Commentary

Novel evidence depicting adverse long-term outcomes linked to tonsillectomy: a spotlight on overtreatment

Nikhil Nair Hariharan[a] and Kashyap Patel[b]

[a]Department of Biochemistry and Biomedical Sciences, McMaster University, Hamilton, Canada

[b]Faculty of Health Sciences, McMaster University, Hamilton, Canada

Abstract

Tonsillectomies (TEs) are the first line of treatment when patients present with recurrent tonsillitis, peritonsillar abscesses or obstructive sleep apnea. Though TEs have modest efficacy, they remain a common pediatric surgery in Canada. TEs are now viewed as a prophylactic measure used to prevent tonsil-related diseases. Simultaneously, there is a lack of evidence-based decision-making when recommending TEs, leading to overtreatment. Novel findings indicate that pediatric TE patients have an increased risk of complications and poor long-term outcomes including respiratory, infectious, and allergic disorders. A need for alternatives to TEs is evident; less invasive interventions with fewer perioperative complications and lifelong morbidities warrant further research. To prevent unnecessary adverse outcomes, healthcare providers should opt for more selective and evidence-based TE recommendations. Meanwhile, it is also imperative that physicians clearly communicate the potential quality of life implications associated with TEs. Healthcare and social mores surrounding TEs need to change towards a more evidence-based practice that focuses on improving patients' quality of life. This commentary examines the current role of TEs, their long-term outcomes, and the implications of overtreatment.

Keywords: pediatric, tonsillectomy, tonsil-related diseases, tonsil-related surgery, evidence-based, overtreatment

Corresponding author: hariharn@mcmaster.ca

Introduction

A tonsillectomy (TE) is the surgical removal of tonsils and is commonly performed in children. This procedure involves the dissection of the peritonsillar space and ligation of the relevant blood vessels to maintain hemostasis. This surgery is often accompanied with an adenoidectomy (AE), the removal of adenoids, and is mainly performed in patients presenting with recurrent tonsillitis, peritonsillar abscesses or obstructive sleep apnea[1].

TEs have become exceedingly prevalent in contemporary practice. Data reporting in Canada found 3606 children from the age of 0 to 4 years underwent TEs in 2016-2017, making it the most common surgical procedure in that age group. This continues to be a problem in children aged 5 to 17 years, where 3714 individuals underwent TEs during the same period[2]. According to a Cochrane Review on the efficacy of TEs for treating tonsillitis, the benefits conferred by patients were small. It indicated a minor reduction in sore throat episodes when compared to non-surgical treatment[3]. This implies that a large cohort of patients undergo TEs despite their modest benefits[4].

A UK cohort study followed 15,760 children aged 0 to 15 years who underwent TEs from 2005 to 2016 and evaluated the incidence of evidence-based indications for TEs[5]. Evidence-based indications for TEs according to the Paradise criteria include tonsillar tumours, symptoms fitting the Paradise criteria as well as periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome (see Table 1)[5]. The study found that the proportion of non-evidence-based TEs was much higher than evidence-based TEs, with "seven in eight children unlikely to benefit"[5]. Instead of being recommended using the Paradise Criteria, TEs are now viewed as a prophylactic measure that serve to prevent any tonsil-related diseases[6-8]. Thus, TEs are not always performed through an evidence-based approach.

Next, the frequency of perioperative complications and morbidities are discussed. Postoperative hemorrhage is a potentially life-threatening major complication incurred by 0.1% to 4.8% of all pediatric patients[9]. TEs can be achieved through cold dissection, which involves "cold" surgical instruments, or through electrosurgery which entails bipolar diathermy. Multiple studies demonstrate higher risks of postoperative secondary hemorrhage after electrosurgery for TE when compared to cold dissections[5,10-12]. According to a nationwide study done in the United States, nearly 3.6% of children are readmitted to hospitals following TEs primarily due to hemorrhages (26%), post-TE pain (16%) and dehydration (47%)[13]. Furthermore, a Thai study indicated that 48% of TE patients reported wound pain and 29% reported dysphagia[14]. Another minor TE complication includes postoperative taste disturbance; 8.6% of patients in a study evaluating this outcome experienced this and it usually lasted for 1.5 months[15]. TEs present a risk of major complications and adverse outcomes including postoperative hemorrhage, readmission to hospital, and temporary changes of sensation on the tongue. Patients and their surgeons should consider this procedure carefully.

