 - 25% of the infected people), due to a temporary decrease in immunity. An after-effect of bacterial superinfection might lead to some cases of hearing loss associated with the infection.

Varicella Zoster Virus, VZV, is part of the *Herpesviridae* family. Initially, VZV caused a primary infection that can have expressed symptoms or be asymptomatic. Afterwards the virus can remain latent for a long period, in the neurons in different parts of the body. Reactivation of the latent VZV in ganglion *geniculi* causes Ramsay Hunt syndrome or herpes zoster oticus through the development of inflammation of the ganglion and inflammation of the facial nerve. Involvement of cranial nerve VIII ensues from transfer of the virus from the ganglion which is nearly located or directly from the facial nerve in the internal auditory canal. Symptoms include paralysis of the facial nerve, herpetiform vesicles, severe otalgia, SNHL (24% of the affected patients), tinnitus and vertigo [10].

SNHL is unilateral and can vary from mild, high frequency to profound hearing loss but is usually mild to moderate. It can sometimes occur suddenly as a first manifestation of herpes zoster oticus. Patients with HZO have changes in BAEP followed by cochlear and retrocochlear dysfunction [11].

Haemorrhage of the cochlear nerve and destruction of the apex of the organ of Corti can be observed. Loss of cells of the ganglion *geniculi* with neuronal swelling and chromatolysis, perivascular lymphocytic infiltrate, nerve demyelination and axonal loss are also observed. Hearing loss following HZO can be reversed after treatment while recovery from facial paralysis is reported less frequently. Severity of the facial paralysis not always correlates with the severity and prognosis of the auditory and vestibular symptoms.

Permanent hearing impairment occurs in about 5% of the cases of HZO [12]. In these cases SNHL is

caused by damage in the cochlea and in the more proximal auditory pathways. Hearing aids can be used to improve mild to moderate deafness (socially appropriate hearing to profound hearing loss).

Other viral infections such as West Nile Virus, the human parvovirus B19, lymphocytic choriomeningitis virus are potentially connected with acquired hearing loss including that with sudden hearing loss.

Meningitis

Hearing loss is a well-documented complication of bacterial meningitis. Systematic review and meta-analysis of 132 articles has reported 33.6% frequency of hearing loss, due to bacterial meningitis caused by various agents (*Str. Pneumoniae*, *H.influenzae B*, *Neiss. meningitides*, etc.) [13]. Although *H.influenzae* type B meningitis is most common, hearing loss occurs with higher frequency after pneumococcal meningitis in infants over one-month age.

A matter of dispute is the exact location of the damage in hearing loss caused by meningitis, whether it is in the hair cells, the terminal branches of the auditory nerve or the auditory nerve itself. Hair cells, terminal branches and the cell bodies of the nerve fibres are surrounded by perilymph and endolymph fluid. Medications and/or bacterial infections are the most probable causes for the damage of hair cells and the nerve [14]. Serial BAEP recordings during the first 48 hours from the beginning of their impact have demonstrated early occurrence of hearing loss. All changes in BAEPs disappear within two weeks from monitoring without registered cases of later hearing loss or recovery. This suggests that the functional status of peripheral neurons of auditory pathways is intact in children with congenital deafness compared with those who have lost their hearing after meningitis. Hearing loss caused by bacterial meningitis starts during meningitis and the cases of hearing loss do not decrease after specific antibacterial treatment. Although, in some cases, acute otitis media with direct spread through the labyrinth window can precede the onset of the disease it is more likely bacterial toxins to penetrate through the cochlear aqueduct or through the internal auditory canal, thus leading to perineuritis or neuritis of CN VIII and/or purulent labyrinthitis. Other pathophysiological mechanisms participating in hearing loss include serous or toxic labyrinthitis, thrombophlebitis or embolisation of the labyrinth vessels, hypoxia or anoxia of CN VIII and the central auditory pathways.

In children with bilateral sensorineural hearing loss



after bacterial meningitis, cochlear implantation is a successful remedy for rehabilitation of hearing. Surgical treatment has to be performed quickly because of labyrinthine ossification occurring as a complication of meningitis.

Intake of ototoxic medications

Hearing loss resulting due to ototoxic medications from the group of aminoglycosides such as gentamicin, and toxic substances such as lead, is a rare and preventable cause for sensorineural hearing loss. Some medications cause irreversible deafness, while intake of others leads to hearing loss which can be reversed when medications are stopped. There seems to be an idiosyncratic and genetic susceptibility to ototoxic medications [15]. Medication-induced hearing impairments are usually bilateral, symmetrical and of variable severity. Loss of hearing is progressive, initially affecting high frequencies.

Borradori et al [16] have identified ototoxicity closely related to a prolonged administration and higher total dose of ototoxic drugs, particularly aminoglycosides and furosemide. Salamy et al [17] find a high risk of hearing loss when furosemide is administered in the neonatal period in greater amounts, for longer durations and in combination with aminoglycosides.

Risk of hearing loss caused by intake of ototoxic medications also exists in patients with malignant tumours treated with cisplatin. Other medications known to induce sensorineural hearing loss are acetylsalicylic acid, chloramphenicol, chloroquine phosphate, dihydrostreptomycin, neomycin, nortriptyline, pharacetin, polymyxin B, streptomycin, vancomycin.

Hearing loss has been reported in association with prenatal exposure to alcohol, trimethadione, and methyl mercury as well as in prenatal iodine deficiency.

Neonatal wards differentiate a group of children who are at risk for hearing loss, combining the impact of factors such as ototoxic medications used during treatment in the units, extracorporeal membrane oxygenation and continuous ventilation and hyperbilirubinemia in some of the young patients.

Stay in a neonatal intensive care unit

It is clear from research that the most frequent risk factors for hearing loss in neonatal intensive care units are ototoxic medications (44,4%), low weight at birth (17,8%), assisted ventilation lasting 5 days (16,4%), low Apgar scores (13,95%) [18].

Hypoxia, hyperbilirubinemia and, to a lesser degree, exposure to ototoxic medications determine hearing loss in the neonatal intensive care unit.

Hypoxia varies from apnoea, low Apgar score or more often documented as $PO_2 < 50$ mm Hg.

Hyperbilirubinemia is a factor related with sensorineural hearing loss in neonatal intensive care units and also with auditory neuropathy. Specific deviations in the auditory evoked responses have been demonstrated in the presence of hyperbilirubinemia. These aberrations disappear after blood exchange transfusion and bilirubin levels return to normal. DeVries et al [19] have found that a higher mean duration of hyperbilirubinemia (48 hours versus 24 hours) and low birth weight is associated with higher risk of sensorineural hearing loss.

Persistent pulmonary hypertension and extracorporeal membrane oxygenation are indicators for hearing monitoring, performed every six months until the age of three, since delayed onset of sensorineural hearing loss has been reported.

Interruption of blood flow to the cochlea is another theorized cause for sudden hearing loss. It usually leads to cochlear fibrosis and ossification which are well-visualized on MRI.

Acoustic trauma

Loud noise is one of the main reasons for hearing loss. Although acoustic trauma can sometimes be considered a rough equivalent of noise-induced hearing impairment including chronic cases, their clinical course and treatment outcomes differ. Noise-induced hearing loss can be divided into acute and chronic and chronic is further divided into two types - occupational (in the majority of cases) and non-occupational.

Acute noise-induced hearing loss is also two categories: one is acoustic trauma and the other is acute noise-induced hearing loss (such as hearing loss related with listening to loud music at concerts).

Acoustic trauma happens instantly, for example, with a gun-shot or an explosion. Immediately after the explosion, a mechanical injury is induced since the noise level physically exceeds the 'elastic limit' of the peripheral auditory mechanism. This type of trauma is caused by an extremely intense level of noise (≥ 130 dBA). On the other hand, acute noise-induced hearing loss is usually caused after some exposure time, from several minutes to several hours. After attending a concert people might experience ringing sounds or muffled ears. This type of impairment is mainly caused by metabolic damage due to 'excitotoxicity' from exposure to intense sound of around 100–120 dBA.



Outer hair cells in the cochlea when initially exposed to loud noise suffer from reversible damage which causes temporary threshold shift of hearing; if a person is exposed long enough, the damage remains permanent. Standard tone threshold audiometry does not record these early changes and until hearing loss can be detected by the audiogram, permanent damage is caused to the outer hair cells. Occupational guidelines for industry noise exposure require employees exposed to sound levels above 85dB (A) to be provided with personal protective equipment.

It has been proved that above 85 dB the likelihood for acquiring permanent damage of hair cells quickly increases, with a seemingly slight increase in the level of decibels. As logarithmic scales are used to measure decibels, for every 3-4 dB increase in sound pressure the permissible time for exposure to noise above 85 dB is halved [20].

Acute noise-induced hearing loss is considered to be reversible to some degree. Currently, several treatment methods are used in clinical practice for the recovery of hearing: steroids, hyperbaric oxygen therapy and dextran being the most widely spread. Exposure to more than 140 dB peak sound pressure can cause an immediate, profound and permanent deafness [21].

Head trauma

It is well known that fractures of the temporal bones are associated with SNHL. Hearing loss resulting from concussion and traumatic brain injury is less often recognised in the absence of apparent temporal bone fractures.

Cochlear concussion presents with a PTA result from 2000 to 4000 Hz in the absence of temporal bone fracture or other organic pathology following the head trauma.

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Airway management for microlaryngeal surgery

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Abstract

Theoretical basis: Microlaryngeal surgery can be conducted in an awake patient, frequently under conscious sedation, or with the patient anesthetized. The ventilation options under general anesthesia consist of "tube" (i.e., endotracheal intubation) and "tubeless" techniques, with the latter represented by the techniques of Spontaneous ventilation, Apneic intermittent ventilation (AIV), and Jet Ventilation (JV). **Results:** The use of a small (5.0-mm ID) MLT tube with positive-pressure ventilation remains the standard for airway management in most nonlaser microlaryngeal surgery, and it is associated with minimal or no intraoperative complications. Spontaneous ventilation is rarely used in adult microlaryngeal surgery, but it is commonly employed in the pediatric patient population. AIV remains a relatively popular technique for microlaryngeal surgical procedures of short duration in some surgical centers. Superimposed High-Frequency Jet Ventilation (SHFJV), which combines high-frequency and low-frequency ventilation modes, has been used effectively in surgical treatment of high-grade laryngeal and tracheal stenosis. **Conclusion:** General anesthesia for microlaryngeal surgery represents a unique example of close cooperation between the surgeon and the anesthesiologist.

Key words: Microlaryngeal surgery, general anesthesia, ventilation techniques.

Literature review

Microlaryngeal surgery can be conducted in an awake patient, frequently under conscious sedation, or with the patient anesthetized. The ventilation options under general anesthesia consist of "tube" (i.e., endotracheal intubation) and "tubeless" techniques, with the latter represented by the techniques of Spontaneous ventilation, Apneic intermittent ventilation (AIV), and Jet Ventilation (JV).^{1,2}

Awake airway surgery

For selected patients, many laryngoscopic procedures can be safely and effectively performed in an office-based setting, including diagnostic endoscopy, laser surgery, microlaryngeal surgery for cancer screening and biopsies, and therapeutic vocal cord injections. The key to success for office-based surgery remains adequate topical and regional anesthesia of the patient's airway, which is usually performed by the surgeon and typically follows preparation of the patient for awake oral and nasal flexible fiberoptic intubation. Although highly motivated patients can undergo office-based laryngoscopic surgery strictly under local anesthesia, most desire sedation and amnesia.

If presence of the anesthesiologist is requested, the main objectives are to monitor for possible local anesthetic toxicity, to supplement local anesthesia with a rapidly titratable and reversible state of sedation, and to treat acute hyperdynamic respons-

es that can occur in up to 20% to 30% of patients, despite seemingly adequate topical anesthesia of the airway.³ Judicious use of intravenous opioids or sedatives/hypnotics, or both, is paramount, because a loss of patient cooperation may result in intraoperative injury. Sedation of the patients with obstructive sleep apnea and morbid obesity should be performed with extreme caution.^{4,5}

Asleep airway surgery

General anesthesia for microlaryngeal surgery represents a unique example of some of the conflicting intraoperative goals that exist between the surgeon and the anesthesiologist with regard to the patient's airway control and maintenance. For the surgeon, ideal operating conditions would be completely unobstructed surgical visualization, unimpeded surgical manipulation, and absence of movement in the surgical field. From the anesthesiologist's perspective, the ideal anesthetic technique would allow adequate protection of the patient's lower airway from aspiration and the use of stable, controlled mechanical ventilation with the ability to measure the concentration of anesthetic gases, peak inspiratory pressure (PIP), inspired oxygen concentration (FiO_2), and end-tidal carbon dioxide level (EtCO_2). In most cases, these objectives can be balanced by the use of a small microlaryngeal tracheal tube (MLT tube), maximizing the patient's safety and the success of surgery.

Endotracheal intubation with microlaryngeal tracheal tubes

The use of a small (5.0-mm ID) MLT tube with positive-pressure ventilation remains the standard for airway management in most nonlaser microlaryngeal surgery, and it is associated with minimal or no intraoperative complications.^{6,7} Adequate gas exchange can be maintained through small-ID ETTs in most adult patients, unless the duration of surgery approaches 2 hours. Even then, despite a consistent trend toward progressive hypercapnia and respiratory acidosis, the pH and EtCO_2 values remain within physiologic range.^{8,9}

With most glottic pathology originating in the anterior two thirds of the larynx, consistent positioning of a small MLT tube between the arytenoid cartilages in the posterior part of the glottis leaves most of the surgical field unobstructed to the surgical view and manipulations. Even with many posterior glottic disorders, it may be possible for the surgeon

to gently displace the MLT tube anteriorly with the microsurgical cupped forceps or to perform the surgery using the specially designed posterior glottic laryngoscopes.^{10,11,12}

However, if the posterior glottis is occupied by a significant surgical pathology (e.g., posterior glottic or subglottic stenosis, transglottic tumor), use of alternative, tubeless ventilation techniques becomes necessary. Because of the surgeon's preference, tubeless ventilation can also be requested as a primary ventilation mode from the outset of the procedure.

Tubeless techniques Spontaneous Ventilation

Spontaneous ventilation is rarely used in adult microlaryngeal surgery, but it is commonly employed in the pediatric patient population, for whom it offers the additional ability to evaluate dynamic airway function and the level of obstruction.^{13,14} Although this technique offers free access to the larynx, it does not provide a still surgical field for precision surgery, it affords no protection of the lower airway, and it contaminates the OR environment. Deep planes of anesthesia are usually required to blunt the laryngeal responses and to prevent patient movement, which tends to provoke cardiovascular instability and ventilatory compromise (i.e., hypoxemia, hypercarbia, and short periods of apnea).¹⁵ The protagonists of spontaneous ventilation technique may wish to routinely supplement general anesthesia with topical or local anesthesia of the airway (usually done by the surgeon after deployment of suspension laryngoscopy), which facilitates maintenance of a more stable and lighter plane of anesthesia, promotes hemodynamic and respiratory stability, and decreases the incidence of intraoperative laryngospasm.¹⁶

Apneic intermittent ventilation

AIV remains a relatively popular technique for microlaryngeal surgical procedures of short duration in some surgical centers. Compared with spontaneous ventilation, it affords more stable and controlled anesthetic conditions, as well as full muscle relaxation. After induction of anesthesia, the patient's lungs are ventilated by a face mask or an LMA, which is followed by a period of apnea to allow deployment of a suspension laryngoscope by the surgeon. The patient's trachea is subsequently intubated by the surgeon with a small-diameter,



preferably uncuffed ETT that is placed through the lumen of the laryngoscope, and the patient's lungs are hyperventilated with an FiO_2 of 1.0. The ETT is then removed to provide a fully unobstructed and still surgical view of the larynx. The ETT is withdrawn and reinserted as frequently as necessary to maintain an oxygen saturation by pulse oximetry (SpO_2) of 90% or greater and EtCO_2 between 40 and 60 mm Hg, allowing periods of apnea up to 5 to 10 minutes in healthy adult patients.^{17,18} TIVA is typically used for maintenance. Monitoring the hypnotic state of anesthesia is advisable during AIV, because the incidence of awareness and recall may reach 4% (30 times higher than in the general surgical population), especially when the inhalational agents are used to supplement intravenous anesthesia.^{19,20}

The disadvantages of AIV include slowing the pace of surgery, disruption of the surgical field, possible trauma to the vocal cords and lower airway due to repeated endotracheal intubation, and a propensity for laryngospasm. In a study of more than 350 patients, the incidence of intraoperative laryngospasm with AIV was 1.4%. The AIV may not be suitable for patients with significant lung or cardiovascular disease, and it leaves the patient's lower airway unprotected to aspiration.

Jet Ventilation

Supraglottic JV (i.e., jet nozzle above the glottic opening) for microlaryngeal surgery can be performed through the side port of a suspension operating laryngoscope, with the jet cannula attached to the lumen of the laryngoscope or through a specialized jet laryngoscope.^{21,22,23}

Subglottic JV (i.e., jet nozzle below the glottic opening) is established by bypassing the larynx from above (i.e., translaryngeal or transglottal approach) or below (i.e., percutaneous approach) through the Cricotracheal membrane (CTM) or the upper Transtracheal Jet Ventilation (TTJV) rings. Transglottal JV typically employs specialized, laser-safe, small-diameter, orally placed, double-lumen catheters, in which the large port is used for jetting and the smaller lumen for monitoring the distal airway pressure and respiratory gases.^{24,25}

Long, single-lumen catheters (typically 1.5- to 3-mm ID), some of which are laser resistant, may be used and can be placed through the oral or nasal route, however, they lack concurrent monitoring capability.^{26,27,28} Alternatively, a small-diameter,

movable, metal jet cannula can be passed through the glottis by the surgeon after the suspension laryngoscope is in position.²⁹ For transglottal JV, midtracheal placement of the catheter or cannula is usually preferred. TTJV is typically administered through a long catheter or Ravussin-type cannula.³⁰ For TTJV catheter or cannula placement, the use of an flexible fiberoptic bronchoscope (FFB) or a rigid bronchoscope may be advocated to monitor the procedure and to minimize the risk of unnoticed posterior tracheal wall laceration, which may lead to submucosal gas injection and barotrauma.³¹ Use of a rigid bronchoscope with the bevel turned posteriorly may be especially efficacious, because the posterior tracheal wall is protected by the bronchoscope from the needle entry. For transglottal JV and TTJV, endoscopic control also allows adjustment of the position of the distal end of the catheter or cannula to optimize high frequency jet ventilation (HFJV).

Compared with endotracheal intubation, supraglottic and subglottic JV techniques have distinct advantages of providing the surgeon with an enlarged, clear or minimally impeded, and undistorted view of the endolarynx and facilitating surgical access. Although supraglottic and subglottic ventilation techniques can use low-frequency jet ventilation (LFJV), HFJV, or superimposed high-frequency jet ventilation (SHFJV) modes, the use of these modes in clinical practice is usually more restrictive.^{32,33,34}

The use of manual supraglottic LFJV (i.e., Venturi jet ventilation) at a rate of less than 60 breaths/min continues to predominate in clinical practice, probably because of the low cost and easy accessibility of manual JV devices.^{35,36} Although an overall incidence of complications with manual supraglottic LFJV may be low (0.42%), a survey of 229 U.K. centers revealed that it was responsible for most major complications (e.g., significant hypoxemia, barotrauma, unplanned admission to the intensive care unit) and for all deaths, especially when applied subglottically. This suggests that LFJV should be reserved for uncomplicated, elective procedures of short duration and that it may not be regarded as a standard of practice for microlaryngeal surgery.

