## Adenotonsillectomy Complications: A Meta-analysis

Graziela De Luca Canto, DDS, MsC, PhD<sup>a,b</sup>, Camila Pachêco-Pereira, DDS<sup>b</sup>, Secil Aydinoz, MD<sup>c</sup>, Rakesh Bhattacharjee, MD<sup>d</sup>, Hui-Leng Tan, MBBS<sup>e</sup>, Leila Kheirandish-Gozal, MD, MSC<sup>d</sup>, Carlos Flores-Mir, DDSC, MSc, DSc, RCDC(C)<sup>b</sup>, David Gozal, MD, MBA, FAAP<sup>d</sup>

**abstract BACKGROUND AND OBJECTIVE:** Complications after adenotonsillectomy (AT) in children have been extensively studied, but differences between children with and without obstructive sleep apnea (OSA) have not been systematically reported. Our objective was to identify the most frequent complications after AT, and evaluate if differences between children with and without OSA exist.

**METHODS:** Several electronic databases were searched. A partial gray literature search was undertaken by using Google Scholar. Experts were consulted to identify any missing publications. Studies assessing complications after AT in otherwise healthy children were included. One author collected the required information from the selected articles. A second author crosschecked the collected information and confirmed its accuracy. Most of the selected studies collected information from medical charts.

**RESULTS:** A total of 1254 studies were initially identified. Only 23 articles remained after a 2-step selection process. The most frequent complication was respiratory compromise (9.4%), followed by secondary hemorrhage (2.6%). Four studies compared postoperative complications in children with and without OSA, and revealed that children with OSA have nearly 5 times more respiratory complications after AT than children without OSA (odds ratio = 4.90; 95% confidence interval: 2.38–10.10). In contrast, children with OSA are less likely to have postoperative bleeding when compared with children without OSA (odds ratio = 0.41; 95% confidence interval: 0.23–0.74).

**CONCLUSIONS**: The most frequent early complications after AT are respiratory compromise and secondary hemorrhage. Based on the current limited evidence, children with OSA appear to have more respiratory complications. Conversely, hemorrhage appears to be more frequent in children without OSA.

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<sup>a</sup>Department of Dentistry, Federal University of Santa Catarina, Florianopolis, Santa Catarina, Brazil; <sup>b</sup>School of Dentistry, Faculty of Medicine and Dentistry, University of Alberta, Alberta, Canada; <sup>o</sup>Gulhane Military Medical Academy, Istanbul, Turkey; <sup>d</sup>Division of Biological Sciences, Department of Pediatrics, Pritzker School of Medicine, University of Chicago, Chicago, Illinois; and <sup>e</sup>Royal Brompton Hospital, Imperial College, London, United Kingdom

Dr De Luca Canto worked on study conceptualization, design, data collection, data analysis, drafted the initial manuscript, and critically reviewed the manuscript; Dr Pachêco-Pereira worked on study conceptualization, design, data collection, data analysis, and manuscript preparation; Dr Aydinoz worked on data collection, data analysis, and manuscript preparation; Drs Bhattacharjee, Tan, and Kheirandish-Gozal worked on data analysis and manuscript preparation; Drs Flores-Mir and Gozal worked on study conceptualization, design, data analysis, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

www.pediatrics.org/cgi/doi/10.1542/peds.2015-1283

DOI: 10.1542/peds.2015-1283

Accepted for publication Jul 7, 2015

Address correspondence to David Gozal, MD, FAAP, Department of Pediatrics, University of Chicago, 5721 S. Maryland Ave, MC 8000, Suite K-160, Chicago, IL 60637. E-mail: dgozal@uchicago.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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Obstructive sleep apnea (OSA) is widely recognized as a potential cause of significant morbidity in children.<sup>1,2</sup> OSA symptoms include habitual snoring and reporting of disturbed unrefreshing sleep, frequently accompanied by excessive daytime sleepiness, and daytime neurobehavioral and mood problems.<sup>3</sup> The prevalence of OSA is markedly variable during childhood (1%-5%), with age, gender, and ethnicity as major contributors.<sup>2,4–6</sup> However, independently of the lowest or the highest reported prevalence, OSA is a relatively frequent condition that imposes a high degree of disease burden, thereby requiring timely diagnosis and effective treatment.

The first-line treatment of pediatric OSA is provided through either medical or surgical procedures on the basis of the underlying severity of the condition as defined by overnight polysomnography (PSG).<sup>3</sup> Medical treatments in mild cases may include weight loss management in overweight children, intranasal steroids, leukotriene modifiers, and oral or topical descongestants.<sup>3</sup> However, in the majority of cases, adenoidectomy and tonsillectomy (AT) remains the most common surgical procedure performed for OSA in children,<sup>7</sup> with more than 530 000 of these procedures being performed annually in the United States alone.8 Similarly, AT is traditionally performed in cases fulfilling the criteria of recurrent tonsillitis, which in the past accounted for the majority of AT surgeries, before being surpassed by OSA indications.<sup>9</sup> As with most surgical procedures, AT involves potential intraoperative risks and postoperative complications. Among the latter, minor complications include pain, nausea, vomiting, and dehydration.<sup>10</sup> However, more serious complications may occur, such as hemorrhage, respiratory decompensation, velopharyngeal incompetence, subglottic stenosis, and rarely death.11

Some authors<sup>12–16</sup> have suggested that differences in the frequency of these complications could be present after AT in children with OSA and children without OSA. Because these complications can have a significant impact on the burden of care, the purpose of this systematic review was (1) to identify the most frequent postoperative complication during the first 3 weeks after AT, and (2) to critically evaluate the differences comparing children with OSA and children without OSA. These findings should help in making physicians aware of potential complications after this type of surgical procedures in specific target populations.

#### **METHODS**

This systematic review was done adhering to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses checklist.<sup>17</sup>

#### **Diagnostic Terminology**

All terms that indicated OSA,<sup>1</sup> including sleep disordered breathing (SDB), sleep-related breathing disorder, and OSA syndrome, were all considered synonymous of OSA for this submission.

#### **Protocol and Registration**

The systematic review protocol was registered at the International Prospective Register of Systematic Reviews<sup>18</sup> under number CRD42015016102.

