ACTA OTORHINOLARYNGOLOGICA ITALICA 2021;41(SUPPL.1):S138-S144; doi: 10.14639/0392-100X-suppl.1-41-2021-14

Surgical multidisciplinary approach in the management of odontogenic or non-odontogenic neck infections

Gestione chirurgica multidisciplinare delle complicanze cervicali nelle patologie odontogene o non odontogene

Francesca Cambria[1], Massimo Fusconi[1], Francesca Candelori[1], Massimo Galli[2], Francesca Romana Federici Stanganelli[2], Federico Venuta[3], Valentino Valentini[1], Marco de Vincentiis[2]

[1] Department of Sense Organs, University Sapienza of Rome, Italy; [2] Department of Oral and Maxillo-Facial Surgery, University Sapienza of Rome, Italy; [3] Department of Thoracic Surgery, University Sapienza of Rome, Rome, Italy

SUMMARY

In recent years, in our university hospital, the number of odontogenic and non-odontogenic abscesses has been rapidly increasing. We included 70 patients from January 4th 2018 to February 19th 2020 affected by the odontogenic ones. Deep neck infection can spread to the chest and is associated with high morbidity and mortality. The purpose of this mini-review is to demonstrate that, in case of complications, a multidisciplinary approach is needed to treat these infections, so that all practitioners should work together to achieve the patient's rapid recovery.

KEY WORDS: multidisciplinary team, head-neck, dental disease, abscesses

RIASSUNTO

Negli ultimi anni, nel nostro ospedale universitario, il numero di ascessi cervicali, odontogeni e non odontogeni, si è mostrato in rapido aumento. Dal 4 gennaio 2018 fino al 19 febbraio 2020 abbiamo valutato 70 pazienti affetti da ascessi di natura odontogena. Le infezioni degli spazi profondi del collo possono portarsi fino al torace ed hanno un alto tasso di morbilità e mortalità. Lo scopo di questo studio è di dimostrare che, in caso di complicanze, è richiesto un approccio multidisciplinare per trattare queste patologie. Quindi tutti gli specialisti coinvolti dovrebbero collaborare per ottenere una rapida ripresa delle condizioni del paziente.

PAROLE CHIAVE: *team multidisciplinare, testa-collo, patologie odontogene, ascessi*

Introduction

Dental infections are very common and are mainly due to dental caries. They affect mostly men, between the third and fifth decades, with underlying systemic disease (as diabetes), from a rural background, with poor oral hygiene and lack of dental care [1-3]. The clinical progression of these infections can lead to the appearance of an abscess. Deep neck abscesses of non-dental origin can be caused by peritonsillar or retropharyngeal abscess, sialoadenitis, epiglottitis, cervical lymphadenitis, jugular intravenous drug use and trauma, as well as iatrogenic causes including infection of surgical wounds [4]. The abscesses have many complications that affect the head-neck district. They are potentially lethal, and consist of upper airway obstruction, mediastinitis, necrotizing fascitis, thoracic empyema, jugular vein thrombosis, sepsis, orbital abscess and osteomyelitis [5-8].

Received: November 10, 2020
Accepted: February 25, 2021

Correspondence
Massimo Fusconi
Department of Sense Organs, Sapienza University, Umberto I Hospital
viale del Policlinico 155, 00161 Rome, Italy
E-mail: massimo.fusconi@uniroma1.it

Funding
None.

Conflict of interest
The Authors declare no conflict of interest.

How to cite this article: Cambria F, Fusconi M, Candelori F, et al. Surgical multidisciplinary approach in the management of odontogenic or non-odontogenic neck infections. Acta Otorhinolaryngol Ital 2021;41(SUPPL.1):S138-S144. https://doi.org/10.14639/0392-100X-suppl.1-41-2021-14

With the advent of modern antibiotics, the mortality rate associated with complications has significantly decreased [8]. The treatment of complications often requires a multidisciplinary surgical approach that can involve the otolaryngologist, the dentist, the maxillofacial and thoracic surgeons and sometimes the general surgeon.

