Laser tonsil treatment under local anesthesia: a patient-friendly effective alternative?

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LASER TONSIL TREATMENT

UNDER LOCAL ANESTHESIA:

A patient-friendly effective alternative?

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PREFACE

My decision to pursue medicine was inspired early on by my father, a multifaceted physician who is a neurologist, psychiatrist, and acupuncturist. With an open mind, I began my studies, eager to explore the many possibilities within the field. During my clinical rotations, I developed an interest in ENT surgery, a specialty where I took my first steps as a physician in The Hague.

In seeking further growth, I was offered several research projects. However, these were often fully developed topics that left little room for my own input. Having already gained experience with smaller studies, I knew I wanted to take on a larger project, something that would demand time and dedication, but also genuinely motivate me.

That opportunity came at Haga Hospital in The Hague, where the ENT team, uniquely in the Netherlands and beyond, performed outpatient laser tonsil treatments without general anesthesia. As a senior house officer (ANIOS), I regularly performed the procedure myself and became intrigued by both its potential and the controversy surrounding it. Although a small cohort study was underway, I saw that its design and scale were insufficient to convincingly demonstrate the procedure's value. Yet the popularity of the treatment was undeniable, with patients traveling from across the Netherlands (and beyond) to The Hague for this less invasive option.

The theory behind this selective approach, treating only the symptomatic tissue, resonated with me. Prof. Henk Blom's enthusiasm was contagious, and together we decided to thoroughly investigate the value of laser tonsillotomy. Although previous attempts had been made, these projects had stalled before completion. The result of our renewed effort now lies before you, presented in the following chapters.

Today, I am working as an ophthalmologist. Combining my passion for ophthalmology with ENT research has been both challenging and rewarding. Reflecting on this project, I see it as an incredibly enriching experience in many ways. Beyond scientific growth, I gained insight into the broader research landscape: from grants being unexpectedly withdrawn and other resistance from those skeptical of innovative approaches. At the same time, I experienced the positives: doors that opened in the name of science, the unwavering support of loved ones, and the tangible impact research can have. Our work has helped this procedure evolve from a controversial method to a recognized and insured treatment within Dutch healthcare.

I dedicate this thesis to my parents, who have always stood by me unconditionally, enabling me to pursue my goals, for which I am deeply grateful.

Thank you for your interest in our research. I hope you enjoy reading it!

Justin Wong Chung

"Progress is impossible without change, and those who cannot change their minds cannot change anything." *George Bernard Shaw*