#### **Study Design**

A systematic review that evaluated (within 3 weeks) postoperative complications after AT in children with OSA and children without OSA aimed at answering 2 specific questions:

- 1. What are the most frequent immediate postoperative complications after AT?
- 2. Do children with OSA and children without OSA differ in the frequency of immediate postoperative complications after AT?

#### **Eligibility Criteria**

#### Inclusion Criteria

 Clinical studies that evaluated (within 3 weeks) postoperative complications after AT in children with OSA and children without OSA (0-18 years old).

• No language restriction was set. Complications were defined as any deviation from the usual postoperative recovery course that required intervention. All reported complications were reviewed to determine type, occurrence time, and need for an extended hospital stay and/or intensive care unit (ICU) monitoring.<sup>19</sup>

#### Exclusion Criteria

The studies were excluded in 2 phases.

In phase 1 (titles and abstracts) the following exclusion criteria were applied:

- 1. Studies that targeted a different condition.
- 2. Studies in adults.
- 3. Reviews, letters, conference abstracts, editorials, case-series studies.
- 4. Studies in which the cohort sample included subjects previously diagnosed with genetic syndromic patients (eg, Down syndrome, craniofacial anomalies, neuromuscular disorders, chromosomal abnormality, etc), coagulation disorders, or cerebral palsy.

In phase 2 (full-text) these additional exclusion criteria were applied:

5. Studies that did not reveal complications during the first 3 weeks of follow-up.

#### **Information Sources**

Detailed individual search strategies for each of the following bibliographic databases were developed: Cochrane, Embase, Medline, PubMed, Web of Science, and Literatura Latinoamericana e do Caribe em Ciências da Saúde. A partial gray literature search was taken by using Google Scholar. The end search date was January 3, 2015, across all databases. The references cited in the selected articles were also checked for any additional references that could have been inadvertently omitted during the electronic database searches. In addition, experts in the field of sleep, otolaryngology, and/or respiratory medicine were approached to identify any missing important publication. Experts were identified based on the main reference list, such that authors who had (as a first/senior author) > 6 publications in this main search were contacted, and were asked to identify the 10 most important publications regarding AT postoperative complications.

#### Search

Appropriate truncation and word combinations were selected and

adapted for each database search (Supplemental Table 4). All references were managed by reference manager software (RefWorks-COS, ProQuest, Bethesda, MD) and duplicate hits were removed.

#### **Study Selection**

The selection was completed in 2 phases. In phase 1, 2 reviewers (Drs De Luca Canto and Pachêco-Pereira)

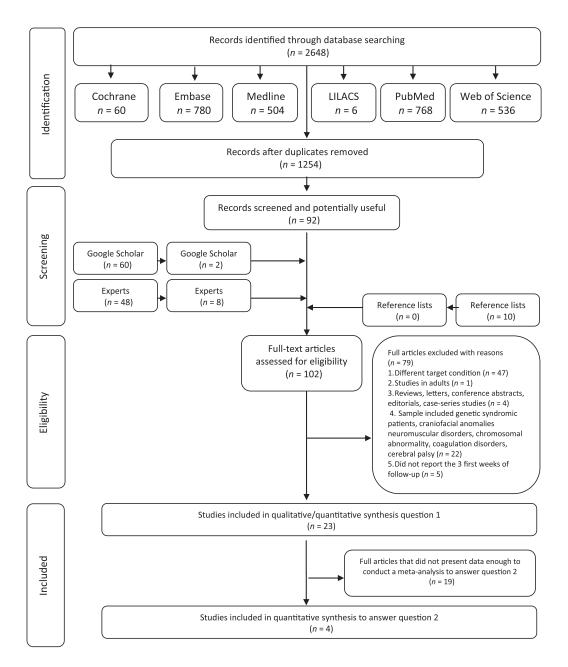


FIGURE 1

Flow diagram of literature search and selection criteria. Adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.<sup>17</sup>

independently reviewed the titles and abstracts of all identified electronic database citations. A third author (Dr Aydinoz) read all abstracts selected to reach the final decision. This was important when disagreements emerged between the 2 initial evaluators. Any studies that did not fulfill the inclusion criteria were discarded.

In phase 2, the same 2 reviewers (Drs De Luca Canto and Pachêco-Pereira) independently participated in phase 2. The reference lists of all included articles were critically assessed by 1 examiner (Dr De Luca Canto). Selected studies were read by both examiners (Drs De Luca Canto and Pachêco-Pereira). Any disagreement in either phase was resolved by discussion and mutual agreement between the 3 reviewers (Drs De Luca Canto, Pachêco-Pereira, and Aydinoz).

A fourth author (Dr Gozal) was involved when controversy arose in the process of reaching a final decision either in phase 1 or 2. Final selection was always on the basis of the full-text of the publication.

#### **Data Collection Process**

One author (Dr De Luca Canto) collected the required information from the selected articles. A second author (Dr Pachêco-Pereira) crosschecked all the collected information and confirmed its accuracy. Again, any disagreement in either phase was resolved by discussion and mutual agreement between the 3 reviewers (Drs De Luca Canto, Pachêco-Pereira, and Aydinoz). The fourth author was involved as required, to enable formulation of the final decision (Dr Gozal).

#### **Data Items**

The following information was recorded: author(s), year of publication, country, study design, recruitment method, follow-up length, sample size, participant's age, complication type, surgery type, results, and main conclusion. If the required data were not complete, attempts were made to contact the authors to retrieve the missing information.

#### **Risk of Bias in Individual Studies**

The methodology of selected studies was evaluated by using the Meta-Analysis of Statistics Assessment and Review Instrument.<sup>20</sup> Two reviewers (Drs De Luca Canto and Pachêco-Pereira) scored each item with "yes," "no," "unclear," or "not applicable," and assessed independently the quality of each included study. Disagreements between both reviewers were resolved by a third reviewer (Dr Aydinoz).

#### **Summary Measures**

Early (within 3 weeks) postoperative complications after AT were considered as the main outcome. Any type of outcome measurement was considered (categorical and continuous variables).

#### **Synthesis of Results**

Studies that revealed postoperative prevalence but did not directly compare OSA and non-OSA groups were analyzed through a metaanalysis performed with MedCalc (MedCalc Software, Ostend, Belgium). Studies that directly compared children with OSA and children without OSA were analyzed through a meta-analysis by using Review Manager 5.2 (RevMan, The Nordic Cochrane Centre, Copenhagen, Denmark).