High-quality evidence such as systematic reviews and meta-analyses on the benefits and harms of alternative treatment options is required to improve patient outcomes. An American review by Cooper et al. recently analyzed the knowledge gaps in the current literature concerning

TEs. As only 11% of the studies were relevant to evidence-based practice, current otolaryngologic research lacks strong evidence on the clinical practice guidelines of TEs[16]. This commentary considered studies from a wide variety of countries to ensure an international consensus. The medical literature was assessed by relevance to this commentary. Forward reference searching from the Byars et al. article was used to find studies that further examined the risk posed by TEs.

Table 1. Paradise Criteria, an evidence-based approach to assess the need of tonsillectomies[5].

Criterion	**Definition**
Minimum frequency of sore throat episodes	At least seven episodes in the previous year, at least five episodes in each of the previous two years, or at least three episodes in each of the previous three years
Clinical features	Sore throat plus at least one of the following features qualifies as a counting episode: ● Temperature of greater than 100.9 degrees Fahrenheit ● Cervical adenopathy (tender lymph nodes or lymph node size greater than 2 cm) ● Tonsillar exudate ● Culture positive for group A B-hemolytic streptococcus
Treatment	Antibiotics administered in the conventional dosage for proved or suspected streptococcal episodes
Documentation	Each episode of throat infection and its qualifying features substantiated by contemporaneous notation in a medical record If the episodes are not fully documented, subsequent observance by the physician of two episodes of throat infection with patterns of frequency and clinical features consistent with the initial history

Long-term implications of TEs and adverse effects

Novel evidence has indicated that TEs increase the risk of a wide variety of diseases. A recent cohort study done in Denmark was the first to evaluate the relationship between the long-term risks of allergic, infectious, and respiratory diseases in adults who underwent the removal of tonsils, adenoids, or adenotonsillectomies (ATEs) in the first nine years of childhood[17]. This population-based cohort followed 1,189,061 children born between 1979 and 1999. There were 60,667 surgical patients which included 17,460 AEs, 11,830 TEs, or 31,377 ATEs, who were compared to 1,157,684 controls. The data extracted from Danish registries covered 10-30 years of medical history and found a 17% increase in risk for allergic and infectious diseases in the ATE group (RR: 1.17; 95% CI: 1.10-1.25; n=37618; p-value<0.00064)[17]. Out of the 28 disease groups (such as infectious, inflammatory, circulatory, etc.), 78% of them had small but significant increases in relative risk after correcting for subgroup analyses. The most noteworthy

finding was that TEs led to a 2.72-fold increase in relative risk (RR: 2.72; 95% CI: 1.54-4.80; n= 22684; p-value<0.00064) compared to controls for the incidence of upper respiratory tract diseases[17]. These results concur with another study that indicated a 1.96-fold increase in the relative risk (RR: 1.96; 95% CI: 1.14-3.36; n=41; p-value=0.020) of asthma for adults who underwent AE/TE in their childhood[18]. The NNH was 5 for the TE group, meaning that one in five patients develops an upper respiratory tract disease. Furthermore, AEs were associated with a 2-fold increase in the risk (RR: 2.11; 95% CI: 1.53-2.92; n=701; p-value<0.00064) for chronic obstructive pulmonary disorder (COPD)[17]. Tonsils are lymphatic tissue that initiate immune responses through B-cell and T-cell lymphocytes to airborne antigens in the mouth and nose. They are also the most immunologically active between the ages of 3 and 10 years[19]. Therefore, removing tonsils can impair immune function and expose patients to respiratory diseases. There is a strong correlation between these surgeries and the incidence of respiratory diseases.

