The assessment of risk factors associated with difficult intubation as endocrine, musculoskeletal diseases and intraoral cavity mass: A nested case control study

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ABSTRACT

BACKGROUND: The predictive factors of difficult airway have been studied to reduce especially the incidence of unanticipating difficult intubation, provide patient safety, and avoid wasting resources. In this study, it was aimed to investigate whether endocrine, musculoskeletal diseases, presence of intraoral mass, and demographic factors have predictive values in the evaluation of difficult airway as well as frequently used airway assessment tests.

METHODS: This study was designed a nested-case control study. After eligibility criterions, totally 1012 patient data were collected, 92 of them were difficult intubation, 920 of them were non-difficult intubation patients (1: 10 ratio). Demographic characteristics of the patients (age, gender), body mass index (BMI), Mallampati, Cormack-Lehane Score (CLS), sternomental distance (SMD), inter incisor gap (IIG), type of surgery, endocrine, musculoskeletal and cardio-pulmonary diseases, and the presence of intraoral mass were compared between groups.

RESULTS: Age >52 years, male gender, ASA 3–4, higher BMI, CLS 3–4, Mallampati 3–4, IIG <4 cm, and SMD <10 cm were found statistically significant in terms of difficult intubation. Besides, a statistically significant relationship was found when the groups were compared in the presence of intraoral mass (17.57 times higher, p<0.05), endocrine diseases (3.51 times more common, p<0.05) and musculoskeletal system diseases (4.5 times higher, p<0.05).

CONCLUSION: In this study, it was demonstrated that endocrine disorders such as diabetes mellitus and thyroid disorders, musculoskeletal system diseases, and the presence of intraoral cavity mass should be used as predictors for difficult intubation with commonly used airway assessment tests.

Keywords: Diabetes mellitus; difficult intubation; intraoral cavity mass; risk factors; thyroid disorders.

INTRODUCTION

Difficult airway is defined as difficulty with mask ventilation, endotracheal intubation, or both by an experienced clinician. ^[1] Endotracheal intubation and airway management can be challenging especially for clinicians working in emergency department, intensive care units and operating rooms.^[2] Although some clinical features and tests were described for predicting difficult airway, sometimes an unpredictable difficult airway may be encountered. It has been estimated that 2.1% of people are difficult to intubate and 45.7% of these problems are unanticipated.^[3] The difficult airway is closely related to patient factors, the clinical setting, and the skills of the practitioner and the difficulty in the airway can be congenital or acquired.^[1]

In the pre-operative assessment, to identify potentially difficult airway, inter incisor gap (IIG) measurement, Mallampati score, neck mobility, sternomental distance (SMD), and history of difficult airway have been used, Cormack-Lehane score (CLS) which is evaluated during the laryngoscopy also can be used for defining difficult intubation, despite these

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evaluations and methods, the clinicians can encounter unanticipating difficult intubation cases. It was reported that the tests as Mallampati, IIG, SMD–alone, or combined to predict difficult intubation with direct laryngoscopy have limited sensitivity, specificity, positive, and negative predictive value, especially in the patients without a pathology of the airway. ^[4] Therefore, the evaluation of clinical features as obesity, previous surgery affecting neck mobility, or mouth opening as maxillofacial surgery and comorbidities that impair temporomandibular joint mobility may guide clinicians in terms of predicting difficult airway.^[5]

In this study, the primary aim is to assess and compare comorbidities of musculoskeletal system, endocrine, cardiac and pulmonary diseases, obesity, the presence of intraoral cavity tumor, and surgery types (elective or emergency operation) with other mostly studied parameters such as age, gender, body mass index (BMI), Mallampati, CLS, SMD, and IIG among patients with difficult airway and non-difficult airway.

MATERIALS AND METHODS

Ethics

This study was conducted in Mersin University Faculty of Medicine, Department of Anesthesiology and Reanimation in Turkey and was approved by the Mersin University Clinical Research Ethics Committee.