The subglottic HFJV mode (respiratory rate of 100 to 300 breaths/min; tidal volumes [Vt] of 1 to 3 mL/kg), delivered through specialized automated jet ventilators, is typically used. Compared with

supraglottic LFJV, in which intermittent apnea is frequently required due to significant vocal cord movement, subglottic HFJV significantly reduces laryngeal motion and affords a quiet surgical field without the need for interrupting ventilation. If vocal cord movement becomes a problem, HFJV driving pressure can be decreased, and the respiratory frequency can be increased to provide a smoother gas flow, or the ventilator can be turned off during particularly delicate parts of the procedure.³⁴

Despite very small V_t values, CO_2 elimination during subglottic HFJV is facilitated by the upstream turbulent convective flow of CO_2 along the decreasing gradient from the alveoli to the conducting airways. The alveolar-arterial CO_2 gradient in patients with normal lung function is largely maintained within normal range.³⁷

In contrast to supraglottic LFJV, with which contamination of the lower airway due to air entrainment is possible, a continuous, upward-directed flow of gas during subglottic HFJV creates a positive-pressure build-up, preventing blood and surgical debris from being directed down an unprotected airway. Alternatively, initiation of the subglottic HFJV can be held off until the suspension laryngoscope is deployed, and ventilation is supported conventionally through a face mask or the LMA.

On emergence from anesthesia, small V_t values and low peak and mean airway pressures associated with subglottic HFJV enable the patient to breathe spontaneously, facilitating a transition to adequate spontaneous ventilation.^{38,39} This transition can be further assisted at the end of surgery by increasing the frequency of ventilation to 300 breaths/min, increasing FiO_2 to 1.0, and setting a ventilator driving pressure at about 0.8 bar, which enables almost continuous flow of O_2 and apneic oxygenation, as well as a rise in the carbon dioxide (CO_2) level. If the conversion to spontaneous ventilation through a small subglottic catheter proves difficult, the patient's airway can be supported through a face mask, LMA, or ETT, as required. If obstructive airway lesions exist, subglottic HFJV must be used with extreme caution. If upper airway obstruction is greater than 50%, the position of the jet nozzle should be proximal to the site of the obstruction to prevent barotrauma, or the obstruction must be bypassed by a rigid bronchoscope first.

Total outflow obstruction with resultant barotrauma during subglottic HFJV can be quickly precipitated

by or closure of the vocal cords due to inadequate depth of anesthesia or inadequate muscle relaxation. Modern automated jet ventilators incorporate multiple safety features, including automatic ventilator shutdown, if the user-preset pressure limits are exceeded. This design has enabled some experienced providers to successfully use high-frequency TTJV in patients with massive supraglottic lesions and severe airway compromise, for which the use of supraglottic or subglottic JV was not possible or surgically feasible. The presence of a second anesthesiologist to facilitate monitoring and maintenance of an upper airway was required and deemed an important safety factor in preventing intraoperative pressure-related complications in all cases.

Compared with the transglottal approach, high-frequency TTJV is associated with a significantly higher combined major and minor (e.g., transient hypoxemia) complication rate and it represents an independent risk factor for complications during JV for microlaryngeal surgery. Modern automated JV may not be able to remediate all possible causes of barotrauma associated with high-frequency TTJV; complications may be related to the TTJV catheter insertion problems, laryngospasm, and high-pressure episodes (e.g., coughing, active expiration) during the recovery period.

SHFJV, which combines high-frequency and low-frequency ventilation modes, has been used effectively in surgical treatment of high-grade laryngeal and tracheal stenosis, even with a remaining glottic opening as small as 2 to 3 mm.⁴⁰ SHFJV is delivered supraglottically through a specialized jet laryngoscope, which incorporates welded low-frequency and high-frequency jet nozzles.⁴¹ As the streams (LFJV of 12 to 20 breaths/min; HFJV of 100 to 900 breaths/min) get simultaneously directed from the ventilator toward the center of the distal end of the jet laryngoscope, LFJV entrains air and produces cyclic changes in V_t (similar to supraglottic LFJV), facilitating maintenance of PaCO_2 at near-normal limits and allowing HFJV to be adjusted as needed. HFJV builds up a continuous PEEP and promotes alveolar recruitment, maintaining PaCO_2 even in the presence of the low FiO_2 required for laser surgery.^{42,43} Safety of SHFJV is enhanced by an integrated port for continuous pressure (PIP and PEEP) and gas (FiO_2 and EtCO_2) monitoring at the end of the jet laryngoscope and of an automatic pressure-triggered



ventilator shutdown feature, similar to an isolated HFJV mode.

To achieve adequate SHFJV, it appears to be sufficient to generate a PIP of 15 to 30 cm H₂O, as measured at the end of the jet laryngoscope, which closely correlates with the PIP at the glottic and tracheal levels (i.e., no further increase in pressure occurs in the distal airway). The PEEP values may not exceed 2.5 to 5 cm H₂O. As a result, no adverse hemodynamic effects and barotrauma were observed in more than 1500 adult and pediatric patients who had undergone supraglottic SHFJV for laryngotracheal surgery, and endotracheal intubation was required in only 3 patients (0.2%), with concomitant significant restrictive or obstructive pulmonary disease. Due to the HFJV component, vocal cord movement is greatly attenuated during SHFJV. If a perfectly still surgical field is requested by the surgeon, HFJV can be further increased, LFJV decreased or stopped, or a short period of full apnea instituted.^{40,41}

SHFJV is a completely tubeless, laser-safe, open breathing system that allows a fully unobstructed surgical field. It enables an easy switch between different JV modes and parameters, and it offers greater versatility and ventilation capabilities over the single-frequency JV techniques, especially in patients with preexisting compromised gas exchange. However, its effective use requires optimal laryngoscope alignment and adjustability in relation to the glottic opening.

Despite the increased safety profile of SHFJV, clinical monitoring of the patient to prevent barotrauma should remain the standard of care for all JV techniques. Close cooperation between the surgeon and the anesthesiologist is essential. If the operating laryngoscope moves or is removed and obstructs the airway without a warning to the anesthesia team, major barotrauma may result. Ensuring an adequate level of anesthesia, analgesia, muscle relaxation and close monitoring of vital signs and chest excursions are essential for the patient's safety.

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Awake or asleep approach to difficult airway during microlaryngeal surgery

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Abstract:

Introduction: Patients presenting for microlaryngeal surgery frequently have a difficult airway. The chosen approach to this airway depends on the pathology and the patient's symptoms. The **Aim** of the study is to determine the safest anesthesiological approach to difficult airway during microlaryngeal surgery. **Materials and Methods:** A prospective cohort study including 200 patients undergoing microlaryngeal surgery in the Department of Otorhinolaryngology at the University Hospital "Queen Giovanna" - ISUL, Sofia, in the period 2014-2019; Medical University-Sofia. Preoperative examination of the larynx is performed in all patients by Storz 8402 ZX fiber optic laryngoscope with video capability. **Results and discussion:** In 76% of the patients the tumor mass causing obstruction is localized in the area of the larynx, and in 24% of them the tumor mass is localized in the area of the hypopharynx. In 20% of the patients with 3rd degree of laryngeal obstruction an awake tracheostomy is chosen as a primary approach because of impossible intubation. The same approach is chosen in all of the patients presenting with respiratory failure at rest. In 25% of the patients with tumor mass causing hypopharyngeal obstruction an awake tracheostomy is chosen as a primary approach because of impossible intubation. **Conclusion** The decision to proceed with an awake or asleep approach to an anticipated difficult airway depends on the degree of laryngeal or hypopharyngeal obstruction and the experience of the anesthesiologist.

Key words: microlaryngeal surgery, anesthesiological approach, laryngeal obstruction, hypopharyngeal obstruction

Introduction

Patients presenting for microlaryngeal surgery frequently have a difficult airway. The chosen approach to this airway depends on the pathology and the patient's symptoms. In situations with critical airway compromise, an awake tracheostomy may be warranted from the outset, but it may prove to be technically challenging or impossible and may require general anesthesia. Even if an awake tracheostomy is chosen as a primary approach, full backup preparation for alternative airway management is necessary. Video laryngoscopy reliably improves laryngeal exposure by at least one grade, allows continuous observation of the entire intubation procedure by the entire team, and may therefore be a near-ideal technique for managing difficult airways in patients presenting for microlaryngeal surgery. Choosing the video laryngoscopic device depends on the operator's preference and must consider the nature and location of the lesions. The strongest predictor of the technique failure was altered neck anatomy with presence of a surgical scar, radiation changes, or a mass. Factors indicating difficult intubation also need to be considered.^{13,14,15} These conditions are frequently encountered in patients presenting for microlaryngeal surgery.^{1,2,3,4,5}

Material and methods

A prospective cohort study including 200 patients undergoing microlaryngeal surgery in the Department of Otorhinolaryngology at the University Hospital "Queen Giovanna" – ISUL, Sofia, in the period 2014-2019; Medical University-Sofia. Preoperative examination of the larynx is performed in all patients by Storz 8402 ZX fiber optic laryngoscope with video capability. The degree of laryngeal obstruction is determined by modified Cotton-Myer scale with 4 degrees of obstruction: up to 50% (1st degree), 51–70% (2nd degree), 71–99% (3rd degree) and full obstruction (4rd degree). In all patients we used quamatel 20 mg for premedication. For induction in general anesthesia we used propofol 2.5 mg . kg⁻¹ and succinylcholine 1 mg . kg⁻¹ as muscle relaxant. Endotracheal intubation was performed by endotracheal tube № 6.0 or № 6.5 from the anesthesiologist and mechanical ventilation was performed. For maintenance of general anesthesia we used sevoflurane inspiratory concentration of 2.5 vol. % and fentanyl 4-5 µg . kg⁻¹. for pain relief.

Results

We found that 86% of the patients were men and 14% were women (fig.1).

In 76% of the patients the tumor mass causing obstruction is localized in the area of the larynx, and in 24% of them the tumor mass is localized in the area of the hypopharynx (fig.2).

From the patients with tumor mass causing laryngeal obstruction 39.5% are with 1st degree of obstruction, 26.3 % are with 2nd degree, 31.6% are with 3rd degree and 2.6% are with respiratory failure at rest (fig.3).

In 20% of the patients with 3rd degree of laryngeal obstruction an awake tracheostomy is chosen as a primary approach because of impossible intubation. These are 5.3% of all patients with tumor mass causing laryngeal obstruction. The same approach is chosen in all of the patients presenting with respiratory failure at rest. These are 2.6% of all patients with tumor mass causing laryngeal obstruction (fig.4).

In 25% of the patients with tumor mass causing hypopharyngeal obstruction an awake tracheostomy is chosen as a primary approach because of impossible intubation (fig.5).

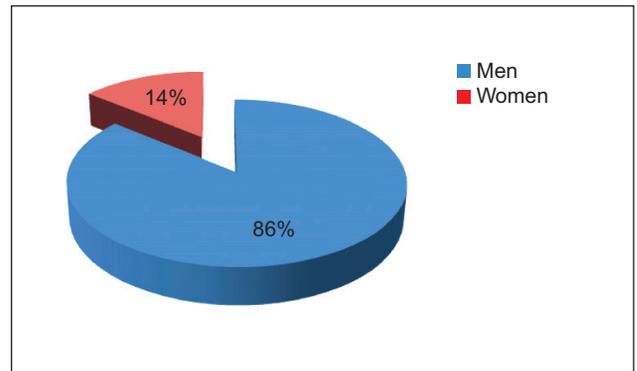


Figure 1. Distribution according to gender.

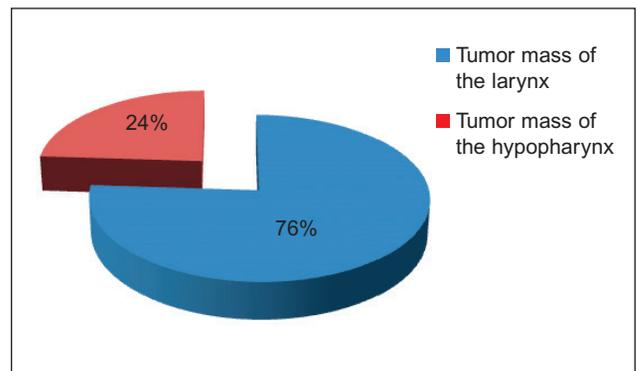


Figure 2. Distribution according to localization of the tumor mass.

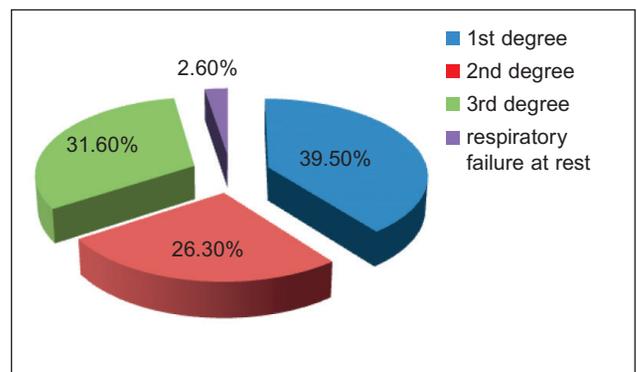


Figure 3. Distribution according to the degree of laryngeal obstruction.

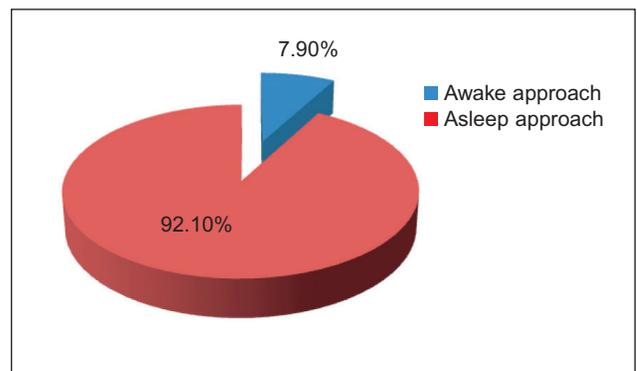


Figure 4. Awake or asleep approach in patients with tumor mass causing laryngeal obstruction.

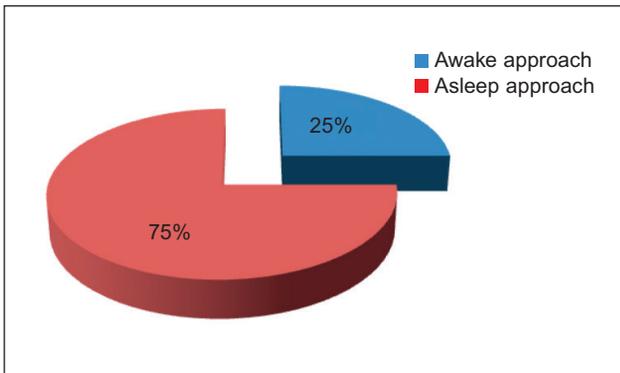


Figure 5. Awake or asleep approach in patients with tumor mass causing hypopharyngeal obstruction.

Discussion

The decision to proceed with an awake or asleep approach to an anticipated difficult airway should follow the American Society of Anesthesiologists (ASA) difficult airway algorithm, with special attention directed to predictors of difficult mask ventilation, impossible mask ventilation, and their association with difficult intubation.⁶ The anesthesiologist also should review the pertinent preoperative findings identified on flexible fiberoptic laryngoscopy, chest radiography, CT, and MRI and should discuss these findings with the surgeon.

If an asleep approach to the difficult airway is chosen, several preformulated alternative airway management plans must be in place before induction of anesthesia. If the airway is marginal, the patient's neck should be prepped, and the surgical team should be present on induction, ready to perform an emergent cricothyrotomy or tracheostomy, or to employ rescue techniques such as a rigid bronchoscope.^{7,8} In experienced hands, rigid bronchoscopy may be used to rescue failed direct laryngoscopy and failed intubation and to manage a "cannot intubate, cannot ventilate" (CICV) situation. It also serves as an indispensable tool for managing acute airway obstruction resulting from foreign bodies, hemoptysis, or tumors.⁹ After the bronchoscope is placed into the patient's trachea by the surgeon, manual or jet ventilation can commence in a safe manner through the lumen of the bronchoscope.

Patients with an advanced airway obstruction and inspiratory stridor at rest comprise some of the most feared and complicated cases for the anesthesiologist. The incidence of difficult mask ventilation and impossible mask ventilation among patients with severe stridor and upper airway obstruction

of more than 75% of the lumen reaches 40% and 6%, respectively,¹⁰ compared with 1.4% and 0.15% for the general surgical population.¹¹ These patients frequently present for microlaryngeal surgery on an emergent or semi-emergent basis, yet they require a systematic and thoughtful approach by the anesthesiologist and the surgeon. The nature of the obstructing lesion (e.g., vascular, submucosal, pedunculated, inflammatory) and its location (e.g., supraglottic, glottic, subglottic, midtracheal, lower tracheal, and bronchial [mediastinal]) may require completely different intubation considerations and approaches.

In the context of laryngeal surgery, the optimal technique of airway management of the stridorous patient with an advanced proximal airway obstruction (i.e., supraglottic, glottic, and subglottic levels) remains a subject of controversy. An awake flexible fiberoptic intubation, inhalational induction, and intravenous induction with muscle relaxants have been used successfully, but none should be considered fail-safe.¹² Thorough preoperative discussion of the surgical pathology and formulation of closely coordinated airway management plan with the surgeon are essential for safe management of these patients.

In the patients with tumor mass causing hypopharyngeal obstruction an awake tracheostomy is more often compared with patients with tumor mass causing laryngeal obstruction because the size of the tumor mass prevents intubation or the use of supraglottic devices. On the other hand, unsuccessful attempts for intubation in patients with laryngeal obstruction can lead to laryngeal trauma, hemorrhage and subsequent impossible ventilation. Therefore, our advice is in patients with obstruction of the larynx 3rd to 4th degree or respiratory failure at rest, the tracheostomy should be performed in the awake state of the patient under local anesthesia with preservation of spontaneous breathing. The assessment of the possibility of intubation in a patient with 3rd degree laryngeal obstruction depends on the clinical symptoms, the fiberoptic laryngoscopy, the results of the CT or MRI and to the greatest extent on the experience of the anesthesiologist.

Conclusion

The decision to proceed with an awake or asleep approach to an anticipated difficult airway depends on the degree of laryngeal or hypopharyngeal obstruction and the experience of the anesthesiologist.

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Correlations between malocclusion and anomalies in the posture

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Abstract:

Posture is understood as the relative position of various body segments in relation to each other and relative to the environment. Postural control is characterized by the ability to adapt our use of sensory information to changing tasks and environmental conditions. Malocclusion and incorrect body posture are two very common issues in growing subjects and especially in patients with mixed dentition, where it is still possible to intervene to modify and correct both conditions. In order to perform a correct diagnosis and an orthodontic treatment plan, the relationships between occlusion and posture should be evaluated to establish the most appropriate strategy of treatment and an interdisciplinary approach between different health-care professionals. The aim of this study is to investigate the possible relationship between malocclusion and body posture anomalies.

Key words: malocclusion, posture, balance

Introduction

Posture is understood as the relative position of various body segments in relation to each other and relative to the environment. Thus, humans can take an infinite number of positions during daily and sport activities, such as standing, walking, running, throwing an object, etc. The posture in which both feet are in contact with the ground indicates the position commonly known as bipedal upright posture. The control of posture is essential for successfully achieving motor actions and implies the control of body position in space, with the double purpose of orientation and stability. (9, 12) Postural orientation involves proper positioning of the body segments relative to each other and to the environment. Stability during quiet standing involves the maintenance of the center of mass projection within the boundaries of the base of support.

Posture control is characterized by the ability to adapt our use of sensory information to changing tasks and environmental conditions. This process involves determining the accuracy of incoming sensory inputs and selecting the most appropriate sense for the context and changing the relative weighting of sensory inputs for postural control depending on their accuracy for orientation. (22)

Several factors may modify body posture and balance, among these dental malocclusion has great relevance. (17) Analyzing the occlusion can identify if the individual has physiological or pathologi-

cal relationship between the dental arches, which is also known as malocclusion. (13)

Aim: The aim of this study is to investigate if there is a connection between malocclusion and body postural anomalies.

Material and methods

The following scientific databases were included for the study: MEDLINE, Scopus, EMBASE and PubMed, with a time period from 1989 to 2020. For the search the keywords - malocclusion, posture and balance were used.