TEs are also associated with an increased risk for cancers. A German case-control study found a statistically significant OR of 1.4 (OR: 1.4; 95% CI: 1.0-1.9; n=136; p-value<0.05) of developing acute leukemia in children who had undergone TEs[20]. In addition, a Taiwanese nationwide cohort study concluded that TE patients had a significantly higher risk of developing cancer during their 3-year follow-up period (IRR: 1.54; 95% CI: 1.05-2.25; n=103; p-value<0.05)[21]. Moreover, an American case-control study that examined pre- and post-menopausal women uncovered a correlation between TEs and increased likelihood of breast cancer in premenopausal women (OR: 1.50; 95% CI: 1.08-2.08; n=169; p-value=0.02)[22]. A possible explanation is that tonsils produce immune cells and removing them may impair immunosurveillance[22]. As TEs have been repeatedly associated with a higher overall risk of developing cancer, overtreatment should be cause for caution.

TEs and AEs are also associated with developing inflammatory disorders. Studies have correlated TEs with an augmented risk for inflammatory bowel disease. A systematic review concluded that though there is no definitive association between TEs and ulcerative colitis, there is a positive relationship between TEs and Crohn's disease (OR: 1.37; 95% CI: 1.16-1.62; n=7666; p-value<0.05)[23]. Increased risk of appendicitis and sarcoidosis in adults has also been linked with TEs and AEs in foreign studies[24,25]. A Swedish cohort study found that adults and children who received a TE had a significantly increased standardized incidence ratio (SIR: 1.34; 95%CI 1.30-1.37; n=5357; p-value not reported) of developing autoimmune disorders[26]. Given the long-term effects and impaired quality of life experienced with these inflammatory disorders, it is important for practitioners to weigh the risk and benefit of TEs.

As there are a myriad of disorders including respiratory tract infections, cancers, and inflammatory disorders that correlate with these surgeries, it is valuable to explore alternatives.

Table 2. A summary of the studies examined and used in this section.

Studies				Findings	
Authors	**Population**	**Condition**	**Methods**	**Ratio**	**95% CI**
Byars et al.	Adults who underwent TEs or AEs in the first 9 years of their lives	Upper respiratory tract diseases	Population-based cohort	RR: 2.72	1.54-4.80
		Allergic and infectious diseases		RR: 1.17	1.10-1.25
		COPD		RR: 2.11	1.53-2.92
Yurtsever et al.	Adult with an average age of 42.5	Asthma	Retrospective cohort	RR: 1.96	1.14-3.36
Schüz et al.	Pediatric population (ages 0-14)	Acute leukemia	Case-control	OR: 1.4	1.0-1.9
Sun et al.	Adult population with and without tonsillectomy	Different cancers	Nationwide population-based cohort study	IRR: 1.54	1.05-2.25
Brasky et al.	Pre- and post-menopausal women	Breast cancer	Population-based case-control	OR: 1.50	1.08-2.08
Sun et al.	Adults from GI and outpatient clinics	Crohn's disease	Systematic review and meta-analysis	OR: 1.37	1.16-1.62

Reform to medical practice and education

Given the short and long-term adverse effects of TEs and that many are performed without sufficient clinical indication, healthcare providers need to re-evaluate their approach to TEs and also identify better alternatives. A retrospective chart review found that radiofrequency tissue volume reduction (RFTVR) reduced tonsil size by 86% while cold dissection removed 100% on average. However, the study found that the radiofrequency coblation group (n=50) experienced significantly fewer days of pain, reduced activity and required fewer days of medication compared to the cold dissection group (n=50; p-value<0.0001)[27]. RFTVR only requires local anesthesia, making it potentially less harmful than TEs which require general anesthesia. RFTVR also minimizes pain, with patients returning to normal function within two days of the procedure, unlike TEs for which the average recovery time is seven days[28]. Though this alternative was only tested in adults and its long-term effects have not been studied, it is a promising avenue that should be explored in the pediatric population as it can both prevent patient discomfort and increase quality of life in the short-term.

Currently, patients seek TEs as a preventative approach to avoid potential tonsillitis[6-8]. This mentality ultimately puts patients at unnecessary risk. Evidence-based protocols should be taught by educators and followed by healthcare providers to prevent overtreatment. In the case of TEs, overtreatment seems to be more harmful than beneficial for both the patients and the medical system in the long-term. To further curtail overtreatment, medical educators ought to emphasize the importance of assessing their necessity. Educational reform also needs to emphasize the importance of communicating risks. Physicians and specialists must be equipped to clearly communicate the short- and long-term risks to the patients and/or their guardians. According to a recent update to the American Clinical Practice Guideline on Pediatric TEs,

effective communication is identified as a quality improvement opportunity for physicians. It outlines that physicians can better communicate surgical and postoperative complications. This implies that there is room for improvement in the quality of communication between physicians and their patients. The guideline also notes that patient expectations can be improved through education. One of the major changes to the guideline was incorporating new evidence into practice and addressing patient opinions[29]. Patients must understand that what seems to be a prophylactic measure is, in reality, a major surgical procedure with risks and complications that can and should be avoided if possible. Hence, a tripartite approach to overtreatment could include improvements to patient education, establishing and following specific evidence-based protocols and considering alternate treatment plans.