Study Design

A nested case–control research design was used in patients who had general anesthesia in the operating room of Mersin University Medical Faculty Hospital Operating Rooms, in which those with intubation difficulties were compared with patients who had no difficulties.

Patient Selection

Between January I, 2019, and January I, 2021, the data of total 1012 patients who meet the inclusion and exclusion criteria were collected. Of these 1012 patients, 92 patients were recorded as "difficult intubation" to the Hospital Data System, 920 were the patients who had no difficulty of airway management. The data of the patients were recorded with a study form that included patients' age, gender, BMI, American Society of Anaesthesiologists (ASA) physical status, the presence of comorbidities, diseases related to endocrine, musculoskeletal, cardiac, pulmonary system, department of surgery, surgery type (emergent or elective), the presence of intraoral cavity mass, Mallampati score, measurements of IIG, SMD, and CLS parameters. The files of the patients were collected from the Department of Anesthesiology Archive. Patients operated in the Mersin University Medical Faculty Hospital, on the specified dates, aged ≥18 years, endotracheal intubation method was used to provide airway were included to the study. Whereas, being operated outside of the specified dates, aged <18 years, other than endotracheal intubation method was used to provide airway patients and patients with congenital syndromes causing airway abnormalities were excluded from the study. Patients were grouped as "difficult intubation" Group DI, and "non-difficult intubation" Group NI.

Statistical Analysis

When the Odds ratio (OR) of the predicted factors to be associated with difficulty intubation is 1.5 times (the least clinically significant), the confidence interval (CI) width is accepted for 25% (for a fairly reliable range) and the prevalence of difficult intubation is 13.8%.^[6] While the minimum number of patients to be included in the study is 700, the maximum number of patients that can be included in the study is 1200. The number of difficult intubated patients was matched 1:10 to the number of non-difficult intubated. Parametric tests were used without the normality test due to the Central Limit Theorem compatibility.^[7] In the analysis of the data, the mean and standard deviation, minimum and maximum values of the features, median and guartiles of 25-75%; frequency and percentage values were given when defining categorical variables. Chisquare was used to evaluate the relationship between categorical variables, and z-test statistics were used to evaluate the difference between two independent ratios. Student's t-test statistics to compare the means of two independent groups and ANOVA test to compare the means of more than two independent groups were evaluated with the Tukey statistic in pair-wise comparison (post hoc) in case of difference with ANOVA. The OR of the factors predicted to be associated with difficult intubation was given with 95% CI. The statistical significance level of the data was taken as p<0.05. In the evaluation of the data, www.e-picos.com, NY, New York software, and MedCalc statistical package program were used.

RESULTS

Between January I, 2019, and January I, 2021, 123 patients were reported as difficult intubation. Of them 13 patients were aged <18 years, laryngeal mask was used in 10 patients and eight patients had congenital abnormalities. Therefore, 31 patients were excluded from the difficult intubation group and 92 were included in this group. According to the statistical method, the control group was 920 patients. The data of non-difficult intubated patients were collected from the Department of Anaesthesiology Archive. A total of 1012 patients who underwent general anesthesia were included in the study.

According to the intubation status; there was a significant difference between the mean age, BMI, and sternomental measurement (cm) (p<0.05). Furthermore, gender, ASA Score, Mallampati, and CLS and IIG were found statistically significant (p<0.05) and are shown in Table 1.

The relationship between existing comorbidities, diseases related to endocrine, cardiac, pulmonary, musculoskeletal sys-