#### **Risk of Bias Across Studies**

We assessed the clinical heterogeneity (by comparing variability among the participant's characteristics, type of interventions and outcomes studied), methodological heterogeneity (by comparing the variability in study design and risk of bias), and statistical heterogeneity (by comparing variability in the intervention effects in the different included studies).

#### **RESULTS**

#### **Study Selection**

During the initial search (phase 1), 1254 different citations were identified across the 6 electronic databases. Then, after a comprehensive evaluation of the abstracts, only 92 articles were deemed potentially relevant, and were selected for phase 2 assessment. An additional 60 citations from Google Scholar, and another 48 citations from content experts were also considered. Of these 108 articles (not initially included among those from the electronic databases), only 10 were deemed appropriate for phase 2 assessments. No additional study that might have been inadvertently missed by the search procedures was identified after further reviewing the reference list of the 102 studies. From these remaining studies, 79 were subsequently excluded (Supplemental Table 5). Thus, only 23 studies were retained for the final meta-analysis aimed at answering the first question. From these 23 studies, only 4 studies differentiated between OSA and non-OSA groups, and were used in the meta-analysis aiming to answer the second question. All of these articles were identified from the main electronic search. A flowchart of the process of identification, inclusion, and exclusion of studies is shown in Fig 1.

#### **Study Characteristics**

The 23 studies that were retained to address question 1 revealed the following postoperative complications: respiratory complications, 12,13,16,19,21-33 hemorrhage, 15,21,25,26,28,30,34-38 pain,<sup>27,28</sup> nausea,<sup>27,34</sup> vomiting,<sup>27,35</sup> refuse to drink,<sup>35</sup> inadequate oral intake,<sup>21</sup> dehydratation,<sup>28,29,34</sup> fever,<sup>24,29</sup> dysphagia,<sup>28,34</sup> and cardiac complications.<sup>35</sup>

