

Risk factors for deep neck infection in patients with sore throat and neck pain

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ABSTRACT

BACKGROUND: Deep neck infection (DNI) is a potentially life-threatening disease because infections spread quickly, causing serious complications. Therefore, more attention is needed than other neck infections, but there are many difficulties due to isolation guidelines in the period of coronavirus disease 2019 pandemic. We investigated the early predictability of DNI through patient symptoms at the first emergency department encounter.

METHODS: This was a retrospective study of patients with suspected soft-tissue neck infections from January 2016 to February 2021. Symptoms were retrospectively analyzed in fever, foreign body sensation, chest discomfort/pain, submandibular pain, odynophagia, dysphagia, voice change, and severe pain. Furthermore, baseline characteristic data, laboratory findings, and pre-vertebral soft-tissue (PVST) thickness were evaluated. DNI and other neck infections were diagnosed through computed tomography. Logistic regression analysis was conducted to determine the independent factors for predicting DNI.

RESULTS: In the 793 patients included in the study, 267 (33.7%) were diagnosed with DNI, and 526 (66.3%) were diagnosed with other soft-tissue neck infections. In the comparison between the two groups, C-reactive protein (CRP), sodium, PT (INR), foreign body sensation, chest discomfort/pain, submandibular pain, odynophagia, dysphagia, severe pain, and PVST thickness showed statistically significant differences. Independent factors for predicting DNI were severe pain (odds ratio: 6.336 [3.635–11.045], $p < 0.001$), foreign body sensation (odds ratio: 7.384 [2.776–19.642], $p < 0.001$), submandibular pain (odds ratio: 4.447 [2.852–6.932], $p < 0.001$), and dysphagia (odds ratio: 52.118 [8.662–313.588], $p < 0.001$) among symptoms and CRP (odds ratio: 1.034 [1.004–1.065], $p = 0.026$) and PT (INR) (odds ratio: 29.660 [3.363–261.598], $p = 0.002$) in laboratory tests. PVST thickness at C2 (odds ratio: 1.953 [1.609–2.370], $p < 0.001$) and C6 level (odds ratio: 1.179 [1.054–1.319], $p = 0.004$) was also shown as an independent variable for prediction.

CONCLUSION: Among patients with sore throat or neck pain, patients with dysphagia, foreign body sensation, severe pain, and submandibular pain are more likely to have DN. DNI can cause serious complications; therefore, patients with the above symptoms should be closely observed due to the potential for significant complications.

Keywords: COVID-19; deep neck space infection; delayed treatments; emergency department; signs and symptoms; sore throat.

INTRODUCTION

Deep neck infection (DNI) can result from cellulitis or abscesses in the potential spaces of the neck and fascial planes. The use of improved antibiotics and oral hygiene have significantly reduced the incidence of DNI and its complications.^[1]

Nevertheless, globally, DNI is still a common and life-threatening disease, and the patients usually present to the emergency department (ED). The life-threatening complications of DNI include upper airway obstruction, cervical necrotizing fasciitis, mediastinitis, and septic shock.^[2–4] Unlike other soft-tissue neck infections, which are appropriately treated with

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antibiotics, DNI with complications may require incision and drainage or surgical debridement.^[5,6] Therefore, early diagnosis of DNI is important in patients with symptoms such as sore throat or neck pain that may also appear with other soft-tissue neck infections.

On March 11, 2020, the World Health Organization declared coronavirus disease 2019 (COVID-19) a pandemic.^[7] In South Korea, the first case of COVID-19 was reported on January 20, 2020, and the number of confirmed cases increased rapidly in February 2020.^[8] Accordingly, the Korean government raised the level of COVID-19 infectious disease crisis alert to “serious” on February 23, 2020.^[9] To prevent infection, hospitals have established isolation guidelines for treatment such as, wearing certified personal protective equipment (PPE) and using isolation rooms. Therefore, patients with suspected soft-tissue neck infections and having sore throat or neck pain were also treated according to isolation guidelines, which had resulted in delays in processes. The gold standard investigation for the diagnosis of DNI is computed tomography (CT). However, in isolated patients, the CT process is considerably delayed owing to the requirement for wearing PPE and limited facilities. Moreover, it is difficult to continue monitoring the worsening of symptoms because the isolation room, where medical staff is present and is structurally away from the scanning room, and only a limited number of medical personnel are available.