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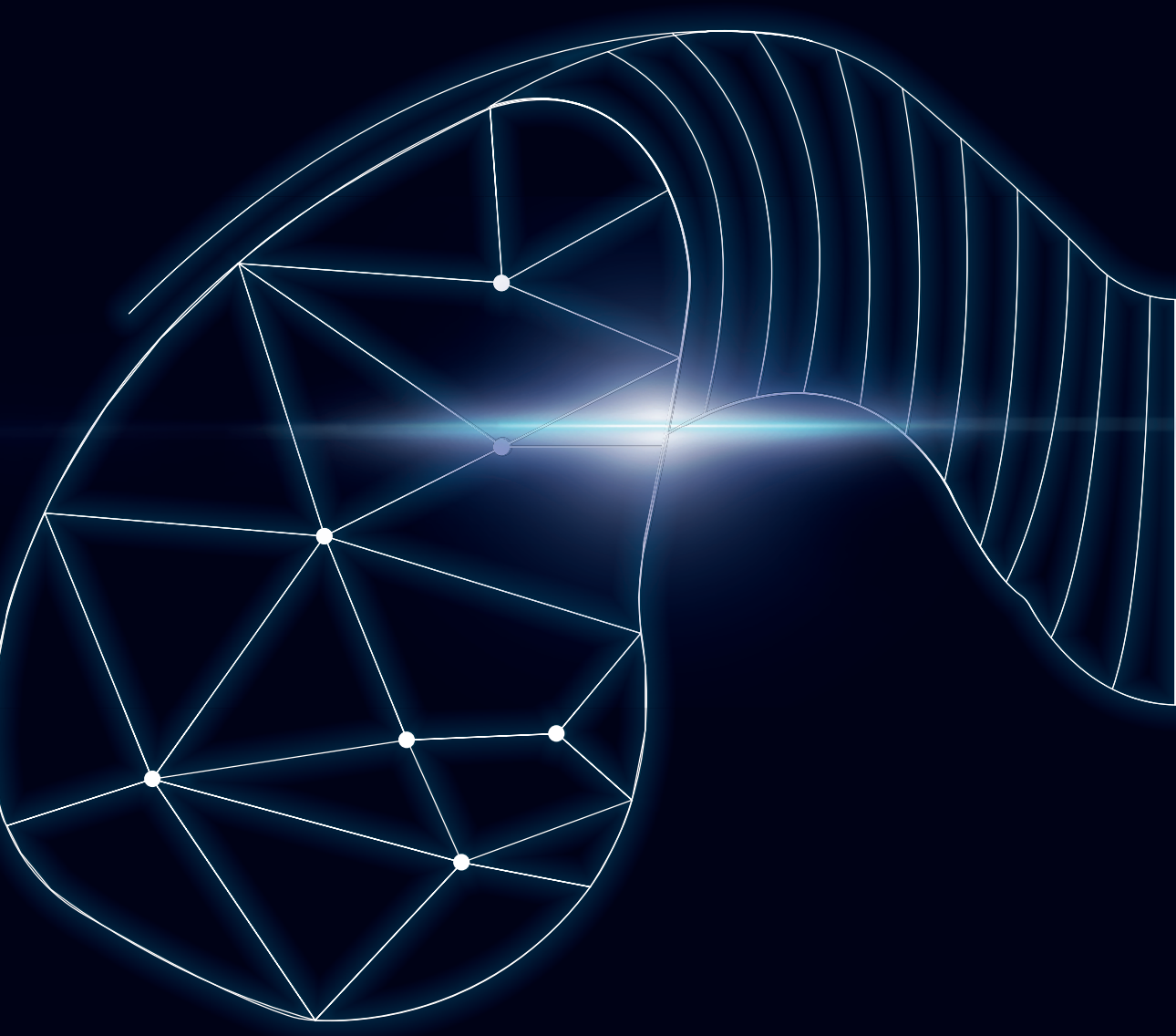