Source	Country		Source Country Sample			Results		Additional Data
		и	Characteristics	Overall, % <sup>a</sup>	Hemorrhage, % <sup>b</sup>	Respiratory Complications, %	Other, %	
Ahmad et al 2010 <sup>25</sup>	Malaysia	267	OSA or RT or other (unclear	7.2	Primary: 1.9	Extubation failure: 0.4	Infection: 1.1	Increase in risk with every 1 min
			IL FOG WAS DEFIGITIED		Secondary: 1.9		Other: 1.9	morease in duration of surgery Primary hemorrhage (OR: 1.05; 95% CI: 1.01-1.09 min: P = .020)
								Respiratory complications (OR: 1.08; 95%, CI: 1 01–1 16, min. P – 024)
Baguley et al 2014 <sup>31</sup>	Australia	100	0SA (confirmed by PSG)	11.0	NA	Left recovery with oxygen prescribed:	Major complications:	apnea/hypopneia index (AHI)
						11.0	zero	cutoff above which oxygen
								supplementation was given (0K: 1 135: 95% CI: 0 99–1 3: P – 07)
Brown 2006 <sup>23</sup>	Canada	54	OSA (confirmed by PSG or	61.1	NA	Overall: 61.1 <sup>ª</sup> (reintubation, ventilation,	NA	Risk factors: Associated medical
			cardiorespiratory sleep			and/or administration of racemic		condition or 8.15; 95% Cl: 1.81–36.73
			studies or oximetry or			epinephrine or salbutamol, oxygen		Preoperative saturation nadir less than
			awake capillary carbon diovida tansion)			administration, reintubation in the recovery room for resouratory		80% OB: 5.54: 95% CI: 1.15—26.72
						compromise)		Atropine administration at induction
								decreased the risk of postoperative
								respiratory complications (0R: 0.18;
								95% CI: 0.11–1.050)
Del-Rio Camacho	Spain	229	0SA (confirmed by PSG)	3.5	Primary: 1.3	2.2	NA	OSA group (3.23%) vs non-OSA group
et al 2014 <sup>16</sup>			and RT					(1.47%), presented a higher
								incidence of respiratory
								complications (not statistically
								significant, $P = .39$ )
								All respiratory complications took
								place in the immediate postoperative
ľ								period.
Hadden et al 2011 <sup>27</sup>	United States	102	0SA and others (unclear	100	NA	Respiratory events: 26.5ª	Pain: 66.7 <sup>a</sup> Nausea	Ι
~~~			if PSG was performed)				and vomiting: 6.9ª	
Hamada et al 2015 <sup>37</sup>	Japan	147	0SA (confirmed by home-PSG)	7.4	Primary: 5.4	NA	NA	AT can be performed without major commissations
Lalakea et al 1000 <sup>21</sup>	Ilnited States	134	DSA (unclear if DSG was	K.	Drimary 16	Zeno	Vomiting and or	The complication rate did not vary
		5	performed) and RT	0	0.1	2	inadequate oral	significantly with the duration of
			-				intake: 3.7	postoperative observation $(P = .71)$
Ma et al <sup>32</sup>	China	86	0SA (confirmed by PSG)	6.8	Zero	Postoperative desaturation: 6.8	NA	Children with desaturation after
								tonsilletomy and adenotonsillectomy
								had significant higher mean BMI z
								score than children Without desaturation (P = 014)
Muninnobpamasa	Thailand	481	OSA (unclear if PSG was	91.3	Primary: 4.1	Anesthetic (partial airway obstruction	Dvsphagia: 29.0	The average length of hospital stav was
et al 2012 <sup>28</sup>			performed), RT, neritonsillar abscess		Secondary: 3.9	that needed airway intervention): 1.6	Dehydration: 4.6 Dain: 48 1	3.6 d and readmissions 3.7%.
			and others				- 40.1	

**TABLE 1** Summary of Descriptive Characteristics of Included Studies to Answer Question 1 (n = 23)

TABLE 1 Continued								
Source	Country		Sample			Results		Additional Data
		и	Characteristics	Overall, % <sup>a</sup>	Hemorrhage, % <sup>b</sup>	Respiratory Complications, %	Other, %	
Nixon et al 2005 <sup>22</sup>	Canada	10	0SA (confirmed by PSG)	10.0	NA	Intervention for respiratory compromise: 10	NA	1
Onotai and Lilly-Tariah	Nigeria	100	0SA (confirmed by	9.0	Primary: 4.0	2.0	Cardiac: 1.0	Mortality was recorded in 3% because
2013 <sup>30</sup>	)				Secondary: 2.0			of severe respiratory distress and
			ear infection					cardiac arrest.
Perkins et al 2012 <sup>15</sup>	United States	9023	30	2.3	Primary: 0.5	NA	NA	Children with OSA were half as likely to
			chronic tonsillitis,		Secondary: 1.8			hemorrhage compared with chronic
L								tonsillitis patients ( $P = .04$ )
Rakover et al 1997 <sup>55</sup>	Israel	363	SO	9.9	Primary: 3.9	NA	NA	Three was no increase in the rate of
			performed), RT,		Secondary: 1.9			postoperative hemorrhage and of
			and others					readmissions among the children
								discharged from the hospital after
								the operation, compared with those
								hospitalized. There was no
								correlation between type of
								procedure: tonsillectomy or AT and
								postoperative complications.
Riaz et al 2009 <sup>13</sup>	Saudi Arabia	60	OSA (confirmed by PSG)	50.0	NA	Desaturation <95%, cough, stridor,	Nausea and	The complications at extubation
			and RT			laryngospasm: 41.7	vomiting: 8.3	(cough, laryngospasm, postoperative
								nausea, and vomiting) were higher
								in OSA group, but not statistically
								significant; $P > .05$ ).
								At the time of extubation, desaturation
								was significantly higher in OSA
								was significantly ingred in OCA prolin (43.3% vs.6.6% P = 002
								Stadp (+0.000 to 0.000, r = .002, OR = 10.70)
								Mono actionto of DCA Amoun accuined
								Mure patients of upa group required
								0Xygen (bo.3% VS 10%, P < .UU1,
								UK = 15.54).
								Six children from 0SA group required
								insertion of an oropharyngeal
								airway. No child from the non-0SA
								group required it $(P = .023)$ .
Ruboyianes 1996 <sup>19</sup>	United States	44	OSA (confirmed by PSG)	32.0	Zero	Intermittent obstruction: 2.3	NA	Factors associated with development of
						Upper airway obstruction, pulmonary		complications included age $< 3$
						edema: 4.5		(P = .10), thin body habitus
						IInner airway ohstruction nueumonia:		(P - 0.07) and acuite airway
								V = 0.21, and added an way obstruction ( $P < 0.01$ )
						Ctrictor otolootooio. 0 2		
						upper airway eueria: 4.0		
						Laryriguspasiri: 4.0		
						iransient upper airway obstruction: 2.5		
						Central apnea: 2.3		
						Viral bronchitis: 2.3		

Source	Country		Sample			Results		Additional Data
		и	Characteristics	Overall, % <sup>a</sup>	Hemorrhage, % <sup>b</sup>	Respiratory Complications, %	Other, %	Ι
Sanders et al 2006 <sup>12</sup>	Mexico	82	0SA (confirmed by PSG) and RT	78.0	NA	Medical intervention (the need for oral airway, oxygen to keep 0 <sub>2</sub> saturations >92%, assisted ventilation and reintubation in recovery: 22.0	Pain: 56.0	0SA group had more respiratory complications than non-0SA (5.7 vs 2.9, $P = .0001$ ).
Shakeel et al 2012 <sup>38</sup>	United Kingdom	106	0SA (unclear if PSG was performed) and RT	7.6	Primary: 0.9 Secondary: 6.7	M	И	Secondary hemorrhage versus: Indication for surgery 0SA versus recurrent tonsililitis (0R. 0.180, 95% Cl: 0.02–1.82) Obstructive symptoms to recurrent tonsililitis (0R. 1.004; 95% Cl: 0.09–11.03)