In the past and recently, sore throat or neck pain has been the most common chief complaints of patients with suspected soft-tissue neck infections presenting to the ED.^[10,11] Among neck infections, DNI may require life-saving airway interventions such as intubation and tracheostomy, as well as surgical drainage of abscesses. Therefore, emergency physicians should keep this entity at the top of their differential diagnoses. We aimed to determine the differences between DNI and other soft-tissue neck infections among patients with suspected soft-tissue neck infections who visited the ED. In particular, since isolation guidelines could cause delays in treatment, we investigated whether DNI could be predicted early based on symptoms during the first visit.

MATERIALS AND METHODS

Study Design and Population

In this retrospective study, we analyzed patients who visited the ED at a tertiary university hospital from January 2016 to February 2021. The inclusion criteria were as follows: (1) age ≥ 18 years and visited the ED with complaints of sore throat or neck pain, (2) neck CT was performed, and (3) the diagnosis, including DNIs and other soft-tissue neck infections, was confirmed in the ED. CT reading for the final diagnosis was performed by expert radiologists of the hospital. The exclusion criteria were as follows: (1) history of swallowing a foreign body or trauma and (2) DNI diagnosed at another hospital before visiting the ED. The enrolled patients were

divided into the DNI group and other soft-tissue neck infections group, and comparisons were made between the two groups. This study was approved by the institutional review board of our hospital, and the requirement for written informed consent from patients was waived (IRB No. 2021-10-053-001).

Data Collection and Outcome Measurement

Data were collected from electronic medical records of eligible patients in a picture archiving and communication system (PACS; Maroview 5.4, Infinitt, Seoul, Republic of Korea). The study variables included patient demographics, vital signs at the initial visit to the ED, laboratory findings, and clinical outcomes (i.e., general ward or intensive care unit (ICU) admission, length of hospital stay, and mortality). As in other studies,^[12,13] on a sagittal CT image, the distances from the midpoints of the vertebral bodies of C2 and C6 to the closest points in the air column in trachea were measured to determine the thickness of the pre-vertebral soft-tissue (PVST) swelling caused by the spread of inflammation. Other combined symptoms including fever (initial body temperature ≥ 37.5), foreign body sensation, chest discomfort or pain, submandibular pain, odynophagia, dysphagia, and voice change were retrospectively reviewed from medical records. The classification of other combined symptoms was similar to that in other studies.^[14-16]

We also used the numeric rating scale (NRS) to measure the intensity of pain or discomfort. The scale was divided into two categories. NRS 0–2 indicates tolerable pain that does not require measures to relieve it, and NRS 3–10 indicates pain beyond discomfort that requires measures to relieve it.

The outcomes of this study were factors that can predict DNI early, including symptoms during the first encounter with the patient and differences between DNI and other soft-tissue neck infections.

Statistical Analysis

We used an independent t-test to ascertain the differences among continuous variables, including age, vital signs, laboratory findings, and PVST thickness. Pearson’s Chi-square test was used for categorical variables, including sex, ED disposition, and clinical signs. Continuous variables are presented as mean \pm standard deviation, and categorical variables are presented as count (percentage). Multivariate logistic regression analysis was conducted using the statistically significant factors in the univariate analysis to determine the independent factors for the prognosis of DNI. Statistical analysis was performed using SPSS (version 26.0; SPSS Inc., Chicago, IL, USA). Results were considered as statistically significant at a $P < 0.05$.