Results and discussion

Malocclusion and incorrect body posture are two common issues in growing subjects and especially in patients with mixed dentition. In the specified period it is still possible to intervene to modify and correct both conditions. In order to perform a correct diagnosis and an orthodontic treatment plan, relationships between occlusion and posture should be evaluated. This is done in order to establish the most appropriate strategy of treatment and an interdisciplinary approach between different healthcare professionals. (6)

Malocclusion can be defined as an imbalance between the masticatory system and neuromuscular temporomandibular joint. It is considered as a result of the sum of genetic, environmental and postural

elements therefore of multifactorial origin. (18)

Deformations in occlusion can occur in the three anatomical planes. Paying attention to the sagittal plane, three occlusion classes are found. The first, Class I, is the physiological relationship between the teeth, where the mesiobuccal cusp of the maxillary first molar occludes with the buccal groove of the mandibular first molar (normocclusion). The Class II or overshoot, occurs when the mesiobuccal cusp of the maxillary first molar occludes anterior to the buccal groove of the mandibular first molar. Class II malocclusion can be further subdivided into two types, differing by the position of incisors. In class II, division 1 cases maxillary incisors are tilted outwards which creates significant overjet and deep bite occlusion. In class II, division 2 maxillary lateral incisors are tilted labially. Finally, in class III cases, mesiobuccal cusp of the maxillary first molar occludes posterior to the buccal groove of the mandibular first molar. (4)

Many other types of malocclusion are found in the literature, for instance, the posterior crossbite consisting of an abnormal relationship in the lateral direction of one or more teeth of the maxillary, mandibular, or both, resulting in a disability performing the normal occlusion and open bite where there is a lack of contact between the incisors. (2)

For the period 1989-2020, 189 review and 1 739 research articles were published. Results from some of the studies are presented in Table 1.

Tabl. 1. Studies and main results.

Year	Authors	Objective	Population	Main results
2010	Perinetti et al. [17]	To investigate whether malocclusion is related to postural changes in young people.	122	Few data were considered significant, including the primary phase of teeth and malocclusion classified as overbite shown to be associated with the center of gravity changes measured by the pressure pad.
2011	Aldana et al. [1]	To test the null hypothesis: "there is no relationship between malocclusion and postural changes of head and neck."	116	Among the results were found associations between anti-clockwise rotation skull with Class III mandibular posterior rotation with dolichofacial individuals and Class II with the tongue position at rest.
2011	Perillo et al. [16]	To investigate the relationship between malocclusion and Helkimo Index ≥ 5 with postural changes in children and young people.	1178	The correlation between patients with malocclusion and Helkimo Index ≥ 5 with the worst asymmetry trunk and better performance in the Fukuda test was found.
2012	Deda et al. [5]	Comparing a group of patients with malocclusion with a control group and investigate whether there are differences between head posture.	25	Regarding the evaluation by photogrammetry, there was no significant difference between groups. Clinical inspection has achieved significant results, where 100% of Class II subjects had forward head and 73.3% in the control group, showed neutral head position.



2013	Silvestrini-Biavati et al. [20]	To investigate the incidence of malocclusion with ocular convergence and postural disorders.	605	93.8 to 94.2% of the entire sample, consisting of individuals with and without malocclusion presented symmetry of the lower limbs. For gait disturbance, no significant differences were found between the occlusal classes.
2014	Park et al. [14]	To investigate the prevalence of nasal septal deviation and concha bullosa among patients with malocclusion as common anatomical variations that can affect nasotracheal intubation in comparison with previous studies.	634	Septal deviation was found in 402 patients (63.4%). Concha bullosa was found in 328 patients (51.7%). Both of them were found in 238 patients. Three hundred twenty-five patients had the middle concha bullosa, sorted by type into true (182), lamella (80) and bulbous type (33), while for 30 patients, combination of two or more types were observed. That more closely preoperative evaluation is necessary for patients with malocclusion planning on surgery using nasotracheal intubation.
2016	Lopatiéné et al. [11]	To evaluate the relationships between hard and soft tissues and upper airway morphology in patients with normal sagittal occlusion and Angle Class II malocclusion according to gender.	114	Cephalometric analysis applied in our study showed that Angle Class II patients with significantly decreased facial convexity angle, increased nasomental, upper lip-chin, and lower lip-chin angles, and upper and lower lips located more proximally to the E line more frequently had constricted airways.
2018	Yogi et al. [23]	To evaluate a possible association between overall functional impairment and malocclusion in this population	70	The results showed that the type of Cerebral palsy, the degree of motor involvement, and the presence of parafunctions are important factors to be considered to establish a correct diagnosis of malocclusion in persons with Cerebral palsy.

Several studies have examined the correlation between malocclusion and parameters of body posture in the sagittal and frontal planes. Results identified a connection between structural orthopaedic diseases and occlusal morphology. (9, 10)

Segatto et al. found that children with various spinal deformities have a high number of malocclusions (19), and Ben-Bassat et al. proved that patients with idiopathic scoliosis showed more asymmetric features characteristic of malocclusion than a random control group. (3) Moreover, children with congenital hip dislocation are more predisposed to the development of a lateral cross-bite. (7) However, the results from studies looking at the correlation between poor body posture and dental occlusion are conflicting.

Sinko et al. compared body posture in 29 Class II and Class III patients, and found that the apex of the thoracic kyphosis was more cranial in Class III patients than in Class II patients or healthy controls. (21)

Based on these, it is observed that only the orthodontic treatment is not sufficient for the correction of postural dysfunctions possibly generated by mal-

occlusion. Perez et al. (15) suggests that other factors may be associated with postural changes (such as age, the type of teeth and others), and sometimes overlaps a malocclusion.

This review also includes two studies that used body balance in their methods. The first, of Perinetti et al. (17), aimed to investigate whether malocclusion was correlated with postural changes in young individuals, and it used a sample of 122 young people, between 10 and 16 years with malocclusions. The anteroposterior and lateral deviations have been verified by pressure platform on two conditions: mandibular relaxation and dental intercuspation. Few data were considered significant, including malocclusion classified as overbite shown to be associated with anteroposterior and lateral changes the center of gravity body. However, significant variables considered corresponded to 3-9% of the evaluation carried out, not being sufficient, according to the authors, to attest to the modification of postural stability.

In the second study Perillo et al. (16) assessed body balance, investigating the relationship between malocclusion and Helkimo Index ≥ 5 with postural changes in 1178 young people from 11 to 19 years.

Posture was analyzed by static evaluation (tilt and trunk asymmetry) and dynamic (Test of Fukuda steps, validated for balance assessment). A significant correlation was found between patients with malocclusion and Helkimo Index ≥ 5 - worse asymmetry trunk and better performance in the Fukuda test. These results show that individuals with malocclusion can develop a change of static equilibrium, but not significant when evaluated dynamically. Perillo et al. (16) also assume that the greater activation of postural muscles in these individuals may have positively influenced the Fukuda test, increasing their performance.

Aldana et al. (1), through a cross-sectional study, sought the relationship between malocclusion and postural abnormalities of the head and neck. For this, they used a sample of

116 malocclusion patients who have undergone orthodontic treatment. Thus sought associations between craniocervical Rocabado analysis, the cephalogram and functional evaluation of the language. Weak associations were found between the counterclockwise rotation skull with Class III, the mandibular posterior rotation and dolichofacial and facial individuals and Class II with the tongue position at rest.

Deda et al. (5) in their study, compared the position of the head in different classes (Class I, II and III) by photogrammetry and clinical inspection the

sample of twenty-five patients diagnosed with malocclusion. There was no significant difference between classes and influenced malocclusion on the angle head-neck evaluated by photogrammetry. However by clinical inspection, he noticed a pattern in head position in individuals Class II, where 100% had forward head. Another significant value was observed in the control group, who did not have changes in occlusion, where 73.3% had neutral head position.

Silvestrini et-Biavati al. (20) analyzed the incidence of malocclusion correlating with posture and disorders of ocular convergence. In a sample of 605 children, they found that 93.8 to 94.2% of the entire sample, consisting of individuals with and without malocclusion presented symmetry of the lower limbs. The study also evaluated the presence of gait disturbance, without any significant differences between the occlusal Classes.

Conclusion

Further research could help to reveal more details on the correlations between body posture and malocclusions from a pathogenic and clinical point of view. Scientists doubt whether the diseases occur simultaneously or they are dependent on the each other. It is not known for sure as well if one of the two is treated, there would be an influence on the other.

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Difficult airways in ENT surgery

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Abstract

Theoretical basis: Airway management for laryngeal surgery require the anesthesiologist to be adept with various methods of managing the difficult airway and performing airway exchange, to competently execute intraoperative ventilation strategies, to be proficient with inhalational and total intravenous anesthesia, and to quickly tailor anesthetic techniques to the various durations of the surgical cases. **Results:** When the surgical site is within or near the airway, coordination between the anesthesia and surgical teams is essential to consider the need for an ETT, which tube type to use, the oxygen enrichment plan, and mode of ventilation. The presence of laryngeal carcinoma requires precise assessment of the feasibility of endotracheal intubation. Tracheostomy can be safely performed under general anesthesia with laryngeal mask ventilation. The essential requirements for precision microlaryngeal surgery and optimal preservation of function include a clear and still surgical field, absence of patient movement, and allocation of sufficient time to carefully complete the procedure in an unhurried manner. Postoperative hemorrhage is the most serious complication of tonsillectomy. Aspiration of foreign bodies by children is a common problem around the world. **Conclusion:** General anesthesia in ENT surgery represents a unique example of close cooperation between the surgeon and the anesthesiologist.

Key words: Difficult airways, tracheostomy, general anesthesia, airway management.

Literature review

Advances and demands of the new surgical techniques and an expanding patient population that was previously considered unsuitable for surgery have created novel challenges for the anesthesiologist. State-of-the-art anesthesia and airway management for laryngeal surgery require the anesthesiologist to be adept with various methods of managing the difficult airway and performing airway exchange, to competently execute intraoperative ventilation strategies, to be proficient with inhalational and total intravenous anesthesia, and to quickly tailor anesthetic techniques to the various durations of the surgical case.

Laser surgery of the larynx

Laser is an acronym for *light amplification by stimulated emission of radiation*-a highly collimated beam of photons at a single frequency. Lasers are ubiquitous in the modern world and are increasingly used in the operating room (OR).¹ When the surgical site is within or near the airway, coordination between the anesthesia and surgical teams is essential to consider the need for an ETT, which tube type to use, the oxygen enrichment plan, and mode of ventilation. If intubation is planned, then varied intubation options exist and include an assortment of available ETTs and



jet ventilation catheters. A few oxygenation-ventilation strategies include ventilating through a cuffed or tightly fitting ETT, either continuously or intermittently using a ventilator with apnea during episodic removal of the ETT to allow unobstructed access to the surgical field. Either supraglottic or infraglottic catheter positioning may be selected for jet ventilation. In addition, the choice of anesthetic must be considered. There are series using sevoflurane and spontaneous ventilation²; however, volatile anesthetics are not reliably delivered to the patient if jet ventilation is required, and the vapors can pollute the OR. Finally, although the volatile anesthetics currently used in clinical practice are nonflammable and nonexplosive in clinically relevant concentrations,³ when exposed to flame, they may pyrolyse to potentially toxic compounds.⁴ ETT fires have their own set of elevated risks for the patient and require swift corrective measures. With the right conditions and if properly managed an ignited ETT may cause little if any harm. However, catastrophic injury may occur.^{5,6} If ignited and combustion breaches the ETT with its centrally flowing reservoir of oxidizer, a *blowtorch* scenario in the airway can occur. The potential for far-reaching thermal injury to the pulmonary tract exists. In addition, products of complete and partial combustion including smoldering debris, particulate matter, toxic gases, and compounds may cause further insult. When using a laser near the airway, the updated 2013 ASA Practice Advisory strongly agrees that “laser resistant tracheal tubes [and catheters] should be used, and that the tube choice should be appropriate for the procedure and the laser...” If a cuffed tube is used, then the cuff should be filled with saline rather than air whenever feasible.⁷ Methylene blue-dyed saline may help speed identification of cuff breaches.⁸ Added protection from ignition may be achieved by using water-soaked sponges around the tube at the site of work and at the glottis. These sponges may seal leaks of oxygen around an ill-fitting ETT cuff, segregating the higher FiO₂ being delivered to the patient from the ambient air above the glottis and may protect the tube from laser strikes by adding a layer of water-saturated protection.⁹

Total laryngectomy

Laryngeal carcinoma is the eleventh of the most common malignant neoplasms found in men. Epidemiologically it represents 1.6-2% of all

malignant tumors in males and 0.2-0.4% in females¹⁰. Surgical treatment of laryngeal carcinoma, partial or total laryngectomy, is an important part of the complex management of the disease. Total laryngectomy is a surgical procedure during which the larynx is totally removed and the airway is interrupted, respiration being performed through a tracheal stoma resulting from bringing the trachea to the skin in the lower anterior cervical area.¹¹⁻¹⁴ The presence of laryngeal carcinoma requires precise assessment of the feasibility of endotracheal intubation. Expectation of a difficult intubation requires a preliminary preparation for ventilation if endotracheal intubation is not possible. It is important to assess whether endotracheal intubation after induction in general anesthesia is possible or the tracheostomy should be performed in an awake patient with preserved spontaneous breathing under local anesthesia receiving supplementary oxygen via nasal oxygen catheter.¹⁵⁻²² The degree of laryngeal obstruction can be preoperatively evaluated by a detailed description of preliminary performed video laryngoscopy along with computer tomography examination results. The degree of laryngeal obstruction can be categorized using the Cotton-Myer scale for every patient. This evaluation will allow the clinician to choose the proper method for upper airway instrumentation. Induction into general anesthesia and endotracheal intubation as a method for upper airway instrumentation in patients with laryngeal carcinoma is dangerous and under debate because of: expected difficult intubation due to laryngeal obstruction by the tumor, tissue trauma (can cause bleeding and/or edema), transplantation of tumor cells into lower parts of the airways causing stoma recurrence.²³⁻³¹ Tracheostomy can be safely performed under general anesthesia with laryngeal mask ventilation. This method for upper airway instrumentation has been recently introduced for patients with laryngeal carcinoma undergoing laryngectomies in the Department of Otorhinolaryngology at the University Hospital “Queen Giovanna” - ISUL, Sofia, Bulgaria. In a study conducted by Marinov et al. over 60 patients undergoing total laryngectomy, 20 of the patients underwent tracheostomy under general anesthesia and laryngeal mask ventilation. None of them suffered any significant complications, including desaturations, despite of the considerably high degrees of laryngeal obstruction caused by the tumor masses.³²

Microlaryngeal surgery

The essential requirements for precision microlaryngeal surgery and optimal preservation of function include a clear and still surgical field, absence of patient movement, and allocation of sufficient time to carefully complete the procedure in an unhurried manner. The patient's airway must be protected from blood, debris, and irrigation fluid and ventilation must be adequately controlled.³³ The anesthesiologist must safely share the patient's airway with the surgeon, and must be prepared to skillfully and confidently switch from one ventilation technique to another during the case if needed or dictated by surgery. In most surgical procedures, the patient's airway is shared with the surgeon, and immediate access to the airway is difficult or impossible because the operating room (OR) table is turned 90 or 180 degrees away from the anesthesiologist. The ETT must be secured diligently to prevent accidental extubation under the surgical drapes or withdrawal of the ETT into the larynx, resulting in a sudden air leak or possible compression of the anterior branch of the recurrent laryngeal nerve by the ETT cuff.^{34,35} Although advanced airway management techniques can be highly successful when direct laryngoscopy fails, the patient's unfavorable anatomy may not be modifiable for the surgical exposure, which requires the use of the largest operating laryngoscope and placement of the patient's head in the Boyce-Jackson position using a combination of cervical flexion and atlantooccipital extension.^{36,37} If suspension laryngoscopy fails or if the location of the lesion is not easily accessible, it can be performed, to the extent microlaryngeal surgery permits, with the help of the flexible fiberoptic bronchoscope (FFB) inserted through the laryngeal mask airway (LMA).^{38,39,40} The intubating laryngeal mask airway (iLMA) offers certain advantages, such as a rigid, wide metal tube that can accommodate a large-diameter FFB, optimal alignment of the iLMA aperture with the glottic opening, diminished hemodynamic responses compared with suspension laryngoscopy, and superior ventilation capabilities.⁴¹⁻⁴⁴ The iLMA is associated with an outstanding success rate for blind endotracheal intubation in patients with difficult airways. Unfortunately, the manufacturer-supplied iLMA ETTs are too big for most microlaryngeal surgery. An ETT with a smaller inner diameter (ID) (e.g., 5.0-mm ID microlaryngeal tracheal [MLT] tube) is

typically required to maximize the surgical view. Placement of MLT tubes through the iLMA can be achieved with the help of a small-diameter FFB; however, passage of the ETT through the laryngeal inlet into the trachea is blind. Blind advancement of the ETT may cause inadvertent laryngeal trauma and core out pedunculated supraglottic or glottic tumors, nodules, or cysts.⁴⁵ When the FFB route (with or without the use of a supralaryngeal airway device) is chosen for endotracheal intubation, it is advantageous to closely match the outer diameter (OD) of the scope with the ID of the ETT to minimize the risk of complications associated with blind ETT advancement. Use of optical stylets (e.g., Bonfils, Shikani, Clarus Video System) may also be beneficial in that regard, because the ETT will follow the trajectory of the stylet navigated under direct vision through the vocal cords. However, most of the available adult-size stylets require the use of an ETT with a minimum ID of 5.5 to 6.0 mm.

Tonsillectomy

For a patient with a bleeding oropharynx the anesthesiologist should follow the difficult airway guidelines developed by the American Society of Anesthesiologists (ASA). However, these guidelines or other available new or old modalities do not specifically address the management of a bleeding airway.⁴⁶ Furthermore, the risk of aspiration from bleeding is an added challenge that makes it very difficult to secure the airway for surgery. In addition, hemodynamic instability and hypoxia as a result of bleeding and inability to secure the airway can be further compromised with a prolonged or failed intubation.⁴⁷ Postoperative hemorrhage is the most serious complication of tonsillectomy. The common time for postoperative bleeding varies from the first 6 hours to 7 to 8 days postoperatively.⁴⁸ However, bleeding has been reported up to 6 months after tonsillectomy. Most of the bleeding originates from the tonsillar fossa and often requires surgical exploration and hemostasis. Bleeding is usually sudden and occurs most often when the "scab" falls off the tonsil area 7 to 10 days after the surgery. These patients are considered as having a full stomach because constant bleeding results in patients swallowing large amounts of blood. Severe blood loss and a compromised airway are the 2 main reasons for morbidity and mortality of these patients.⁴⁹



Aspiration of foreign bodies

Aspiration of foreign bodies by children is a common problem around the world. Asphyxiation from inhaled foreign bodies is a leading cause of accidental death among children younger than 4 years. The preoperative assessment should determine where the aspirated foreign body has lodged, what was aspirated, and when the aspiration occurred. If the foreign body is located in the trachea, the child is at risk for complete airway obstruction and should be taken urgently to the operating room. Conversely, the risk of complete airway obstruction is less if the object is firmly lodged beyond the carina. It is important to determine the type of foreign body: Organic materials can absorb fluid and swell, oils from nuts cause localized inflammation, and sharp objects can pierce the airway. The time since the aspiration should be established because airway edema, granulation tissue, and infection may make retrieval more difficult with delayed

presentations.⁵⁰ Major iatrogenic complications were specified in 21 studies with 9437 children with aspirated foreign bodies. These complications included laryngeal edema or bronchospasm, pneumothorax, pneumomediastinum, cardiac arrest, tracheal or bronchial laceration, and hypoxic brain damage. These major complications occurred in 91 of these 9437 children (0.96%). Of the 11 cardiac arrests that were reported, 1 occurred after induction of anesthesia in a child who was hypoxic on admission, 5 occurred during bronchoscopy because of hypoxia (3) or bleeding (2), and the remaining 5 were not specified. Twenty-five deaths occurred in the 5 largest series with 5927 children (0.42%).⁵¹⁻⁵⁵ In a study conducted by Marinov et al. the incidence of major complications were 30.83% for tracheal or bronchial laceration, 15.83% for the bronchospasm and 7.5% for the laryngospasm. The reason of this high incidence of major complications is that most of the foreign bodies stayed in airways more than 10 days.⁵⁶

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Applications of acoustic pharyngometry in screening of the sleep-disordered breathing

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Abstract

INTRODUCTION: Acoustic pharyngometry is an inexpensive, quick, non-invasive, and easily repeatable method for localizing the upper airway obstruction in sleep-related breathing disorders.