Table I. Relationship and difference statistics of socio-demographic and clinical characteristics with intubation status				
Variables	Total (n=1012)	Group DI (n=92)	Group NI (n=920)	р
	Mean±SD	Mean±SD	Mean±SD	
Age (years)	48.9±17.6	52.72±14.2	48.6±17.9	0.01
BMI (kg/m²)	25.5±5.29	28.21±4.54	25.56±5.31	<0.001
SMD (cm)	11.23±1.29	10.87±1.16	11.26±1.3	0.005
	n (%)	n (%)	n (%)	
Gender				
Female	493 (48.7)	60 (65.2)	433 (47.1)	0.001
Male	519 (51.3)	32 (34.8)	487 (52.9)	
ASA				
I	298 (29.4)	11 (12)	287 (31.2)	
2	487 (48.I)	43 (46.7)	444 (48.3)	<0.0001
3	201 (19.9)	35 (38)	166 (18)	
4	26 (2.6)	3 (3.3)	23 (2.5)	
Mallampati				
Score				
I.	226 (22.3)	7 (7.6)	219(23.8)	
2	443 (43.8)	21 (22.8)	422 (45.9)	
3	284 (28.1)	31 (33.7)	253 (27.5)	<0.0001
4	59 (5.8)	33 (35.9)	26 (2.8)	
CLS				
I	256 (25.3)	_	256 (27.8)	
П	547 (54.1)	-	547 (59.5)	
Illa	7 (.6)	-	7 (2.7)	<0.0001
IIIb	25 (2.5)	25 (27.2)	_	
IV	67 (6.6)	67 (72.8)	_	
IIG (cm)				
<4	22 (2.2)	15 (16.3)	7 (0.7)	<0.0001
≥4	990 (97.8)	77 (83.7)	913 (99.2)	

Student's t, Chi-square, p<0.05 significance. SD: Standard deviation; DI: Difficult intubation; NI: Normal intubation; BMI: Body mass index; SMD: Sternomental distance; ASA: American Society of Anaesthesiologists; CLS: Cormack-Lehane Score; IIG: Inter Incisor Gap.

tem, department of surgery, surgery type, and the presence of intraoral cavity mass is shown in Table 2.

The ORs and Cls of the factors associated with intubation status are shown in Table 3.

The multivariable logistic regression analysis of the factors associated with intubation status is shown in Figure 1.

While 51.3% of the patients were female, 48.7% of them

were male. Male gender was found statistically significant 2.11 times higher in patients with difficult intubation than in those with non-difficult intubation (p<0.05). The age of the total patients was minimum 18 and maximum 94 years. The mean age and standard deviation were 48.9 ± 17.6 , while the median value was 48. Difficult intubation risk increases 1.02 times with a rate of I year increment in age (p<0.05). The presence of any comorbidity was found 1.95 times higher in patients with difficult intubation than with non-difficult intubation status (p<0.05). It is statistically significant that endocrine disease is 3.51 times more common in patients with difficult intubation status (p<0.05).

The presence of musculoskeletal disease was 4.5 times higher in patients with difficult intubation than with non-difficult intubation (p<0.05).

It was found that statistically significant to have an intraoral cavity mass was 17.57 times higher in patients with difficult intubation than with non-difficult intubation status (p<0.05).

The IIG <4 cm was found statistically significant 25.41 times higher in patients with difficult intubation than in patients with non-difficult intubation (p<0.05).

It was found with each 1 unit increase in BMI, the incidence of difficult intubation status increases 1.11 times (p<0.05).

The analyzes showed that as the SMD ascends 1 cm, the risk of difficult intubation decreases 0.83 times (p<0.05).

DISCUSSION

This study demonstrated that endocrine and musculoskeletal system diseases, obesity, and the presence of intraoral cavity mass should be considered as risk factors for difficult intubation in combination with age, gender, Mallampati, SMD, IIG measurements, and CLS. Ideal scoring system for difficult airway is yet to be defined, this outcome is of great importance for emergency, anesthesia, and intensive care physicians who primarily provide airway management.

The movement of mandibular and atlanto-occipital joint restriction in advanced ages may be resulted in difficulty of airway management. In the literature, Cook et al.^[8] found age >55 years as independent risk factor for difficult airway. The male gender has a tendency for both difficult mask ventilation and intubation and it is shown in various studies.^[3,9] In this study, male gender and age >52 were found statistically significant as risk factors when compared with non-difficult intubated patients.