RESULTS

Baseline Characteristics

A total of 793 patients were enrolled during the study period (Fig. 1). Of these patients, 267 were diagnosed with DNI. A

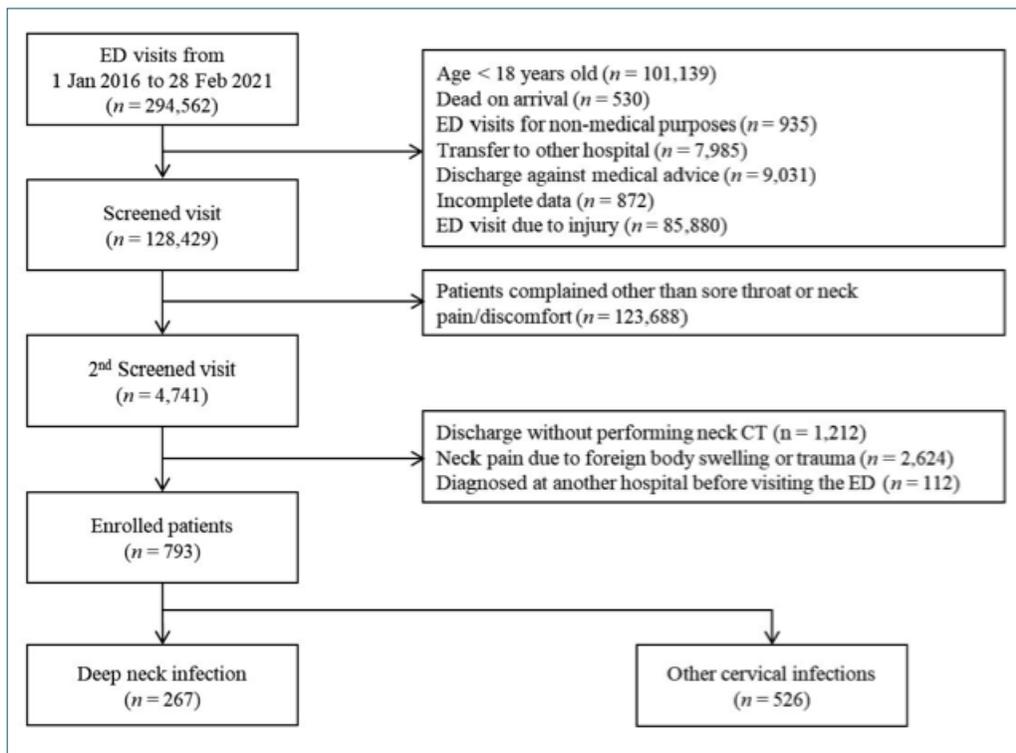


Figure 1. Flow chart.

comparison of the basic characteristics of patients with DNI and other soft-tissue neck infections is presented in Table 1. The mean age of patients was 47.06±18.07 in the DNI group

and 43.26±18 years in other soft-tissue neck infections group (p=0.005). There was no significant difference in sex and vital signs at the ED visit between the two groups. The admis-

Table 1. The baseline characteristics of patients with deep neck infection and other cervical infections

Variable	Deep neck infection (n=267)	Other cervical infections (n=526)	p-value
Age (years) ^a	47.06±18.07	43.26±18	0.005
Sex ^b			0.172
Male	160 (59.9)	289 (54.8)	
Female	107 (40.1)	238 (45.2)	
Vital signa			
Systolic blood pressure (mmHg)	132.53±21.02	133.33±19.89	0.598
Diastolic blood pressure (mmHg)	78.94±13.87	78.8±13.35	0.892
Pulse rate (beats/min)	95±16.79	94.46±19.22	0.698
Respiratory rate (breath/min)	20.14±2.22	19.84±1.87	0.050
Body temperature (°C)	37.43±0.79	37.52±1.05	0.179
Peripheral O ₂ saturation (%)	98.32±1.76	98.11±5.18	0.551
ED disposition ^b			<0.001
Discharge	152 (56.9)	411 (78.0)	
Admission	115 (43.1)	116 (22.0)	
ICU admission ^b	20 (17.4)	9 (7.8)	0.027
Hospital LOS (d) ^a	11.82±16.42	10.83±15.22	0.635
In-hospital mortality ^b	4 (3.5)	2 (1.7)	0.402

^aThe values are given as mean±standard deviation. ^bThe values are given as number (%). ICU: Intensive care unit, LOS: Length of stay, ed: Emergency department.

