

A Meta-analysis Study on Possible Risk Factors for Primary and Secondary Hemorrhage After Tonsillectomy

Tonsillektomi Sonrası Gelişen Primer ve Sekonder Kanamalarda Olası Risk Faktörleri Üzerine Bir Meta-analiz Çalışması

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ABSTRACT Objective: Tonsillectomy is one of the most common surgical operation performed by otorhinolaryngologists, with significantly reduced morbidity and mortality rates due to the operation in parallel with the advances in surgical technique and anesthesia. Post-tonsillectomy hemorrhage (PTH) is one of the most common, most reported, and serious complication of tonsillectomy operations. In this context, the aim of this research is to synthesize and reveal a wide-ranging study through meta-analysis of studies examining the risk factors that may cause primary and secondary hemorrhage in patients who have undergone tonsillectomy surgery using data from relatively small samples. **Material and Methods:** In this study, a meta-analysis of a total of 12 studies on PTH risk factors was conducted. In this meta-analysis, the "effect size" criterion was used, which indicates how much a new method makes a difference compared to the old one. **Results:** As a result of the study, like the literature, the risk of PTH was found to be higher in men than in women in adults, in children under the age of 15, the difference between boys and girls was quite low. It is considered that fewer studies, especially for children under the age of 15, may influence this. In addition, studies have shown that secondary hemorrhage occurs. **Conclusion:** As a result of the study, it was determined that women experience PTH more frequently than men, and secondary PTH risk is higher than primary PTH.

ÖZET Amaç: Tonsillektomi, cerrahi teknik ve anesteziadaki gelişmelere paralel olarak operasyona bağlı morbidite ve mortalite oranlarının önemli ölçüde azaldığı, kulak-burun-boğaz uzmanları tarafından en sık uygulanan cerrahi operasyonlardan biridir. Tonsillektomi sonrası kanama [post-tonsillectomy hemorrhage (PTH)], tonsillektomi ameliyatlarının en yaygın, en çok bildirilen ve ciddi komplikasyonlarından biridir. Bu bağlamda, bu araştırmanın amacı, tonsillektomi ameliyatı geçiren hastalarda birincil ve ikincil kanamaya neden olabilecek risk faktörlerini nispeten küçük örneklemelerden elde edilen verilerle inceleyen çalışmaların metaanalizi ile geniş kapsamlı bir çalışmayı sentezlemek ve ortaya çıkarmaktır. **Gereç ve Yöntemler:** Bu çalışmada, PTH risk faktörleri ile ilgili toplam 12 çalışmanın metaanalizi yapılmıştır. Bu metaanalizde, yeni bir yöntemin eskisine göre ne kadar fark yarattığını gösteren "etki büyüklüğü" kriteri kullanılmıştır. **Bulgular:** Çalışma sonucunda, literatürde olduğu gibi erkeklerde PTH riski erişkinlerde kadınlara göre daha yüksek, 15 yaş altı çocuklarda kız ve erkek çocuklar arasındaki fark oldukça düşük bulunmuştur. Özellikle 15 yaş altı çocuklar için daha az sayıda çalışmanın bunu etkileyebileceği düşünülmektedir. Ek olarak, çalışmalar ikincil kanamanın meydana geldiğini göstermiştir. **Sonuç:** Çalışma sonucunda, kadınların erkeklerden daha sık PTH yaşadığı ve ikincil PTH riskinin birincil PTH'den daha yüksek olduğu belirlendi.

