Original Article

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Relationship between Obstructive Sleep Apnea (OSA) and Difficult Intubation

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ABSTRACT

BACKGROUND AND OBJECTIVE: One of the challenges of patients who are candidates for anesthesia is difficult intubation, which leads to severe complications and even death after anesthesia. The aim of this study is to investigate the relationship between obstructive sleep apnea and difficult intubation through systematic review and meta-analysis.

METHODS: In this review article, observational articles about the relationship between obstructive sleep apnea and difficult intubation were extracted without time limit by searching national and international databases and the keywords were: difficult intubation, problematic intubation, Intra tracheal-endotracheal, difficult airway OSA, OSAS, obstructive sleep apnea, sleep breathing disorder, anesthesia, and their Persian equivalents. Data were analyzed using meta-analysis and fixed effects model. In order to study the heterogeneity and contradictions in the studies, Q Cochrane and I^2 indices were used, respectively.

FINDINGS: Of the 72 found articles, 9 articles with a sample size of 1,126 and an average of 125 subjects were included in the study. The results of this study showed that the relationship between obstructive sleep apnea and difficult intubation is significant (OR = 3.88, CI95% = 2.69 – 5.61). In addition, the results of the analysis based on country showed that the highest and lowest odds ratios were observed in studies conducted in France and Canada, respectively.

CONCLUSION: The results of this study showed that there is a correlation between obstructive sleep apnea and difficult intubation.

KEY WORDS: *Obstructive Sleep Apnea, Difficult intubation, Systematic review, Meta-analysis.*

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Introduction

The obstructive sleep apnea syndrome is one of the most common respiratory disorders during sleep, which affects about 3 to 7 % of the general population and remains undetectable in the majority of cases (1). This disorder indicates stoppage of air flow more than 10 seconds in the airway in an adult person, which is repeated hundreds of times during sleep and causes the breathing to stop for a short time during sleep (2). During these moments, the person wakes up several times with feeling of fatigue, but he/she is not aware of that (3).

This complication may be due to upper airway obstruction, increase in sympathetic activity due to frequent excitation and hypoxia during sleep (4). The vain attempts to breathe during apnea will exacerbate the negative pressure inside the chest, intermittent respiratory interruptions and waking up (5).

In addition to creating multiple problems such as headache, fatigue, decreased consciousness, disrupted sleep patterns and daily functioning, memory impairment, depression, diabetes and impotence in men, the obstructive sleep apnea is associated with the risk of more serious complications such as hypertension, cerebrovascular diseases, ischemic heart disease and accidents (6–8).

In addition, obstructive sleep apnea can reduce the longevity of people (8). Chang et al. reported that the average life expectancy in people with obstructive sleep apnea (58 years) is significantly lower than healthy people (78 years) (9). One of the problems that may be caused by obstructive sleep apnea is difficult intubation during the induction of anesthesia in candidates for surgery (10). A difficult intubation is a clinical condition in which the patient's pharynx view is placed at grade 3 or 4 during laryngoscopy (11). In these cases, the insertion of the tube into the patient's trachea is either not taking place, or hardly done after several attempts, and sometimes there is need for facilitating maneuvers and assisting devices for intubation (12, 13).

Recent studies have shown that difficult intubation occurs in about 3 – 5 % of patients undergoing general anesthesia surgery (14). The reason for difficult intubation in patients with obstructive sleep apnea is the large neck circumference in patients with obstructive sleep apnea based on the STOBBANG screening tool (15, 16).