Table 2. Comparison of clinical factors between deep neck infection and other cervical infections

Variable	Deep neck infection (n=267)	Other cervical infections (n=526)	p-value
Laboratory tests ^a			
White blood cell (10 ⁹ /L)	13.4±4.94	13.22±21.29	0.889
Hemoglobin (g/dL)	13.65±1.63	13.61±1.97	0.804
Platelet (10 ⁹ /L)	250.73±80.7	241.06±85.64	0.129
C-reactive protein (mg/dL)	9.36±8.76	5.86±6.47	<0.001
Aspartate aminotransferase (IU/L)	36.94±136.27	32.33±39.37	0.479
Alanine aminotransferase (IU/L)	36.78±140.44	34.21±75.18	0.741
Blood urea nitrogen (mg/dL)	14±7.38	13.12±6.35	0.084
Creatinine (mg/dL)	0.91±0.52	0.95±0.97	0.467
Glucose (mg/dL)	134.57±62.63	126.91±48.21	0.084
Sodium (mmol/L)	136.36±3.3	136.88±3.56	0.048
Potassium (mmol/L)	4.06±2.26	3.91±0.37	0.137
PT (INR)	1.09±0.25	1.05±0.1	0.001
PTT (sec)	27.9±4.78	27.65±11.58	0.741
Clinical signs ^b			
Fever	114 (42.7)	228 (43.3)	0.861
Foreign body sensation	49 (18.4)	11 (2.1)	<0.001
Chest discomfort/pain	21 (7.9)	12 (2.3)	<0.001
Submandibular pain	135 (50.6)	81 (15.4)	<0.001
Odynophagia	13 (4.9)	9 (1.7)	0.011
Dysphagia	16 (6.0)	2 (0.4)	<0.001
Voice change	10 (3.7)	9 (1.7)	0.076
NRS 3~10	238 (89.1)	307 (58.3)	<0.001
Pre-vertebral soft-tissue diameter ^a			
C2 (mm)	7.34±2.33	5.89±1.85	<0.001
C6 (mm)	15.91±2.29	14.72±1.67	<0.001

^aThe values are presented as mean±standard deviation. ^bThe values are presented as number (%). NRS: Numeric rating scale

sion rate was 43.1% in the DNI group, which was higher than that in the other soft-tissue neck infections group (22.0%; $p<0.001$). Among the admitted patients, the ICU admission rates were higher in the DNI group than in the other soft-tissue neck infections group (17.4% and 7.8%, respectively; $p=0.027$).

Comparison of Clinical Factors between DNI and Other Soft-Tissue Neck Infections

Table 2 summarizes the clinical factors in both groups. The serum C-reactive protein (CRP) level was 9.36 ± 8.76 mg/dL in the DNI patient group, which was higher than that in the other soft-tissue neck infections group (5.86 ± 6.47 mg/dL; $p<0.001$). Serum sodium levels and PT (INR) values were also statistically significant; however, these values did not differ considerably between the two groups. There were statistically significant differences in foreign body sensation, chest discomfort or pain, submandibular pain, odynophagia, dys-

phagia, and NRS scores. Approximately 18.4% of patients with DNI and 2.1% of patients with other soft-tissue neck infections complained of a foreign body sensation ($p<0.001$). Chest discomfort or pain was reported by 7.9% and 2.3% of patients in the DNI group and other soft-tissue neck infections group, respectively ($p<0.001$). Submandibular pain was reported by 50.6% of patients in the DNI group and 15.4% of patients in the other soft-tissue neck infections group ($p<0.001$). Approximately 4.9% of patients in the DNI group and 1.7% of patients in the other soft-tissue neck infections group complained of odynophagia ($p=0.011$). Dysphagia was reported by 6.0% of patients in the DNI group and 0.4% of patients in the other soft-tissue neck infections group ($p<0.001$). When comparing the intensity of pain, 89.1% of DNI groups and 58.3% of other soft-tissue neck infections groups complained of severe pain ($p<0.001$). Furthermore, the thickness of PVST measured at both C2 and C6 levels showed statistically significant differences between the two