Keywords: Tonsillectomy; postoperative hemorrhage; bleeding; postoperative complication

Anahtar Kelimeler: Tonsillektomi; postoperatif hemoraji; kanama; postoperatif komplikasyon

Tonsillectomy is a common otolaryngological operation and complications due to this operation have been reduced with the advances in surgical technique and anesthesia.¹⁻³ Although tonsillectomy is generally a safe operation, arterial damage may occur during the operation due to the

course of the major arteries and their proximity to the operation area, the rich vascular network, and the atypical course of the internal carotid artery.^{4,5} For this reason, postoperative hemorrhage is one of the common complications of tonsillectomy.^{2,3,6,7}

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The incidence of post-tonsillectomy hemorrhage (PTH) has been reported as 0.1-9.3% in the literature. Bleeding within 24 hours postoperatively is called primary hemorrhage, while bleeding after 24 hours is called secondary hemorrhage. Primary hemorrhage is more common and is often associated with insufficient hemostasis, acute vascular injuries or surgical technique; secondary hemorrhage is associated with solid food intake during wound healing, tonsillectomy area infection, nonsteroidal anti-inflammatory medication use or early decomposition of granulation tissue due to idiopathic reasons in the operated area.^{7,8} In addition, secondary hemorrhage is less common and more frightening.^{1,8-11}

The variables affecting PTH are listed as follows: preoperative factors [patient's gender, age, indication for surgery, hematological parameters, physiological oropharyngeal bacterial colonization, genetic disorders affecting the coagulation mechanism, hemorrhage diathesis (susceptibility), use of anticoagulant or antiplatelet medications, lupus, kidney or liver failure, the presence of diseases that can cause hemorrhage such as hypothyroidism, recent viral infections], perioperative factors (surgical technique, experience of the surgeon performing the surgery, intraoperative medicine used including anesthetic agents and steroids, blood loss during the operation, the season and ambient temperature of the operation), postoperative factors (postoperative pain and analgesic control, antimicrobial treatment, time after the operation, postoperative blood pressure, insufficient fluid intake, postoperative saliva content change).^{6,8,10-14} For example, children with tonsillectomy due to chronic tonsillitis have more scars on their tonsils and surrounding tissue, and the tonsils are more difficult to remove.

In this meta-analysis, we aimed to investigate risk factors that may cause primary and secondary hemorrhage in patients who have undergone tonsillectomy.

MATERIAL AND METHODS

METHOD

Meta-analysis method was used in the research. "Meta-analysis" is a method that combines individual studies on a specific subject and synthesizes the re-

sults of the studies by using appropriate statistical methods and aims to reach common results. In the studies conducted in the literature, generally the "p value" is used to evaluate whether the difference between groups is important or not. In meta-analysis studies, the "effect size" criterion is used, which indicates how much a new method makes a difference compared to the old one.¹⁵ All procedures were performed according to the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Various risk factors that can cause primary and secondary hemorrhage after tonsillectomy are mentioned in the relevant literature. In this study, it is aimed to investigate the possible risk factors affecting PTH in a holistic manner by combining the results of studies in the literature on tonsillectomy within certain criteria. Therefore, meta-analysis method was preferred in the study.

SEARCH PLAN AND STUDY SELECTION

In the study, in order to collect data, the keywords "tonsillectomy", "post-tonsillectomy hemorrhage", "tonsillectomy complications" were searched in English, from the National Thesis Center of the Council of Higher Education to reach theses first, and from the Google academic search engine to reach scientific articles. According to Lipsey and Wilson, for a research to be included in the meta-analysis study, it must be within the boundaries of the research and have the necessary statistical data for analysis.¹⁶ In this context, the following criteria were considered when selecting the studies included in the study:

- Studies that are conducted between 2010 and 2020,
- Studies that are examining possible risk factors affecting PTH,
- Studies involving the sample size and average values required for meta-analysis regarding the number of events and averages.

Five databases were searched independently (PubMed, SCOPUS, Embase, Web of Science, and the Cochrane database), including the articles published between 2010-2020. A combination of controlled vocabulary and key terms related to

tonsillectomy and PTH (eg, keywords “tonsillectomy”, “post-tonsillectomy hemorrhage” and “tonsillectomy complications”) was used for searching the databases. The purpose of meta-analysis is to reach all published and unpublished data on the specified subject. In this study, doctoral theses, master theses, articles and case reports were included as data sources and those suitable for analysis were included. Additionally, the reference lists of included articles and recent reviews addressing tonsillectomy in children to identify potentially relevant articles were hand-searched.