AIM: The purpose of this study was to describe the general characteristics of the method of acoustic pharyngometry and to illustrate its differential-diagnostic role concerning the extent of the pharyngeal dysfunction for the first time in Bulgaria.

MATERIALS AND METHODS: Between April 1, 2019 and December 31, 2019, a total of 400 adult subjects, 272 males and 128 females, at a mean age of 50.8 ± 14.1 years from the city of Varna underwent screening examinations for OSA and snoring by using acoustic pharyngometry with Eccovision® acoustic pharyngometer. The acoustic pharyngometric findings of healthy subjects and patients with pharyngeal dysfunction were illustrated and discussed.

RESULTS: There were considerable differences between the values of the pharyngeal volume, mean and minimal cross-sectional areas and minimal distance in healthy subjects and patients with slightly expressed and severe pharyngeal dysfunction causing sleep-related breathing disorders.

CONCLUSION: The detection of these differences in terms of the main acoustic pharyngometric parameters between normal subjects and patients with pharyngeal dysfunction proves that a much broader acoustic pharyngometry application for the screening and early diagnosis of these socially significant disturbances in Bulgaria is undoubtedly beneficial.

Keywords: acoustic pharyngometry, pharyngeal dysfunction, pharyngeal volume, cross-sectional area, sleep-disordered breathing

Introduction

In recent years, evidence accumulates that acoustic pharyngometry is an inexpensive, quick, non-invasive, and easily repeatable method for locating the upper airway obstruction in sleep-related breathing disorders. The acoustic pharyngometry evaluates the static airway during the waking state when there is neuromuscular activation, but disregards dynamic and sleep state changes (1). It demonstrates a significant difference in upper airway cross-sectional area measurements in individuals with and without obstructive sleep apnea (OSA) which proves its great potential in OSA screening (2). The accuracy and reproducibility of acoustic rhinometry and acoustic pharyngometry for tridimensional assessment of airway caliber in various clinical situations are comparable to computerized tomography and magnetic resonance imaging (3).

The acoustic pharyngometry does not involve exposure to radiation, ensures a real-time display of the upper airway and assesses quantitatively the entire airway simultaneously and rapidly. However, this technique requires certain cooperation from the subject, is difficult to perform during sleep, and does not inform about the nasopharynx. Because polysomnography is not a popular screening tool for OSA worldwide yet, the acoustic pharyngometry is needed to screen the patients by localizing the possible narrowing area and predicting the sleep-disordered breathing at the initial patient's

visit. The acoustic pharyngometry can't replace polysomnography in OSA evaluation as it does not assess OSA severity. Being a reliable screening tool, this new method helps primary physician making the decision which patients should be referred to specialized sleep centres for further evaluation and treatment of OSA (4).

General characteristics of acoustic pharyngometry

The acoustic pharyngometry assesses the geometry of the oropharyngeal cavity using a reflected acoustic signal (filtered click) emitted from a device and sent into the oropharynx (5). This principle is based on the relation: $Z=rC/A$ where: Z is impedance (resistance), r is gas density traversed by the acoustic wave, C is the wave velocity, and A is tube diameter (5). If r is a constant and C is equal to 0, the impedance is inversely proportional to tube cross-section: $A=1/Z$.

The amplitude and frequency of reflected waves depend on the airway area, while the time taken for the reflected wave to return is a function of distance. Therefore the relation 'pressure/time' is changed into 'cross-sectional area/distance' (5). Reductions in the anatomical space and particularly in the diameter produce changes in the intensity of the reflected wave and in the time taken for the reflected wave to return from a given anatomical structure to the microphone (6).

The main components of the acoustic pharyngometry parameters are illustrated in Fig. 1. Here belong the basic characteristics of the cross-sectional

area of the pharynx: the specific waves mentioned above, the volume of the pharyngeal space, the mean and minimal cross-sectional area, the single areas of the oropharyngeal junction, epiglottis and glottis, the minimal distance as well as the distances of the oral cavity, oropharynx and hypopharynx.

Our aim was to compare the findings detected by using acoustic pharyngometry between healthy adults and adults with sleep-disordered breathing within the recent prevention programme in the city of Varna.

Materials and methods

Between April 1, 2019 and December 31, 2019, a total of 400 adult subjects, 272 males and 128 females, at a mean age of 50.8 ± 14.1 years from the city of Varna participated in the screening examinations for sleep-disordered breathing kindly sponsored by the Sleep Apnea Prevention Programme of the Municipality of Varna. Acoustic pharyngometry with Eccovision® acoustic pharyngometer (HOOD Laboratories, Boston, MA, USA) in sitting position was used for the first time in Bulgaria in the Division of Otorhinolaryngology, St. Anna Hospital of Varna. Several other appropriate diagnostic methods such as clinical inspection, anterior rhinoscopy, pharyngoscopy, indirect laryngoscopy, and acoustic rhinometry were applied by a highly qualified team of otorhinolaryngologists. All the participants filled-in an Epworth Sleepiness Scale questionnaire and reported their concerns related to sleep-related breathing disorders.

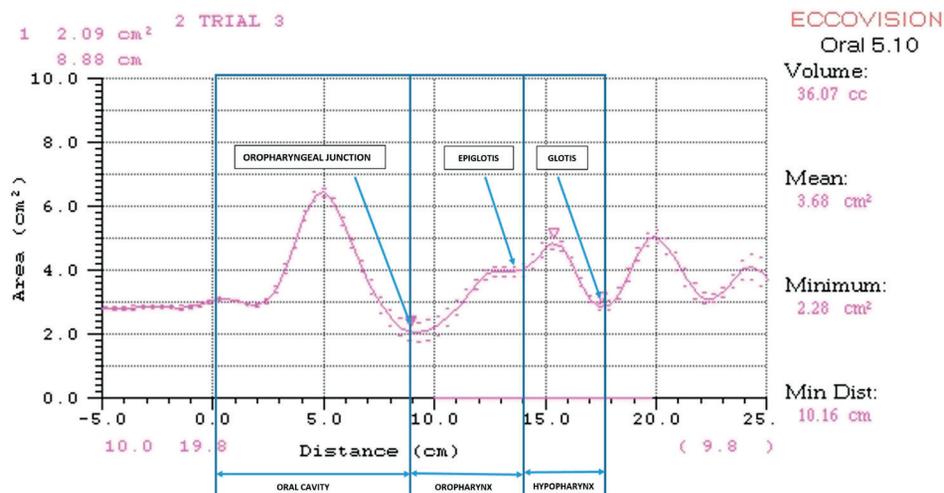


Figure 1. Schematic presentation of the acoustic pharyngometry data



Results

In the present study, we illustrated the normal acoustic pharyngometry patterns in adults without any sleep-disordered breathing in comparison with pathological acoustic pharyngometry findings in patients with a slightly expressed and severe pharyngeal dysfunction.

The normal findings from the acoustic pharyngometry examinations in a 35-year old healthy man and a 27-year old healthy woman were displayed in Fig. 2 and Fig. 3.

The pathological acoustic pharyngometry findings in a 67-year old male patient suffering from arterial hypertension and type 2 diabetes mellitus and diagnosed with slightly expressed pharyngeal dysfunction

due to low soft palate, uvula elongation along with nasal septum deviation and chronic hypertrophic rhinitis were demonstrated in Fig. 4.

The pathological acoustic pharyngometry findings in a 47-year old female patient diagnosed with slightly expressed pharyngeal dysfunction due to low soft palate, uvula elongation along with nasal septum deviation and chronic hypertrophic rhinitis were demonstrated in Fig. 5.

The pathological acoustic pharyngometry findings in a 29-year old male patient suffering from arterial hypertension and diagnosed with severe pharyngeal dysfunction due to low soft palate, uvula elongation along with chronic hypertrophic rhinitis were demonstrated in Fig. 6.

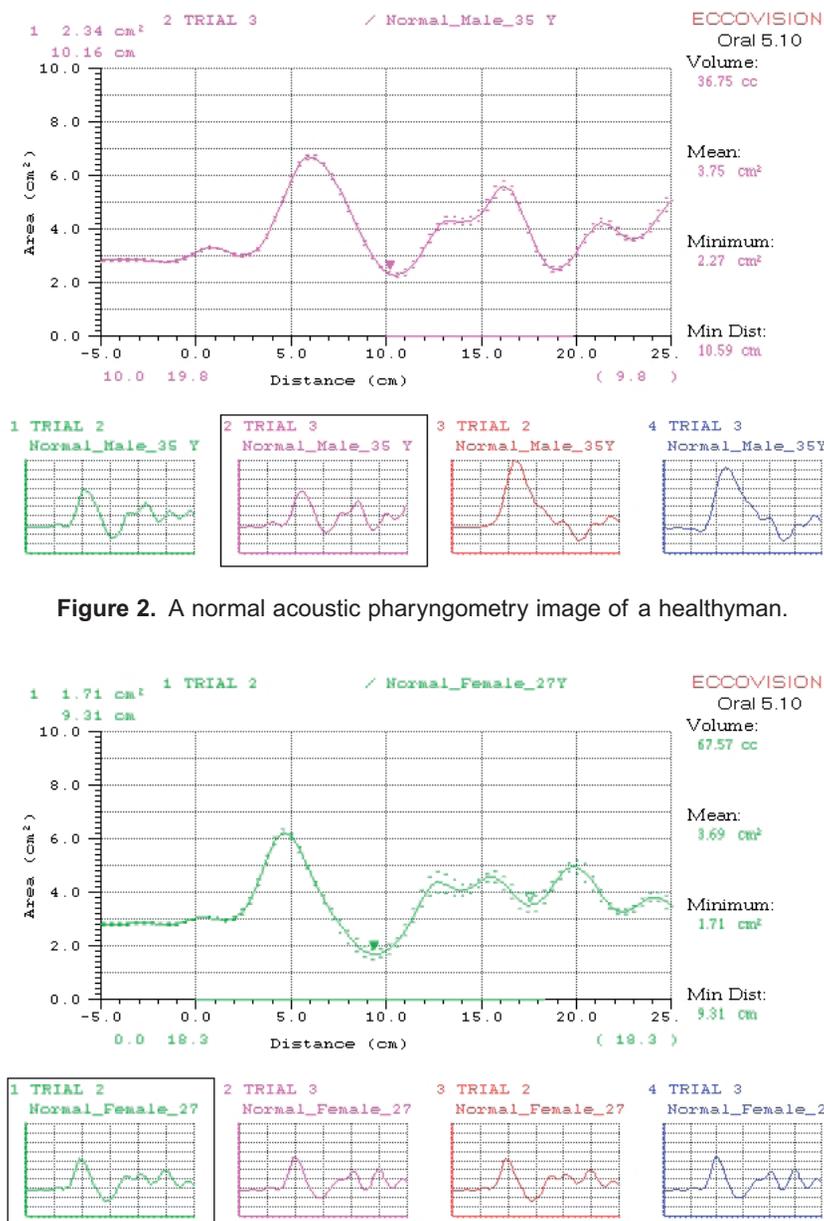


Figure 2. A normal acoustic pharyngometry image of a healthy man.

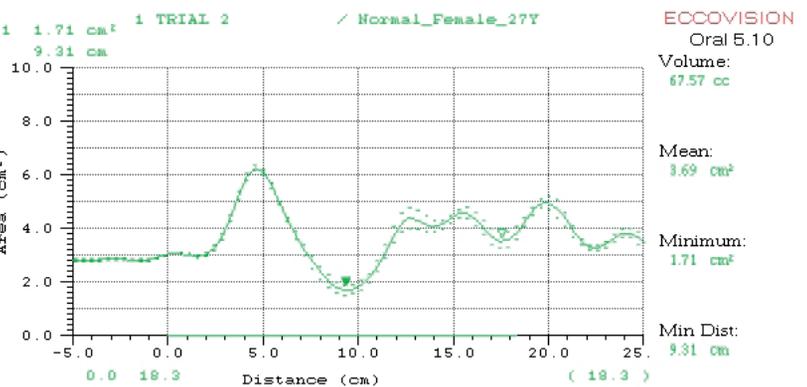


Figure 3. A normal acoustic pharyngometry image of a healthy woman.

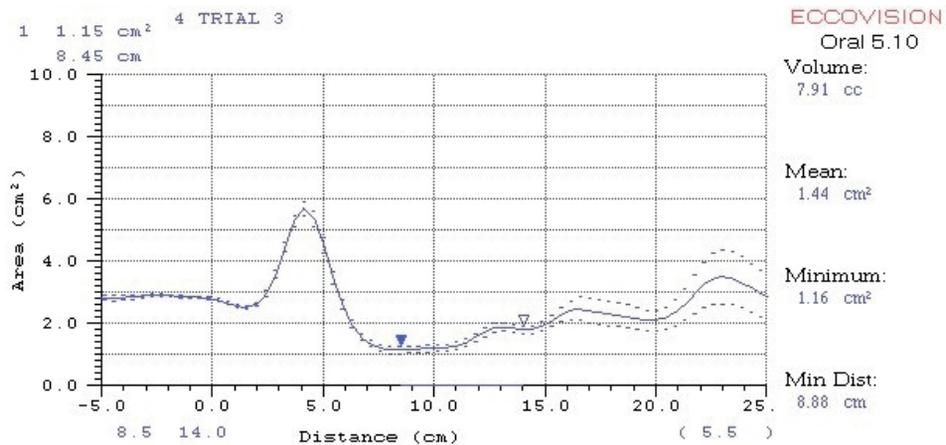


Figure 4. Acoustic pharyngometry changes in a male patient with slightly expressed pharyngeal dysfunction

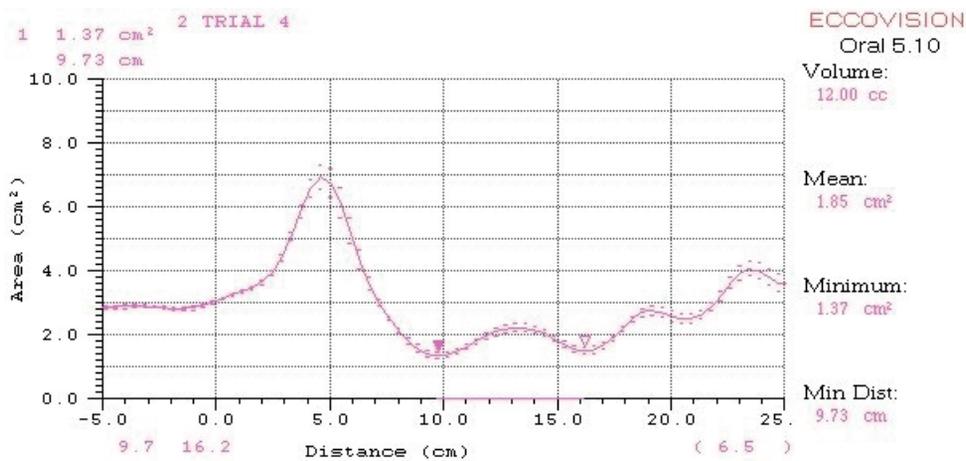


Figure 5. Acoustic pharyngometry changes in a female patient with slightly expressed pharyngeal dysfunction

The pathological acoustic pharyngometry findings in a 62-year old male patient suffering from arterial hypertension and diagnosed with severe pharyngeal dysfunction due to low soft palate, uvula elongation along with chronic hypertrophic rhinitis were demonstrated in Fig. 7.

Discussion

In the men with slight and severe pharyngeal dysfunction, there was a pharyngeal volume reduction towards the value in a healthy man by 4.65 times and 12.46 times, respectively. Concerning the mean and minimal cross-sectional areas, the corresponding figures were the following: by 2.60 times, 6.58 times, 1.96 times and 5.82 times, respectively.

In the women with slight and severe pharyngeal dysfunction, there was a pharyngeal volume reduction towards the value in a healthy woman by 5.63 times and 11.00 times, respectively. Concerning the mean and minimal cross-sectional areas, the corre-

sponding figures were the following: by 1.99 times, 3.73 times, 1.25 times and 3.56 times, respectively. These dramatic differences between the normal and pathological values of the three parameters confirmed the differential-diagnostic role of the acoustic pharyngometry concerning the extent of the pharyngeal dysfunction that underlay the sleep-disordered breathing.

The mean cross-sectional areas and airway volumes in any segments assessed by acoustic pharyngometry in 15 OSA patients are statistically significantly smaller in OSA patients than in 15 healthy controls ($p < 0.05$) (7). The minimal cross-sectional area of the upper airway at end-exhalation is measured in upright position and breathing through the mouth in 60 subjects, 35 males and 25 females at a mean age of 42 years (range, 21-81 years) (2). Their body mass index is 34 ± 8 kg/m², mean apnea-hypopnea index is 33 ± 30 events/hour, and mean Epworth Sleepiness Scale score is 11 ± 6 . In univariate logistic regression analysis, the minimal cross-

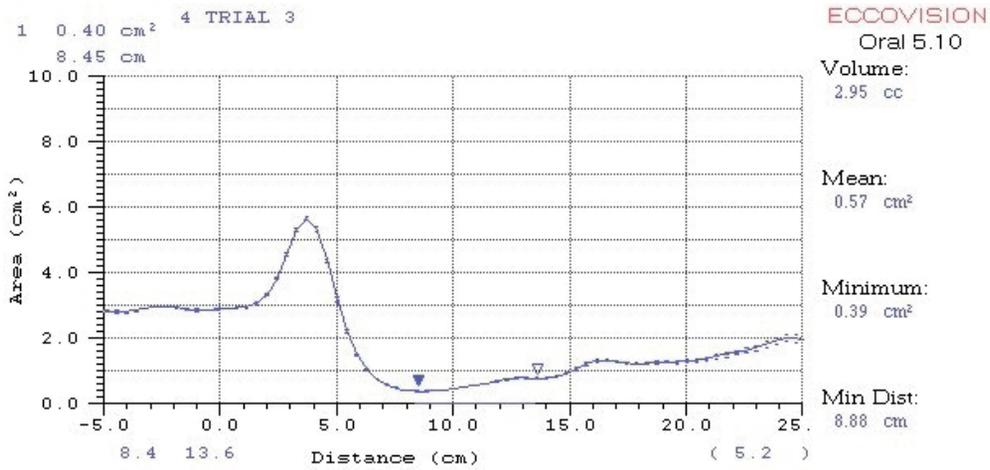


Figure 6. Acoustic pharyngometry changes in a male patient with severe pharyngeal dysfunction

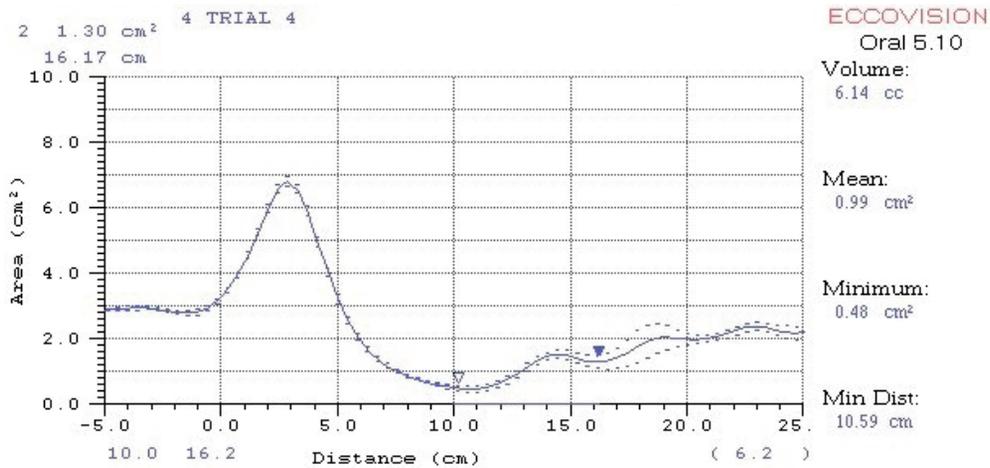


Figure 7. Acoustic pharyngometry changes in a female patient with severe pharyngeal dysfunction

sectional area is a significant predictor of mild to absent OSA (apnea-hypopnea index <15). A multivariate logistic regression model including the minimal cross-sectional area, age, gender, and neck circumference statistically significantly predicts the apnea-hypopnea index <15. The minimal cross-sectional area represents the only significant independent predictor ($p < 0.01$).