Conclusions

Tonsillectomies continue to be recommended at alarming rates in Canada, especially amongst children. Though they could improve the quality of life in the short-term, novel findings suggest that TEs are correlated with multiple severe long-term morbidities and adverse outcomes. In order to mitigate these effects, less invasive alternatives should be explored while avoiding the saturation of invasive surgical procedures. Healthcare providers must effectively communicate risks associated with TEs and dispel them as a prophylactic measure. Evidence-based decision-making, such as the use of the Paradise criteria, is of paramount importance when assessing the need for TEs. Therefore, using clinical criteria outlining when TEs are necessary and investing in researching alternatives are recommended.

Abbreviations

1. TE - tonsillectomy
2. AE - adenoidectomy
3. ATE - adenotonsillectomy
4. PFAPA - Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis
5. RR - risk ratio or relative risk
6. NNT-harm - number needed to treat-harm
7. COPD - chronic obstructive pulmonary disorder
8. OR - odds ratio
9. IRR - incidence rate ratio
10. CI - confidence interval
11. SIR - standardized incidence ratio
12. RFTVR - radiofrequency tissue volume reduction

References

1. Baugh RF, Archer SM, Mitchell RB, Rosenfeld RM, Amin R, Burns JJ, et al. Clinical practice guideline: tonsillectomy in children. Otolaryngol Head Neck Surg. 2011 Jan 01; 144: S1–30.
2. Canadian Institute for Health Information. Inpatient hospitalizations, surgeries and newborn indicators [Internet]. Canada: CIHI; 2018. Available from: cihi.ca/sites/default/files/document/stats_dad_hmdb_ih_1314_en.xlsx
3. Burton MJ, Glasziou PP, Chong LY, Venekamp RP. Tonsillectomy or adenotonsillectomy versus non-surgical treatment for chronic/recurrent acute tonsillitis. Cochrane Database of Systematic Reviews. 2014 Nov 19; 1(11): CD001802.
4. Paradise JL, Bluestone CD, Colborn KD, Bernard BS, Rockette HE, Kurs-Lasky M. Tonsillectomy and adenotonsillectomy for recurrent throat infection in moderately affected children. Am Aca Peds. 2002 Jul 01; 110(1): 7-15.
5. Šumilo D, Nichols L, Ryan R, Marshall T. Incidence of indications for tonsillectomy and frequency of evidence-based surgery: a 12-year retrospective cohort study of primary care electronic records. Br J Gen Pract. 2018 Sept 07; 678: 33–41.
6. Woo J-M, Choi J-Y. Tonsillectomy as prevention and treatment of sleep-disordered breathing: a report of 23 cases. Maxillofac Plast Reconstr Surg. 2016 Nov 25; 38.
7. Bluestone CD. Current indications for tonsillectomy and adenoidectomy. Ann Otol Rhinol Laryngol. 1992 Jan 01; 101: 58–64.
8. Misiukiewicz K, Posner M. Role of prophylactic bilateral tonsillectomy as a cancer preventive strategy. Cancer Prev Res. 2015 Jul 01; 8: 580–582.
9. Wall JJ, Tay KY. Postoperative tonsillectomy hemorrhage. Emerg Med Clin North Am. 2018 May 01; 36: 415–26.
10. Lee MS, Montague ML, Hussain SS. Post-tonsillectomy hemorrhage: cold versus hot dissection. Otolaryngol Head Neck Surg. 2004 Dec 01; 131: 833-836.
11. Gendy S, O'Leary M, Colreavy M, Rowley H, O'Dwyer T, Blayney A. Tonsillectomy—cold dissection vs. hot dissection: a prospective study. Ir Med J. 2005 Nov 01; 98: 243-244.
12. O'Leary S, Vorrath J. Postoperative bleeding after diathermy and dissection tonsillectomy. Laryngoscope. 2009 Jan 03; 115: 591-594.
13. Johnson RF, Chang A, Mitchell RB. Nationwide readmissions after tonsillectomy among pediatric patients - United States. Int J Pediatr Otorhinolaryngol. 2018 Apr 01; 107: 10–3.
14. Muninnobpamasa T, Khamproh K, Moungthong G. Prevalence of tonsillectomy and adenoidectomy complication at Phramongkutklao Hospital. J Med Assoc Thai. 2012 May 01; 95 Suppl 5: S69-74.
15. Tomofuji S, Sakagami M, Kushida K, Terada T, Mori H, Kakibuchi M. Taste disturbance after tonsillectomy and laryngomicrosurgery. Auris Nasus Larynx. 2005 Dec 01; 32: 381–6.

