B-ENT, 2017, **13**, 197-203

Prognosis for deep neck infections of dental origin: a univariate/multivariate analysis

E. Fasanaro[1], *G. Ottaviano*[2], *N. Favaretto*[2], *R. Marchese-Ragona*[2], *S. Sivolella*[3], *A. Bedogni*[4], *L. Giacomelli*[3], *E. Stellini*[3], *A. Martini*[2], *G. Marioni*[2]

[1]Department of Radiotherapy, Veneto Institute of Oncology IOV-IRCCS, Via Giustiniani 2, Padova, Italy; [2]Department of Neurosciences DNS, Otolaryngology Section, University of Padova, Via Giustiniani 2, Padova, Italy; [3]Department of Neurosciences DNS, Odontostomatology Institute, University of Padova, Via Giustiniani 2, Padova, Italy; [4]Department of Neurosciences DNS, Maxillofacial Surgery Unit, University of Padova, Via Giustiniani 2, Padova, Italy.

Key-words. Deep neck infection, dental, odontogenic, prognosis, multivariate

Abstract. *Objectives:* Dental infections can cause deep neck infections. There are still no widely-accepted prognostic factors for the rational diagnosis and treatment of deep neck infections (DNIs) of dental origin. The nature of the risk factors for DNIs of dental origin and their contributions to the outcome were analysed using univariate and multivariate approaches.

Methods: 115 consecutive cases of DNI of dental origin, treated at the Department of Neurosciences of Padova University, between 2000 and 2014, were considered.

Results: Higher than normal leukocyte counts on admission correlated strongly with longer hospital stays (more than seven days) at univariate analysis (Fisher's exact test, p=0.005), and were also independently associated with longer hospital stays at multivariate analysis (p = 0.007, OR = 3.99).

Conclusions: Further investigations are needed to confirm the clinical utility of leukocyte count normalization for safely deciding the optimal hospital stay for patients with odontogenic DNIs, even in the case of incomplete resolution of neck CT signs of infection.

1. Introduction

Deep neck infections (DNIs) (abscesses or cellulitis) are usually bacterial and originate from the upper aerodigestive tract, spreading along the fascial planes, and involving the deep neck spaces.[1] Before the worldwide diffusion of broad-spectrum antibiotics, most DNIs (about 70-80%) resulted from complicated pharyngeal infections.[2] Nowadays, however, despite improvements in dental care and oral hygiene, odontogenic infections are being diagnosed more frequently. A series described by Parhiscar and Har-El[3] revealed a marked prevalence of DNIs due to dental infections (43%), and Stalfors *et al*.[4] likewise found that odontogenic DNIs were the most common (49%). In the experience of Eftekharian *et al*.[5], the dental sources of DNIs were usually periapical infections of the mandibular (second or third) molars.

Generally speaking, odontogenic infections respond well to dental care and antimicrobial therapy.[6] The use of modern antibiotics has significantly reduced the rates of severe complications associated with odontogenic infections, but there has been a growing resurgence of antibiotic resistance.[7] Sometimes dental infections can spread to the deep neck spaces, causing DNIs that require hospitalization and aggressive surgical treatment.[8] According to the available literature, the DNI-related mortality rate ranges globally from 7.1% to 41.7% when local or systemic life-threatening complications occur.[9,10]

The main endpoint of our study was to review our experience of diagnosing and treating DNIs of ascertained dental origin at the Otolaryngology Section, Department of Neurosciences, University of Padova (an academic tertiary referral centre) during the period 2000-2014. A second endpoint was

This study was partly supported by grant No. 60A07-8485/13 (G. Marioni) from the University of Padova, Italy.

to analyse a consecutive case series of odontogenic DNIs using univariate/multivariate statistical models to identify any clinical, radiological or laboratory factors of prognostic value in terms of multiple neck site involvement and length of hospital stay.