Shott et al 1987 <sup>34</sup>	United States	421	0SA (confirmed by PSG)	3.8	Secondary: 2.1	ΝΑ	Nausea and vomiting: 0.5 Dehydration: 0.7 Dysphagia: 0.5	1
Spencer and Jones 2012 <sup>29</sup>	United States	86	OSA (unclear if PSG was performed), RT, and chronic tonsillitis	7.0	N	Reactive airway disease: 1.2	Dehydration: 4.7 Fever: 1.2	I
Vlastos et al 2010 <sup>26</sup>	Greece	910	SO	2.8	Primary: 1.4	1.1	0.3	I
Wang et al 2009 <sup>24</sup>	China	82	0SA (confirmed by PSG)	21.5	Zero	Airway edema with increased snoring, mouth breathing, and apneas in the first night: 17.1; required CPAP in the first 3 d: 3.7	Fever: 0.7	
Wong et al 2007 <sup>36</sup>	China	329	0SA (unclear if PSG was performed) and RT	2.4	Secondary: 2.4	NA	Mortality zero	I
Ye et al $2009^{33}$	China	321	0SA (confirmed by PSG)	11.2	Zero	Overall: 11.2 (required an oropharyngeal or nasopharyngeal airway, had multiple episodes of desaturation, and other respiratory	AN	I

CPAP, continuous positive airway pressure; NA, not applicable, when the item was not evaluated by the study; RT, recurrent tonsilitis. <sup>a</sup> Data were calculated by authors. <sup>b</sup> We considered primary hemorrhage when it occurs in the first 24 h, and secondary hemorrhage when it occurs after 24 h.

						:			
Source	Country	Place of Recruitment	Follow Up	0SA, <i>n</i>	Non-OSA With Tonsillitis, <i>n</i>	Mean Age or Range	Surgery Procedure/ Complication Assessment Location	Results	Main Conclusion
Del-Rio Camacho et al 2014 <sup>16</sup>	Spain	Hospital pediatric department	Once the surgery was finished	93	136	4.97	AT by curettage and tonsillectomy by dissection Complication during anesthetic recovery and while the patients was in the ward or	Hemorrhage: 1.3% Respiratory: 2.2% OSA group (3.23%) vs non-OSA group (1.47%), presented a higher incidence of respiratory complications (not statistically significant, P = .39). All respiratory complications took place in the immediate postoperative period.	Children who undergo AT and have an immediate postoperative period without complications do not need to be admitted to an ICU, even though they present severe 0SA.
Perkins et al 2012 <sup>15</sup>	United States	United States Pediatric hospital	48 h—18 d	267	158	06.9	Tonsillectomy by electrocautery or coblation	Children with 0SA were half as likely to hemorrhage compared with chronic tonsilitis patients ( $P = .04$ ).	Children with 0SA may be less likely to have postoperative hemorrhage than children without 0SA with chronic tonsillitis.
Riaz et al 2009 <sup>13</sup>	Saudi Arabia	Hospital anesthesiology department	Once the surgery was finished	30	30	6.60	AT Recovery room	The complications at extubation (cough, laryngospasm, postoperative nausea, and vomiting) were higher in 0SA group, but not statistically significant!, $P > .05$ ). At the time of extubation, desaturation was significantly higher in 0SA group (43.3% vs 6.8%, P = .002, 0R = 10.70). More patients of 0SA group required oxygen (63.3% vs 10%, $P < .001$ , 0R = 15.54). Six children from 0SA group required insertion of an oropharyngeal airway. No child from non-0SA group required it ( $P = .023$ ).	Children with 0SA operated for AT are at significant risk of certain life-threatening perioperative anesthetic complications.

**TABLE 2** Summary of Descriptive Characteristics of Included Studies to Answer Question 2 (n = 4)

TABLE 2 Continued	nued								
Source	Country	Place of Recruitment	Follow Up	0SA, <i>n</i>	0SA, <i>n</i> Non-OSA With Mean Age Tonsilitis, <i>n</i> or Range	Mean Age or Range	Surgery Procedure/ Complication Assessment Location	Results	Main Conclusion
Sanders et al 2006 <sup>12</sup>	Mexico	Pediatric otolaryngology service from university's hospital	Until discharge of recovery room	61	21	2-16	AT by electrocautery dissection 0SA group had more respiratory compli- than non-0SA (5.7, P = .0001). Supraglottic obstructi breath holding, and desaturation on an induction and eme were the most con complications. Increased severity of weight, and young correlated with an rate of complication Medical intervention necessary in 0SA during recovery ar emergence than in 0SA group (17/51 v	OSA group had more respiratory complications than non-OSA (5.7 vs 2.9, P = .0001). Supraglottic obstruction, breath holding, and desaturation on anesthetic induction and emergence were the most common complications. Increased severity of OSA, low weight, and young age are correlated with an increased rate of complications. Medical intervention was more necessary in OSA group during recovery and emergence than in the non- OSA group (17/61 vs 1/21,	Children with OSA are at risk for respiratory complications after AT. These complications do not prolong the time to discharge.

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ے ا The sample size ranged widely from 102<sup>3</sup> to 9023 subjects.<sup>15</sup> A summary of the study descriptive characteristics can be found in Table 1. The characteristics from the 4 studies selected to answer question 2 can be found in Table 2.

#### **Risk of Bias Within Studies**

The studies selected to answer question 1 were very heterogeneous, 6 of them had high risk of bias, 6 had moderate risk, and only 7 had low risk of bias. None of the studies fulfilled all methodological quality criteria. The studies selected to answer question 2 were more homogeneous, 2 had moderate risk of bias and 1 had low risk. More information about the risk of bias of included studies can be found in Table 3 (summarized assessment) and Supplemental Tables 6 and 7 (detailed assessment).

#### **Results of Individual Studies**

The results of studies selected to answer question 1 are reported in Table 1. The results of the studies selected to answer question 2 are

TABLE 3	Risk of Bias	Summarized
	Assessment	

Source	Risk of Bias
Ahmad et al <sup>25</sup>	Moderate
Baguley et al <sup>31</sup>	Moderate
Brown <sup>23</sup>	Low
Del-Rio Camacho et al <sup>16</sup>	Moderate
Hadden et al <sup>27</sup>	Low
Hamada et al <sup>37</sup>	Low
Lalakea et al <sup>21</sup>	Low
Ma et al <sup>32</sup>	Low
Muninnobpamasa et al <sup>28</sup>	Moderate
Nixon et al <sup>22</sup>	Moderate
Onotai and Lilly-Tariah <sup>30</sup>	High
Perkins et al <sup>15</sup>	Low
Rakover et al <sup>35</sup>	High
Riaz et al <sup>13</sup>	Moderate
Ruboyianes <sup>19</sup>	High
Sanders et al <sup>12</sup>	Low
Shakeel et al <sup>38</sup>	Low
Shott et al <sup>34</sup>	High
Spencer and Jones <sup>29</sup>	Moderate
Vlastos et al <sup>26</sup>	Low
Wang et al <sup>24</sup>	High