16. Cooper CM, Checketts JX, Brame L, Gray H, Downs JB, Vassar M. An analysis of the literature addressing tonsillectomy knowledge gaps. Int Journal of Pediatric Otorhinolaryngology. 2018 Dec 01; 115: 89–93.
17. Byars SG, Stearns SC, Boomsma JJ. Association of long-term risk of respiratory, allergic, and infectious diseases with removal of adenoids and tonsils in childhood. JAMA Otolaryngol Head Neck Surg. 2018 Jul 01; 1;144(7):594–603.
18. Yurtsever N, Soyyigit S, Sozener ZC, Mungan D, Kose SK, Misirligil Z. Is adenoidectomy and/or tonsillectomy a risk factor for allergic diseases and asthma in adulthood? Eurasian J Med. 2018 Oct 01;50(3):152–5.
19. Ramos SD, Mukerji S, Pine HS. Tonsillectomy and adenoidectomy. Pediatr Clin North Am. 2013 Aug 01;60(4):793–807.
20. Schüz J, Kaletsch U, Meinert R, Kaatsch P, Michaelis J. Association of childhood leukaemia with factors related to the immune system. Br J Cancer. 1999 Apr 09;80(3–4):585–90.
21. Sun L-M, Chen H-J, Li T-C, Sung F-C, Kao C-H. A nationwide population-based cohort study on tonsillectomy and subsequent cancer incidence. Laryngoscope. 2015 Jan 01;125(1):134–9.
22. Brasky TM, Bonner MR, Dorn J, Marhsall JR, Vena JE, Brasure JR, et al. Tonsillectomy and breast cancer risk in the Western New York Diet Study. Cancer Causes Control. 2009 Apr 01;20(3):369–74.
23. Sun W, Han X, Wu S, Yang C. Tonsillectomy and the risk of inflammatory bowel disease: A systematic review and meta-analysis. J Gastroenterol Hepatol. 2016 Jun 01;31(6):1085–94.
24. Sawahata M, Nakamura Y, Sugiyama Y. Appendectomy, tonsillectomy, and risk for sarcoidosis – A hospital-based case-control study in Japan. Respir Investig. 2017 May 01; 55: 196-202.
25. Ballester JC, Ballester F, Rubio EC et al. Association between tonsillectomy, adenoidectomy, and appendicitis. Rev Esp Enferm Dig. 2005 Mar 01;97: 179-186.
26. Ji J, Sundquist J, Sundquist K. Tonsillectomy associated with an increased risk of autoimmune diseases: A national cohort study. J Autoimmun. 2016 Jun 22; 72:1–7.
27. Friedman M, LoSavio P, Ibrahim H, Ramakrishnan V. Radiofrequency tonsil reduction: safety, morbidity, and efficacy. Laryngoscope. 2003 May 01;113(5):882–7.
28. Nelson LM. Radiofrequency treatment for obstructive tonsillar hypertrophy. Arch Otolaryngol Head Neck Surg. 2000 Jun 01;1131;126(6):736–40.
29. Mitchell RB, Archer SM, Ishman SL, Rosenfeld RM, Coles S, Finestone SA, et al. Clinical practice guideline: tonsillectomy in children (update)-executive summary. Otolaryngol Head Neck Surg. 2019 Feb 05;160(2):187–205.