2. Materials and methods

2.1. Patients

The study was carried out in accordance with the principles of the Helsinki Declaration. All available records concerning patients treated between April 2000 and September 2014 for DNIs at the Otolaryngology Section of the University of Padova (Italy) were reviewed. Superficial infections, infections due to external (traumatic or surgical) neck injuries and, infections occurring in head and neck tumours, as well as, in patients with active neoplastic diseases, were excluded.

Among the 301 patients admitted with DNIs, for the purposes of the present study we only considered those whose infection was of dental origin, judging from their clinical and radiological findings. Over the period considered, 115 patients (68 males, 47 females; mean age 42.6±18.8 years; median age 38 years) were hospitalized with odontogenic DNIs.

Different treatment approaches were adopted on the grounds of clinical findings (oral cavity exploration, upper aero-digestive tract endoscopy), radiological features (contrast-enhanced computerized tomography [CT], magnetic resonance imaging [MRI], ultrasonography, mandible orthopantogram [OPT]), and microbiological and laboratory evidence.

2.2 Statistical analyses: univariate and multivariate

Fisher's exact test was used in a univariate setting to test the association between various clinical, laboratory, and radiological findings and the prognostic variables: (i) involvement of more than one deep neck site; and (ii) longer hospital stays (more than seven days; 6.91 days was the mean hospital stay for our series).

In the limited number of cases with available data (26 patients), the non-parametric Mann-Whitney *U* Test was used to compare the mean early c-reactive protein (CRP) values of the sub-cohorts with (i) involvement of one *vs* more than one deep neck site; and (ii) long (more than seven days) *vs* short hospital stay.

A p-exclusion value of $p \leq 0.2$ was applied in Fisher's exact test and a final multivariate model was generated. The multivariate statistical analysis was run applying the logistic regression model to calculate the odds ratio (OR) for each variable considered, again with a view to identifying significant independent predictors of: (i) multiple neck site involvement; and (ii) longer hospital stays (more than seven days). The adequacy of the resulting models was ascertained by checking for multicollinearity and goodness of fit.

A p-value <0.05 was considered significant. The STATA 8.1 (Stata Corp, College Station, TX) statistical package was used for all analyses.

3. Results

Before admission, the patients' general practitioners or dentists had already prescribed oral antibiotic therapy in 87 cases (76.65%), and oral steroids in 30 (26.09%), while 21 patients (18.26%) had received no pharmacological treatment prior to their hospitalization.

On admission, physical examination revealed neck swelling (95 cases, 82.61%), trismus (64 cases, 55.65%), and fever (53 cases, 46.09%) as the most common clinical signs. Gum swelling was apparent in 20 patients (17.39%), and oral swelling

Table 1

Main signs and symptoms of odontogenic DNIs at presentation (more than one sign or symptom in some patients).

Signs	**No. of cases**	**%**
Neck swelling	95	82.61
Trismus	64	55.65
Fever	53	46.09
Facial swelling	29	25.22
Gum swelling	20	17.39
Oral swelling	14	12.17
Increased drooling	6	5.22
Symptoms	**No. of cases**	**%**
Neck pain	63	54.78
Odynophagia	46	40.00
Dysphagia	34	29.57
Dysphonia	12	10.43
Gum pain	11	9.57
Dyspnoea	8	6.96

Table 2

DNIs originating from mandibular teeth (more than one tooth was involved in two cases).

Teeth involved	No. of cases	%
First molar	33	35.86
Second molar	28	30.43
Third molar	25	27.17
Premolar	11	11.95
Ceanine	2	2.17
Data unavailable	23	20.00

(not involving gums) in 14 (12.17%). Neck pain (63 cases, 54.78%), odynophagia (46 cases, 40.00%), and dysphagia (34 cases, 29.57%) were the symptoms most frequently reported by patients (Table 1). Laboratory tests identified higher than normal leukocyte counts (reference range 4.5-11.0 cells*10^9/L) in 71/106 cases (66.99%) (data were unavailable for nine patients). Hypertension (13 cases, 11.30%), diabetes mellitus (seven cases, 6.08%), and heart diseases (seven cases, 6.08%) were the most common systemic comorbidities. Eighty-one patients (70.43%) had no associated systemic disorders.