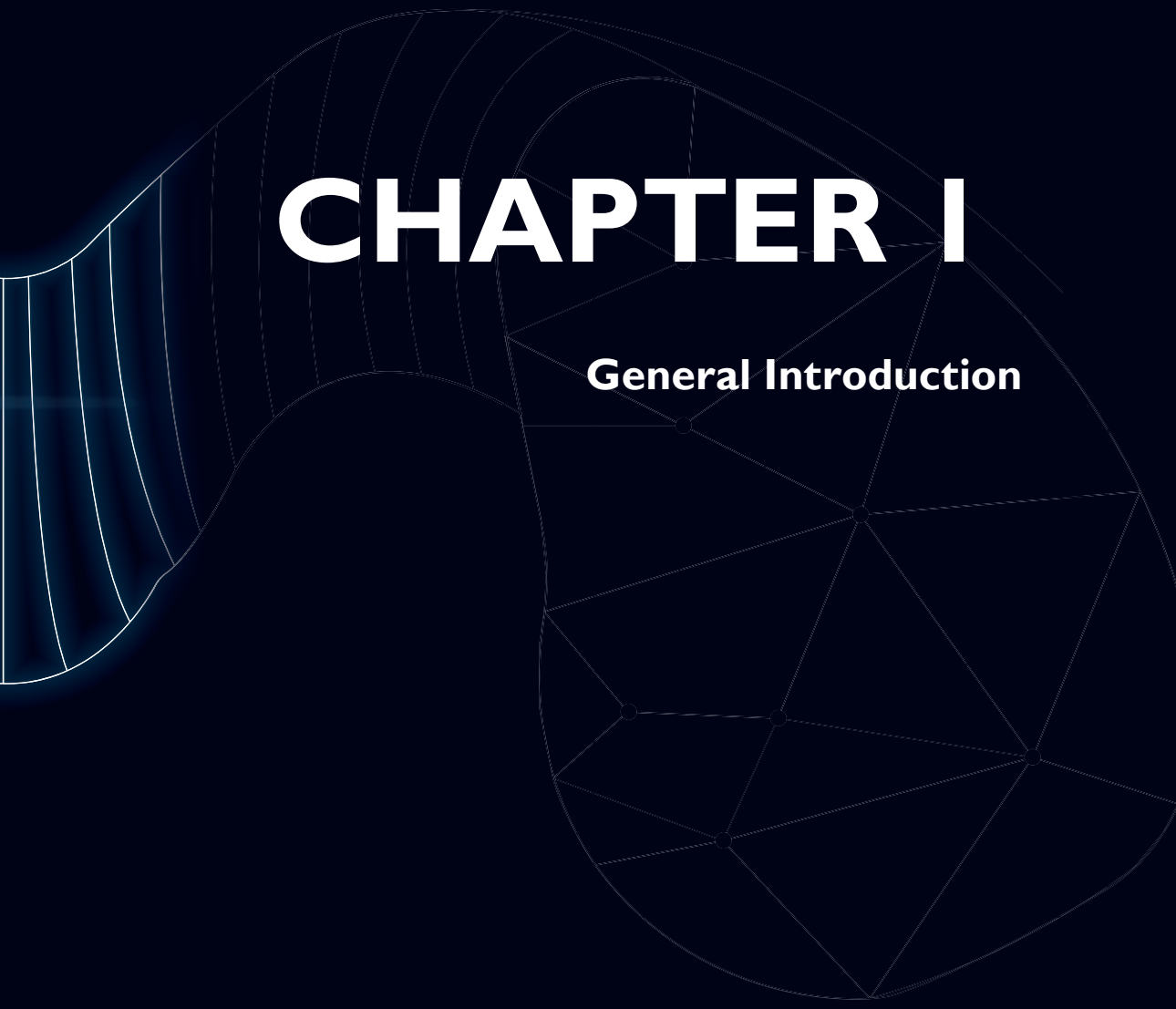

CHAPTER I

General Introduction

PALATINE TONSILS: ANATOMY AND FUNCTION

The palatine tonsils are two lymphoid structures located in the tonsillar sinus, positioned between the palatoglossal and palatopharyngeal arches. The **palatoglossal muscle** forms the anterior pillar, while the **palatopharyngeal muscle** forms the posterior pillar **(Figure 1)**. Each tonsil has a medial surface with up to 15 crypts, increasing antigen exposure, and a lateral surface encapsulated by superior pharyngobasilar fascia and loose areolar tissue. This capsule adheres tightly to the tonsil and extends inward as septa containing nerves, blood vessels, and lymphatic vessels.[1,2]

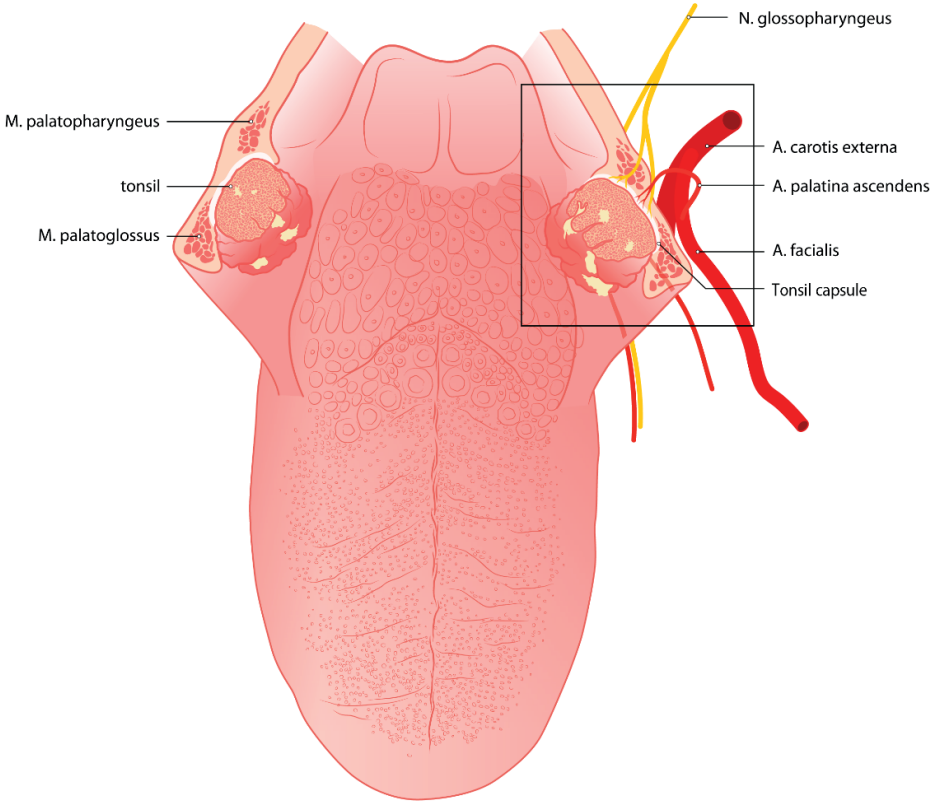

FIGURE 1. PALATINE TONSILS AND SURROUNDING ANATOMY. (NED TIJDSCHR GENEESKD. 2022;166:D6938)