Table 3. Predictive factors for deep neck infection by multivariate logistic regression analysis

Variable	OR	B	p-value
C-reactive protein	1.034 (1.004–1.065)	0.034	0.026
PT (INR)	29.660 (3.363–261.598)	3.390	0.002
Foreign body sensation	7.384 (2.776–19.642)	1.999	<0.001
NRS 3–10	6.336 (3.635–11.045)	1.846	<0.001
Submandibular pain	4.447 (2.852–6.932)	1.492	<0.001
Dysphagia	52.118 (8.662–313.588)	3.954	<0.001
Pre-vertebral soft-tissue diameter at C2	1.953 (1.609–2.370)	0.669	<0.001
Pre-vertebral soft-tissue diameter at C6	1.179 (1.054–1.319)	0.165	0.004

OR: Odds ratio, B: Regression coefficient, Boldface type indicates statistical significance ($P < 0.05$), NRS: Numeric rating scale.

groups (C2: 7.34 ± 2.33 mm vs. 5.89 ± 1.85 mm, $P < 0.001$; C6: 15.91 ± 2.29 mm vs. 14.72 ± 1.67 mm, $p < 0.001$).

Clinical Factors that Predicted DNI

Logistic regression analysis was performed to elucidate factors that could predict DNI in enrolled patients. In univariate analysis, age, CRP, PT (INR), foreign body sensation, chest discomfort or pain, submandibular pain, odynophagia, dysphagia, and NRS 3–10 were significant risk factors for DNI. Multivariate logistic regression analysis was conducted using significant variables in the univariate analysis. In multivariate logistic regression analysis, CRP (odds ratio [OR], 1.034; 95% confidence interval [CI], 1.004–1.065; $p = 0.026$), PT (INR) (OR, 29.660; 95% CI, 3.363–261.598; $p = 0.002$), foreign body sensation (OR, 7.384; 95% CI, 2.776–19.642; $p < 0.001$), NRS 3–10 (OR, 6.336; 95% CI, 3.635–11.045; $p < 0.001$), submandibular pain (OR, 4.447; 95% CI, 2.852–6.932; $p < 0.001$), dysphagia (OR, 52.118; 95% CI, 8.662–313.588; $p < 0.001$), PVST thickness at C2 (OR, 1.953; 95% CI, 1.609–2.370; $p < 0.001$), and PVST thickness at C6 (OR, 1.179; 95% CI, 1.054–1.319; $p = 0.004$) were identified as independent factors that predicted DNI (Table 3).

DISCUSSION

This study compared the baseline characteristics, laboratory test results, and clinical signs between patients with DNI and other soft-tissue neck infections. Some previous studies have reported the characteristics of DNI and described common symptoms.^[17–19] In the present study, we compared these symptoms with those of other soft-tissue neck infections. In the ED, patients with DNI presented with complaints of increased foreign body sensation, chest discomfort or pain, submandibular pain, odynophagia, and dysphagia compared with patients with other soft-tissue neck infections. Moreover, patients with DNI complained of more severe pain. The most common symptom in patients with DNI in this study was severe pain (89.1%). This result is similar to the results of previous studies.^[17,18] Pain was the most common symptom in

patients with other soft-tissue neck infections as well; however, there was a statistically significant difference between the two groups. The second most common symptom in the DNI group was submandibular pain (50.6%), which was the third most common symptom in the other soft-tissue neck infections group (15.4%). Similar to other studies on DNI, fever was found to be the third most common symptom in patients with DNI.^[17,19] Fever was also the second most common symptom in patients with other soft-tissue neck infections; however, there was no statistically significant difference between the two groups, indicating that fever was not a significant symptom for differentiation ($p = 0.861$). Furthermore, significant symptoms for predicting DNI were foreign body sensation and dysphagia. Dysphagia showed the highest OR (52.118; 95% CI, 8.662–313.588) and was identified as an important independent factor for early prediction of DNI.