The source of the DNI (as also assessed by OPT) (Table 2) was a periapical infection or interproximal caries involving the first molar in 33 of the 92 patients with available data (35.86%), the second molar in 28 (30.43%), the third molar in 25 (27.17%), the first or second premolars in 11 (11.95%), and the canine teeth in two cases (2.17%). In two cases there was more than one tooth involved.

The extension of the DNI was assessed mainly on a contrast-enhanced CT, which can also pinpoint the site of a DNI (abscess or cellulitis) in relation to the major vessels. In our series, the submandibular neck space was involved in 110 cases (95.65%), the parapharyngeal space in 18 (15.65%), and the retropharyngeal space in one. The infection involved more than one neck site in 16 cases (13.91%). DNI complications (5.21%) were diagnosed in six patients: four were cases of skin fistulization, one of mediastinitis, and one of pleuritis.

While in hospital, 30 patients (26.09%) were treated with empirical intravenous antibiotic therapy alone (ampicillin/sulbactam 1.5 g three or four times a day, plus metronidazole 500 mg three or four times a day, or cefotaxime 2 g three times a day plus metronidazole 500 mg three or four times a day), with or without intravenous steroids (intravenous betamethasone, 4-12 mg a day). Rehydration was administered as necessary. The thirty patients who only required medical therapy underwent restorative and endodontic therapy on the teeth involved. Eighty-five patients (73.91%) required both medical and surgical therapy (and more than one surgical procedure in some cases). Endoral incision and drainage were performed on 56 patients (48.70%) and tooth extraction on 47 (40.87%) without delay if there was evidence of pericoronitis, extended periodontal lesions, or destructive caries unresponsive to endodontic therapy**.** Neck exploration and drainage via a cervicotomy were performed in 15 cases (13.04%). Surgery was usually prompted by a contrast-enhanced CT showing a significant, encapsulated, hypodense heterogeneous lesion, and/or when clinical and laboratory findings indicated that patients were failing to respond to parenteral antibiotics within 24 to 48 hours, and/or in cases of potentially life-threatening complications. The results of intraoperative bacterial cultures were available for 46 of the 85 patients treated surgically (54.11%). The most frequently isolated bacteria were *Streptococcus viridians sp*, and *Peptostreptococcus,* which were consistent with the dental origin of the DNIs. Table 3 details the available data on the bacteria isolated.

Table 3

Results of 46 available microbiological cultures (more than one pathogen was isolated in some cases).

Pathogens	No. of cases
Streptococcus viridans sp.	17[a]
Peptostreptococcus sp.	15
Gemella morbillorum	5
Staphylococcus epidermidis	2
Streptococcus β-haemolytic groups A or B	2
Fusobacterium species	1
Burkholderia cepacia	1
Prevotella oralis	1
Eikenella corrodens	1
Multiple pathogens	5
Negative culture	6

[a]including *Streptococcus constellatus* (13 cases), *Streptococcus anginosus* (one case) and *Streptococcus viridans* (three cases)

None of the patients required tracheotomy. None died of their odontogenic DNIs or any related complications. After discharge, patients who had received intravenous antibiotic treatment for less than 14 days while in hospital completed at least a two week course of antibiotics, usually with oral amoxicillin clavulanate (1 g three times a day).

3.1. Prognosis: univariate analysis

Fisher's exact test revealed that multiple site involvement was not significantly related with any of the variables considered (Table 4), whereas longer hospital stays correlated strongly with higher than normal leukocyte counts (Fisher's exact test, p = 0.005). The involvement of more than one neck site (p = 0.16) and an interval of more than seven days between the onset of clinical signs of DNI and hospital admission (p = 0.19) were not significantly related to longer hospital stays. For the complete results, see also Table 5.

Considering the limited sub-cohort of patients with available early CRP determinations (26 cases), the Mann-Whitney *U* Test ruled out any significant differences between mean CRP values in patients with multiple *vs* one neck site involvement (111.4±60.2 mg/L *vs* 68.3±43.7 mg/L, p = 0.23) and with longer *vs* shorter hospital stays (90.1±56.5 mg/L *vs* 84.0.3±54.8 mg/L, p = 0.84).