We reviewed the findings on PTH among the included studies. In [Figure 1](#), the summary of flow chart design of the study is presented.

ASSESSMENT OF STUDY RISK OF BIAS AND STRENGTH OF EVIDENCE

The methodologic quality of studies was independently evaluated by two investigators using prespecified questions that were appropriate to each study design to assess the risk of bias of randomized controlled trials and observational studies. Discrepancies in the risk-of-bias assessment were resolved by senior reviewers. Studies with a high risk of bias were not included in our descriptive analyses; however, they were included in the meta-analysis after the determination of the fact that their inclusion did not systematically affect the meta-analysis results. The data were extracted by one investigator regarding: study design; descriptions of study populations, intervention, and comparison groups; and baseline and out-

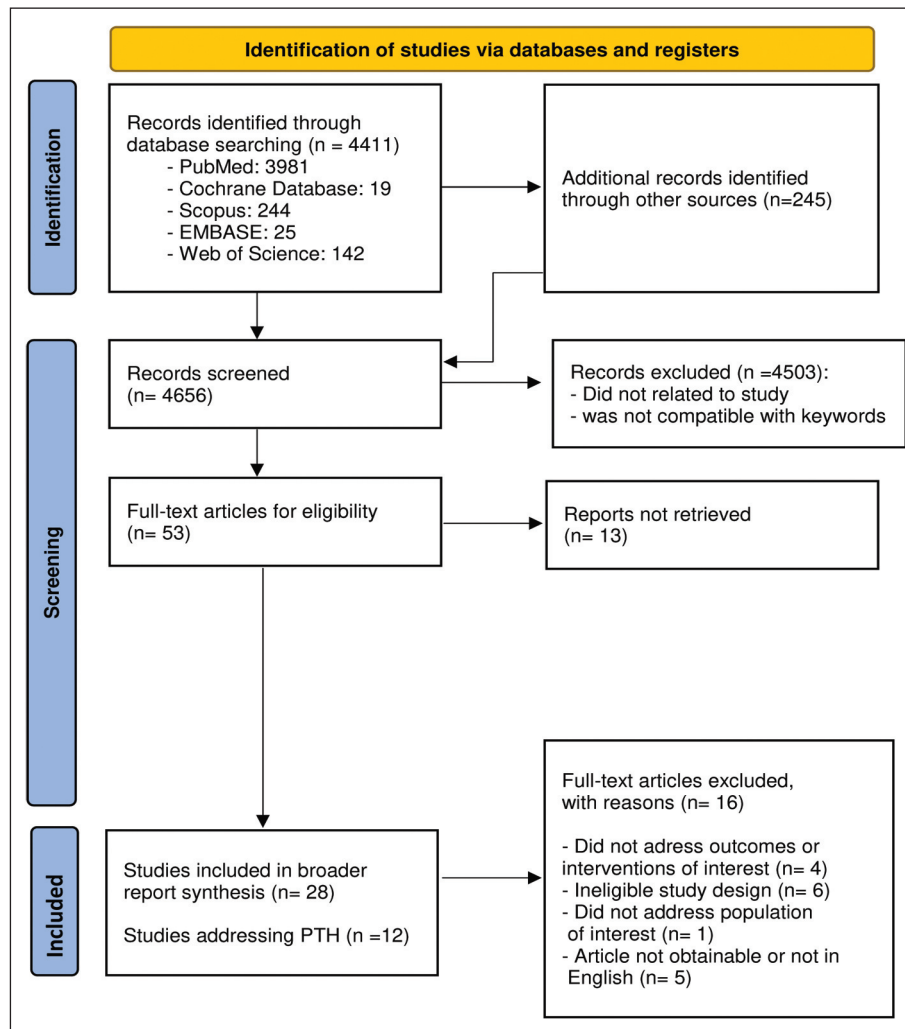


FIGURE 1: Study flow chart. PTH: Post-tonsillectomy hemorrhage.

come data using a standardized form. Another investigator verified the accuracy of the extraction and revised as needed independently.