DNI commonly results from inflammation of the mandibular teeth, tonsils, and parotid glands. It usually extends to the cervical potential space and has a rapid onset and progression, leading to fatal conditions such as airway obstruction, mediastinitis, and sepsis.^[12,20,21] When a patient with suspected DNI visits the ED, the possibility of rapid progression to a critical illness should be considered, even if the patient has mild clinical symptoms and stable vital signs.^[22] For this reason, patients with suspected DNI need close observation and continuous monitoring. However, in the recent COVID-19 pandemic era, emergency physicians are facing difficulties for close observation of patients as well as diagnosis and treatment owing to isolation guidelines such as the use of isolation rooms, and there is concern regarding poor outcomes in patients.^[23–25] Despite the government's efforts, COVID-19 transmission was rapid; thus, it was difficult to contain the disease. Therefore, it has become difficult for several patients with potential infections to visit the ED and seek treatment due to the shortage of isolation rooms.

The technology has been developing every day, and diagnostic methods have also made considerable progress. Diagnostic methods include imaging techniques such as CT, magnetic

resonance imaging, or ultrasound and laboratory tests such as blood tests. The use of CT in the ED is increasing every year.^[26,27] CT is the gold-standard investigation for the diagnosis of DNI because of its high sensitivity to soft-tissue characterization.^[12] At the same time, medical history and physical examinations have been the cornerstone of disease diagnosis and can still provide important clues for diagnosis. In particular, in the COVID-19 pandemic era, diagnosis may be delayed in patients who stay in isolation rooms due to delays related to diagnostic tests such as CT; thus, patients' signs and symptoms during the ED visit may be more important for diagnosing DNI.

We also used laboratory tests and simple radiography as other diagnostic tools that could be performed faster than CT. The serum CRP level in the DNI group was higher than that in the other soft-tissue neck infections group, and the difference was statistically significant ($P < 0.001$). CRP is an acute reactant that increases during infection, trauma, and tissue necrosis. In this study, CRP levels were used to assess the severity of infection and inflammation. CRP levels in patients with DNI are higher than those in patients with other soft-tissue neck infections because DNI is characterized by the spread of inflammation to other sites. This result is similar to those of other studies.^[28,29] On the cervical spine lateral radiograph, the thickness of the soft tissue at the C2 level is considered abnormal if it is 7 mm or more in children and adults, and the thickness at the C6 level is considered abnormal if it is 14 mm or more in children and 22 mm or more in adults.^[30] At the C2 level, the thickness was 7 mm or more in the DNI group, which is considered abnormal and may be helpful for diagnosis. Further, the thickness measured at the C6 level was < 22 mm, but it was thicker than that in patients with other soft-tissue neck infections.

Our study has some limitations. The main limitation was that it was a single-center, retrospective study. To minimize this limitation, we analyzed patients who visited the hospital over several years to include a sufficient number of patients. Nevertheless, caution is needed when generalizing the results, and further multicenter, prospective studies are required. Moreover, there might have been a potential selection bias because only patients who underwent CT for the diagnosis of DNI were selected. Finally, we did not evaluate the medical and drug history of the patients. Some studies have indicated that diabetes mellitus, hypertension, and the use of non-steroidal anti-inflammatory drugs are associated with more severe infections and an increased risk of DNI.^[17,31] In addition, antibiotic use and microbiological analysis were not performed in this study.

Conclusion

Among patients who visited the ED with sore throat or neck pain, those with dysphagia, foreign body sensation, neck discomfort, including severe pain with an NRS score ≥ 3 , and submandibular pain were more likely to have DNI. Other

tests, such as CT or MRI, should be performed for the final diagnosis, but the health of patients with these symptoms is may to worsen rapidly. Therefore, more attention should be paid to the appropriate treatment of the condition. In particular, the results of this study may be useful for efficiently using limited medical personnel during the COVID-19 pandemic period.