3.2. Prognosis: multivariate analysis (Table 6)

The variable CPR was not considered in our multivariate models considering the limited number of cases with available data.

Table 4

Univariate approach: association analyses between multiple site involvement in patients with odontogenic DNIs and, demographic, clinical laboratory and microbiological variables

Variables considered	**p-value**
Sex (M/F)	0.79
Age (<65/≥65 years)	1
Presence of symptoms before admission(>7 days) (yes/no)	0.76
Steroid treatment before admission (yes/no)	0.12
Antibiotic treatment before admission (yes/no)	1
Comorbidities (yes/no)	1
Complications (yes/no)	1
Leukocytosis (yes/no)	1
Microbial growth (yes/no)	1
More than one pathogen (yes/no)	1

Table 5

Univariate approach: association analyses between longer hospital stays (more than seven days) in patients with odontogenic DNIs and demographic, clinical, laboratory, and microbiological variables

Variables considered	**p-value**
Sex(M/F)	0.69
Age (<65 / ≥65 years)	0.43
Presence of symptoms before admission (>7 days)(yes/no)	0.19
Steroid treatment before admission (yes/no)	1
Antibiotic treatment before admission (yes/no)	0.63
Comorbidities (yes/no)	0.27
More than one neck site involved (yes/no)	0.16
Complications (yes/no)	1
Leukocytosis (yes/no)	0.005
Bacterial growth (yes/no)	1
More than one pathogen (yes/no)	1

Table 6

Multivariate analysis for the prognosis of odontogenic DNIs: longer hospital stay (more than seven days)

Prognostic factors	**OR**	**CI 95 %**	**p-value**
Symptoms before hospitalization			
≤7 days	1.00	Reference group	0.12
>7 days	2.05	0.81-5.20	
Leukocyte count			
<11.0 cells x 10^9	1.00	Reference group	0.007
≥11.0 cells x 10^9	3.99	1.45-10.96	
Sites of deep neck spaces involved			
one space	1.00	Reference group	0.45
more than one space	1.54	0.49-4.8	

Neither the time elapsed between the onset of signs or symptoms and admission to hospital (p = 0.12, OR 2.05, CI 95% 0.81-5.20), nor multiple neck site involvement (p = 0.45 OR 1.54 CI 95% 0.49-4.8), were significant independent prognostic indicators of a longer hospital stay when analysed sing multivariate statistics. On the other hand, a higher than normal leukocyte count on admission (p = 0.007, OR = 3.99, CI 95% 1.45-10.96) was independently associated with a longer hospital stay (more than seven days), as summarized in *Table 6*.

4. Discussion

Deep neck infections of dental origin can be caused by caries, periodontitis, periapical abscess, periodontal abscess, pericoronitis, pulpitis, osteitis or infections of the aponeurotic spaces[11], or they can stem from recent dental extractions.

Although odontogenic DNIs can originate from infections in either jaw, mandibular dental infections should be considered as a specific risk factor for DNIs. Alotaibi *et al.*[12] retrospectively assessed a cohort of 97 patients hospitalized for odontogenic DNIs and reported a significantly higher frequency of DNIs in patients with mandibular infections than in those with maxillary ones (29% *vs* 7%), and the hospital stay was also significantly longer for the former than for the latter (mean 5.6 *vs* 3.2 days). A similar retrospective analysis was conducted by Opitz *et al.*[13] on 814 patients with odontogenic infections who received surgical treatment: 14 patients (1.7%) required intensive medical therapy after surgery and one died. The aetiology of all but one of these patients was decay in one or more of the mandibular teeth. Wabik[14] considered 38 patients suffering from odontogenic inflammatory processes in the cervicofacial area, reporting that the inflammation originated from mandibular teeth in 84% of patients, from teeth in both jaws in 11%, and from teeth in the maxilla alone in 5% of cases. Among the mandibular teeth responsible for DNIs, the third molar was the most common cause of inflammation (47%), followed by the second molar (34%) and, then the first (26%). In our series, on the other hand, the most frequent culprit was a periapical infection and interproximal caries of the first mandibular molar (35.86% of the patients with available data), followed by the second and third molars (30.43% and 27.17%, respectively). More than one tooth was involved in two cases.