Mallampati test is a commonly used pre-operative assessment that, in many studies on difficult airway, it is well studied.^[1,4,6] In a study including 102,305 pre-operative adults, Heinrich et

		Total	Group DI (n=92)	Group NI (n=920)	Р
		n (%)	n (%)	n (%)	
Comorbidity	No	548 (54.2)	36 (39.1)	512 (55.7)	0.002
	Yes	464 (45.8)	56 (60.9)	408 (44.3)	
Cardiac	No	713 (70.5)	57 (62)	656 (71.3)	0.06
	Yes	299 (29.5)	35 (38)	264 (28.7)	
Pulmonary	No	895 (88.4)	86 (93.5)	809 (87.9)	0.11
	Yes	117 (11.6)	6 (6.5)	(2.)	
Endocrine	No	840 (83)	57 (62)	783 (85.1)	<0.000
	Yes	172 (17)	35 (38)	137 (14.9)	
Musculoskeletal	No	967 (95.6)	79 (85.9)	888 (96.5)	<0.000
	Yes	45 (4.4)	13 (14.1)	32 (3.5)	
Department	General surgery	161 (15.9)	17 (18.5)	144 (15.7)	
	ENT	176 (17.4)	25 (27.2)	151 (16.4)	0.03
	Urology	132 (13)	7 (7.6)	125 (13.6)	
	Orthopaedics	130 (12.8)	6 (6.5)	124 (13.5)	
	Eye surgery	101 (10)	9 (9.8)	92 (10)	
	Obstetrics	136 (13.4)	8 (8.7)	128 (13.9)	
	Plastic surgery	102 (10.1)	13 (14.1)	89 (9.7)	
	Thoracic surgery	7 (0.7)	1 (1.1)	6 (0.7)	
	Cardiovascular	13 (1.3)	3 (3.3)	10 (1.1)	
	Neurochirurgia	54 (5.3)	3 (3.3)	51 (5.5)	
Surgery type	Emergent	127 (12.5)	7 (7.6)	120 (13)	0.13
	Elective	885 (87.5)	85 (92.4)	800 (87)	
Intraoral cavity mass	No	1004 (99.2)	87 (94.6)	917 (99.7)	<0.000
	Yes	8 (0.8)	5 (5.4)	3 (0.3)	

Table 2. The statistics of relationship and difference of chilical leatures with intubation statu	Table 2.	The statistics of relationshi	p and difference of clinical	features with intubation status
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Student's t, Chi-square, p<0.05 significance. DI: Difficult intubation; NI: Normal intubation; ENT: Ear nose throat surgery.

Variable	Odds Ratio	Lower (95% CI)	Upper (95% CI)	p-value
Age	1.02	1.01	1.03	Significant (p<0.05)
Gender	2.11	1.35	3.3	Significant (p<0.05)
Comorbidity	1.95	1.26	3.03	Significant (p<0.05)
Endocrine disease	3.51	2.22	5.55	Significant (p<0.05)
Musculoskeletal disease	4.57	2.3	9.05	Significant (p<0.05)
Intraoral cavity mass	17.57	4.13	74.75	Significant (p<0.05)
Inter incisor gap	25.41	10.06	64.19	Significant (p<0.05)
Body mass index	1.11	1.06	1.16	Significant (p<0.05)
Sternomental oistance	0.83	0.73	0.95	Significant (p<0.05)

Table 2 Evolution of fee

*Significant at the p<0.05 level (Odds Ratio). CI: Confidence interval.

al.^[10] reported that patients with a Mallampati score of III or IV were 6.5 times more likely to have difficult laryngoscopy. However, they found in the same study that a high Mallampati scores were determined in <50% patients with difficult laryngoscopy, with a sensitivity of 45% and a specificity of 89% and five false-positive cautions for one true prediction of a difficult

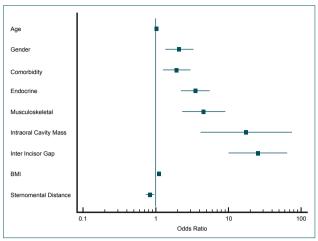


Figure 1.Evaluation of factors associated with intubation status (OR and 95% CI).

airway. In the present study, it was found that the incidence of Mallampati Score I, II, and IV was statistically significant higher in difficult intubated patients than non-difficult intubated patients. Mallampati Score III was detected more in difficult intubation group but it was not statistically significant.