It is reflected by the assessment of the strength of the evidence that the confidence we have in the stability of treatment has an effect on the face of future research. The degree of confidence that the observed effect of an intervention is unlikely to change (ie, the strength of the evidence) is shown as to be insufficient, low, moderate, or high. Five domains are taken as basis for the assessments on consideration of: study limitations, consistency in direction of the effect, directness in measuring intended outcomes, precision of effect, and reporting bias. A prespecified approach described in detail in the full article was used to determine the strength of evidence separately for major intervention-outcome pairs.

The research was begun by primarily examining the abstracts of the studies. Considering the criteria listed above, 28 studies were determined first. When the full texts of these studies were later examined, studies that included descriptive statements explaining the risk factors affecting PTH, but no quantitative data were reported, were excluded and 16 of the studies that were found not to include the sample size, average value and p values required to calculate the effect sizes were also excluded from the study. As a result, 12 studies were included in the meta-analysis. Descriptive information of these studies is presented in Table 1, and quantitative information is presented in Table 2.

STATISTICAL ANALYSIS

The total sample size of the studies included in the analysis is 21,647 patients. The statistical values given in Table 2 vary according to the purpose of these studies; within the scope of this study, studies are classified according to the desired risk factors. According to the quantities given in Table 2, the gender factor in adults in experiencing PTH, the gender factor in children under the age of 15 and the risks of experiencing primary and secondary PTH will be compared.

RevMan 5.3 program was used to perform meta-analysis in the study. First of all, effect sizes of the analyzed articles were calculated, and heterogeneity

TABLE 1: Descriptive information about studies included in the meta-analysis.

Authors	The aim of the study	Sample number
Aksakal ¹⁰	Investigation and comparison of the characteristics of PTH in adult and pediatric patients who underwent tonsillectomy or denotonsillectomy	421
Alvo et al. ¹⁷	Examination of PTHs in children who have undergone tonsillectomy in private and state hospitals	2177
Hoshino et al. ¹⁶	Examination and comparison of patients with PTH according to their obesity status and demographic structure	98
Inuzuka et al. ¹⁹	Examination of PTHs in adult patients	325
Johnston et al. ²⁰	Examination of pediatric patients with PTH according to their infected status	1538
Kim et al. ²¹	Comparison of adults and children experiencing PTH	1489
Kim et al. ²²	Comparative examination of PIT and extracapsular tonsillectomy techniques in pediatric patients	1077
Nami et al. ²³	Investigation of contralateral and ipsilateral hemorrhage and risk factors of patients with PTH	1671
Ordemann et al. ²⁴	Investigation of the effect of age factor on pediatric patients with PTH	1418
Perkins et al. ²⁵	Investigation of the relation between preoperative clinical diagnostic factors and PTH	9023
Spektor et al. ²⁶	Investigation of the relation between preoperative risk factors and PTH in pediatric patients	2237
Seyhun et al. ²⁷	Investigation of the relation between smoking status and PTH in adult patients	364

PTH: Post-tonsillectomy hemorrhage; PIT: Partial intracapsular tonsillectomy.

TABLE 2: Quantitative information about studies included in the meta-analysis.

