Epidemiology of deep neck infection submitted to surgery in a portuguese tertiary hospital centre

Original Article

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Abstract

Objective: Assess epidemiological data and clinical predictors of mediastinitis in deep neck infections (DNI) submitted to surgery.
Study Design: Retrospective observational
Methods: Data analysis of every DNI patient submitted to surgery from January 2015 to December 2021 in the Otorhinolaryngology department of a tertiary hospital center.
Results: A total of 165 patients with a mean age of presentation of 48,5 years were included. The most frequent etiology was odontogenic infection (51,5%) and the most involved cervical space was the submandibular space (60,6%). Furthermore, the most isolated bacteria in patients with and without mediastinitis was Streptococcus spp.
Progression to mediastinitis occurred in 20 (12,1%) patients. In a multivariate analysis, a bilateral DNI location (p=0,015) and a higher neutrophil to lymphocyte ratio (NLR) (0,037) were associated with progression to mediastinitis.
Conclusion: The presence of a bilateral DNI and NLR seem to be the most important clinical predictors of mediastinitis.
Keywords: Deep Neck Infection; Mediastinitis

Introduction

Deep neck infections (DNI) are defined as abscesses or cellulitis located in the cervical spaces limited by the layers of the deep cervical fascia[1]. These infections may rapidly spread through the cervical fascia planes and descend to the mediastinum[2]. Thus, DNI are associated with high morbidity and potentially lethal complications, such as mediastinitis, *Lemierre* Syndrome, and necrotizing fasciitis[3]. To optimize the treatment of DNI, clinicians must be aware of the epidemiology and factors associated with unfavorable outcomes. The objective of this study is to analyze the epidemiology and predictive factors of mediastinitis in DNI.

Methods

This retrospective observational study included adult patients who underwent surgery due to DNI in the otorhinolaryngology department of a tertiary hospital center from January 2015 to December 2021. Exclusion criteria were patients with an isolated peritonsillar abscess and those with a malignant head and neck tumor. All patients were treated according to the department's protocol for DNI. Every patient underwent blood investigations and contrast enhanced computed tomography (CT) prior to the surgery. The type of surgery (intra-oral or external drainage) was selected according to the clinical and imaging examination results, and purulent exudates were collected in every case for microbiological assessment. Antibiotic therapy was initiated empirically with ceftriaxone (1 g/IV/q.12.h.) and clindamycin (600 mg/IV/q.6.h.), and was modified, if required, after antimicrobial susceptibility tests. Drains were placed in every patient who underwent external drainage and daily lavages were performed with *Microdacyn*®. The following data were retrospectively analyzed: patients' demographic variables (age, sex) and clinical history (DNI etiology, previous antibiotic therapy, symptom duration, and other diseases), blood tests at admission (C-reactive protein [CRP], leucocyte count, lymphocyte count, neutrophil count, and neutrophil to lymphocyte ratio [NLR]), purulent exudate cultures, and contrast enhanced CT scan (involved spaces, highest dimensions, infra-hyoid extension, and presence of gas), treatment, hospitalization days and complications of DNI. Furthermore, patients who developed mediastinitis were compared with patients with isolated DNI to assess the prognostic factors related to mediastinitis. A descriptive analysis of the patients' characteristics was performed by using absolute and relative frequencies for categorical variables, mean and standard deviation for normally distributed continuous variables, and median and range for non-normally distributed continuous variables. Normality of continuous variables was assessed with the *Kolmogorov-Smirnov Test*. Associations of different variables with mediastinitis were analyzed using the *Chi-square Test* or *Fischer's Exact Test* for categorical variables, *Student's T Test* for normally distributed continuous variables, and *Mann-Whitney U Test* for non-normally distributed continuous variables. Multivariate logistic regression analysis was performed by taking into consideration age, etiology, laboratory parameters (neutrophil count, lymphocyte count, and NLR), CT parameters (highest dimensions, infra-hyoid extension, and presence of gas), location, and laterality to assess the predictive factors for progression to mediastinitis. All statistical analyses were conducted using the software IBM® SPSS® Statistics version 27, and associations were considered significant when $p<0.05$.