Wong et al <sup>36</sup>	High
Ye et al <sup>33</sup>	Moderate

synthesized below (with additional information in Table 2).

Riaz et al<sup>13</sup> reported that at the time of extubation, desaturation was significantly more frequent in the OSA group (43.3% vs 6.6%, P = .002, odds ratio [OR] = 10.70). Other complications at extubation (ie, cough, laryngospasm, and postoperative nausea and vomiting) were also more frequent in the OSA group, but were not statistically significant (P = .999). In the postanesthesia care unit, the frequency of complications and medical interventions was also higher in OSA group. More patients in the

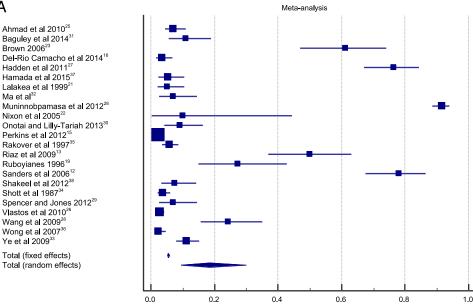
А

Ma et al3

OSA group required oxygen supplementation (63.3% vs 10%, *P* < .001, OR = 15.54). They concluded that children with OSA undergoing AT are at significant risk of certain lifethreatening perioperative anesthetic complications.

Similarly, Sanders et al<sup>12</sup> evaluated the rate of complications experienced by children who undergo AT for OSA, the safety of a standard anesthetic protocol for these children, and preoperative predictors of complications. They found that children with OSA had more respiratory complications than children without OSA (5.7 vs 2.9,

P < .0001). Supraglottic obstruction, breath holding, and desaturation on anesthetic induction and emergence from anesthesia were the most common complications. Increased severity of OSA, low body weight, and young age were associated with an increased rate of complications. Medical intervention was necessary in a higher proportion of children with OSA during recovery and emergence from anesthesia than in the non-OSA group (17/61 vs 1/21, P < .05). However, both groups of children had similar opioid requirements, and the time to discharge from the recovery room was also similar. They concluded



# Meta-analysis: proportion

Meta-analysis		Sample size	Proportion	95% CI
			(%)	
Total (fixed effects)		13 537	5.453	5.076-5.848
Total (random effect	s)	13 537	18.514	9.390-29.865
Test for heterogeneit	у			
Q	309	9.8407		
DF	22			
Significance level	P <	.0001		
$I^2$ (inconsistency)	99.	29%		
95% CI for $I^2$	99.	19–99.38		

Proportion

#### **FIGURE 2**

Forest plot question 1. Frequency of complications after AT in children (question 1). Results from 2 types of meta-analysis: fixed and random effects. A, Forest plot for all postoperative complications. Sample = 13 537. B, Forest plot for respiratory complications. Sample = 3148. C, Forest plot for primary hemorrhage. Sample = 11 760. D, Forest plot for secondary hemorrhage. Sample = 11 090.

that children with OSA are at risk for respiratory complications after AT, but that these complications do not appear to prolong the time to discharge.

Del-Rio Camacho et al<sup>16</sup> found that when considering all children, complications occurred in only 3.5% of children, with 2.2% corresponding to respiratory complications. Children with mild to moderate OSA (3.23% vs 1.47%, *P* = .39) and children with severe OSA (3.77% vs 1.70%, P = .32)presented a higher incidence of respiratory complications, which did not achieve statistical significance. All respiratory complications took place in the immediate postoperative period.

In contrast, Perkins et al<sup>15</sup> hypothesized that a diagnosis of OSA

В

Brown 200623

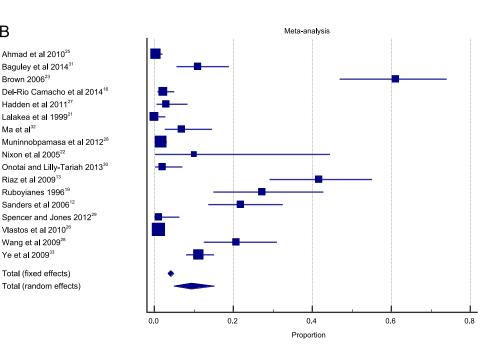
Ma et al<sup>32</sup>

may be protective against postoperative hemorrhage. A total of 9023 tonsillectomy patients were identified. Of these, only 2.4% (n = 212) presented with hemorrhage. There were 48 patients (22.6%) with primary, and 164 patients (77.4%) with secondary hemorrhage, with the majority occurring among children with recurrent tonsillitis. The authors concluded that children with OSA were half as likely to manifest bleeding as a complication after AT when compared with children with chronic tonsillitis (P = .04).

#### **Synthesis of Results**

The meta-analysis was performed in 2 steps. To answer question 1, the 23 studies selected were grouped and a meta-analysis was performed. The heterogeneity between the studies found in the meta-analysis was high; therefore, a random model was choosen.<sup>39</sup> The results from this meta-analysis revealed that the overall frequency of postoperative complications was ~19% (total sample = 13 537; Fig 2A). The most frequent postoperative complications were respiratory compromise (9.4%) in sample = 3148 cases; Fig 2B) followed by secondary hemorrhage (2.6% in sample = 11 090 cases; Fig 2D) and primary hemorrhage (2.4% in sample = 11760; Fig 2C).

To answer the question 2, the 4 studies<sup>12,13,15,16</sup> that directly



#### Meta-analysis: proportion

Meta-analysis	Sample size	Proportion (%)	95% CI		
Total (fixed effects)	3148	4.041	3.382-4.787		
Total (random effects)	3148	9.406	4.916-15.155		
Test for heterogeneity	1				
Q	57.2512				
DF	6				
Significance level	<i>P</i> < .0001				
( ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( ( (	5.52%				
95% CI for $I^2$	94.03–96.64				

FIGURE 2 Continued.

compared an OSA and a non-OSA group, as defined by nocturnal PSG were grouped, and a metaanalysis was performed. Only a meta-analysis with a fixed effect model was performed by using the method of Mantel-Haenszel.39 In this meta-analysis, only data relying on PSG-confirmed OSA and non-OSA were considered. Because of these criteria, different sample sizes emerge in Tables 1 and 2 for the same studies. To perform this metaanalysis, the studies were grouped in 2 groups, A (respiratory complications) and B (bleeding complications). The heterogeneity between the studies found in the meta-analysis was 0% indicating high homogeneity (confirming that

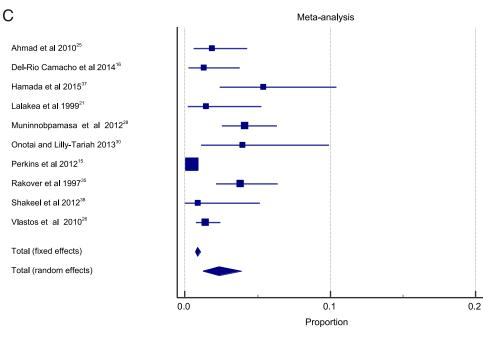
we can analyze these data with fixed effect). The meta-analysis of group A (respiratory complications) included 371 patients (184 with OSA and 187 without OSA) and confirmed that children with OSA appear to have more frequent postoperative respiratory complications after AT than children without OSA (OR = 4.90; 95%) confidence interval (CI): 2.38–10.10). In group B (bleeding complications), 360 children with OSA and 294 children without OSA were included. The meta-analysis confirmed that bleeding is more likely to occur among children without OSA (OR = 0.41; 95% CI: 0.23-0.74; Fig 3).

#### **Risk of Bias Across Studies**

Although the studies had different study design (experimental and descriptive), the main methodological problem concerns the actual subject sample. Most of the studies selected to answer question 1 used a convenience sample from a hospital. Even the experimental studies did not randomly assign participants. Besides this particular issue, most of the observational studies did not perform appropriate statistical analyses.