Patients	Male		Female		Children		Adults		Total PTH		PTH male		PTH Female		PTH children		Primer PTH		Secondary		Blood		Spontaneous		Local		General a	
	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)	(n)
Aksakal ¹⁰	421	205	216	290	131	290	131	16	7	9	7	1	15	2	4	2	10	1	1	2	2	4	4	2	2	10		
Alvo et al. ¹⁷	2177	-	-	2177	-	2177	-	78	38	40	78	5	73	1	58	-	22	5	5	1	1	58	58	-	-	22		
Hoshino et al. ¹⁶	98	56	42	-	98	-	19	15	4	4	-	1	18	-	10	6	3	1	1	-	-	10	10	6	6	3		
Inuzuka et al. ¹⁹	325	250	75	-	325	-	71	65	6	6	-	8	63	-	61	5	5	8	8	-	-	61	61	5	5	5		
Johnston et al. ²⁰	1538	-	-	1538	-	1538	-	84	-	-	84	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-		
Kim et al. ²¹	1489	938	550	1109	380	1109	74	44	30	30	33	0	74	-	53	8	13	0	74	-	-	53	53	8	8	13		
Kim et al. ²²	1077	656	421	1077	-	1077	18	13	5	5	18	-	-	-	15	-	3	-	-	-	-	15	15	-	-	3		
Nami et al. ²³	1671	-	-	-	-	-	116	76	40	40	-	4	112	-	25	30	61	4	4	-	-	25	25	30	30	61		
Ordemann et al. ²⁴	1418	748	670	1418	-	1418	31	17	14	14	31	11	20	-	-	-	-	11	11	-	-	-	-	-	-	-		
Perkins et al. ²⁵	9023	4335	4688	9023	-	9023	242	101	111	111	212	48	164	-	-	-	-	48	48	-	-	-	-	-	-	-		
Spektor et al. ²⁶	2237	-	-	2237	-	2237	91	49	42	42	91	-	91	-	-	-	-	-	-	-	-	-	-	-	-	-		
Seyhun et al. ²⁷	364	218	146	-	364	-	53	44	9	9	-	-	53	-	33	11	21	-	-	-	-	33	33	11	11	21		

Child: <15 years and younger, Adult: >1 year-old, PTH: Post-tonsillectomy hemorrhage.

test was performed. In addition, there is a need to consider the publication bias of the studies analyzed in meta-analysis. In this study, the field bias test was analyzed using the Funnel Plot method.²⁸

RESULTS

GENDER FACTOR OF PATIENTS WITH POST-TONSILLECTOMY HEMORRHAGE

The effect sizes of the studies included in the gender factor analysis of patients with PTH are shown in Funnel Plot Figure 2. In the analysis of gender factors in PTH, the number of male and female patients in the total number of patients, and the studies with exact female and male numbers among patients with PTH were included. In 12 studies selected for meta-analysis, a total of 8 studies showed that these numbers were given exactly. Figure 2 shows that the studies are balanced and closely collected on both sides of the vertical line of effect size. This can be interpreted in such a way that the studies included in the analysis do not have a publication bias.

As seen in Figure 3, 8 studies including a total of 14,214 patients who underwent tonsillectomy operation were analyzed. Of the patients used as samples in these studies; 7,406 people are men, and 6,808 people are women. Regardless of the primary and secondary differentiation of patients, a total of 306 PTH was occurred in male patients and 188 PTH in women patients. As a result of the analysis, it is seen that there is heterogeneity at 95% confidence interval (p<0.05). Looking at the forest plan, it is seen that the general relative risk ratio is in favor of women.

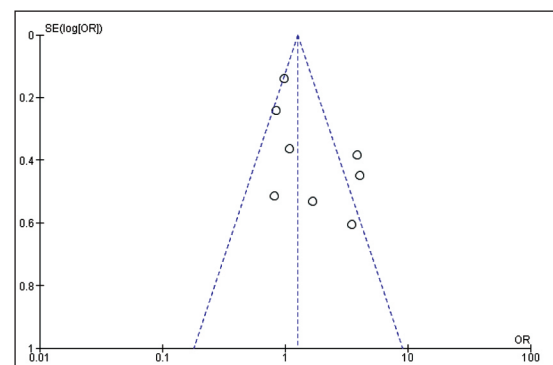


FIGURE 2: Funnel plot of studies included in the gender factor analysis of patients undergoing post-tonsillectomy hemorrhage.