Results

Epidemiology of DNI

A total of 165 patients with DNI were included. The mean age at presentation was 48.5 ± 16.6 years; there was a male predominance (n=106; 64.2%); and 23 patients (13.9%) had diabetes mellitus (DM). The median symptom duration until otorhinolaryngological evaluation was 5 (1–30) days, and 105 (63.6%) patients had taken antibiotics previously, among whom 52.4% were undergoing treatment with amoxicillin with clavulanic acid. Most patients (n=134; 81.2%) underwent external cervical drainage, while the remaining underwent intra-oral drainage (n=31; 18.2%). After surgery, the median hospitalization days were 10.5 (1–133) days, and 40 (24.2%) patients required re-intervention. The reported complications are shown in Figure 1. The most common complication was mediastinitis in 20 (12,1%) patients. The most frequent etiology was odontogenic infection (n=86, 52.1%), while the second most common was tonsillitis (n=42; 25.5%). The etiologies are shown in Figure 2. Furthermore, the most frequently involved neck space was the submandibular space (n=100; 60.6%) followed by the parapharyngeal space (n=69; 41.8%), as illustrated in Figure 3.

Figure 1
Complications of deep neck infections (DNI)

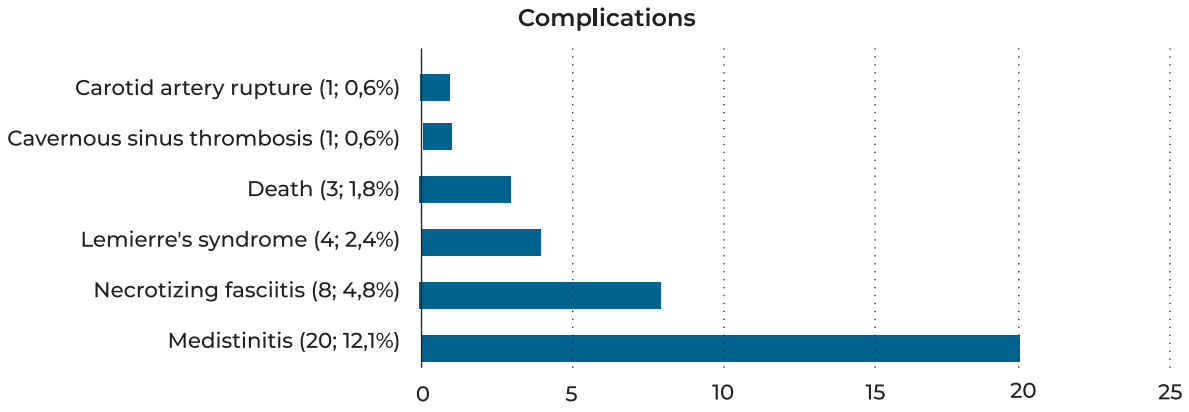


Figure 2
Etiologies of deep neck infections (DNI)