Among 576 subjects, 369 males and 207 females at a mean age of 57 years and with a mean body mass index of 30.3 kg/m^2 , there are 501 patients with OSA and 75 subjects without OSA (1). The mean upper airway cross-sectional area at functional residual capacity in sitting position is significantly smaller in OSA patients than in healthy controls (3.3 cm^2 versus 3.7 cm^2). When controlled for age, sex, body mass index and comorbidities, the odds ratio of OSA increases for every 1-cm^2 decrease of the mean upper airway cross-sectional area at functional residual capacity (odds ratio of 1.62; between 1.23 and 2.13 at 95% confidence interval).

A cut-off value of 3.75 cm^2 , the point with the best sum of sensitivity and specificity, has a sensitivity of 73% and a specificity of 46%.

Initially, 17 middle-aged, morbidly obese men have significantly lower pharyngeal cross-sectional areas at different levels of the pharynx than 20 nonobese male control subjects in the upright and supine position (8). After weight loss, both the mean pharyngeal cross-sectional area and the area at glottis level remain lower in obese than in nonobese subjects.

In 50 patients with severe obstructive sleep apnea-hypopnea syndrome (OSAHS), the distance of minimal cross-sectional area from the nostril is $2.06 \pm 0.12 \text{ cm}$, the pharyngeal cross-sectional area is $0.87 \pm 0.12 \text{ cm}^2$ and the pharyngeal cross-sectional volume is $9.24 \pm 2.31 \text{ cm}^3$ (9). Both pharyngeal cross-sectional area and volume are statistically significantly lower in patients than in control subjects ($p < 0.01$).

Among 350 normal volunteers, 271 males and 79

females, the examinations by acoustic pharyngometry demonstrate a mean pharyngeal area of $3.194 \pm 0.311 \text{ cm}^2$ in males and $2.814 \pm 0.331 \text{ cm}^2$ in females as well as a mean glottic area of $1.06 \pm 0.119 \text{ cm}^2$ in males and $0.936 \pm 0.108 \text{ cm}^2$ in females (6).

Overall and subgroup analyses in 138 OSAHS patients demonstrate that the minimal cross-sectional area of oropharyngeal lumen statistically significantly decreases ($p < 0.05$), whereas that of velopharyngeal lumen does not significantly change with mouth opening ($p > 0.05$) (10). The relative position of tongue to soft palate is the main factor influencing upon the velopharyngeal lumen changes with mouth opening.

In 145 women at a mean age of 42.9 ± 15.1 years, the pharyngeal area at the oropharyngeal junction negatively correlates with body mass index, waist, hip and sagittal abdominal diameter while the mean pharyngeal area does with body mass index and sagittal abdominal diameter in orthostatic position only (11).

Among 35 consecutive male and female patients with obstructive sleep apnea syndrome examined by means of acoustic pharyngometry, body mass index and dimensions of uvula breadth and free oropharynx are significantly related to apnea-hypopnea index (12). In snoring patients with OSA, the mean apnea-hypopnea index is 25.9 events/hour and

the mean pharyngeal area is 1.589 cm^2 while in snorers without OSA, this index is 4.0 events/hour and the mean pharyngeal area is 2.41 cm^2 ($p < 0.001$) (13). The repeatability of pharyngeal cross-sectional area measurements obtained by acoustic pharyngometry is compared between 20 adult normal volunteers, 16 men and four women at a mean age of 35.9 years, and ten adult snorers, nine men and one woman at a mean age of 36.4 years (14). In normal subjects, the mean pharyngeal cross-sectional area is 3.187 cm^2 in the first session, 3.239 cm^2 in the second session at the same-day, and 3.245 cm^2 in the third session after seven to ten days. In the snorers, the corresponding figures are the following: 2.244 cm^2 , 2.237 cm^2 , and 2.238 cm^2 .

Conclusion

Our initial results indicate considerable differences in terms of the main acoustic pharyngometric parameters between healthy subjects, on the one hand, and patients presenting with slightly expressed and particularly with severe pharyngeal dysfunction causing sleep-related breathing disorders, on the other hand. A much broader acoustic pharyngometry application for the screening and early diagnosis of these socially significant disturbances among adults and children in Bulgaria is undoubtedly beneficial and should be recommended.

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Hemodynamic complications during microlaryngeal surgery

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Abstract:

Introduction: Successful anesthetic management of microlaryngeal cases requires a high degree of cooperation with the surgeon, a reciprocal understanding of the potential problems, and adequate preparation on both sides to meet the anticipated challenges that may arise. The **Aim** of the study is to determine the hemodynamic complications during microlaryngeal surgery. **Materials and Methods:** A 5-year prospective cohort study of 200 patients who underwent microlaryngeal surgery in the Department of ENT Surgery; University Hospital "Queen Giovanna"– ISUL; Medical University–Sofia. All patients were monitored and recorded for: Systolic blood pressure (SBP), Diastolic blood pressure (DBP); heart rate (HR); continuous electrocardiography (ECG). The above parameters were recorded and analyzed at predetermined time intervals: 5-th minute before intubation, every 5 minutes after intubation and 5-th minute after extubation. **Results and discussion:** Mean systolic blood pressure of the patients during the operation is 147.33 mmHg, mean diastolic blood pressure is 93.5 mmHg and mean pulse rate is 57.64 beats per minute. 49% of the patients have arterial hypertension I grade during the operation, 28% of them are with isolated arterial hypertension and 23% are with normal blood pressure. 40% of the patients had pulse rate between 45-60 beats per minute during putting on the tube of Kleinsasser, 29% of them had pulse rate >60 beats per minute during putting on the tube of Kleinsasser and 31% had pulse rate <45 beats per minute during putting on the tube of Kleinsasser. **Conclusion:** Microlaryngeal surgery is specific kind of surgery which is characterized by hypertensive hemodynamic. There is a risk of severe bradycardia after putting on the tube of Kleinsasser which can cause hemodynamic instability and even cardiac arrest if not corrected immediately.

Key words: microlaryngeal surgery, hemodynamic complications, hypertensive hemodynamic, bradycardia

Introduction

Successful anesthetic management of microlaryngeal cases requires a high degree of cooperation with the surgeon, a reciprocal understanding of the potential problems, and adequate preparation on both sides to meet the anticipated challenges that may arise.^{1,2} Thorough appreciation by the anesthesiologist of the complexity of the upper airway anatomy, the pathologic process involved, and all steps of the surgical procedure is necessary for devising a rational anesthetic plan and maintaining a good working relationship with the surgeon.³ The expert ability to safely share the patient's airway with the surgeon, in conjunction with an intimate knowledge of possible immediate intraoperative and early postoperative complications of laryngeal surgery, greatly contributes to safe patient management in the perioperative period. Microlaryngeal surgery encompasses a wide range of laryngeal procedures that can be organized in two broad categories: phonosurgery (i.e., benign and malignant vocal cord lesions, laser laryngeal surgery, and vocal cord augmentation) and laryngeal framework surgery (i.e., vocal cord paralysis and motion disorders, scarring, stenosis of the glottic, subglottic, and tracheal areas, and laryngeal trauma). Patients presenting for microlaryngeal surgery may have a variety of comorbidities contributing to their voice symptoms and affecting anesthetic management. Changes in voice quality can be exag-

generated by inadequate airflow production (e.g., chronic obstructive pulmonary disease [COPD]) or vocal fatigue caused by neuromuscular disorders (e.g., myasthenia gravis, muscular dystrophy, Parkinson's disease).⁴ Various rheumatologic and musculoskeletal ailments can alter posture, impairing voice quality, and endocrine disorders, such as hypothyroidism, can cause dysphonia as a result of swelling in the Reinke's space (i.e., superficial lamina propria) of the vocal cords. Many patients presenting for laryngeal surgery have a long history of heavy smoking and drinking.⁵ Many of them are elderly and have cardiovascular disease. Appropriate diagnostic tests are indicated for them as part of the preoperative work-up. The pulmonary status of COPD patients should be optimized to decrease airway reactivity and the possibility of postoperative pulmonary complications.

Material and methods

We obtain approval from local ethical review board and informed consent from all study participants. A 5-year prospective cohort study of 200 patients who underwent microlaryngeal surgery in the Department of ENT Surgery; University Hospital "Queen Giovanna"- ISUL; Medical University-Sofia. In all patients we used quamatel 20 mg for premedication. For induction in general anesthesia we used propofol 2.5 mg . kg⁻¹ and succinylcholine 1 mg . kg⁻¹ as muscle relaxant. Endotracheal intubation was performed by endotracheal tube №6.0 or №6.5 from the anesthesiologist and mechanical ventilation was performed. For maintenance of general anesthesia we used sevoflurane inspiratory concentration of 2.5 vol. % and fentanyl 4-5 µg . kg⁻¹. for pain relief.

All patients were monitored and recorded for: Systolic blood pressure (SBP), Diastolic blood pressure (DBP); heart rate (HR); continuous electrocardiography (ECG). The above parameters were recorded and analyzed at predetermined time intervals: 5-th minute before intubation, every 5 minutes after intubation and 5-th minute after extubation. Descriptive statistical analysis of the results was performed.

European Society of Hypertension (ESH) and the European Society of Cardiology (ESC) classification for arterial hypertension¹⁷ (fig.1):

Results

The mean age of the patients is 59.03 years. According to anesthesia risk assessment 6% of the patients are with ASA 1 class, 24% of them are with ASA 2 class, 68% are with ASA 3 class and 2% are with ASA 4 class.

We found that 86% of the patients were men and 14% were women (fig.2)

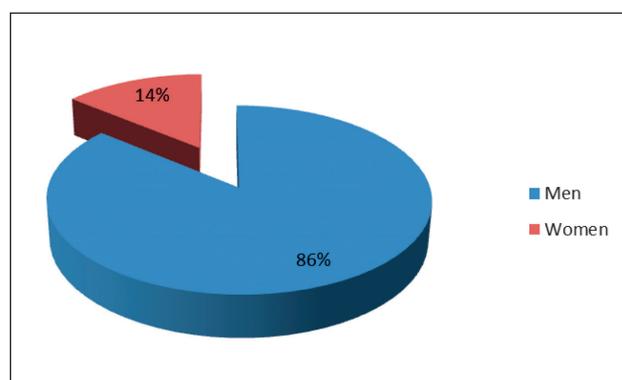


Figure 2. Distribution according to gender.

Category	Systolic blood pressure		Diastolic blood pressure
OPTIMAL	<120 mmHg	and	<80 mmHg
Normal	120-129 mmHg	and/or	80-84 mmHg
High normal	130-139 mmHg	and/or	85-89 mmHg
Arterial hypertension I	140-159 mmHg	and/or	90-99 mmHg
Arterial hypertension II	160-179 mmHg	and/or	100-109 mmHg
Arterial hypertension III	≥180 mmHg	and/or	≥110 mmHg
Isolated systolic hypertension	≥140 mmHg	and	<90 mmHg

Figure 1. Classification for arterial hypertension.



Mean systolic blood pressure of the patients during the operation is 147.33 mmHg, mean diastolic blood pressure is 93.5 mmHg and mean pulse rate is 57.64 beats per minute (fig.3).

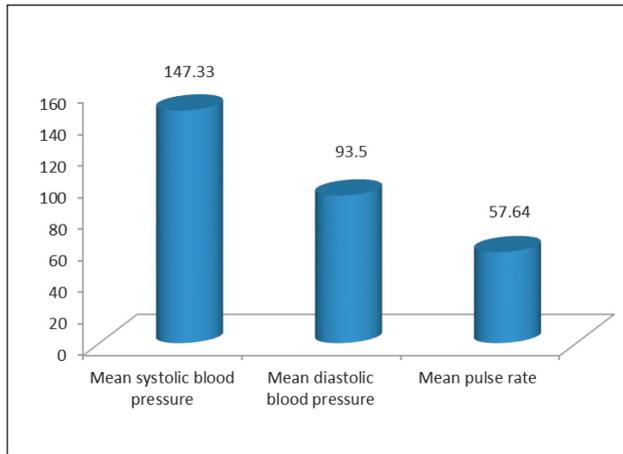


Figure 3. Mean parameters of hemodynamic.

49% of the patients have arterial hypertension I grade during the operation, 28% of them are with isolated arterial hypertension and 23% are with normal blood pressure (fig.4).

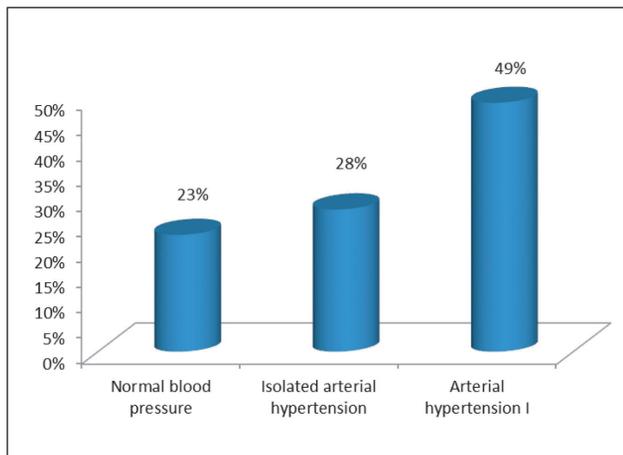


Figure 4. Most of the patient are with hypertensive hemodynamic.

40% of the patients had pulse rate between 45-60 beats per minute during putting on the tube of Kleinsasser, 29% of them had pulse rate >60 beats per minute during putting on the tube of Kleinsasser and 31% had pulse rate <45 beats per minute during putting on the tube of Kleinsasser (fig.5).

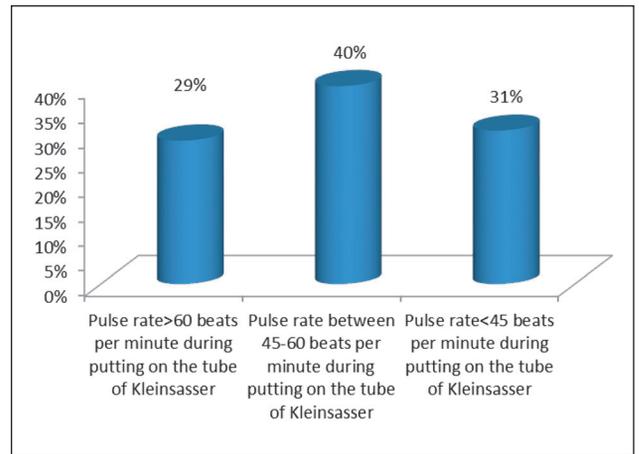


Figure 5. Bradycardia after putting on the tube of Kleinsasser.

Discussion

The essential requirements for precision microlaryngeal surgery and optimal preservation of function include a clear and still surgical field, absence of patient movement, and allocation of sufficient time to carefully complete the procedure in an unhurried manner. The patient’s airway must be protected from blood, debris, and irrigation fluid and ventilation must be adequately controlled.⁶

The anesthesiologist must safely share the patient’s airway with the surgeon, and must be prepared to skillfully and confidently switch from one ventilation technique to another during the case if needed or dictated by surgery.

Performance of conventional and operative direct laryngoscopy, supraglottic tissue distention, and laryngeal stimulation elicit intense cardiovascular responses, resulting in tachycardia, arterial and pulmonary hypertension, and arrhythmias.⁷⁻⁹ Although these responses are usually short lived, myocardial ischemia and compromise of cerebral circulation may occur in high-risk patients, resulting in adverse outcomes.¹⁰⁻¹² Anesthetic technique should ensure a stable plane of anesthesia, nonstimulating emergence from anesthesia, a rapid return of consciousness, and protective airway reflexes, and it should facilitate quick discharge of patients, because most of these surgical procedures are done on an outpatient basis.

In our study the mean age of the patients is 59.03 years which means that these are people in active working age. This kind of operation gives them chance to keep their ability to speak and work normally. On the other hand in this age group the risk of accompanying cardiovascular and respiratory

disease is higher. In this case the risk of hemodynamic complications will be higher. Most of the patients are males 86%. This may be connected with higher incidence of accompanying risk factors like smoking in male group, which is common for Bulgarian population.¹³⁻¹⁶ The anesthesia risk assessment shows that most of the patients are in ASA III class 68%. This means higher risk of accompanying cardiovascular disease and higher risk of hemodynamic complications. 49% of the patients have arterial hypertension I grade and 28% of them are with isolated arterial hypertension during operation despite of higher dosage of opioids and propofol that we used. This may be caused by the strong pain stimulus from the tube of Kleinsasser during the operation. 40% of the patients had pulse rate between 45-60 beats per minute and 31% of them had pulse rate < 45 beats per minute

during putting on the tube of Kleinsasser. This is very dangerous reflex reaction of the heart, which we believe is caused by parasympathetic nervous system, because in some of the cases the pulse rate is corrected after administration of atropine. In other cases when the bradycardia is very severe administration of atropine cannot help so the tube of Kleinsasser must be removed, because there is a risk of cardiac arrest. After removing the tube and administration of atropine the pulse rate is normalized.

Conclusion

Micro-laryngeal surgery is specific kind of surgery which is characterized by hypertensive hemodynamic. There is a risk of severe bradycardia after putting on the tube of Kleinsasser which can cause hemodynamic instability and even cardiac arrest if not corrected immediately.

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Methods for assessment of vocal characteristics in dental treatment

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Abstract:

A phonetically correct articulation after teeth treatment and prosthetics is an important decision for a socially comfortable, meaningful, and high quality life. Dental treatment and prosthetics contribute to the preservation of normal speech ability, beyond just contributing to the preservation and re-establishing of the masticatory and aesthetic functions. While the last two roles of dental treatment and prosthetics are well understood, the phonetic recovering is still poorly comprehended and rather unvalued. The purpose of this article is to review the methods for assessing voice characteristics in dental treatment.

Key words: vocal characteristics, dental treatment, methods, assessment

Introduction

Proper knowledge of phonetics enables dentists to fabricate a prosthesis, which encounters the key objective of oral rehabilitation. (19) Voice quality (VQ) can be broadly defined as a combination of laryngeal and supralaryngeal characteristics in someone's voice, which leads to a long-term effect on perception and makes that voice recognizably different from the others. (16) Methodologically, assessment of VQ can be approached from an articulatory, acoustic or perceptual point of view. The use of phonography to distinguish vocal changes from normal voices has been documented in the literature (14, 18, 24) to list changes in the voice due to fatigue and to assess changes in voice quality after voice therapy (13) or vocal singing training (29, 30). In particular, with regard to the standardization of reference values, there are population studies in Thailand (4), Germany (9) and Finland. (17)

Research also shows that there is a link between vocal tract dimensions and voice quality characteristics (6, 23); between voice disorders and oral muscle disorders (8, 25), as well as a relationship between the severity of temporomandibular disorders and vocal quality. (28)

Although literature demonstrates a link between the characteristics of the stomatognathic system and phonator function, no studies have been found to analyze vocal parameters, taking into account facial type and balanced occlusal condition importance.

Aim: To review the methods for assessing voice characteristics in dental treatment.

Material and methods

The following research databases were used for the study: MEDLINE, Scopus, EMBASE and PubMed from January 2001 to August 2020, focusing on finding methods for assessing changes in voice characteristics in the field of prosthetic dental medicine.

Results and discussion

A phonetically correct articulation after teeth treatment and prosthesis plays an important role for a socially comfortable, meaningful, and high quality life. Dental treatment and prosthetics contribute to the preservation of the normal speech ability, beyond contributing just to the preservation and re-establishing of the masticatory and aesthetic functions. While the last two roles of dental treatment and prosthetics are well understood, the phonetic recovering is still poorly comprehended and rather unvalued.

Phonography is a measure used to record all the capabilities of the larynx in relation to the frequency and intensity of sound, as it covers the highest and lowest frequencies and intensities that the human larynx is capable of producing. (26)

Auditory-Perceptual Evaluation of Voice. The term perceptual evaluation is recommended by the Voice Committee of the International Association of Logopedics and Phoniatrics (IALP) and entails a comparison between the characteristics of the voice of the speaker and those that are considered normal or typical for the listener. (7) Since we are focused on the audible characteristics of the voice, we should point out that many authors expanded this term to auditory-perceptual evaluation. Clinicians and researchers believe that this form of perceptual evaluation is an essential component of voice assessment, diagnosis, and treatment. (5) The most commonly used perceptual evaluation systems have many similarities in terms of the voice features evaluated and definitions of those features. The GRBAS (Grade, Roughness, Breathiness, Asthenia and Strain) (12), CAPE-V (Consensus Auditory-Perceptual Evaluation of Voice) (1), Stockholm Voice Evaluation Approach (11) and the Perceptual Voice Profile (22), for instance, all incorporate the perceptual features.