Difficult intubation and untreated obstructive sleep apnea are two challenges for anesthetists, which may lead to several complications, including hypoventilation, need for reintubation, cardiac dysrhythmia, prolonged healing period, inflammation of the throat and laryngospasm and even in severe cases and in the absence of proper management of doctors, may lead to death (35%) (12, 17). Although a small percentage of candidate patients have obstructive sleep apnea, almost all patients suffer from mild obstructive sleep apnea and more than half of patients have moderate to severe obstructive sleep apnea, which is not diagnosed before surgery at all (18). The results of different studies are somewhat contradictory regarding the relationship between obstructive sleep apnea and difficult intubation. Some studies have shown that there is a relationship between obstructive sleep apnea and difficult intubation (13, 19). However, in other studies, there was no relationship between obstructive sleep apnea and difficult intubation (10,20).

Considering the importance of safe anesthesia during surgery and the possible association of difficult intubation and obstructive sleep apnea and given the relatively contradictory results of studies in this field, achieving a single result and drawing a more complete picture by summarizing and analyzing the studies is essential and important. Therefore, this study examines the relationship between obstructive sleep apnea and difficult intubation through systematic review and meta-analysis.

Methods

The present study is a systematic review and meta-analysis that examines the association between obstructive sleep apnea and difficult intubation in the studies carried out in this regard. To find the relevant studies, national and international databases such as SID, MagIran, Google Scholar, IranMedex, Science Direct, PubMed, ProQuest, Embase and Scopus were used without time limit.

The searched keywords were: difficult intubation, problematic intubation, intra tracheal-endotracheal, difficult airway, OSA, OSAS, obstructive sleep apnea, sleep breathing disorder, anesthesia, and their combination and their Persian equivalents. The references of the reviewed articles were also reviewed to find more articles. Then hand-crafted articles were also done.

After the initial search, the abstracts of the articles and the related cases were selected. In this study,

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observational studies (descriptive, cross-sectional, case-control and prospective cohort), published in Persian and English, that investigated the relationship between the two variables of obstructive sleep apnea and difficult intubation were included in the study. Intervention studies and studies with unspecified method were excluded from the analysis. According to the inclusion and exclusion criteria, the abstracts of the articles were reviewed by two independent researchers and the related items were separated and their full text was extracted.

In order to extract the required information, a form was used that included the name of the first author of the article, the year of publication, the location of the study, the sample size, and the association between obstructive sleep apnea and difficult intubation. In this study, each article was reviewed by two researcher independently. In case of disagreement, the article was judged by the author who was expert in meta-analysis. The STORBE (strengthening the reporting of observational studies in epidemiology) checklist was used to assess the quality of the articles (21). This checklist includes 22 parts.

The maximum score of the checklist was 30 and the minimum score was 15. Articles with score lower than 15 were excluded from the study. The main criterion for selecting the article was the relevance of the article to the subject of the study. Finally, 65 articles were found in the initial search and 7 articles were found after manual search as well as searching in references of the articles (a total of 72 articles) using the mentioned keywords. After studying the title and abstract, 47 articles were excluded due to being irrelevant to the subject of study and the ambiguity of the methodology and finally, 25 Persian or English relevant articles were examined.

Subsequently, 16 articles were excluded because they examined the relationship between other variables such as body mass index, neck circumference and abdominal circumference and difficult intubation in patients with obstructive sleep apnea or did not provide complete information. Finally, 9 studies were analyzed. The search strategy was as follows:
((Difficult Intubation) OR (problematic Intubation) OR (Intra tracheal Intubation) OR (endo-tracheal intubation) OR (difficult airway)) AND ((OSA) OR (OSAS) OR (obstructive sleep apnea) OR (sleep breathing disorder) AND (anesthesia)).

In statistical analysis, considering that the two variables of obstructive sleep apnea and difficult intubation were reported qualitatively as dichotomies (obstructive sleep apnea: has/does not have, and difficult intubation: has/does not have) in the selected studies, the odds ratio effect with 95% confidence interval was used to measure the relationship between obstructive sleep apnea and difficult intubation. The fixed effects analysis of the Mantel-Haenszel model was used to combine the studies.