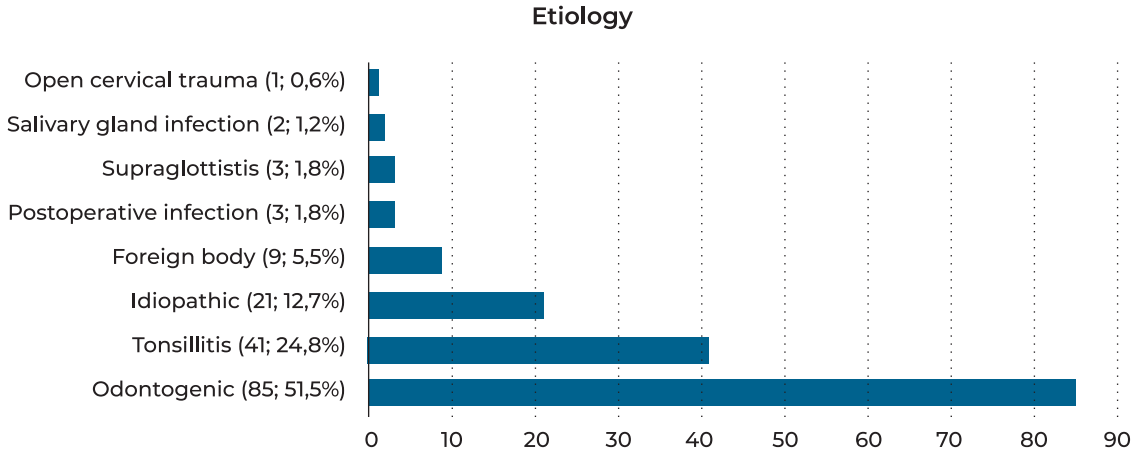
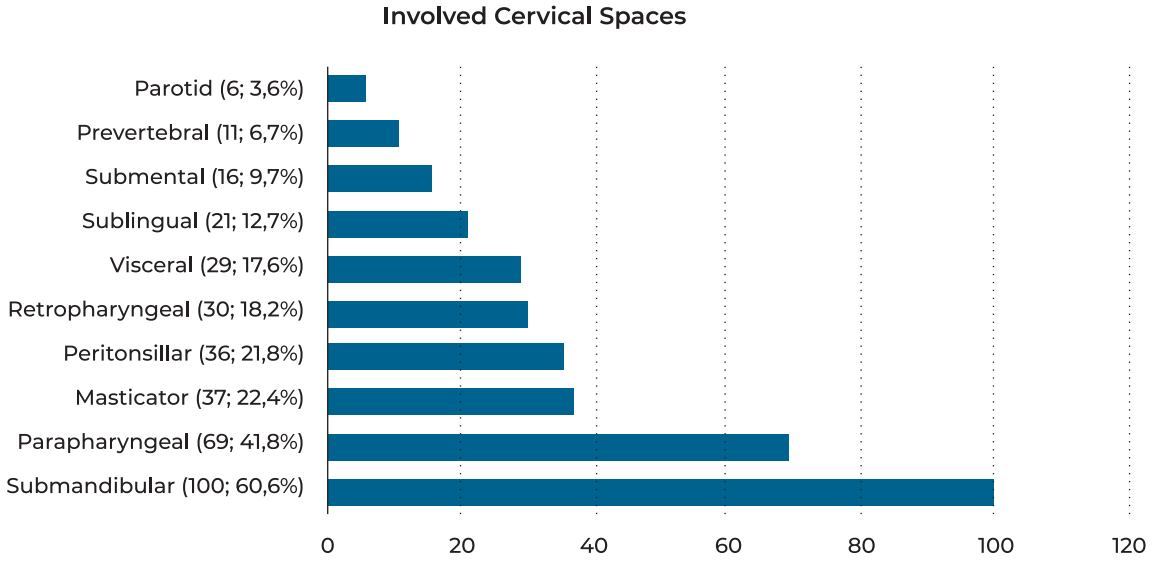


Figure 3
Neck spaces involved in deep neck infections (DNI); the sum of the percentages is higher than 100% because a DNI may involve more than one neck space.



Samples for bacterial cultures were obtained duringsurgeryandtheculturesresultsareshown in Table 1. Among all patients with DNI (n=165), cultures were negative in 76 (46.1%) patients and were positive for multiple bacteria in in 18 (10.9%) patients. The most commonly isolated organisms were *Streptococcus anginosus* in 30 (33.7%) cultures, *Streptococcus constellatus* in 28 (31.4%), and *Prevotella spp.* in 17 (19,1%) cultures. In patients with mediastinitis, cultures were negative in nine (45%) patients and multiple bacteria were isolated in three (15%) patients. The most commonly isolated bacteria in patients with mediastinitis were similar to those reported for all patients with DNI, including *Streptococcus anginosus* in six (54.5%) cultures, *Streptococcus constellatus* in two (18.2%), and *Prevotella spp.* in three (27.3%) cultures.