Perceptual assessment. Speech-language patholo-

gists are increasingly being encouraged to use the new Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) for clinical assessment of voice quality. It provides a standardized framework and procedures for perceptual evaluation of abnormal voice quality that include prescribed speech materials and visual analog scaling of a closed set of perceptual vocal attributes: overall severity of dysphonia, roughness, breathiness, straining, pitch and loudness. (1)

Acoustics assessment. Validity and reliability of acoustic measures currently used in the clinic to objectively assess voice quality (e.g., jitter, shimmer, and noise-to-harmonics ratio) are inherently limited by a reliance on the accurate determination of fundamental frequency (F0), and these measures have been further restricted to the analysis of sustained vowels. (36) One set of approaches is based on cepstral analysis (a spectrum-type method), which is inherently attractive since the cepstrum can be computed for any segment of speech and not just for steady vowel-like sounds. (2, 20, 21)

The second set of recently described acoustic voice measures is based on nonlinear dynamics or chaos analysis (35), which are much more robust with respect to analyzing atypical signals (e.g., aperiodic signals from pathological voices) than the measures currently used for clinical voice assessment.

Aerodynamic assessment. Since the early 1980s, clinical assessment of aerodynamic voice parameters has typically involved extracting assessments of average subglottal air pressures and glottal air flow rates from non-invasive measures of intraoral air pressures and oral air flow rates during the controlled (constant pitch and loudness) repetition of simple syllable strings. It was subsequently shown that important additional information about glottal phonatory status (including the presence of pathology) could be obtained from estimates of the minimum air pressures required to initiate the softest possible voice production—the phonation threshold pressure. Further work using mathematical and physical laryngeal models has further demonstrated that phonation threshold pressure is sensitive to vocal fold thinning, viscous shear properties of the tissue, and vocal tract inertance. (3)

Yan and colleagues have used Nyquist plots, nonlinear processing of both the glottal area extracted from high-speed imaging and from the acoustic signal, to discriminate normal versus pathological voices. (33, 34) The quantification of glottal vari-



ations at a high temporal resolution has also laid the ground work for more sophisticated computer models that can simulate asymmetric vocal fold tissue motion observed in excised larynx preparations (31) and live human subjects. (27, 32)

Hamlet, Geoffrey and Bartlett (10) have analyzed the changes of voice characteristics due to dental prostheses by fitting subjects with experimental dental appliances that artificially lower and retract the alveolar-palatal contour. These authors analyzed acoustically and perceptually the subjects speaking without the prosthesis and with the prosthesis, in the first day and after a week

of prosthesis wearing. They determined that the intelligibility of speech was significantly decreased by prosthesis wearing, especially before the subject had time to adapt to the new condition. Also, these authors found significant sibilant and vowel changes produced due to prosthesis wearing.

Laine (15) analyzed the associations between articulatory disorders and occlusal anomalies in young adults. The main findings are that several types of malocclusions, like mesial molar occlusion, mandibular overjet and lateral crossbite are associated with incorrect articulation of some medio-alveolar consonants, especially /s/. Laine argues that the analyzed occlusal anomalies affect speech primarily by changing the position of the tongue and hyoid bone.

While progresses have been made in the analysis of

the speech quality lowering and in understanding some of the involved mechanisms, the domain is still in its infancy. The main needs are for relating acoustic analysis to the characteristics of the prostheses and to their design.

Correlation of the vocal signal changes with the characteristics of the prosthesis and the specific types of errors in the prosthetic act would be an essential achievement in the way of improving the outcome of the prosthetic act.

Conclusion

We defined several objectives and specific study methods and means for a new field that we called phonetic dentistry. Several plausible mechanisms that affect the phonetic quality of the prosthetic result have been derived based on articulatory mechanisms and on morphologic factors resulting from dentition deficiencies. The relationships between the articulatory facts and the acoustic features have been emphasized and discussed in order to derive acoustic methods and acoustic quantitative indices for assessing the dentition defects.

Some of the correlations between the acoustic features and the dentition deficiencies are already documented in the literature, but much remains to be done for establishing a corpus of knowledge and tools that could constitute the solid foundation of the emerging domain we call phonetic dentistry or gnathophonetics.

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Application of targeted next-generation sequencing in SNHL patients

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Abstract

Sensorineural hearing loss, SNHL, is a complex disease impacted by the interaction of a multitude of endogenous and exogenous factors. Genetic and age-related changes predetermine the state of hearing. Genetic factors and factors affecting development play a key role in the occurrence of SNHL. The goal of this study is to research functioning of the hearing organ in patients with a family history of reduced hearing, to analyse the causes of deafness, to provide an identification strategy of genetic causes and to refer the patient to the most effective treatment.

The study included 192 patients: 178 of them with sensorineural hearing loss and 14 subjects with normal hearing, relatives of the study patients with impaired hearing, of who biological material was also taken to look for mutations associated with hearing. Screening of the patients participating in the study started with searching for mutations in Cx26 (GJB2), Cx30 (GJB6) and Cx31 (GJB3). At the next stage, five families were chosen from the patients without a mutation in the screened genes. They underwent targeted next-generation sequencing in search of rare genes causing SNHL. Clinical, audiological and genetic methods were used in conducting the study.

In 31.77% of the cases the reason for deafness was identified (a genetic reason was found) of which 29.69% cases (n= 57) were mutations in Cx26 (in a homozygous state), corresponding with data published in world's literature on mutations in Cx26 of between 18 to 40% in cases of patients with SNHL. In the remaining 2.08% of the patients, rare mutations responsible for the deafness were identified.

Introduction

Nowadays, there are increased opportunities for diagnostic assessment and treatment of SNHL. In most of the cases, hearing loss has a multifactorial genesis, the causes being both genetic and resulting from environmental factors. A gene mutation can lead to hearing loss. In these cases hearing loss is a monogenetic disorder with autosomal dominant, autosomal recessive, X-linked or mitochondrial inheritance.

Hearing loss can be classified as genetic or non-genetic, depending on the presence of coding mutations; depending on the time of occurrence it can be prelingual or postlingual; and syndromic (a combination of hearing loss and one or more other specific anomalies) or non-syndromic.

Dozens of genetic loci have been identified as the reason for syndromic and non-syndromic hearing loss with various models of inheritance (autosomal dominant, autosomal recessive, X-linked, mitochondrial). The prelingual sensorineural hearing loss is estimated at 1 in 500 children in developed countries as in 80% of the cases hearing loss is genetic. About 80% of the affected have non-syndromic hearing loss while the remaining 20% - syndromic. In 80% of the cases the non-syndromic hearing loss is inherited in a recessive pattern, in 19% the inheritance is autosomal dominant and in less than 1% the modes of inheritance are mitochondrial, miRNA and X-linked [1].

The main goal of our study is to provide an identification strategy of the genetic causes and to refer

the patient to the most effective treatment. For the purposes of implementing that goal, a genetic screening algorithm was developed (Figure 1).

During the screening of the study participants, a mutation in GJB2, the gene encoding protein connexin 26 was identified, as the frequency was 43.75%. In 29.69% of the cases, it involved mutant alleles in a homozygous state, while in 14.06% of the cases mutations were in a heterozygous state.

Mutations in the GJB2 gene are the most frequent cause of monogenic hearing loss, responsible for about half of all the cases of autosomal recessive prelingual hearing loss. It is inherited in an autosomal recessive pattern, which means that two copies of the GJB2 gene have to be changed in each cell to cause a hearing impairment. Mutations in this gene

alter the gap junctions, which causes disruption in the levels of potassium ions in the inner ear.

The screening continued with searching for mutations in the genes GJB6 and GJB3, encoding proteins connexin 30 and connexin 31 respectively. Among the 192 study patients, mutation of the gene encoding Cx30 was not found, which is not unusual in view of its low frequency in the population – 0.65% [2]. Mutations in Cx31 were not identified either.

As a next step in diagnosing hereditary hearing loss, we introduced the application of targeted next-generation sequencing [Figure 1]. We selected families where several members of different generations were affected by SNHL and our aim was to identify rare mutations in genes encoding hearing.

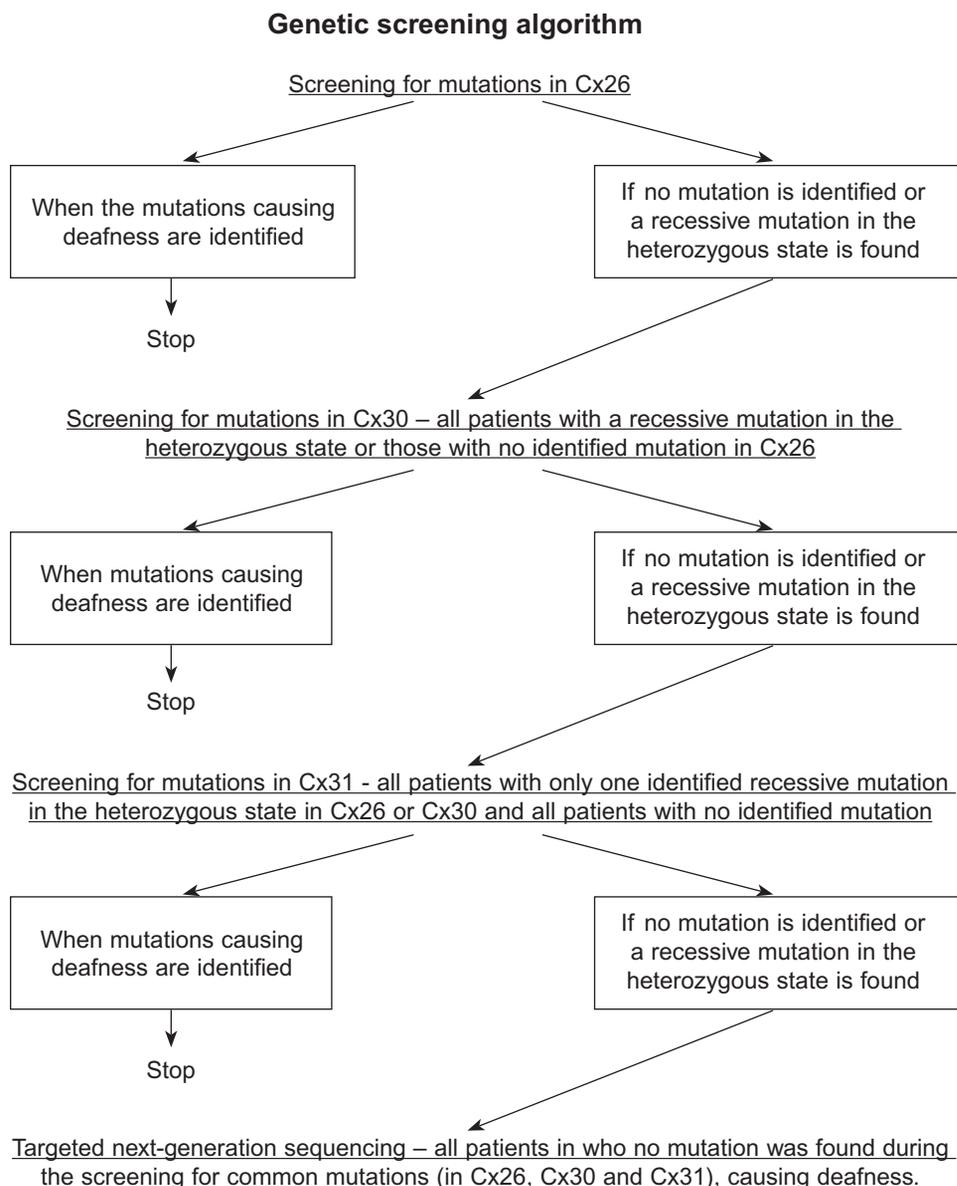


Figure 1. Genetic screening algorithm.



Due to the substantial genetic heterogeneity of deafness, the clinical application of genetic information is still leading to a number of difficulties. It is known that more than 80 genes are related to the non-syndromic hereditary hearing loss. Progress in targeted exome sequencing of selected genes, using massively parallel DNA sequencing allows the successful identification of relatively rare gene mutations [3].

Materials and methods

The study included 192 patients: 178 of them with sensorineural hearing loss and 14 subjects with normal hearing, relatives of the study patients with impaired hearing, of who biological material was also taken to look for mutations associated with hearing.

According to anamnestic data in 54.17% (n = 104) of the cases hearing loss occurred prelingually, before development of speech, in 38.54% (n = 74) of the cases postlingually, after acquiring speech and 7.29% (n = 14) of the cases had socially adequate hearing ability.

The diagnosis was established through pure-tone threshold audiometry of all participants over 6 years of age. Play audiometry was performed in patients between the age of 3 and 6 and for children younger than 3, BAEPs were used. Otoscopy, tympanometry and reflexometry were performed in all participants.

When selecting the patients the following criteria were met:

- Patients were studied regardless of their age, gender and ethnicity;
- Enrolled patients had bilateral sensorineural hearing loss, irrespective of the degree of hearing loss;
- The study also included normally hearing subjects with a family history of SNHL;
- All study participants have a normal ENT status and respectively normal middle ear pressure;
- Patients with syndromic sensorineural hearing loss were not studied;
- In studied patients, hearing impairments caused by exogenous factors such as craniocerebral trauma, noise trauma, exposure to loud noise were excluded.

The mean age of the study participants was 20.4 years, the youngest being two-months old and the oldest one - 70 years old.

From the study patients 73.44% (n = 141) identi-

fied themselves as Bulgarians, 16.15% (n = 31) as Roma, 5.73% (n = 11) as Turks and 4.69% (n = 9) came from mixed marriages.

According to the Bulgarian standards 55.73% (n = 107) of the study patients had deafness, 18.75% (n = 36) of them were with severe deafness (hearing loss between 60 and 90 dB), 18.3% (n = 35) with moderate (hearing loss from 30 to 60 dB), and 7.9% (n = 14) of the subjects had normal hearing.

Methods

For the purposes of the genetic testing DNA was isolated with CHEMAGEN® magnetic separation station. The aim of the isolation was to receive high molecular weight DNA with minimal impurities such as protein, RNA and glycoproteins. A new trend in the methods for isolation of high molecular weight DNA is through automated magnetic separation, which was used in this study.

The quality of the received high molecular weight DNA was defined through agarose gel electrophoresis using 0.8% agarose gel and 1xTBE (tris, borate, EDTA buffer). Concentration of the isolated DNA was estimated with the spectrophotometer NanoDrop™.

To perform the targeted next-generation sequencing we used TruSight One Kit for the preparation and the platform MiSeq, Illumina for the sequencing. Preparation of the libraries was done according to the manufacturer's requirements. [Figure 2]

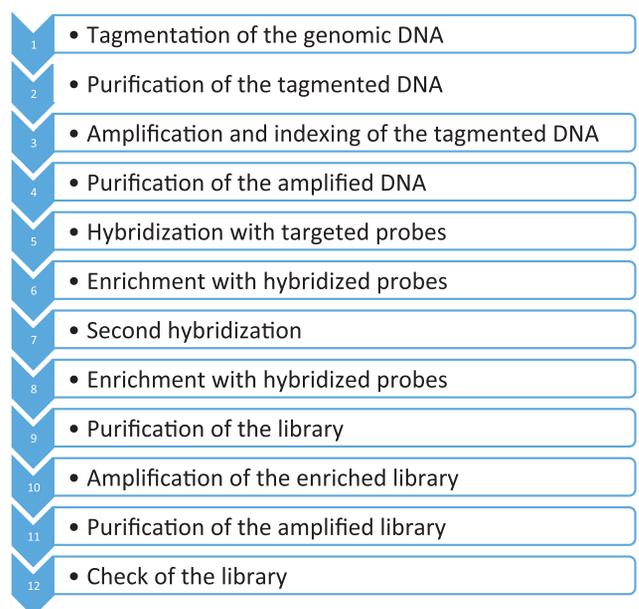


Figure 2. Main steps in preparation of libraries

Bioinformatics methods

The obtained data was processed with VarSeq® (Golden Helix, Inc., Bozeman, MT, www.golden-helix.com), a software package, and the analysis included:

- Alignment and mapping of reads to the human reference genome HG19;
- Removal of duplicate reads, indel realignment and base quality score recalibration (BQSR);
- Identification of human reference genome variants;
- Annotation of public databases on population frequencies, position in the corresponding protein and mRNA, pathogenicity predictions, evolutionary conservatism, etc;
- Prioritizing the identified variants through filtering.

The functional impact of the candidate mutations was assessed *in silico*, using prediction programmes to determine the possible phenotypic impact on the variant. For predicting the effect of missense mutations, the following tools were used: SIFT <http://sift.jcvi.org/>, Polyphen-2 <http://genetics.bwh.harvard.edu/pph2/>, MutationTaster <http://www.mutationtaster.org/>, Meta-SNP <http://snps.biofold.org/meta-snp/>, MutationAssessor (mutationassessor.org), Provean (provean.jcvi.org), LRT (Chun and Fay, 2009), VEST 3 (Carter H. et al, 2013), MetaSVM; for variants potentially leading to changes in the splicing: Automated Splice Site

And Exon Definition Analyses <http://splice.uwo.ca/>, NetGene2 <http://www.cbs.dtu.dk/services/NetGene2/>, Human Splicing Finder <http://www.umd.be/HSF3/HSF.html>.

Results

From the 192 study patients, in 31.77% (n = 61) a mutation causing hearing loss was identified while in 68.23% (n = 131) of the cases the reason for hearing loss remained unclear. After performing genetic tests in 43.75% (n = 84) of the cases, a mutation in GJB2 was identified, the gene encoding protein connexin 26, as this percentage included both heterozygous and homozygous mutations. In 2.08% (n= 4) of the cases mutations causing hearing loss were found in genes other than connexin genes. In 54.17% (n = 104) no mutations involved in hearing were identified. [Figure 3]

In 29.69% (n = 57) of the tested patients, it was found that the hearing loss is caused by a homozygous mutation in the gene encoding protein Cx26. In 14.06% (n = 27) of the study group, mutations were identified in the gene encoding protein Cx26 in a heterozygous state. In those patients, the reason for the hearing loss remained undefined. In 2.08% (n= 4) of the cases mutations causing hearing loss were found in genes other than GJB2 gene. In 54.17% (n = 104) of the tested the reason for hearing loss was not identified. [Figure 4]

In 57.89% (n = 110) of the cases the hearing loss

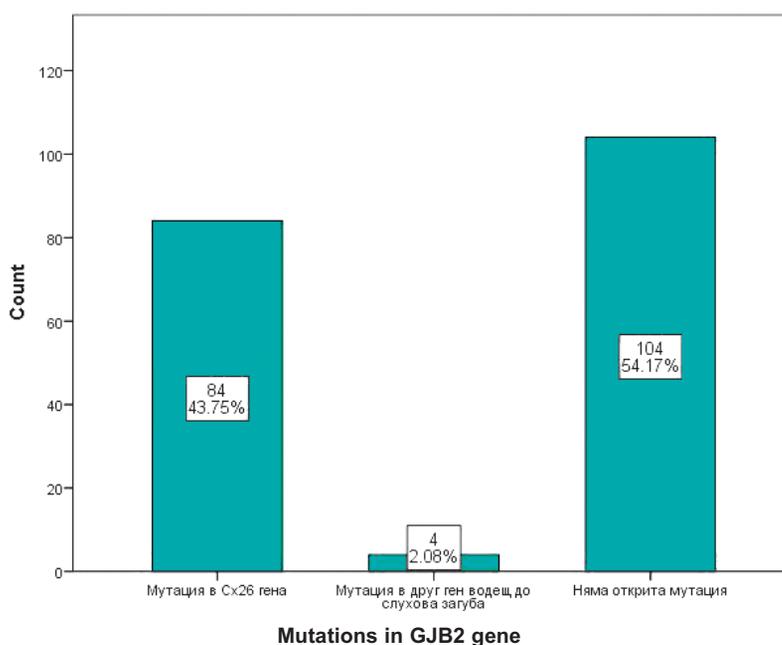


Figure 3: Types of genetic mutations in the study.