#### **DISCUSSION**

AT is a relatively common procedure in clinical otolaryngology practice and usually follows referrals from



#### Meta-analysis: proportion

Meta-analysis	S	Sample size	Proportion (%)	95% CI
Total (fixed effects)	1	1760	0.873	0.713-1.058
Total (random effec	ts) 1	1760	2.378	1.230-3.890
Test for heterogen	eity			
Q	82.98	51		
DF	9			
Significance level	P < .0	0001		
$I^2$ (inconsistency)	89.15	5%		
95% CI for $I^2$	82.17	/93.40		

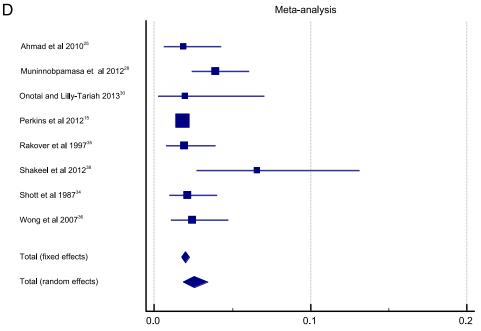
FIGURE 2 Continued. primary care physicians.<sup>25</sup> It is the current treatment of choice for treatment of OSA in children, when indicated, due to its perceived efficacy and cost effectiveness.<sup>40</sup>

Currently guidelines used by clinicians to identify children who are appropriate candidates for AT have indications based primarily on obstructive and infectious causes.<sup>41</sup> Before 1995, the major indication for AT was recurrent tonsillitis, with OSA being a distant second. However, in the past 10 years the number of children referred for OSA-related AT surgery has increased markedly, reflecting an increased awareness and improved diagnosis of OSA by pediatricians and other primary care physicians.<sup>36</sup>

This systematic review investigated the available evidence about the most frequent early postoperative complications after AT, and also evaluated potential differences in the associated complications between children with OSA and those without OSA. Regarding the most frequent early postoperative complications, respiratory compromise and hemorrhage were the most frequent, followed by pain, fever, nausea and vomiting, and dehydration. Infection and cardiac complications were rare. These results are in agreement with the available literature.<sup>3,21,29,35,37</sup>

Mortality rates of AT have been estimated between 1 in 16 000 and 1 in 35 000 cases.<sup>42</sup>

Nixon et al<sup>22</sup> demonstrated that sleep-related airway obstruction is a common postoperative complication leading to significant oxyhemoglobin desaturations after AT in children with severe OSA. Episodes of desaturation occurred during the first postoperative night in all 10 children studied, and these desaturation episodes were predominantly caused by upper airway obstruction. Several mechanisms may explain ongoing upper airway obstruction after AT, including copious nasal secretions





#### Meta-analysis: proportion

Meta -analysis	Sample size	Proportion (%)	95% CI
Total (fixed effects)	11090	1.993	1.741-2.270
Total (random effects	) 11090	2.564	1.829–3.419
Test for heterogene	ity		
Q	6.0921		
DF	7		
Significance level	P = .0243		
	56.50%		
95% CI for $I^2$	4.24-80.24		

FIGURE 2 Continued.

A	OSA	A	Non-C	SA		OR		OR	
Study or Subgroup	Events	Total	Events	Total	Weight,%	M-H, Fixed, 95% C	:1	M-H, Fixed, 95% CI	
Del-Rio Camacho et al 2014 <sup>16</sup>	3	93	2	136	24.8	2.23 (0.37 - 13.63)	X		_
Riaz et al 2009 <sup>13</sup>	22	30	8	30	33.7	7.56 (2.41 - 23.75)			
Sanders et al 2006 <sup>12</sup>	52	61	12	21	41.6	4.33 (1.42 - 13.24)			
Total (95% CI) Total events	77	184	22	187	100.0%	4.90 (2.38 – 10.10	)	•	
Heterogeneity: $\chi^2 = 1.32$ ,	2.542						0.01	0.1 1 10 100	1
Test for overall effect: $Z =$	4.30 (P	< .000	1)					Non-OSA OSA	
В									

Б	OSA		Non-OSA		OR		OR
Study or Subgroup	Events	Total	Events	Total	Weight,%	M-H, Fixed, 95% C	M-H, Fixed, 95% CI
Del-Rio Camacho et al 2014 <sup>11</sup>	δ 1	93	2	136	4.7	0.73 (0.07 - 8.15)	
Perkins et al 2012 <sup>15</sup>	21	267	28	158	95.3	0.40 (0.22 - 0.73)	
Total (95% CI)		360		294	100.0	0.41(0.23 – 0.74)	•
Total events	22		30				
Heterogeneity: $\chi^2 = 0.23$ , df = 1 ( <i>P</i> = .63); l <sup>2</sup> = 0%							0.01 0.1 1 10 100
Test for overall effect: $Z = 2.96$ ( $P = .003$ )							Non-OSA OSA

#### FIGURE 3

Forest plot question 2. Postoperative respiratory and bleeding complications after AT in children with OSA and children without OSA. Children with OSA were at significantly higher odds for respiratory complications (A), and conversely children without OSA were at increased odds for hemorrhage after surgery (B). A, Forest plot for post-AT respiratory complications. B, Forest plot for post-AT bleeding complications.

after surgery, and reactive, postsurgical edema in the adenoid and tonsillar beds. Thus, the first night after AT will usually manifest marked sleep disturbance, airway obstruction, and desaturation.<sup>22</sup>

In this systematic review, we found a very high frequency of pain as the major complication of AT, with some of the included studies revealing exceedingly high rates of pain,12,27,28 such that the frequency of overall postoperative complications when pain was included in the metaanalysis reached the vicinity of 20%. even after random effects were accounted for. Under these circumstances, the frequency of respiratory compromise after AT was 9.4% and primary and secondary hemorrhage prevalence was 2.4% and 2.6%, respectively. Of note, although postoperative bleeding can be a serious complication after AT,<sup>21</sup> it rarely requires transfusion.<sup>30</sup> Thus, AT has substantial postoperative morbidity, and identification of children at risk for either respiratory compromise or bleeding would be

obviously important, particularly because the majority of AT surgeries are conducted in outpatient settings.

In this context, our meta-analysis highlights 2 relevant clinical practice points. The presence of OSA significantly increases the odds for postoperative respiratory complications, with children with OSA exhibiting a nearly fivefold increase in the odds of developing respiratory complications when compared with children without OSA. These findings concur with previous studies that suggested that as the severity of OSA increases, the probability of respiratory complications after AT increases as well.43-45 Children with OSA not only had more frequent complications during induction and emergence from anesthesia, they were also more likely to require supplemental oxygen, oral or nasal airway insertion, or assisted ventilation in the immediate postoperative period.12 Thus, identification of children at higher risk for respiratory complications before AT can help in formulating