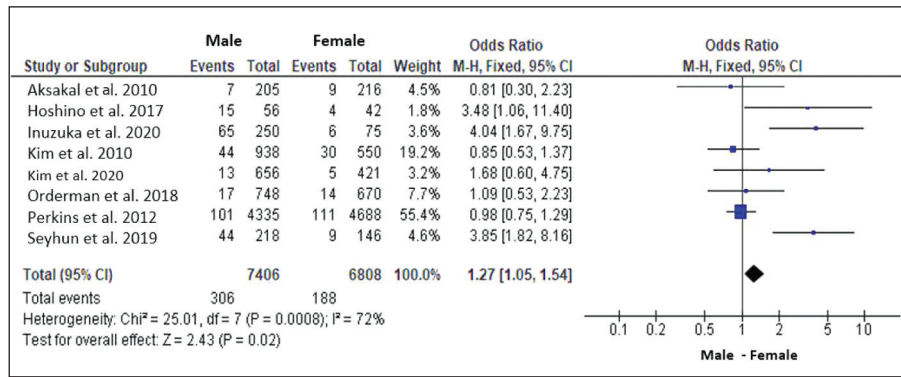


FIGURE 3: Gender factor of patients with PTH.

One of the risk factors examined within the scope of meta-analysis is the analysis of PTHs occurring as primary and secondary in patients. In 10 of the studies examined in this context, it was seen that the total number of PTH and the number of primary and secondary PTH were given and these studies were included in the analysis. Quantitative data and forest plot of the analysis are shown in Figure 4. A total of 761 PTH cases occurred in the patients followed up as a sample in the studies, 78 of them were primary and 683 were secondary hemorrhage.

Another issue addressed in the studies is the evaluation of the risk of experiencing PTH in chil-

dren under 15 years of age. In this context, meta-analysis of studies with quantitative information regarding risk factors in boys and girls under the age of 15 have been made, and the results obtained are shown in Figure 5.

A total of 3 studies on children were included in the meta-analysis. A total of 16,264 pediatric tonsillectomy cases were examined in these studies. A total of 317 PTH cases were encountered, 162 of which were in boys and 155 were in girls. As seen in the Forest Plot, the studies examined show that the relative risk factor for children under the age of 15 is very close to the 1 line, and there is a very small difference in favor of girls.

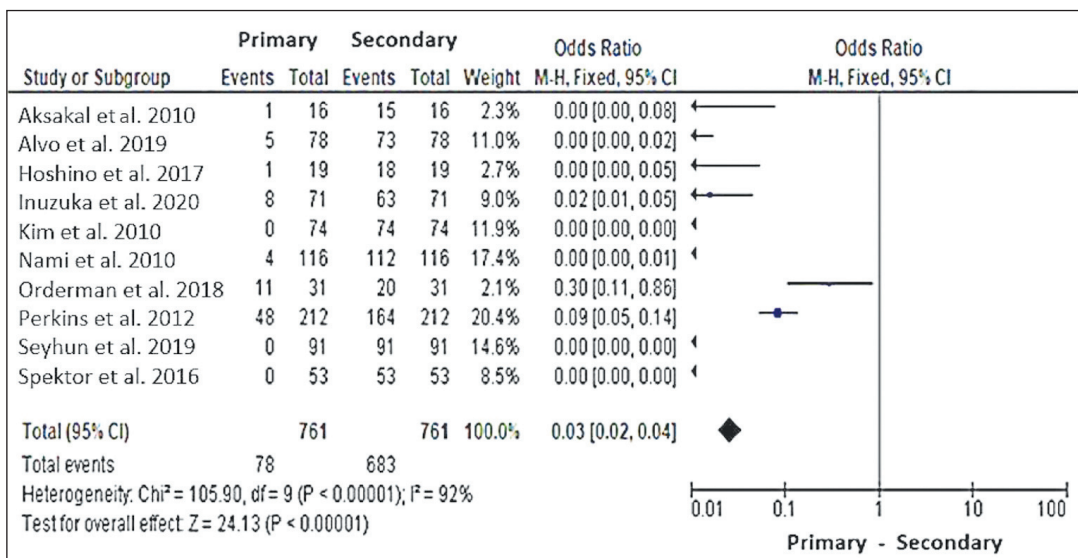


FIGURE 4: Primary and secondary PTH status.