Odontogenic neck infections

As Buckley et al., in the last few year, we have seen an increasing number of patients who went to the emergency room for neck abscesses due to dental infections [2]. The bacteria responsible for dental infection are often the ones of the dental plaque. In fact, Buckley [2] and Prabhu et al. [9] proved, from the pus samples, that Streptococcus Spp and Staphylococcus Aureus were the most common bacteria found. WHO Global Oral Health Data Bank reports that dental caries is still a major health problem in most industrialized countries as it affects 60-90% of school-aged children and the vast majority of adults [10]. It is one of the most frequent causes of consultation on dental issues. In most cases the origin of the infections are the inferior molars, and the periapical periodontitis is determined by caries in 90% of cases. (Figs. 1, 2) As Martins and Chagas said in their paper review, when the infections are immediately localized and diagnosed, the treatment is based on dental care such as endodontic therapy or removal of the infected part, usually one or more teeth, combined with specific antibiotic therapy, if necessary [11].

Pulp necrosis, caused by dental caries, represents the most common way of diffusion. The bacteria responsible for the caries, after causing septic pulpitis and pulp necrosis, reach the periapical region through the root canal region [12]. Pulp necrosis can also be caused by periodontal diseases: the periapical region's contamination happens after the propagation of the infective process through a deep periodontal pocket [13]. It is even possible a retrograde contamination of the apex: infective processes, passing through surrounding anatomical structures (for example a maxillary sinusitis or a cystic infected lesion), can extend to the periapical region of the adjacent tooth, causing its necrosis. Therefore, it is necessary to check the vitality of the teeth that could have been infected.

Regarding pericoronitis, the incomplete eruption of a tooth can promote the bacterial proliferation in the region between the crown of the tooth and the surrounding soft tissues. In case of more aggressive forms, it can extend to the outlying tissues [14].

Typical signs and symptoms of cervical complications from dental origin are fever, neck mass, lymphadenopathy, trismus and odynophagia. It is important to support clinical diagnosis with contrast-enhanced CT imaging and ultrasound.

Figure 1. Ludwig angina, bilateral submandibular phlegmon caused by lower molars caries.

Non-odontogenic neck infections

Deep neck infections of non-dental origin are mainly due to peritonsillar abscesses, adenoiditis, epiglottitis, sialadenitis and otomastoiditis. Peritonsillar abscess is the most common deep infection of the head and neck. Most cases are consequences of recurrent or chronic bacterial tonsillitis, leading to abscesses in the parapharyngeal space. It is most common in patients 20-40 years of age, with no gender predilection. Although rare in childhood, peritonsillar abscess has a greater risk of airway obstruction in paediatric population than in adults. Patients may present with changes in voice, odynophagia, drooling, dysphagia, trismus, and systemic symptoms such as malaise and fever. The most common pathogens are β-*Haemolytic Streptococcus*, *Pneumo-*

Figure 2. Left parapharyngeal and cheek phlegmon caused by upper third molar dysodontiasis.