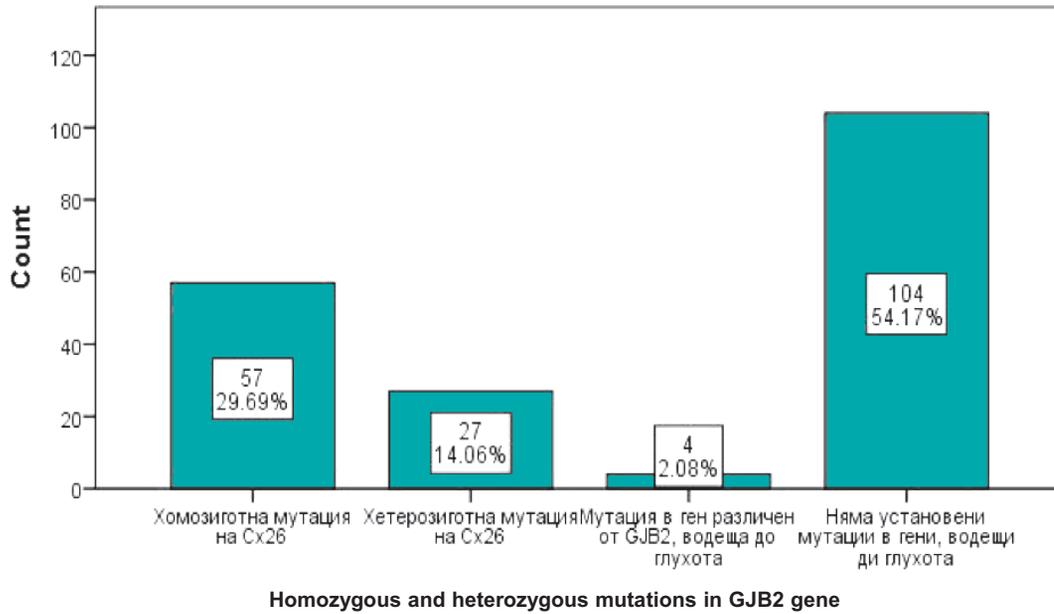


Figure 4: Types of genetic mutations in the study.

had no progression; patients with prelingual hearing loss belonged to that group. In the remaining 42.11% (n = 80) of the cases hearing deteriorated over time. When comparing progression of hearing loss with regard to the impairment onset, it can be seen that the lack of progress in the hearing impairment in cases of prelingual deafness, i.e. 50.57% (n = 89), dominated over the presence of progression found in 7.39% of the cases. Progression in hearing loss dominated in the postlingual impairment – in 36.93 % (n = 65) over the lack of progression – in 5.11% of the cases.

A comparison was made of the presence of a genetic mutation in patients of Bulgarian, Turkish, Roma and mixed ethnic origin and the results did not show statistical significance – p = 0.217. Mutations in genes causing a hearing impairment were distributed regardless of the ethnic origin. [Figure 5] Statistical significance was found (p < 0.05) between the presence of mutations in the genes responsible for hearing and the onset of the hearing impairment. Comparing the group of patients with hearing loss caused by a mutation with the group

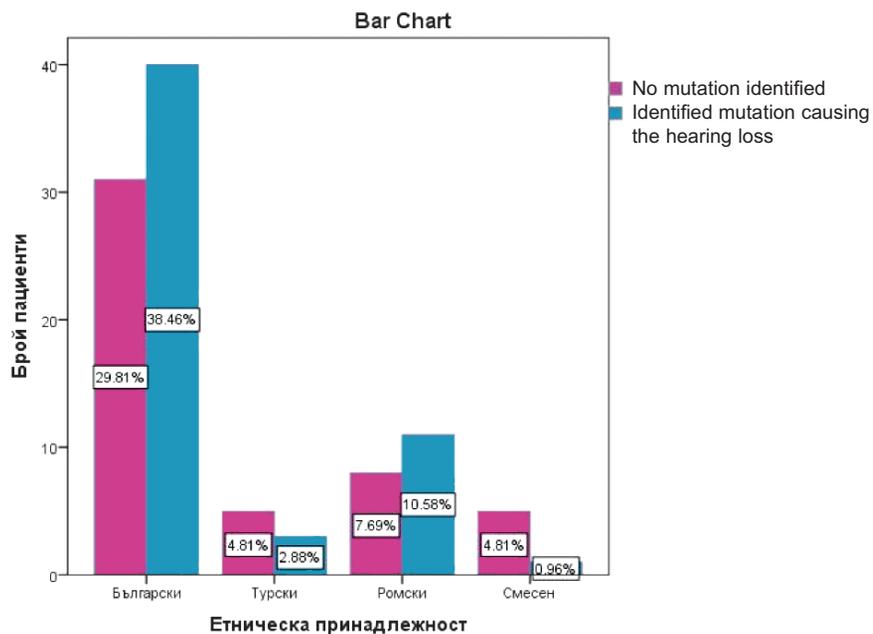


Figure 5. Genetic mutations based on ethnicity.

of patients without identified mutations in genes involved in hearing, predominance of prelingual hearing loss was observed in patients with proven genetic deafness. In patients with no identified mutations, the distribution between prelingual and postlingual onset of the hearing impairment was approximately the same. [Figure 6]

Among the selected five families who underwent targeted next-generation sequencing, no proband was a carrier of mutations in Cx26 (GJB2), Cx30 (GJB6) and Cx31 (GJB3) [Figure 7]. After performing the targeted next-generation sequencing among the selected families, interesting results were received for all who were expected to have gene mutations responsible for hearing. In families: №1, №2 and №4, no currently known mutations were identified in genes associated with hearing.

In family №3, through CNV analysis, in the tested patient a duplication of 51 base pairs in the OTOA gene was found (16:21679026-21679076), affecting exon 3 and partially intron 1-2 and intron 2-3. CNVs have been increasingly associated with non-syndromic hearing loss [4].

In family №5 the replacement, p.Gly285Ser, is a mutation leading to loss of functions and has a strong dominant-negative effect on the wild type KCNQ4 channels [5]. It has been proven that in *Xenopus* oocytes the mutation leads to lack of K⁺ currents [6]. Dysfunction of KCNQ4 is associ-

ated with degenerative processes that have been observed in many other genetic diseases affecting the nervous system. Therefore, hearing loss in patients with mutations in that gene progresses and inheritance in them is autosomal dominant.

Discussion

Among the Bulgarian population, the most common mutation in gene GJB2 is c.35delG, found in 43.75% of the study patients with SNHL: 29.69% in a homozygous state and in 14.06% of the cases in a heterozygous. It was identified in patients from Bulgarian and Turkish ethnic origin but not in patients from the Roma ethnic group. Carrier frequency of different mutations in GJB2 differs globally.

According to literature data and in conclusion from our experience with the study group of patients with SNHL, genetic testing must start with search of mutations in the GJB2 gene, as the most common cause of deafness in the Bulgarian population. Therefore screening for mutations among the study participants started with Cx26 gene. Ethnic origin plays an important role in the distribution and frequency of mutations, as it is clear from the obtained results in Ashkenazi Jews (167 delT), Asians (23delC), Caucasians (35delG). These observations were confirmed by our results as well. In the Bulgarian population, among the

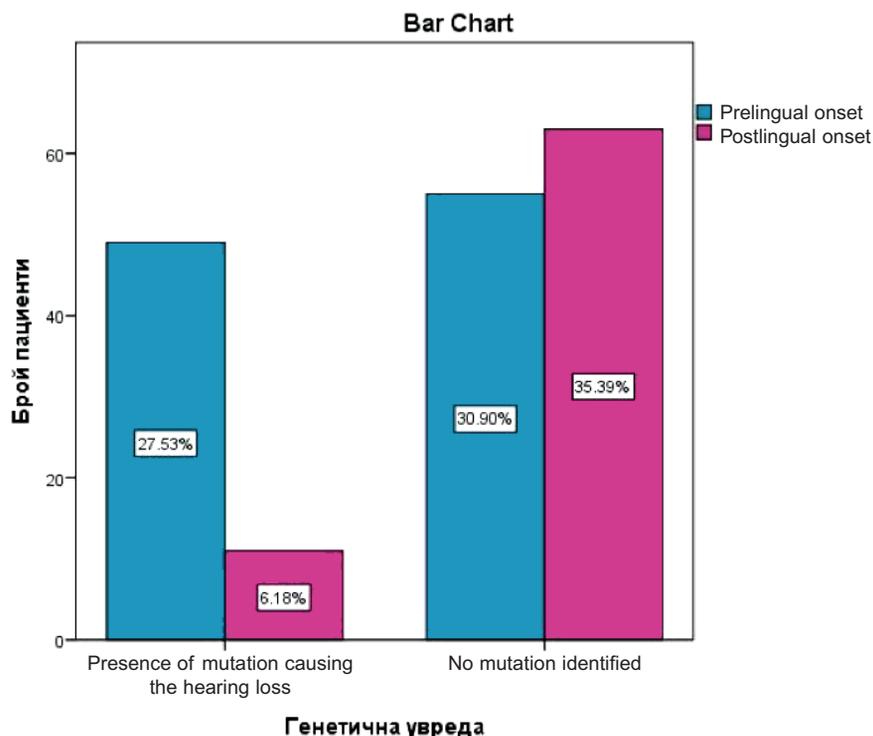


Figure 6. Presence of genetic mutation in connection with the hearing loss onset

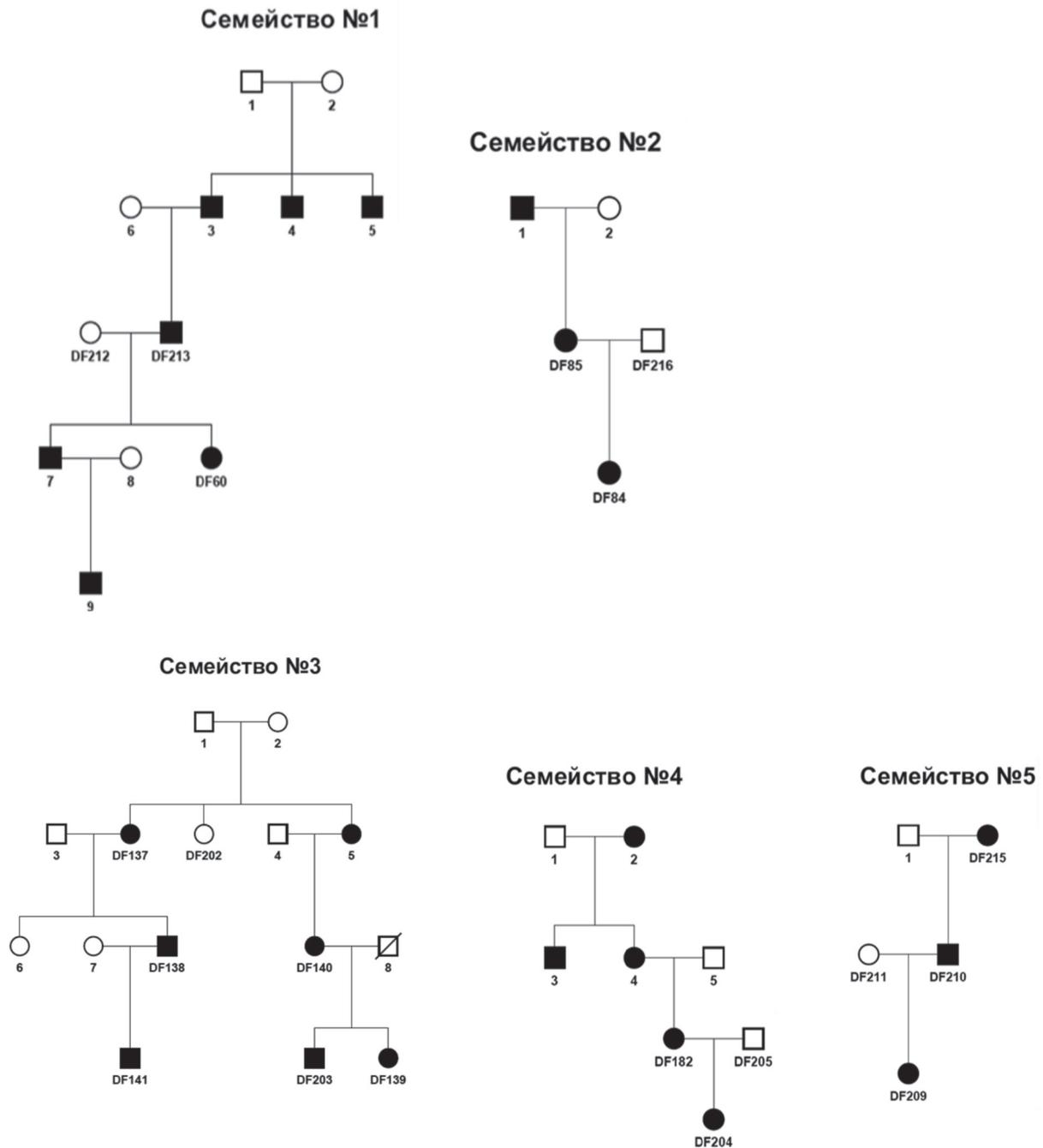


Figure 7. Family trees of the studied families. In family №1 probrand is DF60; in family № 2 probrand is DF84; in family № 3 probrand is DF139; in family № 4 – DF182; in family № 5 – DF210.

tested Roma group with SNHL a high frequency of mutation p.W24X in a homozygous state was observed.

As a next step in diagnosing hereditary hearing loss, following the screening for mutations in connexin genes, we introduced the use of targeted next-generation sequencing in patients in whom such mutation was not found or it was in a heterozygous state.

We selected families where several members of

different generations had SNHL and our aim was to identify rare mutations in genes responsible for hearing. After performing the targeted next-generation sequencing among the selected families, interesting results were received for all who were expected to have gene mutations responsible for hearing.

In family №3, in the tested probrand, through CNV analysis, a duplication of 51 base pairs in the OTOA gene (16:21679026-21679076) was found,

affecting exon 3 and partially intron 1-2 and intron 2-3.

In family №5 the replacement, p.Gly285Ser, is a mutation leading to loss of functions. The hearing loss progresses in patients with mutations in that gene. Inheritance in them is autosomal dominant. Cases of autosomal recessive inheritance have also been reported in carriers of mutations in *KCNQ4*. Wasano K. et al reported on a family with autosomal recessive form of non-syndromic hearing loss who had mutation c.1044_1051del8 in a homozygous state. The proband was diagnosed with severe hearing loss that was either congenital or with an onset in early childhood. The proband's daughter was a heterozygous carrier of the mutation but she had no hearing impairment [Wasano K. et al, 2015].

The found variant in *KCNQ4* co-segregated with the disease in the family and explained the occurrence of the hearing loss. Mutations in that gene have been associated with progressive hearing loss with a postlingual onset. In the proband's daughter the hearing impairment was diagnosed

at the age of 3 months. Currently in literature, there are no described cases of carriers of mutation c.853G>A (p.Gly285Ser), with a congenital hearing impairment. In that girl, the presence of a variant in another gene or the same gene might have aggravated the clinical phenotype.

Conclusion

Hearing screening in order to identify deafness needs to start in neonatal units within 48 hours after birth. An important step is referring the child to an audiologist in case negative OAEs are registered. The next step is BAEP testing.

Hearing loss is the only sensory deficit, which can be successfully treated even with regard to profound deafness. Cochlear implants have a positive effect in speech production and speech perception. A significant positive change in cognitive ability and reading is achieved, strongly expressed in children with *GJB2* mutation, which causes an isolated impairment in the cochlea without impairment of cranial nerve VIII or the CNS.

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Relationship between body posture and dento-facial deformities

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Abstract:

The aim of this study is to investigate the possible relationship between dento-facial deformities, craniofacial morphology and body posture anomalies. It is recommended that specialists in orthodontics give attention to the cervical vertebral column area on profile radiographs to include any deviations in the cervical vertebral column morphology and head posture, while considering diagnosis and evaluation of etiology in orthodontic patients with skeletal craniofacial deviations and in patients with obstructive sleep apnea (OSA).

Key words: dento-facial deformities, craniofacial morphology, malformation, posture

Introduction

It is recommended that specialists in orthodontics give attention to the cervical vertebral column area on profile radiographs to include any deviations in the cervical vertebral column morphology and head posture, while considering diagnosis and evaluation of etiology in orthodontic patients with skeletal craniofacial deviations and in patients with obstructive sleep apnea (OSA).

Craniofacial morphology described on profile radiographs is an important diagnostic tool in orthodontic treatment planning. Björk's analyses were some of the earliest cephalometric analyses that described the vertical and horizontal relationships of the jaws with the cranial base as well as the interrelationship between the jaws. Furthermore, the relation between jaws, teeth, and alveolar bone was described. In 1955, Björk (3) conducted the first human growth study using implants, which resulted in the discovery of the rotation of the jaws. In the following years, cephalometric analyses were further developed to include analyses of growth and treatment changes and, to some extent, prediction of the growth. (4)

Later, cephalometric analyses were performed on the cervical vertebral column area. It was found that the dimensions of the first cervical vertebra (C1), the atlas, and the posture of the head and neck were associated with factors such as craniofacial morphology, including the cranial base, (7, 9, 19, 20) upper airway space, (15, 17) and, to some extent, occlusion (7, 8, 18) and temporomandib-

ular disorders. (11, 20, 32) Many cross-sectional studies agree on the relationship between extended head posture and craniofacial structures. (7, 9, 20) In subjects with extended head posture, increased anterior facial height, reduced sagittal jaw dimensions, and a steeper inclination of the mandible were generally observed. When the head was bent in relation to the cervical column, a shorter anterior facial height, larger sagittal jaw dimensions, and a less steep inclination of the mandible were observed.

Some longitudinal studies (16) likewise demonstrated that growth changes in head posture were related to corresponding changes in the growth pattern of the facial skeleton. When the head was extended, a reduced forward rotation of the mandible was observed. Some studies have also shown that the transverse dimensions of the maxilla and the maxillary dental arch width were associated with the posture of the head and neck. An increased occurrence of posterior crossbite and a smaller width of the maxilla were observed in subjects with an extended head posture. (1, 10, 12)

Many cephalometric studies have been performed on patients with OSA, and most authors agree that craniofacial morphological and postural characteristics exist in patients with OSA, such as reduced posterior airway space, abnormally long soft palate, low position of the hyoid bone, and an extended head posture. (5, 33)

Aim: The aim of this study is to investigate the possible relationship between dento-facial deformities, craniofacial morphology and body posture anomalies.

Material and methods

The following scientific research databases were included in the study: MEDLINE, Scopus, EMBASE and PubMed, with a time period between 1955 and 2020. For search the keywords - dento-facial deformities, craniofacial morphology, malformation, posture and balance were used.

Results and discussion

Anomalies of the cervical vertebral column morphology of the upper 5 cervical vertebrae (C1-C5) on a lateral skull radiograph are usually divided into 2 main categories: fusion anomalies and posterior arch deficiency. (14)

Fusion anomalies are fusion, block fusion, and occipitalization. (29) Fusion is defined as fusion

of one unit with another at the articulation facets, neural arch, or transverse processes. Occipitalization is the term for assimilation, either partially or completely, of the atlas (C1) with the occipital bone. The definition of block fusion was modified according to Sonnesen and Kjær (21) - a fusion of more than 2 units at the vertebral bodies, articulation facets, neural arch, or transverse processes. Posterior arch deficiency consists of partial cleft and dehiscence. (14) Partial cleft is a failure of the posterior part of the neural arch to fuse. Dehiscence is defined as failure to develop part of a vertebral unit.

Deviations of the cervical column morphology occur in healthy subjects with neutral occlusion and normal craniofacial morphology as well as in patients with craniofacial syndromes, deviating craniofacial morphology, and severe malocclusion traits.

A recent study found that fusions between the upper cervical vertebrae (C2 and C3) occurred in 14.3% of healthy subjects. (21) Fusions of the upper cervical column within that range are thus considered normal.