SMD and IIG measurements which performed preoperatively are also searched in various studies and still these are being used in combination with Mallampati Score.^[11] Prakash et al.^[12] studied the relationship between SMD and difficult laryngoscopy comprehensively, the cutoff value of SMD was found 14.75 cm for predicting difficult laryngoscopy with a sensitivity of 66% and their results showed that SMD was not correlated with difficult laryngoscopy. In another study, the cutoff value of SMD as a predictor for difficult intubation was found <13 cm.^[13] In this study, the cutoff value of SMD was analyzed <12.03 cm. These different values may be resulted in anatomic characteristics of patients among countries. The narrow IIG has been used for prediction of difficult airway and the value that determined for prediction is between 3.0 and 5.0 cm. $^{\left[12\right] }$ In this study, the IIG value was classified as 4 cm< and \geq 4 cm and a statistically significant difference was shown between difficult intubation and <4 cm.

CLS is a laryngoscopic view grading, and Grade 3 (3a, 3b) and 4 is defined as difficult intubation.^[12] Major disadvantage is that utilization of CLS is only restricted to direct laryngoscopy and especially in unanticipating difficult intubation cases, it has limited effect by itself. Furthermore, CLS can be used in predicting difficult intubation but in combination with other screening tests. In this study, the results of CLS evaluations were demonstrative, while CLS Grades I, 2, and 3a were not seen in any difficult intubation patients, Grades 3b and 4 were not seen in any of the non-difficult intubation patients.

In this study, also the ASA physical status ASA was evaluated and compared for both groups and found statistically significant difference in difficult intubation patients who were ASA 3 and 4 by a majority. Selvi et al.^[14] also found higher ASA scores in difficult intubation patients. Although Endlich et al.^[6] showed that the ASA score had little influence to predict difficult intubation, in the literature and in this study, it was shown that high ASA score could be a warning risk factor with other factors in suspected patients for difficult airway management.

With the increasing incidence of obesity in the population,^[15] in many researches, the relationship between obesity and difficult intubation has been studied.^[16,17] The cutoff value of BMI is varied between 30 and 50 kg m², where Riad et al.^[18] found that morbidly obese (BMI \geq 50 kg m²) were 5 times more likely to experience difficult intubation, in another study, BMI \geq 30 kg m² was described as a risk factor for it.^[19] In this article, only compared means was used for BMI, and the result was found statistically significant (OR; 1.1). The difficult intubation most probably is due to increased neck circumference and neck immobility; therefore, it is an independent risk factor according to this study.

The intraoral cavity masses are severe problems for airway management and the most challenging part of the anesthesia practice in these patients is to prevent a secure airway. If the oral cavity mass is diagnosed as cancer, the patient receives radiotherapy to head-and-neck as first choice which is a recognized risk factor for difficult airway management.^[20] The intraoral cavity masses were assessed as space occupying lesion and the presence of intraoral cavity mass was 17.57 times higher in patients with difficult intubation than with non-difficult intubation status in the present research.

The ENT surgery has more potential airway risks among other surgical departments. In almost every patient who undergoes head-and-neck surgery, the difficult airway instruments should be readily available. For the surgical issue, it was found that difficult intubation was significantly encountered in ENT surgery.

The musculoskeletal system diseases are very diverse and can affect almost any part of the body, also these are closely related to difficult airway because of the atlanto-occipital and/ or temporomandibular joint involvement.^[21] The research data are very limited about the relationship between musculoskeletal system diseases and difficult airway, the majority of the publications are in the form of case reports. With the results of this study, it was shown that patients with musculoskeletal disease are 4.5 times more likely to be difficult to intubate statistically significant than patients without these diseases.