coccus, Staphylococcus aureus and Haemophilus influenzae.
Infection, that penetrates the fibrous tonsillar capsule and the peritonsillar space, may continue to extend into the masticator, parapharyngeal, or submandibular space. Imaging is not performed routinely as the diagnosis is clinical. However, CT with contrast agent is used if the diagnosis is uncertain, and typically shows fluid density with peripheral enhancement adjacent to an inflamed tonsil.
Infections of the retropharyngeal space generally result from the spread of infection from one site with a primary drainage route to the lymph nodes of the retropharyngeal space. In these cases, the causes can be otitis, pharyngitis, tonsillitis and infections of the oral cavity [5].
An abscess occupying the retropharyngeal space can also derive from adenoiditis. The retropharyngeal lymph nodes affected by the infection become enlarged and suppurate. On contrast-enhanced CT, a retropharyngeal abscess appears as a collection of low attenuating fluids that dilates the retropharyngeal space with enhancement of the peripheral border (Fig. 3).
Deep neck infections may also be due to sialadenitis, that are multifactorial diseases that can be acute or chronic. The most frequent cause of purulent sialadenitis is sialolithiasis. Salivary duct stones are present in sialadenitis which involves approximately 10-20% of parotid glands and 80-90% of the submandibular glands. Since obstruction of the salivary duct plays a significant role in sialadenitis, most cases occur in the submandibular glands, which are most frequently affected by sialolithiasis. CT is one of the main modalities for evaluation for sialadenitis and can demonstrate an enlarged salivary gland with increased attenuation, increased enhancement poorly defined borders, surrounding fat stranding, lymphadenopathy, and thickening of platysma and adjacent cervical fascia. Ultrasound is a valid alternative even if it turns out to be a less accurate examination. MRI makes it possible to distinguish acute and chronic sialadenitis.
The submaxillary gland can be the origin of an infectious process that reaches the perivisceral space directly or remains confined to the submaxillary lodge itself [15]. The different evolution depends on some anatomical variants. The middle cervical fascia can completely circumscribe the submaxillary lodge separating it from the perivisceral space. In other cases, the middle cervical fascia inserting itself on the hyoid bone (Charpy-Moresten anatomical variant) or on the sheath of the digastric muscle (Truffert anatomical variant), does not reach the medial aspect of the mandible resulting in a communication between the submaxillary lodge and the perivisceral space.
Due to a similar etiopathogenesis, a phlegmon or perivisceral abscess can originate from the parotid gland; the invasion of the perivisceral space is caused by the lack of a true capsule on the deep edge of the gland.
Bezold's abscess is a rare complication of acute otomastoiditis in which the infection erodes, through the medial cortex, the tip or internal surface of the mastoid and causes abscess formation in the sternocleidomastoid muscle that extends into the infratemporal fossa. Due to the depth of the cervical fascia that surrounds the sternocleidomastoid and trapezius muscles, the abscess is impalpable. As the mastoid sinus pneumatises late in childhood, Bezold's abscess occurs more frequently in adults. Due to its proximity to the internal jugular vein, the thrombosis is a possible complication [16].

Antibiotics

Antibiotic therapy for deep neck space infections is based on broad-spectrum antibiotics such as penicillin based,