Ethics Committee Approval: This study was approved by the Ewha Womans University Mokdong Hospital Animal Experiment Ethics Committee (Date: 24.11.2021, Decision No: 2021-10-053-001).

Peer-review: Externally peer-reviewed.

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ORIJİNAL ÇALIŞMA - ÖZ

Boğaz ağrısı ve boyun ağrısı olan hastalarda derin boyun enfeksiyonu için risk faktörleri

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AMAÇ: Derin boyun enfeksiyonu (DBE), enfeksiyonun hızla yayılarak ciddi komplikasyonlara neden olma ihtimalinden dolayı potansiyel olarak yaşamı tehdit eden bir durumdur. Bu nedenle, diğer boyun enfeksiyonlarından daha fazla dikkat gerektirir. Ancak COVID-19 pandemisi döneminde izolasyon yönergeleri nedeniyle birçok zorluk yaşanmıştır. Acil serviste ilk karşılaşıldığında var olan hasta semptomları aracılığıyla DBE'nun erken öngörülebilirliğini araştırdık.

GEREÇ VE YÖNTEM: Bu çalışma, Ocak 2016'dan Şubat 2021'e kadar yumuşak doku boyun enfeksiyonu şüphesi olan hastaların retrospektif bir incelemesidir. Semptomlar; ateş, yabancı cisim hissi, göğüs rahatsızlığı/ağrı, submandibular ağrı, odinofaji, disfaji, ses değişikliği ve şiddetli ağrı olarak geriye dönük analiz edildi. Ayrıca temel karakteristik veriler, laboratuvar bulguları ve prevertebral yumuşak doku (PVYD) kalınlığı değerlendirildi. Bilgisayarlı tomografi (BT) ile DBE ve diğer boyun enfeksiyonları teşhis edildi. Derin boyun enfeksiyonunu öngörmek üzere bağımsız faktörleri belirlemek için lojistik regresyon analizi yapıldı.

BULGULAR: Çalışmaya alınan 793 hastanın 267'sine (%33.7) DBE, 526'sına (%66.3) diğer yumuşak doku boyun enfeksiyonları tanıldı. İki grup arasındaki karşılaştırmada, C-reaktif protein (CRP), sodyum, PT (INR), yabancı cisim hissi, göğüs rahatsızlığı/ağrı, submandibular ağrı, odinofaji, disfaji, şiddetli ağrı ve PVYD kalınlığı, istatistiksel olarak anlamlı farklılık gösterdi. Derin boyun enfeksiyonunu öngörmek için bağımsız faktörler; semptomlar arasından şiddetli ağrı (odds ratio: 6.336 (3.635–11.045), p<0.001), yabancı cisim hissi (odds ratio: 7.384 (2.776–19.642), p<0.001), submandibular ağrı (odds ratio: 4.447 (2.852–6.932), p<0.001) ve disfaji (odds ratio: 52.118 (8.662 – 313.588), p<0.001) ve laboratuvar testleri arasından CRP (odds ratio: 1.034 (1.004–1.065), p=0.026) ve PT (INR) (odds ratio: 29.660 (3.363 – 261.598), p=0.002) idi. C2 seviyesindeki (odds ratio: 1.953 (1.609–2.370), p<0.001) ve C6 seviyesindeki (odds ratio: 1.179 (1.054–1.319), p=0.004) PVYD kalınlığı da öngörü için bağımsız birer değişken olarak gösterildi.

TARTIŞMA: Boğaz ağrısı veya boyun ağrısı olan hastalarda disfaji, yabancı cisim hissi, şiddetli ağrı ve submandibular ağrısı olanların DBE olma olasılığı daha yüksektir. Derin boyun enfeksiyonu ciddi komplikasyonlara neden olabilir; bu nedenle, yukarıdaki semptomlara sahip hastalar önemli komplikasyon potansiyeli nedeniyle yakından izlenmelidir.

Anahtar sözcükler: Acil servis; belirti ve bulgular; boğaz ağrısı; COVID-19; derin boyun enfeksiyonu; gecikmiş tedaviler.

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