Prognostic factors for progression to mediastinitis

In univariate analysis, progression to mediastinitis was associated with older age (p=0.007); tonsillitis (p<0.001); bilateral involvement (p<0.001); laboratory parameters such as neutrophilia (p=0.002), lymphopenia (p<0.001), and elevated NLR (p<0.001); and CT parameters such as higher dimensions (p<0.001), infra-hyoid extension (p<0.001), and presence of gas (p<0.001). Furthermore, parapharyngeal (p=0.029), retropharyngeal (p<0.001), prevertebral (p<0.001), and visceral (p<0.001) locations were associated with mediastinitis, while a submandibular location (p<0.001) was a protective factor.

In multivariate analysis of age, etiology, laboratory parameters (neutrophil count, lymphocyte count, and NLR), CT parameters (highest dimensions, infra-hyoid extension, and presence of gas), location, and laterality, the only factors associated with progression to mediastinitis were NLR (p=0.037) and bilateral involvement (p=0.015).

Table 1
Results of bacterial cultures in patients with deep neck infections

Culture	Control (n=165)	Mediastinitis (n=20)
Negative	76 (46,1%)	9 (45 %)
Multiple bacteria	18 (10,9%)	3 (15%)
Gram (+) aerobic		
Steptococcus pyogenes	3 (3,4%)	0
Streptococcus anginosus	30 (33,7%)	6 (54,5%)
Streptococcus constellatus	28 (31,4%)	2 (18,2%)
Streptococcus epidermidis	2 (2,2%)	0
Streptococcus mitis	2 (2,2%)	0
Steptococcus agalactiae	1 (1,1%)	0
Staphylococcus aureus	8 (9%)	1 (9,1%)
Gram (-) aerobic		
Pseudomonas aeruginosa	1 (1,1%)	1 (9,1%)
Klebsiella pneumoniae	1 (1,1%)	0
Anaerobic		
Prevotella spp.	17 (19,1%)	3 (27,3%)
Fusobacterium spp.	7 (7,9%)	0
***Enterobacter** spp.*	3 (3,4%)	1 (9,1%)
Eikenella spp.	3 (3,4%)	0
Proteus spp.	1 (1,1%)	0

Table 2
Univariate analysis for factors associated with progression to mediastinitis

		Control (n=145)	Mediastinitis (n=20)	P
Sex[1]	Male (n=104)	62,8%	65%	1,00
Age[2]		47 ± 16,1	60,2± 16,6	**0,007**
Diabetes mellitus[1] **(n=23)**		13,1%	20%	0,487
Etiology[1]	Idiopathic (n=21)	11%	25%	**<0,001**
	Tonsillitis (n=42)	22,8%	45%	
	Odontogenic (n=86)	56,6%	10%	
	Others (n=16)	9,7%	20%	
Previous antibiotic therapy[1] **(n=104)**		64,1%	57,9%	0,619
Symptom duration in days[3]		5 ± 4	4 ± 3	0,224
Laboratory parameters	CRP[2]	175,86 ± 112,82	256,17 ± 125,03	0,708
	Leucocytes[2]	15,58 ± 6,08	15,37 ± 6,64	0,642
	Neutrophils %[3]	79,6 ± 14	87 ± 7,1	**0,002**
	Lymphocytes %[3]	9,8 ± 10	4,9 ± 4	**<0,001**
	NLR3	8 ± 10	18 ± 18	**<0,001**
CT scan parameters	Highest Dimension[3]	43 ± 21	130 ± 81	**<0,001**
	Infra-hyoid Extension1 (n=64)	30,6%	90,5%	**<0,001**
	Presence of Gas1 (n=39)	16,7%	75%	**<0,001**
Involved neck spaces[1]	Peritonsillar (n=36)	20%	35%	0,247
	Masticator (n=36)	24,1%	5%	0,079
	Parotid (n=6)	4,1%	0%	0,610
	Submandibular (n=98)	65,5%	15%	**<0,001**
	Sublingual (n=21)	14,5%	0%	0,079
	Submental (n=16)	10,3%	5%	0,696
	Parapharyngeal (n=68)	37,9%	65%	**0,029**
	Retropharyngeal (n=30)	11,7%	65%	**<0,001**
	Prevertebral (n=11)	3,4%	30%	**<0,001**
	Visceral (n=29)	10,3%	70%	**<0,001**
Location[1]	Unilateral (n=134)	86,2%	45%	**<0,001**
	Bilateral (n=31)	13,8%	55%	
Surgery[1]	External Drainage (n=132)	79,3%	85%	0,767
	Intra-oral Drainage (n=33)	20,7%	15%	