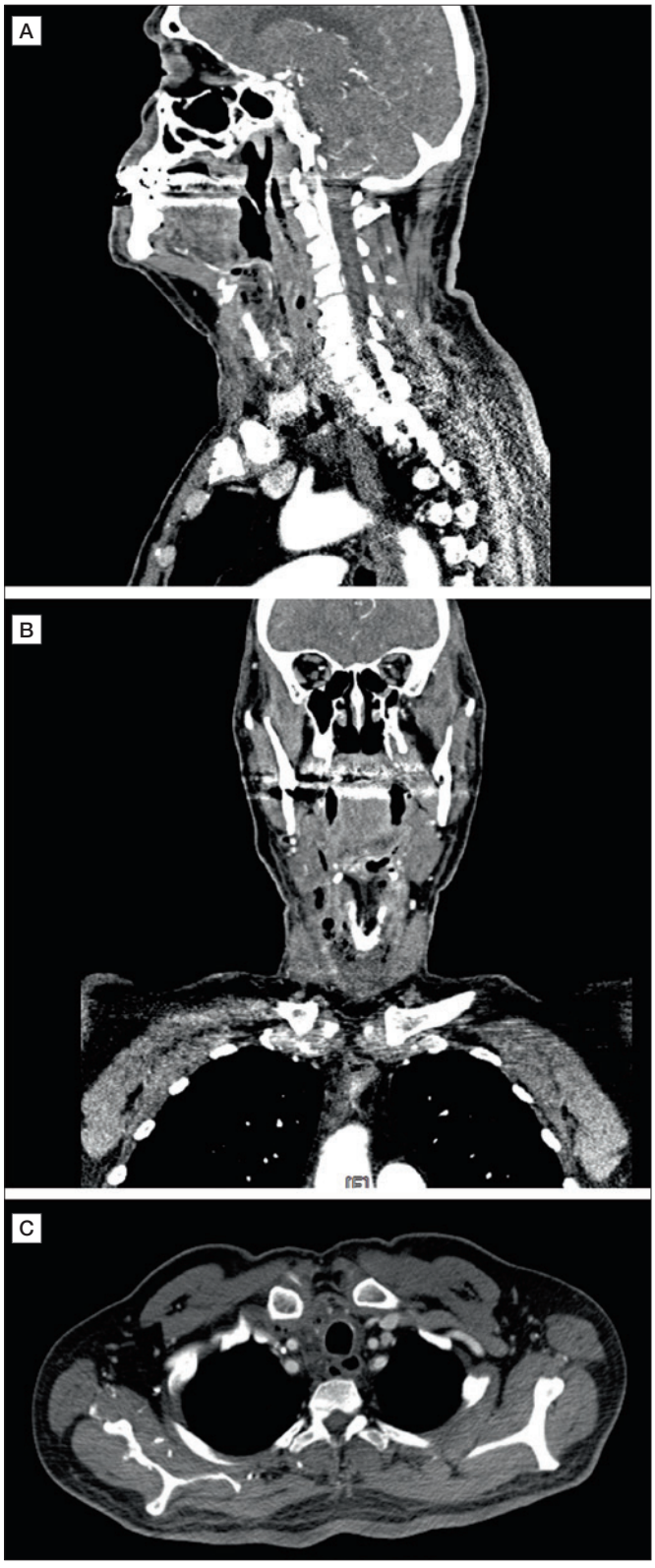

Figure 3. Odontogenic abscess of the upper right arch, partial obstruction of the upper airway. The head, neck and chest CT scan, with contrast medium, documented a phlegmon that reached the mediastinum, through the perivisceral space. (**A**) coronal plane; (**B**) sagittal plane; (**C**) axial plane.

clindamycin, and metronidazole [17]. The literature supports also the use of corticosteroids [18]. The antibiogram is also useful to test the material taken during the operation and to identify the bacteria and to start a target therapy. For this reason, beside surgery, supportive care is unavoidable.

Multidisciplinary management of deep neck infections

Without treatments, the infection can spread into surrounding tissues. When there is airway impairment, sepsis, descending infection, abscess larger than 3 cm, involvement of deep neck spaces or the failure of antibiotics therapy, surgical drainage is necessary. The airway management can be challenging. The main reason for ENT consultation is the evaluation of the air tract [19]. The purpose of the surgery is to eliminate the triggering cause, to drain the purulent material and preserve the airway patency. We need a laryngoscopy to evaluate the obstruction generated at the level of the oropharynx (glossoptosis) or the laryngo-pharynx (peripharyngeal oedema). Compared with elective intubation, emergency intubation is therefore associated with an elevated risk of complications and severe adverse events such as aspiration, a fall in oxygen saturation, or even death. For these reasons, according with Rombey and Shieren, it is better recommended to secure patient's airway via awake fiberoptic intubation and video laryngoscopy [20], that allow intubation of more challenging patients. They are performed under local anaesthesia and sedation and should be performed by an experienced anaesthesiologist. Fang et al. [21] and Ahuja et al. [22] showed that emergent awake tracheostomy should be considered in patients with impeding airway obstruction and is a safe and effective method to secure an airway in these patients. Some studies advocate early tracheotomy in severe deep neck infections in order to decrease the hospitalization in intensive care unit and related complications. Moreover, in severe cases of airway oedema, a prolonged intubation is required, and early tracheostomy can offer several benefits in ICU care compared to intubation such as for example avoiding laryngeal injury caused by prolonged intubation, facilitating nursing care, improving patient comfort by reducing the need for sedation, reducing the need for mechanical ventilation and making faster the discharge. Adley et al. evaluated scientific articles relating to a period of time of thirty years and said that there was a significant difference in favor of early tracheostomy in adults and pediatric group as early tracheostomy was superior regarding reduced duration of mechanical ventilation, with less mortality rates and less duration of stay in ICU [23].

In the case of abscesses of odontogenic origin, to treat the infections of cervical space a surgical approach in team with the dentist is almost mandatory, since in most cases it is necessary to perform the extraction of one or more dental elements. As Heim and Warwas proved quite recently, this better happens during the execution of an exploratory cervicotomy [24]. Odontogenic infections spread from mandible or maxilla into the sublingual, submandibular, or masticatory spaces and then into the parapharyngeal space. For this reason, the site of neck incision depends on the affected area. In any case the surgical incision should be placed in healthy skin, when possible, not at the site of maximum fluctuance, because these wounds tend to heal with an unsightly scar. It should be into a natural skin fold, in a dependent position.