The forest plot, with a 95% confidence interval, was used for visual representation of combined studies. Cochran's Q test and I^2 indices were used to examine the heterogeneity and contradictions in the studies. In addition, the effect of small studies and publishing error was investigated using Begg and Egger's tests and Begg's funnel plot diagrams. Subgroup analysis was used to investigate the relationship between obstructive sleep apnea and difficult intubation based on the type of study and location of the study. Sensitivity analysis was also used to evaluate the effect of each study on the odds ratio. Data analysis was performed using STATA software version 14 and $p < 0.05$ was considered significant.

Results

In the initial search, a total of 72 studies were identified, among which 9 studies entered the final analysis based on inclusion and exclusion criteria. The screening process and the selection of related articles are presented in PRISMA flow diagram in Fig 1. In this meta-analysis, 9 articles with a sample size of 1126 and an average of 125 samples in each study were analyzed. The highest and lowest sample sizes were related to the studies by Acar et al. (12) and Chung et al. (33 patients) (9), respectively (Table 1).

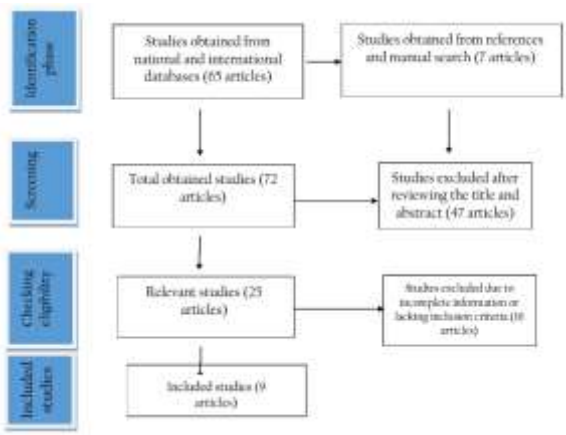

Figure 1. Flowchart of selecting studies to enter the meta-analysis (PRISMA Diagram)

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The review of studies showed that the association between obstructive sleep apnea syndrome and difficult intubation was significant (OR = 3.88, CI-95%= 2.69–5.61). Among the examined articles, only the study of Brodsky et al. showed no significant association between obstructive sleep apnea syndrome and difficult intubation (22) (OR=0.76, CI-95%=0.23 – 2.54) (Fig 2). The results of the sensitivity analysis also showed that in the absence of Brodsky’s study, a significant change was observed in the estimation of the odds ratio and this study alone had a significant effect on the estimation of the odds ratio. According to the results of the sensitivity analysis, after exclusion of Brodsky’s study, the estimation of odds ratio decreased from 3.88 with 95% confidence interval of 2.69 – 5.61 to 4.64 with 95% confidence interval of 3.13 – 6.87 and the I^2 index decreased from 35.9% to zero. The results of the analyses based on the type of study showed that the relationship between obstructive sleep apnea syndrome and difficult intubation was not significant based on the type of study and the type of study has no effect on these two variables.

Accordingly, the highest odds ratio was in case-control studies (OR = 6.38, CI-95%= 3.49–11.69), and the lowest odds ratio was in cross-sectional studies (OR=3.5, CI-95%=1.86–6.58) (Fig 3). The results of the analyses based on country showed that the highest and lowest odds ratios were respectively found in studies in France (OR=7.21, CI-95% = 2.88–18.10) and Canada (OR = 1.3, CI-95% = 0.62 – 2.71). Based on the reported results, publication bias was not observed in the results of this study (p=0.132) (Fig 4).