a safe anesthetic strategy for children with OSA, and should be pursued in future prospective large-scale studies.13 In contrast. our metaanalysis indicated that the presence of tonsillitis in children without OSA increased the odds for hemorrhagic complications. Children without OSA with tonsillitis appear to have 2.5-fold increases in the odds for bleeding complications when compared with children with OSA. Perkins et al<sup>15</sup> suggested that either OSA is protective against postoperative hemorrhage or that recurrent tonsil infection increases the risk for bleeding through undefined mechanisms, most likely involving increased vascularity of tonsillar and surrounding upper airway tissues.

Despite the current guidelines from the American Academy of Pediatrics, several important obstacles have thus far precluded widespread implementation of PSG for OSA, such as cost and reduced availability.<sup>3</sup> However, a definitive diagnosis of OSA requires a PSG, and our current findings further suggest that among children with OSA, the risk of postoperative respiratory complications is high. Children with OSA are clearly at higher anesthetic risk than are patients with normal upper airway function. Anesthesiologists should routinely screen patients for snoring, airway dysfunction, airway anatomic disorders, and other coexisting diseases that can increase risk from OSA in the postoperative period. Despite the pressure to reduce costs, both surgeons and anesthesiologists should improve screening procedures, perhaps develop alternate surgical approaches, to decrease the risks.<sup>46</sup>

Thus, systematic implementation of PSG-based OSA diagnosis could potentially enable delineation of PSGbased criteria that would inform ear, nose and throat (ENT) surgeons on the presence of specific children with higher respiratory risk, and thus improve peri- and postoperative phase planning, while ascertaining that highrisk patients undergo surgery in a medical center capable of monitoring and treating more complex pediatric patients postoperatively.<sup>3</sup>

Raman et al<sup>47</sup> established guidelines for patients undergoing AT resulting in an overall reduction in unanticipated admissions. The authors emphasize that guidelines could be universally applied in an outpatient screening process for identification of at risk surgical patients. This would aid in identifying those patients who may not be ideal candidates for outpatient surgical facilities.

Future prospective studies may address the development of screening tools for patients in need of additional education in normal and abnormal postoperative symptomatology or health care support. This may ultimately lower postoperative emergency department visits and overall health care cost associated with this procedure.<sup>48</sup>

#### Limitations

Most of the selected studies were retrospective. Documentation of a respiratory complication was collected from medical charts. It is likely that minor complications that did not require sentinel event reporting, hospital readmission, or operative intervention were not taken into account in the published literature. In most studies, the criteria used to establish the diagnosis and severity of OSA relied on clinical assessment, rather than PSG. Therefore, accurate stratification of OSA severity is not possible to enable aforementioned OSA severity stratification of postoperative risk.

Notwithstanding that our findings emanate from a meta-analysis of the pertinent published studies, caution should be exercised because the sample size was relatively small, and thus does not enable irrefutable evidence to unequivocally answer the 2 questions from this systematic review. This is even more noticeable for the second question.

#### CONCLUSIONS

The most frequent complications after AT include respiratory compromise and secondary hemorrhage. Based on the current limited evidence, children with OSA appear to have more respiratory complications after AT than children without OSA. In contrast, hemorrhage appears to be more frequent in children without OSA.

#### ACKNOWLEDGMENTS

We thank the experts who kindly responded to specific questions during the conduct of this research: Dr Karen A. Brown at McGill University Health Centre and The Montreal Children's Hospital; Dr Ronald D. Chervin at the University of Michigan; Dr Ron B. Mitchell at the University of Texas Southwestern and Children's Medical Center Dallas; and Dr Hawley E. Montgomery-Downs at West Virginia University.

#### **ABBREVIATIONS**

AT: adenoidectomy and tonsillectomy
CI: confidence interval
ICU: intensive care unit
OR: odds ratio
OSA: obstructive sleep apnea
PSG: polysomnography
SDB: sleep disordered breathing

FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Drs Gozal and Kheirandish-Gozal are supported by National Institutes of Health (NIH) grant HL-65270. Dr Bhattacharjee is supported by a scientist development grant from the American Heart Association (3SDG14780079).

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

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**BREAKING DARWIN'S RULES:** My second son loves to fish. He mostly surfcasts in salt water and fly fishes in fresh water. While he likes to catch bigger rather than smaller fish, he is always happy just to be fishing. We do have one rule, however. Regardless of the size of the fish we catch, unless the fish is badly hurt, we always release the fish back to the water from which it came. We usually spend a bit of time making sure the fish has the energy to swim away and not become game for a larger fish. Our theory is that even big fish have the right to get bigger and lead productive adult lives. Unfortunately, conservation policies and fishing practices of most fishermen encourage keeping the largest fish caught.

As reported in The New York Times (Science: August 20, 2015), humans tend to hunt and eat mature adult animals, those in their prime reproductive years. This is in sharp distinction to what happens in the wild where the young, the small, and the weak tend to be the ones killed by other animals. Humans, as amazing predators, have changed the rules of some species from "survival of the fittest" to "survival of the smallest". This can be seen in the Atlantic cod population. Large female cod produce far more eggs than smaller cod. As the cod population plummeted due to overfishing, quotas were established so that only the largest cod could be kept. This led to selection pressure favoring the survival of smaller cod and those that bred earlier and hence, produced smaller numbers of eggs.

Unfortunately, fishing and hunting practices are unlikely to change as sport fisherman and hunters like to pose with larger fish and trophies. Still, I hope that some will realize that the biggest is not always the best, and either return the fish to the water or settle for smaller fish or game while hunting.

Noted by WVR, MD