Drainage of the submandibular space can be required a subperiosteal intraoral and an extraoral incision. For the external approach the incision should be done approximately 3 to 4 cm below the angle of the mandible. The incision is performed on skin and subcutaneous tissues, to the platysma. The platysma is divided with electrocautery or sharp dissection. Superficial and middle cervical fascia are cut in parallel to the inferior border of the mandible. The dissection continues in a superior-medial direction to enter the submandibular space.

Drainage of the lateral pharyngeal space is approached mainly through an external approach. In this case, neck dissection can be performed according to Paul André's approach [25]. Once reached the SCM muscle, the incision is carried down to the superficial and middle cervical fascia, and the carotid sheath is identified and opened. Dissection is carried superiorly along the vessels.

In order to reach abscesses affecting the perivisceral space up to the base of the neck, it is possible to extend the Paul André's incision or perform a horizontal or median arch-shaped incision about 3 cm above the sternum dimple. In this case, the perivisceral space surrounding the thyroid and larynx is reached after incision of the superficial and middle cervical fascia.

In people who have large retropharyngeal space abscesses, an external approach is needed. The carotid sleeve is mobilized medially, so it is possible to reach the deep cervical fascia and if necessary, the prevertebral fascia. In selected cases, with single-chamber and circumscribed abscess cavities, endopharyngeal access to the abscess is possible [26-31].

After the abscess has been drained, the drains are placed [32,33]. To date, it is not clear if it is better use passive drains than open ones. Passive drains are made of latex, polypropylene, or silastic rubber. These include Penrose drains and glove finger. They work by capillary action, gravity, overflow, or fluctuations of pressure gradients caused by body movement. To reduce the risk for ascending infection, passive drains should be covered with a sterile bandage that is placed and aseptically exchanged. if it does not, fluid can lead to severe skin irritation and excoriation in addition to increasing the risk for ascending infection [34].

Active drains, like Jackson-Pratt ones, are closed systems that collect fluid into a reservoir. This decreases the risk for ascending infection and can reduce exposure of hospital staff or other patients to contaminated fluid. Active drains apply an artificial pressure gradient to pull fluid or gas from a wound or body cavity [35].

Through the perivisceral space or the vascular space the infectious process can reach the anterior mediastinum, differently when the abscess involves the third or fourth cervical lodge, respectively the perivisceral space and the prevertebral space, it can reach the chest, causing posterior mediastinitis. In fact, Endo et al. classified descending mediastinitis according to the degree of diffusion of infection diagnosed by computed tomography. Localized descending mediastinitis, type I, is localized in the upper mediastinal space above the carina. Diffuse descending mediastinitis, type IIA, is extended to the lower anterior mediastinum and type IIB reach both anterior and posterior lower mediastinum [36].

Surgery is a complex procedure; thoracotomy and extended cervicotomy is the gold standard approach, as Corsten and Taylor assert in their papers [4,37]. The goal is to drain all the suppurated fluids, to save the organs from the close pus and fibrin collections. These operations give the chance to native tissues to regenerate consequently. Drainages and tissue stimulating dressings can be left in each corner of the affected areas after debridement. More recently, the armamentarium has been improved with a new technology that has shown promising results; the VAC-therapy seems to be associated to a faster resolution of the local tissue damage and some studies has encouraged to use this device more extensively [38].

Conclusions

The number of cervical deep infections has been rapidly increasing in the last years. Abscesses of odontogenic and non-odontogenic origin have a strong tendency to spread between the tissues and to invade the deep spaces of the neck down to the chest. The main reason for ENT consultation is the evaluation of the airway but in many cases, thoracotomy and extended lateral/anterior cervicotomy is required in order to drain all the suppurated fluids. In this scenario, a multidisciplinary approach involving the ENT surgeon, the dentist, the thoracic surgeon and the infectivologist, is the best option to treat such a challenging complication of several head and neck pathologies.

Acknowledgements

The authors would like to thank Galli Carlotta, Franceschini Carlo and Raponi Ingrid who helped to write this article.