Odontogenic infections generally remain localized and heal without complications, providing that appropriate therapy is administered and patients are physiologically immunocompetent.[13] However, in some cases, the infection can spread from the structures supporting the affected tooth along the planes of limited resistance to the fascial spaces in the vicinity. Involvement of the submandibular space can also cause Ludwig's angina (bilateral cellulitis of the submandibular, sublingual and, submental spaces), which may also involve the pharyngo-maxillary and retropharyngeal spaces. In our series, the submandibular space was the most frequently involved neck space (in 100 out of 115 patients), judging from clinical and radiological examinations. Although clinical examination alone seems to underestimate the extent of the disease in 70% of DNIs[15], endoscopy is essential for analysing the need for airway support in patients at risk of Ludwig's angina, as well as in the event of clinical symptoms such as trismus (this applied to 64 of our 115 patients). Diabetes mellitus[16], a history of immunosuppression after transplant surgery, radiation therapy, chemotherapy, HIV infection, and chronic alcohol abuse are known predisposing factors.[13,17] Opitz *et al.*[13] reported that indolence seems to be an additional feature of odontogenic infections in some patients, and may contribute to the severe course of their infection due to their delay in seeking medical treatment. Other reported risk factors for patients with DNIs might include low socio-economic circumstances[17], low levels of formal education, and living more than one hour away from a tertiary care center.[18] The aggressiveness of some odontogenic DNIs may be partially explained by: (i) a poly-microbial aetiology, i.e., the presence of both aerobic and anaerobic bacteria which supports odontogenic infection; individual members of the group of bacteria produce metabolites essential to the growth of other microorganisms, creating a pH favourable to their growth in the environment, or consuming oxygen and thus facilitating anaerobic growth[19]; (ii) the prevalence of penicillin-resistant bacteria isolated in dental infections and abscesses (which ranges from 5% to 20% of cases [20]), as well as the presence of biofilm (which induces the bacteria within the matrix to grow more slowly, a lower drug uptake and the reduced effectiveness of these the drugs[21]); (iii) a sometimes inappropriate use of drugs before hospitalization, which may mask signs of infection by changing its clinical presentation[22]; and/or (iv) circulatory disorders, i.e., slower circulation as a result of blood vessel dilation at the inflammatory focus. These reasons may also explain the frequent need for surgery: tissue oxygenation can modify the environment, inducing the regression of the infection, while removing the source of the dental infection leads to normalization of the local (and systemic) situation.

It is very important to establish which variables influence the onset and prognosis of odontogenic DNIs, and, especially, the factors that turn a local

process into a systemic and potentially complicated disease**.** We therefore applied univariate and multivariate analyses to investigate the multifaceted nature of the risk factors associated with odontogenic DNIs and their respective contributions to the clinical outcome**.** In the available literature on DNIs of dental origin, there are few investigations based on multivariate analysis, and their findings are not easy to compare because different diagnostic and therapeutic methods were adopted, and different variables considered. Although some authors focused on the occurrence of complications in cases of dental DNI and on longer hospital stays, none of the clinical variables considered were unequivocally confirmed as having an independent significant prognostic role. Applying multivariate statistical approaches, Rasteniene *et al*.[23] assessed 285 patients admitted to a medical centre for acute odontogenic maxillofacial infections: they found that the main determinants of the length of hospital stay were the extent of the odontogenic infection and the need for an extra-oral incision to drain the infection. Flynn[24] examined 37 consecutive patients admitted for severe odontogenic infections, and found that only treatment variables (failure of antibiotics and need for re-surgery) and anatomical features (extent or site of the infection) independently predicted a longer hospital stay. Christensen[25] considered 318 patients admitted for odontogenic infections, and showed that leukocytosis and bilateral infections on admission were associated with a shorter hospital stay; as a possible explanation for this result, the author said that such features might be associated in many cases with the need for immediate or more aggressive surgical management, a condition that would have assured a more effective treatment and a consequently earlier discharge**.** Conversely, a higher than normal leukocyte count was the only factor in our series that independently predicted a longer hospital stay. Normalization of the leukocyte count could be seen as a strong indicator of clinical improvement, even if the resolution of the infection still appears incomplete on radiology.