[1] Chi-square or Fischer's Exact Test; presented as percentage; [2] Student T-Test; presented as mean ± standard deviation; [3]Man-Whitney U test; presented as median ± interquartile range; CRP, C-reactive protein; CT, computed tomography; NLR, neutrophil to lymphocyte ratio.

Table 3
Multivariate analyses for factors associated with progression to mediastinitis

		Odds ratio	95% Confidence interval	P
Age		1,03	0,99 – 1,66	0,157
Etiology				0,294
	Idiopathic			
	Tonsillitis[1]	0,88	0,12 – 6,34	0,908
	Odontogenic[1]	1,64	0,17 – 15,31	0,663
	Others[1]	0,18	0,02 – 1,85	0,149
Laboratory	Neutrophils %	0,93	0,82 – 1,06	0,269
	Lymphocytes %	0,89	0,72 – 1,09	0,255
	NLR	1,08	1,00 – 1,15	**0,037**
CT Scan	Highest dimension	1,01	0,99 – 1,03	0,297
	Infra-hyoid extension	2,93	0,53 – 16,18	0,218
	Presence of Gas	0,31	0,06 – 1,44	0,134
Involved Neck Spaces	Submandibular[2]	1,24	0,28 – 5,38	0,777
	Parapharyngeal[2]	3,28	0,95 – 11,25	0,061
	Retropharyngeal[2]	0,43	0,05 – 3,38	0,420
	Prevertebral[2]	5,89	0,54 – 64,04	0,145
	Visceral[2]	2,03	0,42 – 9,93	0,380
Location	Bilateral Abscess[3]	8,28	1,51 – 45,36	**0,015**

[1] In comparison with idiopathic; [2] In comparison with all others; [3] In comparison with unilateral abscess; CT, computed tomography; NLR, neutrophil to lymphocyte ratio

Discussion

The main objective of this study was to evaluate the clinical data, including the symptoms, etiology, blood tests, cultures, CT scans, and treatment, to identify the predictors of mediastinitis in patients with DNI who underwent surgery in the Otorhinolaryngology department of a Portuguese tertiary hospital center. The most common etiology of DNI was odontogenic and the most frequently involved cervical space was the submandibular space. The most frequently isolated bacteria were the *Streptococcus spp.* Furthermore, it was found that the factors predicting the progression to mediastinitis were the presence of a bilateral abscess and high NLR.

The mean age at presentation was 48.5 years and there was a slight male predominance (63.5% men). The demographic results in this study were in accordance with the findings of previous studies[4, 5, 6]. Regarding etiology, odontogenic infection was the most frequent cause of DNI, which is in line with the results of other studies[6, 7]. Although some studies have reported tonsillitis to be the most frequent cause of DNI, these studies reported a higher number of idiopathic infections, which may have led to bias[4, 5]. Moreover, the most frequently involved neck space in DNI seems to be the submandibular space[6, 7, 8], which further supports the role of odontogenic infection in the pathogenesis of most DNI.