Table 1. Specifications of studies included in the meta-analysis

Difficult Intubation Measurement Tools (D.I)	Cormak and Lehane scale	Cormak and Lehane scale/atlanto-occipital joint extension measurements	Malllampati Classification	Mallampati classification	Cormak and Lehane Grade	Malllampati Classification	Operator Intubation Difficulty Scale Score/Cormak and Lehane Grade	Cormak and Lehane Grade	Mallampati Classification/Number of intubation attempts
OSA Measurement Tools	Berlin questionnaire	Polysomnography	STOBBANG tools	Apnea–hypopnea index	Polysomnography	Medical diagnosis	Polysomnography	Apnea–hypopnea index	Examination of neck, mouth and snore
Odds ratio (OR)	3.60	4.07	5.81	3.38	1.73	9.46	5.80	10.71	0.76
95% confidence interval	1.55 – 8.39	1.54 – 10.76	1.57 – 25.52	1.31 – 8.70	0.40 – 7.46	2.63 – 33.46	1.62 – 20.81	2.14 – 53.56	0.23 – 2.54
OSA(-)/ D.I(-)	98 (66.7%)	30 (76.9%)	114 (57%)	63 (68%)	6 (18.2%)	58 (44.3%)	87 (48.3%)	75 (97.4%)	38 (38%)
OSA(+)/D.I(-)	49 (33.3)	18 (45%)	72 (36%)	29 (32%)	9 (27.3%)	47 (35.9%)	75 (41.7%)	28 (78.1%)	50 (50%)
OSA(-)/D.I(+)	10 (35.7%)	9 (23.1%)	3 (1.5%)	9 (39%)	5 (15.1%)	3 (2.3%)	3 (1.7%)	2 (2.6%)	6 (6%)
OSA(+)/D.I(+)	18 (64.3%)	22 (55%)	11 (5.5%)	14 (61%)	13 (39.4%)	23 (17.5%)	15 (8.3%)	8 (21.9%)	6 (6%)
Sample size	175	79	200	115	33	131	180	113	100
Mean age	69.9	49.7	47.9	38.5	56.5	45	44.1	53.8	44
Type of study	Cross-sectional	Case-control	Prospective	Cross-sectional	Prospective	Case-control	Case-control	Case-control	Prospective
Country	Iran	Turkey	Turkey	South Korea	Canada	France	South Korea	France	United States
Year	2016	2015	2014	2011	2008	2008	2006	2002	2002
Auther	Farajzadeh[13]	Akkurt [15]	Acar [12]	Lee S J [16]	Chung [9]	Gonzalez[24]	Kim &Lee Jeong [23]	Siyam & Dan Benhamou[20]	Brodsky [22]

OSA: Obstructive sleep apnea, DI: Difficult Intubation

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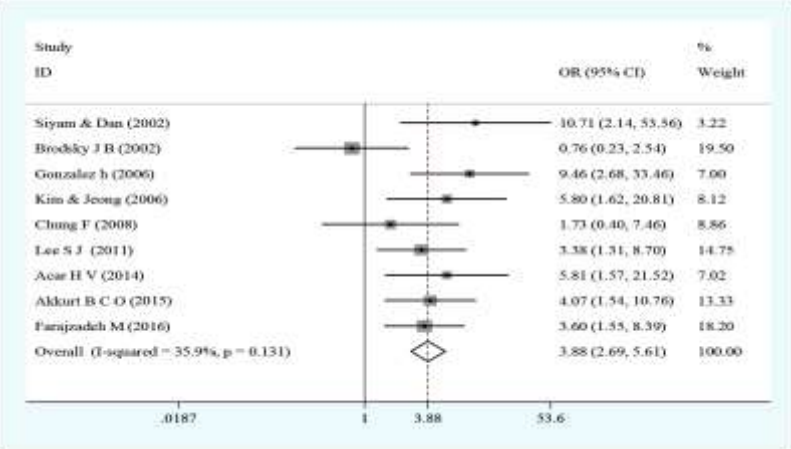

Figure 2. Accumulation graph of investigating the relationship between obstructive sleep apnea syndrome and difficult intubation. The 95% confidence interval for each study is in the form of horizontal lines around the primary average. The lozenge sign is the result of a combination of studies with a 95% confidence interval.