The main strengths of the present study include: (i) our clearly-defined patient inclusion and exclusion criteria (only patients with a clinically and radiologically confirmed dental site of origin to their DNIs were considered); (ii) the consecutive nature of the series; and (iii) the reasonably well-defined diagnostic and therapeutic protocols adopted in close cooperation with the dentists and/or maxillofacial surgeons at our department. As for the data analysis, ours is one of the few investigations on odontogenic DNIs to have been based on both univariate and multivariate statistical approaches. On the other hand, the main weaknesses of our study concern: (i) the retrospective setting; (ii) the fact that, in some cases, it was impossible to contact the dentists who had treated the patients before they were hospitalized; and (iii) the fact that microbiological investigations were not performed for all patients who underwent surgical drainage.

Conclusion

We believe that using multivariate statistical models to investigate DNIs of dental origin can contribute to the development of guidelines for a rational diagnosis and treatment of this condition, reducing the rates of severe complications and the costs of hospitalization. This approach could also make it easier to compare different studies and enable meaningful meta-analyses, possibly shared by otolaryngologists, dentists and maxillofacial surgeons. Further investigations are needed to confirm the clinical utility of leukocyte count normalization for safely deciding the optimal hospital stay for patients with odontogenic DNIs, even in the case of the incomplete resolution of neck CT signs of infection.

Acknowledgement

The authors thank Frances Coburn for correcting the English version of this article.

References

1. Celakovsky P, Kalfert D, Tucek L, Mejzlik J, Kotulek M, Vrbacky A, Matousek P, Stanikova L, Hoskova T, Pasz A. Deep neck infections: risk factors for mediastinal extension. *Eur Arch Otorhinolaryngol*. 2014;271(6):1679-1683.
2. Plaza Mayor G, Martínez-San Millán J, Martínez-Vidal A. Is conservative treatment of deep neck space infections appropriate? *Head Neck.* 2001; 23(2):126-133.
3. Parhiscar A1, Har-El G. Deep neck abscess: a retrospective review of 210 cases *Ann Otol Rhinol Laryngol.*2001;110(11):1051-1054.
4. Stalfors J, Adielsson A, Ebenfelt A, Nethander G, Westin T. Deep neck space infections remain a surgical challenge. A study of 72 patients. *Acta Otolaryngol.* 2004;124(10):1191-1196.
5. Eftekharian A, Roozbahany NA, Vaezeafshar R, Narimani N. Deep neck infections: a retrospective review of 112 cases. *Eur Arch Otorhinolaryngol.* 2009;266(2), 273-277.