References

1 Fusconi M, Greco A, Galli M, et al. Odontogenic phlegmons and abscesses in relation to the financial situation of Italian families. Minerva Stomatol 2019;68:236-241. https://doi.org/10.23736/S00264970.19.042766

2 Buckley J, Harris AS, Addams-Williams J. Ten years of deep neck space abscesses. J Laryngol Otol 2019;133:324-328. https://doi.org/10.1017/S0022215119000458

3 Jayagandhi S, Cheruvu SC, Manimaran V, et al. Deep neck space infection: study of 52 cases. Indian J Otolaryngol Head Neck Surg 2019;71(Suppl 1):923-926. https://doi.org/10.1007/s12070-019-01592-3

4 Taylor M, Patel H, Khwaja S, et al. Descending cervical mediastinitis: the multidisciplinary surgical approach. Eur Arch Otorhinolaryngol 2019;276:2075-2079. https://doi.org/10.1007/s00405-019-05471-z

5 Hansen BW, Ryndin S, Mullen KM. Infections of deep neck spaces. Semin Ultrasound CT MR 2020;4:74-84. https://doi.org/10.1053/j.sult.2019.10.001

6 Rzepakowska A, Rytel A, Krawczyk P, et al. The factors contributing to efficiency in surgical management of purulent infections of deep neck spaces. Ear Nose Throat J 2019;145561319877281. https://doi.org/10.1177/0145561319877281

7 Lawrence R, Bateman N. Controversies in the management of deep neck space infection in children: an evidence-based review. Clin Otolaryngol 2017;42:156-163. https://doi.org/10.1111/coa.12692

8 Fiorella ML, Greco P, Madami LM, et al. New laboratory predictive tools in deep neck space infections. Acta Otorhinolaryngol Ital 2020;40:332-337. https://doi.org/10.14639/0392-100X-N0790

9 Prabh SR, Nirmalkumar ES. Acute fascial space infections of the neck: 1034 cases in 17 years follow-up. Ann Maxillofac Surg 2019;9:118-123. http://doi.org/10.4103/ams.ams_251_18

10 WHO Global Oral Health Programme, https://www.who.int/health-topics/oral-health/

11 Martins JR, Chagas OL Jr, Velasques BD, et al. The use of antibiotics in odontogenic infections: what is the best choice? A systematic review. J Oral Maxillofac Surg 2017;75:2606.e1-2606.e11. https://doi.org/10.1016/j.joms.2017.08.017

12 López-Marcos JF. Aetiology, classification and pathogenesis of pulp and periapical disease. Med Oral Patol Oral Cir Bucal 2004;9(Suppl):52-62. PMID: 15580137

13 Grönholm L, Lemberg KK. The role of unfinished root canal treatment in odontogenic maxillofacial infections requiring hospital care. Clin Oral Investig 2013;17:113-121. https://doi.org/10.1007/s00784-012-0710-8

14 Zehnder M. Endodontic infection caused by localized aggressive periodontitis: a case report and bacteriologic evaluation. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2001:440-445. https://doi.org/10.1067/moe.2001.117270

15 Hedge A, Mohan S. Infections of the deep neck spaces. Singapore Med J 2012;53:305-311; quiz 312.

16 Malik K, Dever LL, Kapila R, et al. Bezold's abscess: a rare complication of suppurative mastoiditis. IDCases 2019;17:e00538. https://doi.org/10.1016/j.idcr.2019.e00538

17 Plum AW, Mortelliti AJ, Walsh RE. Microbial flora and antibiotic resistance in odontogenic abscesses in upstate New York. Ear Nose Throat J 2018;97:e27-e31. https://doi.org/10.1177/0145561318097001-207

18 Tansey, JB, Hamblin J, et al. Dexamethasone use in the treatment of pediatric deep neck space infections. Ann Otol Rhinol Laryngol 2020;129:376-379. https://doi.org/10.1177/0003489419890349

19 Almutairi DM, Alqahtani RM. Deep neck space infections: a retrospective study of 183 cases at a tertiary hospital. Cureus 2020;12::e6841. https://doi.org/10.7759/cureus.6841

20 Rombey T, Schieren M, Pieper D. Video versus direct laryngoscopy for inpatient emergency intubation in adults. a systematic review and meta-analysis of randomized controlled trials. Dtsch Arztebl Int 2018;115:437-444. https://doi.org/10.3238/arztebl.2018.0437

21 Fang CH, Friedman R. Emergent awake tracheostomy – the five-year experience at an urban tertiary care center. Laryngoscope 2015;125:2476-2479. https://doi.org/10.1002/lary.25348