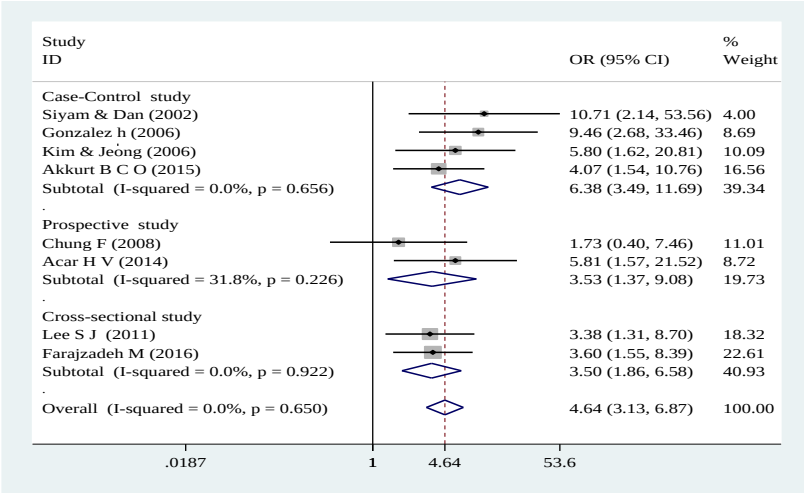

Figure 3. Accumulation graph of investigating the relationship between obstructive sleep apnea syndrome and difficult intubation based on the type of study. The 95% confidence interval for each study is in the form of horizontal lines around the primary average. The lozenge sign is the result of a combination of studies with a 95% confidence interval.

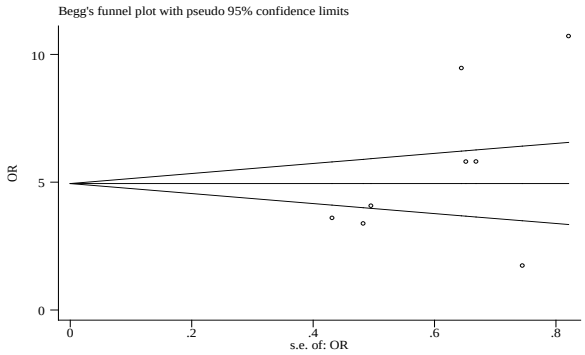

Figure 4. Bug Fillon Plate Bias Selected Studies

Discussion

The overall result of this meta-analysis showed that there was a significant relationship between obstructive sleep apnea syndrome and difficult intubation, and the odds ratio of obstructive sleep apnea syndrome in subjects with difficult intubation was 3.88 times higher than subjects with normal intubation. In this research, all studies except for the

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study of Brodsky et al. (22) showed a direct and significant relationship between obstructive sleep apnea syndrome and difficult intubation. In the study of Brodsky et al., 100 obese subjects who were candidates for elective surgery with BMI of more than 40 kg/m ^{2} were examined.

In this study, the Mallampati Classification method and the number of attempts for intubation were used to measure difficult intubation. Brodsky's study showed that there was no correlation between obstructive sleep apnea syndrome, obesity and BMI and difficult intubation. The reason for the difference between the results of this study and other studies may be due to differences in the research community and the tools for assessing obstructive sleep apnea. The results of different studies showed that the use of various tools to diagnose obstructive sleep apnea syndrome and difficult intubation can affect the relationship between them (19, 25).