6. Seppänen L,Rautemaa R, Lindqvist C, Lauhio A. Changing clinical features of odontogenic maxillofacial infections. *Clin Oral Investig.* 2010;14(4):459-465.
7. Jaunay T, Sambrook P, Goss A. Antibiotic prescribing practices by South Australian general dental practitioners. *Aust Dent J.* 2000;45(3):179-186.
8. Hwang T, Antoun JS, Lee KH. Features of odontogenic infections in hospitalised and non-hospitalised settings. *Emerg Med J.* 2011;28(9):766-769.
9. Marioni G, Staffieri A, Parisi S, Marchese-Ragona R, Zuccon A, Staffieri C, Sari M, Speranzoni C, de Filippis C, Rinaldi R. Rational diagnostic and therapeutic management of deep neck infections: analysis of 233 consecutive cases. *Ann Otol Rhinol Laryngol.* 2010;119(3):181-187.
10. Staffieri C, Fasanaro E, Favaretto N, La Torre FB, Sanguin S, Giacomelli L, Marino F, Ottaviano G, Staffieri A, Marioni G. Multivariate approach to investigating prognostic factors in deep neck infections. *Eur Arch Otorhinolaryngol.* 2014;271(7): 2061-2067.
11. Maestre-Vera JR. Treatment options in odontogenic infection. *Med Oral Patol Oral Cir Bucal.* 2004;9 Suppl:25-31;19-24.
12. Alotaibi N, Cloutier L, Khaldoun E, Bois E, Chirat M, Salvan D. Criteria for admission of odontogenic infections at high risk of deep neck space infection. *Eur Ann Otorhinolaryngol Head Neck Dis*. 2015;132(5):261-264.
13. Opitz D, Camerer C, Camerer DM, Raguse JD, Menneking H, Hoffmeister B2, Adolphs N. Incidence and management of severe odontogenic infections-a retrospective analysis from 2004 to 2011. *J Craniomaxillofac Surg.* 2015;43(2):285-289.
14. Wabik A, Hendrich BK, Nienartowicz J, Guziński M, Sąsiadek MJ. Odontogenic inflammatory processes of head and neck in computed tomography examinations. *Pol J Radiol.* 2014;79:431-438.
15. Reynolds SC, Chow AW. Life-threatening infections of the peripharyngeal and deep fascial spaces of the head and neck. *Infect Dis Clin North Am*. 2007;21(2):557-576.
16. Jin L, Zhang T. Deep neck infections: A retrospective study of 142 patients. *B-ENT.* 2014;10(2):127-132.
17. Horváth T, Horváth B, Varga Z, Liktor B Jr, Szabadka H, Csákó L, Liktor B. Severe neck infections that require wide external drainage: clinical analysis of 17 consecutive cases. *Eur Arch Otorhinolaryngol.* 2015;272(11):3469-3474.
18. Barber BR, Dziegielewski PT, Biron VL, Ma A, Seikaly H. Factors associated with severe deep neck space infections: targeting multiple fronts. *J Otolaryngol Head Neck Surg.* 2014;43(1):35. [Epub ahead of print]
19. Fating NS, Saikrishna D, Vijay Kumar GS, Shetty SK, Raghavendra Rao M. Detection of Bacterial Flora in Orofacial Space Infections and Their Antibiotic Sensitivity Profile. *J Maxillofac Oral Surg.* 2014;13(4):525-532.
20. Jundt JS, Gutta R. Characteristics and cost impact of severe odontogenic infections. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2012;114(5):558-566.
21. May JG, Shah P, Sachdeva L, Micale M, Kruper GJ, Sheyn A,Coticchia JM. Potential role of biofilms in deep cervical abscess. *Int J Pediatr Otorhinolaryngol.* 2014;78(1):10-13.
22. Boscolo-Rizzo P, Stellin M, Muzzi E, Mantovani M, Fuson R, Lupato V, Trabalzini F, Da Mosto MC. Deep neck infections: a study of 365 cases highlighting recommendations for management and treatment. *Eur Arch Otorhinolaryngol.* 2012;269(4):1241-1249.
23. Rastenienė R, Aleksejūnienė J, Pūrienė A. Determinants of length of hospitalization due to acute odontogenic maxillofacial infections: a 2009-2013 retrospective analysis. *Med Princ Pract*. 2015;24(2):129-135.
24. Flynn TR, Shanti RM, Hayes C. Severe odontogenic infections, part 2: prospective outcomes study. *J Oral Maxillofac Surg.* 2006;64(7):1104-1113.
25. Christensen B, Han M, Dillon JK. The cause of cost in the management of odontogenic infections 2: multivariate outcome analyses. *J Oral Maxillofac Surg*. 2013; 71(12):2068-2076.

Elena Fasanaro, MD
Department of Radiotherapy, Veneto Institute of Oncology IOV-IRCCS,
Via Giustiniani 2
35128 Padova
Italy
Tel. +39 049 8217937
Fax: +39 049 8212958
E-mail: elena.fasanaro@alice.it