Previous studies have established an association between malformations of the upper cervical vertebrae and patients with cleft lip and palate. (6, 31) Recently, an association was also found between malformation of the upper cervical vertebrae not only in patients with condylar hypoplasia, (21) but also in adult orthodontic surgical patients with skeletal deep bite, (23) skeletal mandibular overjet, (24) skeletal horizontal overjet, and skeletal open bite. These studies showed that cervical column deviations occurred in 72.7% of the condylar hypoplasia group, 41.5% of the deep-bite group, 61.4% of the mandibular-overjet group, 52.9% of the horizontal-overjet group, and 42.1% of the open-bite group. Deviations occurred significantly more often in all 5 patient groups compared with the control group. This indicates that morphologic deviations of the upper cervical vertebrae are not only associated with malformation of the jaws but also with craniofacial morphology and occlusion.

A study of adults found that fusion between C2 and C3 was significantly associated with posture of the head and neck. (21) In this study, the cervical vertebral column was approximately 5° more curved, and the inclination of the upper cervical spine was 8° more backward in adults with fusion.

Accordingly, associations have been reported



between craniofacial morphology and head posture, between OSA, craniofacial morphology, and head posture (Fig. 1), and between morphological deviations of the cervical vertebral column and craniofacial syndromes (2, 6, 13, 30, 31) and cleft lip and/or palate.

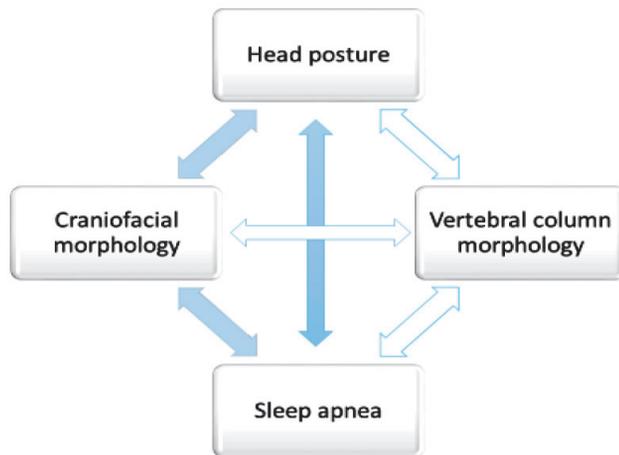


Figure 1. Schematic illustration of associations between craniofacial morphology, head posture, cervical vertebral column morphology, and sleep apnea.

A series of studies were performed on associations between morphological deviations of the cervical vertebral column and the craniofacial morphology in adult patients with severe skeletal malocclusion traits. (21, 23, 26, 27) In these studies, it was revealed that fusion of the cervical vertebral column was associated with craniofacial morphology. A significant association between fusion and a large craniofacial base angle, between fusion and retrognathia of the jaws, and between fusion and inclination of the jaws was found in patients with severe skeletal malocclusions, indicating an association between fusion of the cervical vertebral column and craniofacial morphology, including a large cranial base angle.

Recently, morphological deviations of the cervical vertebral column have been described in healthy subjects with neutral occlusion and normal craniofacial morphology (21, 25) and in patients with severe skeletal malocclusion traits, such as skeletal deep bite, skeletal open bite, skeletal maxillary overjet, and skeletal mandibular overjet. (21, 23, 26, 27)

A study on cervical vertebral column morphology in patients with OSA found that the prevalence of fusion anomalies of the cervical vertebral col-

umn was 46%. (28) In addition, the prevalence of fusion anomalies of the cervical vertebral column occurred significantly more often and at a lower level in the column in patients with OSA compared with subjects with neutral occlusion and normal craniofacial morphology. (28) Fusion anomalies occurred in the OSA patients as fusions between the second and third vertebrae, the third and fourth vertebrae, or between the fourth and fifth vertebrae. Block fusions occurred in the OSA patients in combination with fusions and block fusions. (28)

An association between posture of the head and neck and the cervical vertebral column morphology has been found in a recent study on subjects with neutral occlusion and normal craniofacial morphology. (22) The study showed that the cervical lordosis was significantly more curved in subjects with fusion than in subjects without fusion. Furthermore, the inclination of the upper cervical column was more backward in subjects with fusion than in subjects without fusion. (22) The findings of this recent study indicate an association between fusion of the cervical column and the posture of the neck. (22)

The findings described earlier indicate that fusion of the cervical vertebral column is associated with occlusion, craniofacial morphology, and head posture in nonsyndromic patients.

Conclusion

It is suggested that head posture has an impact on the development and function of the craniofacial morphology, and that the morphological patterns of the upper cervical vertebrae could play a role in the etiology of patients with OSA. Deviations of cervical vertebral column morphology were significantly associated with a large sagittal jaw relationship, retrognathia of the jaws, a large inclination of the jaws, and a large cranial base angle. Furthermore, deviations in the cervical vertebral column morphology were significantly associated with extension of the head in relation to the cervical vertebral column. The associations between cervical column morphology, craniofacial morphology, and head posture have not previously been described in preorthodontic children with horizontal maxillary overjet. These new findings are considered to be important for the diagnosis and more accurate treatment of children with horizontal maxillary overjet.

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Differentiated chondrosarcoma originating in the cricoid cartilage of the larynx: evaluation and treatment. Clinical case presentation

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Abstract

Background

Modern medicine has focused much of its activity and scientific endeavours on the fight against malignant diseases. The goal of our clinical case presentation is to introduce the evaluation and treatment of a rare head and neck tumor, the laryngeal chondrosarcoma (CS). In such rare malignancies the end results of the treatment plan are associated with multiple cofactors that influence strongly the course of the disease.

Materials and methods

In our clinical case we have described the investigations and chosen tactics of treatment, applied to our patient, in a chronological manner, some immediate results, but also the long-term consequences of the management of this disease.

Results

In our opinion, the outcomes in this patient's case were prompted not only by the specifics of this malignant disease, but also by the interpretation of the instrumental examination and the decision-making regarding the initial treatment. In addition to that, the decisions taken by the patient also play an important role in the clinical course. We want to point out that the achieved results and outcomes could be unpredictable - due to the coincidence of circumstances - and different, in comparison to the cases described in most literature.

Conclusions

1. The relatively simple diagnostics with modern diagnostic methods and the abundance of options for surgical treatment or even combination therapy in complicated cases, do not create difficulties in the management of typical chondrosarcoma of the larynx. However, its treatment requires the efforts of several medical specialties - Surgery, Medical oncology, Medical imaging, Radiation therapy, Physiotherapy and Rehabilitation, Psychology and others.
2. Neither RT nor chemotherapy are recommended therapeutic options, except in some rare individual cases.
3. Conservative surgery tends to be adequate only if performed properly and timely as thus ensures long-term remission or cancer-free life. Radical surgical treatment is recommended in advanced cases.

Introduction

Laryngeal carcinoma accounts for 1-2% of all human malignancies, but as a malignancy of the head and neck, it is the most common tumor. According to their histogenesis, malignant diseases of the larynx are divided into epithelial and mesenchymal. CS of the larynx is a rare pathology, approximately from 0.07% and up to 0.2% (or up to 1% by others) of all head and neck malignancies, although it is the most common mesenchymal origin neoplasm of the larynx. Only 2-5% of all chondrosarcomas arise in the head and neck, where the majority of them develop in the maxilla, but other typical localizations include the nasal septum, the voice box, and other parts of the skull. The most frequent location is posterior lamina's internal surface of the cricoid, almost 80% of the cases of laryngeal CS; the thyroid cartilage, especially the inferolateral wall, is affected in about 20% of cases respectively, followed by the arytenoid cartilage, the vocal cords, the hyoid bone and the epiglottis. There have also been cases when more than one cartilage is involved. In our case, the patient's tumor was located in the plate of the cricoid cartilage and the first tracheal ring.

Case report

M.P., a 62-year-old man, non-smoker, with a concomitant disease - Arterial hypertension second degree. The patient was admitted to the clinic for diagnostic clarification and treatment, with com-

plaints of voice change, dry spastic cough and moderate shortness of breath. The complaints had been ongoing for about three months and were progressing. Physical examination: Blood pressure 138/68 mm Hg, pulse 90 beats / minute, body temperature 36.7° C, pronounced inspiratory dyspnea, inspiratory stridor and circulation in the jugulum. Paraclinic - normal. Chest X-ray: Expanded and enlightened lung fields. There was no evidence of an active pulmonary process. The hila were unenlarged, compacted. Cardiovascular shadow - within normal limits in regard to age. Indirect laryngoscopy - a tumor formation subchordally to the right, greatly narrowing the endolarynx. We concluded that there are indications for performing an emergency tracheostomy.

After the tracheostomy, a CT scan was performed. Description: Presence of a tracheostomy. CT data of a soft tissue formation, with the presence of a coarse calcification in it, involving, two-thirds of the cricoid ring originating from right to left, which has stenosed the subglottic lumen. The described formation has a very rich blood supply. It has an axial plane size of 98.8 / 65.5 mm. Several (more than three) lymph nodes are present bilaterally around the described formation. They have preserved fat centers and sizes up to 8.1 mm. CT shows destruction of the cricoid cartilage on the right side. Microlaryngosurgery was performed in a planned manner. Under general anesthesia, material was taken and sent for histological examination.

Histology findings: the sample coincides with the morphology of a differentiated chondrosarcoma. After the obtainment of the histological result, total laryngectomy was performed under general anesthesia. The skin-platysma flap was incised by a "U" shaped cut of skin and subcutaneous tissue. The larynx was skeletonized and mobilized, we ligated and cut a., v., n., Laryngeus supp. bilaterally. The larynx was removed. Hemostasis. Plasticity of the pharyngostomy. Drainage, layered suture, dry sterile bandage. Intraoperative - infiltrative growth, covering the entire larynx, more to the right, without infiltration of the surrounding tissues. Histology findings: "Islands" of hyaline cartilage with increased cellularity and nuclear atypism and binuclear cells. Highly differentiated chondrosarcoma. On the 3rd postoperative day the patient stood up alone, ambulated, and had normal peristaltic. We removed the drainage. After the initial wound healing, the patient was discharged from the clinic in good general condition. We did not recommend adjuvant irradiation as a postoperative therapeutic option.

Almost a year and four months after the primary operation, the patient was admitted to the clinic with complaints of "swelling" of the neck bilaterally, more to the right, ongoing for about two months. During the native CT examination of the cervical region, large soft tissue growths were found, more pronounced on the right side with numbness in them. Multicolored soft tissue areas were scanned

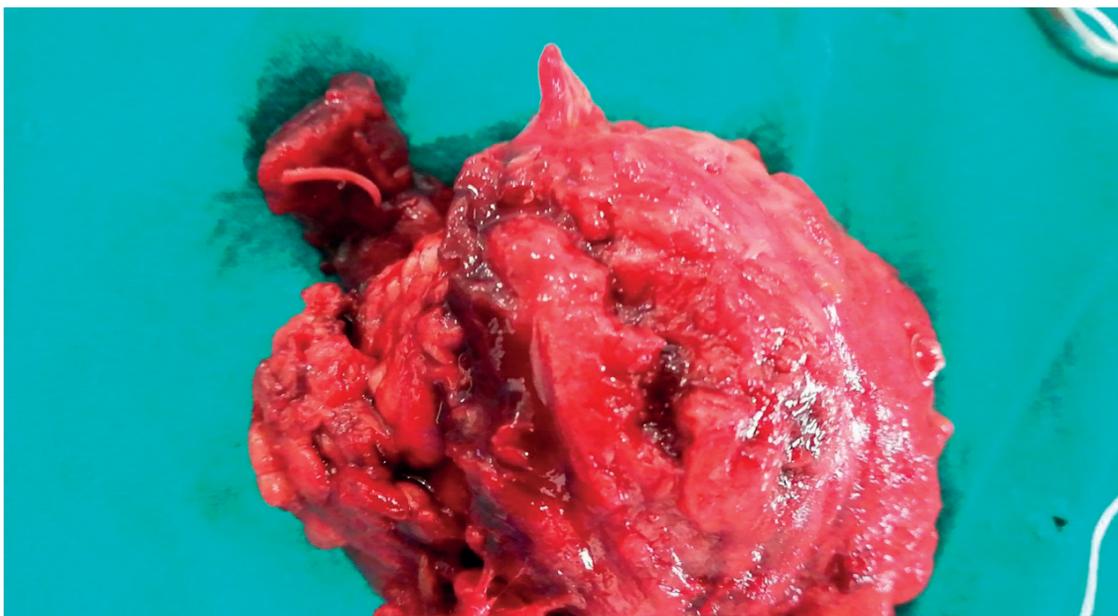


Fig. 1. Highly differentiated chondrosarcoma with infiltrative growth, covering the entire laryngeal cavity, more to the right side.



along the course of the two mm. Sternocleidomastoidei due to enlarged lymph nodes. An incision was made on the right side of the neck under general anesthesia. Gradually, an egg-sized tumor mass, located precarotidly, was dissected and removed. A second walnut-sized tumor mass was removed from the tracheostomy area on the right. Hemostasis was performed, aspiration drainages were placed. Layered suture, dry sterile bandage. Histology findings: soft tissues with infiltration of chondrosarcoma. After a smooth postoperative period and the initial wound healing, the patient was discharged from the clinic in good general condition. To date no further progress has ever been marked in the person's record at the outpatient clinic.

Discussion

Patients with laryngeal CS exhibit a variety of symptoms as a result of tumor growth, including dyspnea, dysphagia, hoarseness, airway obstruction, even stridor, or pain, but mostly – hoarseness and difficulty in breathing. Vocal cord stiffness is observed due to the involvement of the cricoarytenoid articulation, and not because of a lesion of the recurrent nerve. Men are affected more frequently than women, usually during the middle to later decades of life. The male to female ratio is from 3 : 1 to as high as 10 : 1. Chondrosarcomas mostly occur between 40–80 years of age with a peak in the seventh decade of life. The average age for diagnosis is usually between 64 and 66 years, thus coinciding with the maximum cartilage ossification. No definitive etiology for laryngeal CS is known, although the most commonly accepted version is an initial disordered ossification of the laryngeal cartilages. Ionizing radiation is among the etiological factors, which play a significant part. Many authors describe the evolution of the tumor against the background of multiple trauma and operations. Tobacco abuse is likely to have an influence on the development of CS, even though two thirds of the patients report not having such a habit in their medical history. Ultimately, no correlation with nicotine dependence or alcohol abuse was revealed. The transformation of chondroma to CS also deserves our attention. Ischemic changes in the chondroma due to a mechanical trauma may be a precursor to malignisation or a more aggressive biological behavior. The frequent correlation between chondroma and chondrosarcoma supports this theory. Studies reveal that it may reach 60.4%

correlation rate. Irradiation is yet another therapeutic option, although according to most literature sources no effect has been found. The differential diagnosis for CS of the larynx is practically limited to chondroma, chondrometaplasia, and tracheopathia osteoplastica. Rare examples of other sarcomas have been described in the larynx and hypopharynx, such as liposarcoma, osteosarcoma, angiosarcoma, synovial sarcoma, malignant fibrous histiocytoma, Kaposi's sarcoma, leiomyosarcoma. CS are characterised by a low tendency to spread further to the regional lymph nodes, but additional aggressive mesenchymal components could rarely develop in the lesion. High-grade tumours tend to be more associated with higher recurrence rate. Larger studies report an overall recurrence rate of 16% to 18%. The recurrence development is more expectable if the primary neoplasm has been excised partially. The curative potential of total laryngectomy after recurrent laryngeal CS is comparable to that of initial radical surgery. Tumour-related fatal outcomes are occasional and happen when relapses with unpredictable growth or involvement of nearby greater vessels and aggressive spreading proceed. Metastases, most common to the lung, bones and liver, have been described in about 2% to 10% of the reported cases of laryngeal CS. The 5-year survival rate is 90%, while the 10-year survival rate decreases to 80.9%. The diagnosis is based on morphological findings, and histopathology takes an exclusive role in diagnosing CS. CT scanning of the neck with contrast is a standard method for evaluating CS of the larynx, while simultaneously allowing preoperative planning. Due to the slow growing manner of this tumor, a displacement rather than invasion of the surrounding structures is observed. Ultrasound investigation can be useful if doubtful abnormalities in the neck regions are suspected. Modern treatment guidelines assume surgery as a treatment of choice. Adequate conservative surgery must allow for eradication of the cancer within safe margins. Wide surgical excision is the principal goal. Seeking acceptable functional results always is the aim, especially when the lesion exceeds not more than half of the cricoids' perimeter, and if the histological grade is low. The extent of resection to ensure control depends on the site, size and wideness of the lesion – debulking alone, hemi- or partial laryngectomy can definitely all be adequate. Attention should be paid to the resection of the external perichondrium. Salvage

laryngectomy becomes necessary if the cancer is larger, comes with infiltration in the surrounding tissues or an organ-sparing surgery can no longer be applied.

The role of radiotherapy is uncertain, even controversial, because these CS rarely respond to radiation treatment. Their non-responsiveness to radiation therapy limits therapeutic options. Laryngeal CS does not respond to chemotherapeutic agents.

Conclusions

The relatively simple diagnostics with modern diagnostic methods and the abundance of options for surgical treatment or even combined therapy

in complex cases, do not create difficulties in the treatment of the typical chondrosarcoma of the larynx. However, their treatment requires the joint efforts of several medical specialties - Surgery, Medical oncology, Medical imaging, Radiation therapy, Physiotherapy and Rehabilitation, Psychology and others. Radiation therapy and chemotherapy are not recommended as therapeutic options, except in some rare individual cases. Conservative surgery tends to be adequate if performed properly and timely. Conservative surgery tends to be adequate only if performed properly and timely as thus ensures long-term remission or cancer-free life. Radical surgical treatment is recommended in advanced cases.

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Calendar

	Course	
13	<u>13th Annual EUROHNC - European Head & Neck Course</u>	
Jan 2021	HNS/Oncology/Salivary Glands Poznań, Poland	
	Congress/Conference	
08	<u>ERS 2021</u>	
May 2021	Rhinology/Skull Base/Allergy Thessaloniki, Greece	
	Congress/Conference	
19	<u>15th Congress of European Federation of Audiology Societies 2021</u>	
May 2021		
	Otology/Audiology/Neuro-Otology	
	Sibenik, Croatia	
26	Congress/Conference	
May 2021	<u>13th Congress of the European Laryngological Society</u>	
	Laryngology/Phoniatrics Berlin, Germany	
	Congress/Conference	
24	<u>14th Congress of the European Skull Base Society</u>	
Jun 2021	Rhinology/Skull Base/Allergy Riva del Garda, Italy	
	Congress/Conference	
30	<u>ECHNO 2021 - 9th European Congress on Head & Neck Oncology</u>	
Jun 2021	HNS/Oncology/Salivary Glands Brussels, Belgium	
	Congress/Conference	
10	<u>EAACI 2021 Hybrid Congress</u>	
Jul 2021	Rhinology/Skull Base/Allergy Krakow, Poland	
	Congress/Conference	
08	<u>EAONO 2021</u>	
Sep 2021	Otology/Audiology/Neuro-Otology London, United Kingdom	
	Congress/Conference	
15	<u>EAFPS 2021 - Annual Meeting of the European Academy of Facial Plastic Surgery</u>	
Sep 2021		
	Facial Plastic Surgery	
	Nice, France	
06	Congress/Conference	
Oct 2021	<u>30th Congress of Union of the European Phonitricians</u>	
	Laryngology/Phoniatrics	
	Antalya, Turkey	
06	Congress/Conference	
Nov 2021	<u>15th Congress of the European Society of Pediatric Otorhinolaryngology</u>	
	General ORL Marseille, France	

IN MEMORIAM



Prof. Georgi Georgiev

Dear colleagues and friends,

Today 8.11.2020, one of the greatest Bulgarian otorhinolaryngologists,
Prof. Georgi Georgiev, passed away.

For a long time he was the head of the Department of Medical University of Sofia!

He was one of our teachers and a prominent surgeon in the fields of otology,
rhinology and head and neck surgery.

Prof. Georgiev has published many scientific articles and textbooks, organizer of many courses,
symposia, congresses and conferences!

He has been a member of the international board of the international bulletin
of otorhinolaryngology since its inception in 2005.