22 Ahuja V, Chachra A. Awake tracheostomy in a child with respiratory distress due to retropharyngeal abscess. Anaesth Rep 2020;8:e12047. https://doi.org/10.1002/anr3.12047

23 Adly A, Youssef TA, El-Begermy MM, et al. Timing of tracheostomy in patients with prolonged endotracheal intubation: a systematic review. Eur Arch Otorhinolaryngol 2018;275:679-690. https://doi.org/10.1007/s00405-017-4838-7

24 Heim, N, Warwas FB, Wiedemeyer V, et al. C. T. The role of immediate versus secondary removal of the odontogenic focus in treatment of deep head and neck space infections. A retrospective analysis of 248 patients. Clin Oral Investig 2019;23:2921-2927. https://doi.org/10.1007/s00784-018-02796-7

25 Guillier, D, Moris, V, Al Hindi, et al. Surgical approaches in neck dissection: Comparing functional, oncologic and aesthetic aspects of transverse cervicotomy to Paul André's approach. Annales de Chirurgie Plastique Esthétique 2018;63:140-147. https://doi.org/10.1016/j.anplas.2017.07.017

26 Cramer JD, Purkey MR, Smith SS, et al. The impact of delayed surgical drainage of deep neck abscesses in adult and pediatric populations. Laryngoscope 2016;126:1753-1760. https://doi.org/10.1002/lary.25835

27 Boscolo-Rizzo P, Stetlin M, Muzzi E, et al. Deep neck infections: a study of 365 cases highlighting recommendations for management and treatment. Eur Arch Otorhinolaryngol 2012;269:1241-1249.

28 Freeman RK, Vallières E, Verrier ED, et al. Descending necrotizing mediastinitis: an analysis of the effects of serial surgical debridement on patient mortality. J Thorac Cardiovasc Surg 2000;119:260-267.

29 Johnson R, Stewart M. The contemporary approach to diagnosis and management of peritonsillar abscess. Curr Opin Otolaryngol Head Neck Surg 2005;13:157-160.

30 Gallo, O, Mannelli G, et al. How to avoid life-threatening complications following head and neck space infections: an algorithm-based approach to apply during times of emergency. When and why to hospitalise a neck infection patient. J Laryngol Otol 2017;132:53-59. https://doi.org/10.1017/s0022215117002201

31 Coticchia, JM, Getnick, GS, et al. Age-, site-, and time-specific differences in pediatric deep neck abscesses. Arch Otolaryngol Head Neck Surg 2004;130:201. https://doi.org/10.1001/archotol.130.2.201

32 Hyun, SY, Oh HK, et al. Closed suction drainage for deep neck infections. J Cranio-Maxillofac Surg 2014;42:751-756. https://doi.org/10.1016/j.jcms.2013.11.006

33 Flynn TR, Hoekstra C, Lawrence FR. The use of drains in oral and maxillofacial surgery: a review and a new approach. J Oral Maxillofac Surg 1983;41:508-511. https://doi.org/10.1016/0278-2391(83)90241-0

[34] Raves JJ, Slifkin M, Diamond DL. A bacteriologic study comparing closed suction and simple conduit drainage. Am J Surg 1984;148:618-620. https://doi.org/10.1016/0002-9610(84)90336-2

[35] Alexander JW. Bacteriologic comparison of closed suction and Penrose drainage. Am J Surg 1984;148:699. https://doi.org/10.1016/0002-9610(84)90355-6

[36] Endo S, Murayama F, Hasegawa T, et al. Guideline of surgical management based on diffusion of descending necrotizing mediastinitis. Jpn J Thorac Cardiovasc Surg 1999;47:14-19. https://doi.org/10.1007/bf03217934

[37] Corsten MJ, Shamji FM, Odell PF, et al. Optimal treatment of descending necrotising mediastinitis. Thorax 1997;52:702-708. https://doi.org/10.1136/thx.52.8.702

[38] Glass GE, Murphy GF, Esmaeili A, et al. Systematic review of molecular mechanism of action of negative-pressure wound therapy. Br J Surg 2014;101:1627-1636. https://doi.org/10.1002/bjs.9636