The data of the patients were assessed about endocrine diseases such as thyroid disorders and diabetes mellitus in this study, because it is known that both of these diseases are related to difficulty in airway management. In a study by Oria et al.,^[22] it was reported that difficult tracheal intubation is 10 times higher in patients suffering from long-term

diabetes mellitus as compared to those without diabetes. In another study from India also indicated that incidence of difficult intubation in patients with diabetes mellitus is high. ^[23] Furthermore, thyroid disorders can lead difficulty in airway management; in a retrospective study by Kalezić et al., ^[24] 2379 patients were collected and the incidence of difficult intubation was found 6.81% in their study, though the reason of difficult intubation in majority of the patients was found tracheal dislocation/stenosis. According to the results of our study, it is determined that endocrine diseases are 3.51 times more common in patients with difficult intubation than with non-difficult intubation.

Conclusion

The expected difficult intubation is important but when the preparations are well designed, the adverse effect of the laryngoscopy and intubation may be alleviated. The main problem is the unexpected difficult intubation cases and to demonstrate risk factors in addition to other commonly used airway assessment tests are essential. Due to the results of this research, it can be recommended that endocrine diseases such as diabetes mellitus thyroid disorders, musculoskeletal system disorders, and the presence of intraoral cavity mass should be used as predictors for difficult intubation. Examining more clinical features in addition to the frequently used and well known airway assessment tests will be beneficial in reducing complications due to difficult intubation.

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ORİJİNAL ÇALIŞMA - ÖZ

Zor entübasyonla ilişkili endokrin, kas-iskelet hastalıkları ve intraoral kavitede kitle gibi risk faktörlerinin değerlendirilmesi: Kohort içinde olgu kontrol çalışması

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AMAÇ: Zor havayolu saptanmasında kullanılan prediktif faktörler ile ilgili çalışmalar, özellikle beklenmeyen zor entübasyon insidansını azaltmak, hasta güvenliğini sağlamak ve kaynak israfını önlemek için yapılmaktadır. Bu çalışmada, sıklıkla kullanılan hava yolu değerlendirme testlerinin yanında, endokrin, kas-iskelet sistemi hastalıkları ve intraoral kavitede kitle varlığının zor havayolu değerlendirmesinde prediktif değerlerinin araştırılması amaçlanmıştır.

GEREÇ VE YÖNTEM: Bu çalışma iç içe vaka kontrol (nested case-control) çalışması olarak tasarlanmıştır. Dahil edilme kriterlerine uyan, 92'si zor entübasyon, 920'si zor olmayan entübasyon hastası (1: 10 oranı) olmak üzere toplam 1012 hasta verisi toplandı. Hastaların yaş, cinsiyet, vücut kitle indeksleri (VKİ), Mallampati, Cormack-Lehane Skoru (CLS), sternomental mesafe (SMM), kesici dişler arası boşluk (KDB), cerrahinin tipi, endokrin, kas-iskelet sistemi ve kardiyo-pulmoner hastalıklar ve ağız içi kitle varlığı gruplar arasında karşılaştırılmıştır.

BULGULAR: Yaş >52 yıl, erkek cinsiyet, ASA 3-4, yüksek VKİ, CLS 3-4, Mallampati 3-4, KDB <4 cm ve SMM <10 cm olması zor entübasyon açısından istatistiksel olarak anlamlı bulunmuştur. Ayrıca, ağız içi kitle varlığı (17.57 kat daha fazla, p<0.05), endokrin hastalıkları (3.51 kat daha sık, p<0.05) ve kas-iskelet sistemi hastalıkları (4.5 kat daha yüksek, p<0.05) varlığında grupların karşılaştırılmasında istatistiksel olarak anlamlı bir ilişki bulunmuştur.

TARTIŞMA: Bu çalışmada, diyabet ve endokrin bozuklukları gibi endokrin hastalıkların, kas-iskelet sistemi hastalıklarının ve ağız içi kitle varlığının yaygın olarak kullanılan hava yolu değerlendirme testleri ile birlikte zor entübasyon için prediktif faktör olarak kullanılabileceği gösterilmiştir. Anahtar sözcükler: Diyabet; intraoral kavite kitleleri; risk faktörleri; tiroid hastalıkları; zor entübasyon.

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