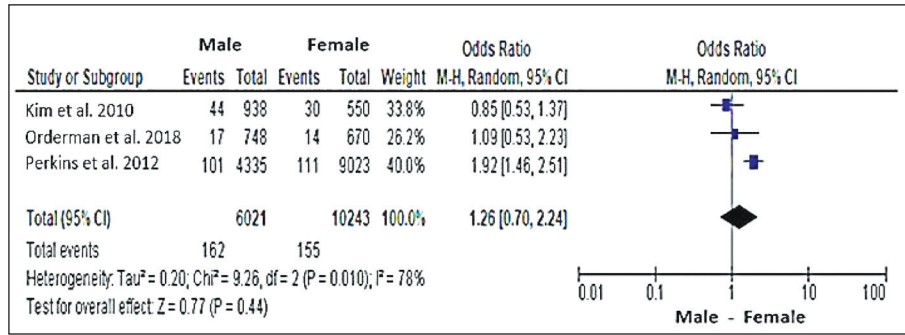


FIGURE 5: Gender factor in PTH cases in children under 15 years of age.

DISCUSSION

Tonsillectomy is one of the most common surgical operations in the ear nose throat field. Although it is a very safe operation with the developing techniques in general, there is a risk of postoperative hemorrhage and the risk of arterial damage during the operation due to the course of the major arteries and their proximity to the operation area, rich vascular network and atypical course of the internal carotid artery.

Tomkinson et al. in their study of 17,680 patients, found that the risk of PTH was greater in patients older than 12 years than in patients younger than 12 years old.²⁸ Kaya and Mutlu examined PTH risk factors with a sample of 667 patients. In their study on a group of 498 adults and 178 children, they found hemorrhage at a rate of 21.3% in adults and 4.3% in children after tonsillectomy.⁷ As a result of the study, they concluded that the risk of PTH increases with increasing age. It was seen that the risk of PTH in adults was higher than in children in the meta-analysis conducted in this study which is similar to the results obtained studies in the literature.

Some studies in the literature reveal that primary hemorrhage is more than secondary hemorrhage, while others argue the opposite.^{13,29} Çakır et al., in their study with a sample of 40 patients, reported that secondary hemorrhage was more common in patients with PTH.⁹ Likewise, in the study performed by Yorgancılar et al. on 23 patients, it was concluded that 4 patients had primary hemorrhage and 19 patients had secondary hemorrhage. In this meta-analy-

sis study, it was found that the risk of secondary hemorrhage was higher than primary hemorrhage.³⁰

There are studies in the literature suggesting that there is a high risk factor against male gender in terms of hemorrhage risk factors after tonsillectomy operation.¹¹ There are also studies suggesting that there is no difference in risk by gender in terms of risk factors for hemorrhage after tonsillectomy surgery.³¹ As can be seen from Table 2, where the quantitative data of 12 studies included in the meta-analysis are presented, it will be seen that in 10 of the 12 studies, male patients who underwent tonsillectomy operation are more than female patients. As a result of the meta-analysis, it was found that the risk ratio is higher in men than in women.

In this study, risk factors of PTH occurring after tonsillectomy were discussed. In total, 12 studies meeting the criteria were included in the analysis. The general gender factor was analyzed in 8 of the studies. A comparison between secondary and primary hemorrhage was made with 10 of the studies. In 3 of the studies, the prevalence of PTH in children by gender was analyzed.

CONCLUSION

As a result of the study, the risk of PTH was found to be higher in men than in women in adults. In children under the age of fifteen, the difference between boys and girls was quite low. It is considered that fewer studies, especially for children under the age of fifteen, may influence this. In addition, studies have shown the factors that is related to secondary hemorrhage occurrence.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, ex-

pertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Sinem Gökçe Kütük; **Design:** Sinem Gökçe Kütük; **Control/Supervision:** Sinem Gökçe Kütük; **Data Collection and/or Processing:** Sinem Gökçe Kütük; **Analysis and/or Interpretation:** Sinem Gökçe Kütük, Fatih Bora; **Literature Review:** Sinem Gökçe Kütük, Fatih Bora; **Writing the Article:** Sinem Gökçe Kütük, Fatih Bora; **Critical Review:** Sinem Gökçe Kütük, Fatih Bora.

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