Most studies agree that *Streptococcus spp.* are the most common bacteria isolated in DNI cultures[4, 6, 8]. However, the most frequently isolated *Streptococcus* subtypes differ from study to study, which may be related to the different bacterial epidemiology in different

countries. In the present study, the most frequent isolated bacteria were *Streptococcus anginosus*, *Streptococcus constellatus,* and anaerobic species, the most common being *Prevotella spp*. In accordance with the findings of Kimura et al., the bacteria isolated in patients with DNI with and without mediastinitis seemed to be similar[4].

DNI may rapidly spread through the neck to the mediastinum, leading to potential life-threatening complications such as mediastinitis, necrotizing fasciitis, *Lemierre's* Syndrome, cavernous sinus thrombosis, carotid artery rupture, and death. Thus, it is important to be aware of the factors that can potentially lead to these complications to optimize the treatment in patients with DNI. Older age at presentation was associated with progression to mediastinitis in the present study. Previous studies have also shown that older age in patients with DNI is associated with the involvement of multiple spaces, complications, multiple surgical interventions, and prolonged hospitalization[9]. Although we found no association between DM and progression to mediastinitis, a meta-analysis reported that DM was associated with a higher rate of complications and involvement of multiple spaces[10]. While tonsillitis was associated with progression to mediastinitis in the present study, other studies did not find any association[4, 11]. Further studies are required to understand if there is an association between the etiology of DNI and progression to mediastinitis.

Kimura et al. found in an adjusted analysis that age ≥55 years, NLR ≥13, and CRP ≥30 mg/dL were clinical predictors of mediastinitis [4], which further supports our finding of an association between NLR and mediastinitis. NLR reflects the dynamic relationship between the innate and adaptive immune responses and is used as a marker of systemic inflammation[12]. It is a sensitive and non-specific marker of systemic infection, sepsis, and bacteremia, and higher values are associated with worse prognosis[12]. It is easy to measure and fast responding to inflammatory changes with dynamic alterations that may even precede the alterations in the clinical state [12]. Thus, NLR should be determined in every patient with DNI in order to assess the probability of complications such as mediastinitis. Since CRP is an acute inflammatory protein with higher levels associated with sepsis and poor prognosis[13], it was expected that there would be an association between CRP and mediastinitis, but it was not found in the present study. Although further studies are required to explore if CRP might be a potential clinical predictor of complications of DNI, our results show that NLR might be a more significant clinical predictor in comparison to CRP.

CT parameters may also be adequate to predict progression to mediastinitis[4]. In the present study, there was an association with the highest dimensions on CT scan, presence of gas, and infra-hyoid extension. Furthermore, involvement of parapharyngeal, retropharyngeal, prevertebral, or visceral spaces was associated with risk of mediastinitis, in accordance with what has been previously reported[8, 11]. In contrast, we have found no previous reports of a protective association between submandibular space involvement and DNI complications.

This study had a large sample size compared to those of most previous studies, which enabled an adjusted analysis of clinical predictors of mediastinitis. In multivariate analysis, only NLR and bilateral DNI were significantly associated with progression to mediastinitis. Thus, these two factors may be the most important clinical predictors of mediastinitis.

This study has several limitations. Firstly, since this was a retrospective observational study, there might be bias and limitations in data collection. For example, there inadequate data to assess the causes of re-intervention. Furthermore, only a small number of patients developed complications other than mediastinitis, which did not allow the evaluation of clinical predictors of different complications. Lastly, some patients with DNI were treated by stomatology, maxillofacial, or

general surgery departments (n=78) during the study period. While these patients were not included in the analysis, this may have led to bias that may influence the generalization of results.

Conclusion

The most frequent DNI etiology was odontogenic infection and the most common abscess location was the submandibular space. Furthermore, *Streptococcus spp.* were the most frequently isolated organisms in DNI cultures. The presence of a bilateral DNI and NLR seem to be the most important clinical predictors of mediastinitis.

Conflicts of Interest

The authors declare that there is no conflict of interests regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and to the 2013 Helsinki Declaration of the World Medical Association.

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Availability of scientific data

There are no datasets available, publicly related to this work.

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