Difficult intubation is known to be a major risk factor for anesthesia, which has serious complications and even leads to death in some cases (18). Different methods have been introduced to detect difficult intubation; however, no unified and comprehensive definition has been announced to be agreed by the experts in this field. Of the 9 studies selected for this meta-analysis, four studies used the Mallampati Classification (12, 16, 22, 24) and five studies used Cormack – Lehane (9, 13, 15, 20, and 23) for the detection of difficult intubation. Moreover, in addition to Cormack – Lehane method, other methods such as Operator Intubation Difficulty Scale Score (OIDS) (23) and Atlanto-Occipital Joint Extension Measurements (15) were used in two studies. Furthermore, the number of attempts to perform intubation was also used to detect difficult intubation in the study of Brodsky et al. (22), in addition to the Mallampati method. In Brodsky's study, items such as neck circumference, mouth opening, thyromental distance, and snoring has been used to measure obstructive sleep apnea syndrome, while other studies used the common tools for diagnosing obstructive sleep apnea syndrome, such as Polysomnography (9, 15 and 23), Apnea-Hypopnea Index (16 and 20), Medical Diagnosis, Berlin Questionnaire (13) and STOBBANG Questionnaire (12).

The size, shape and volume of the contents of the mouth, throat, larynx and neck in people with obstructive sleep apnea syndrome are fundamentally different from healthy subjects, which makes intubation difficult for them (15 and 19). In addition, decreased mandibular length, elevated hyoid bone, and retarded position of a maxillary fracture observed in patients with obstructive sleep apnea syndrome may lead to difficult intubation in these patients (26). Another reason that may affect the results of the studies is the choice of the type of laryngoscopy blade (MacIntosh or Miller) for laryngoscopy in patients. The MacIntosh blade is curved and causes less damage to the tissues in the mouth during laryngoscopy, while the Miller blade is straight and provides a better view (27). The Brodsky's study uses a MacIntosh blade, while the blade type is not mentioned in other studies. Other reasons for the difference between the results of Brodsky's study and other studies may be related to the position of patients' head and body during intubation. Brodsky only mentioned the head and neck extension as the position of patients' head and body during intubation, while in some studies, the positions of Ramp, HELP, and Sniff have been referred to as the position used for intubation (9, 12, 16, 24).

Other studies did not mention head and neck positions. According to the results of this meta-analysis, the type of study (cohort, case – control, and cross – sectional) did not play a role in the relationship between obstructive sleep apnea syndrome and difficult intubation. Furthermore, of all studies conducted in different countries in the world, only the study of Brodsky (United States) showed no significant relationship between the two variables of obstructive sleep apnea syndrome and difficult intubation. Studies have shown that race has a dramatic effect on anatomy of the head and neck, and the genetic difference between the American society and the Asian and European societies can justify this (1). The results of this study showed that there is a relationship between obstructive sleep apnea syndrome and difficult intubation.

Considering the increasing role of anesthesiologists as one of the most important people involved in reducing the complications of anesthesia in patients undergoing surgery, as well as the strong recommendation of the American Society of Anesthesiologists to identify patients with obstructive sleep apnea syndrome and even those suspected of the disease and proper management of anesthesia and intubation of these patients (14–16), it is very important to provide a reliability and validity tool for the screening and diagnosis of patients with obstructive sleep apnea syndrome before intubation;

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That's because obstructive sleep apnea syndrome leads to difficult intubation and causes damage to the tissues in the mouth and post-anesthetic complications. The gold standard instrument in the diagnosis of obstructive sleep apnea syndrome is polysomnography (1), but the high cost, long detection time and lack of access to sleep centers in all areas makes it difficult to use this tool. Therefore, it is necessary to use some screening tools in the operating rooms to diagnose obstructive sleep apnea syndrome. Furthermore, according to the results of various studies, the Mallampati method has been suggested as a suitable predictive method for the diagnosis of difficult intubation and obstructive sleep apnea syndrome, which can be used by the experts (12). Anesthesiologists can also use the fiberoptic laryngoscopy method and the video laryngoscope for cases in which their intubation appears to be difficult (28). One of the limitations of the study was the fact that only articles entered the meta-analysis process that reported odds ratio or reported data in a way that odds ratio could be calculated. Another limitation of this study was the small sample size (1126 people). Other limitations of this study were failure to investigate the effect of the type of laryngoscopy blade used for laryngoscopy and its association with intubation, which was due to the fact that the authors did not refer to the type of blade used for intubation.

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