Larger nerves and vessels lie within the capsule, supplying the tonsil, while smaller ones supply the crypts. Arterial supply comes mainly from branches of the external carotid artery: the tonsillar, lingual, ascending palatine, ascending pharyngeal, and descending

palatine arteries. Venous drainage starts in small veins that form two plexuses, and drains via paratonsillar veins into the facial and internal jugular veins. Sensory innervation is through the lesser palatine branches of the maxillary nerve (CN V2) and the glossopharyngeal nerve (CN IX).[3,4]

The tonsillar crypts are lined with ciliated non-keratinized squamous epithelium which traps pathogens and facilitates lymphoid activation, including germinal centers and mantle zones, leading to effective T- and B-cell immune response.[5]

The function of the tonsil is the same throughout life, but there are differences between children and adults. In children, the tonsils are proportionally larger and play a key role in the developing immune system, contributing significantly to local innate immunity as children are more susceptible to respiratory infections. As the immune system matures, the tonsils shrink in adults, reflecting a reduced role in local immune defense with fewer B and T cells and lower bacterial load.[6] However, they remain part of Waldeyer's ring, a larger local lymphoid structure, and continue contributing to the adaptive immune response, offering protection against respiratory and gastrointestinal infections. Consequently, tonsil removal in adults has minimal impact on the overall immune function, as the remaining lymphoid tissues can compensate. Any reduction in local immunity is generally minor and clinically insignificant.[7]

TONSIL-RELATED CONDITIONS AND THEIR IMPACT

Tonsillar disorders are prevalent and can significantly affect patients' quality of life. Common tonsil-related afflictions in adults include *acute and chronic tonsillitis*, *obstructive sleep apnea syndrome (OSAS)*, and *halitosis*.

Tonsillitis affects millions worldwide, leading to a substantial healthcare burden. In the United States, tonsillitis accounts for an estimated 40 million cases annually, representing over 5% of medical consultations. In France, around 9 million new cases are diagnosed each year. In Spain, 4 million annual cases constitute up to 15% of primary care visits.[8] In Germany, over 120,000 patients are treated for acute tonsillitis each year, with chronic tonsil and soft palate conditions being the 7th most common health issue among women and the 6th among men.[9,10] Although international data highlight the significant burden of tonsil-related conditions, the prevalence among adults in the Netherlands has historically been unclear.

Recurrent tonsil infections can progress to chronic tonsillitis with persistent symptoms such as sore throat, difficulty swallowing, and halitosis significantly impacting daily activities and overall well-being.[12]

OSAS is a common condition, which can be caused by large tonsils. The prevalence of OSAS is on the rise and is currently estimated at 6-17% in adults.[13] Although paediatric OSAS is often due to enlarged tonsils and adenoids, adult OSAS is typically caused by other factors such as obesity (up to 70% of patients), older age, and lifestyle factors like alcohol consumption and smoking.[14,15]

Halitosis has a wide range of causes, including tonsillar debris or stones (tonsillolithiasis). Halitosis affects around 24-41% of the population, but the true prevalence may be higher, as stigma often prevents individuals from seeking help and treatment.[17]

Tonsil-related conditions not only affect individual health but create significant socio-economic challenges as well.[11] A 2008 cost-of-illness study estimated adult pharyngitis-related costs in the United States around $1.2 billion per year.[18] These costs include direct healthcare-related costs, such as consultations and surgeries, and indirect costs from missed workdays and reduced productivity. Tonsil complaints are often chronic and recurrent which leads to high societal costs and strain on healthcare systems worldwide.

Treatment of common tonsil diseases

Given the prevalence of tonsil-related conditions, appropriate management strategies are critical.

Non-surgical management

Non-surgical interventions are the first line of treatment for mild or early-stage tonsil diseases. Acute tonsillitis, typically viral and self-limiting, can be managed with rest and hydration. Antibiotics are reserved for bacterial infections or cases at high risk of potential complications such as endocarditis and rheumatoid arthritis.[19] Symptom relief can be achieved with acetaminophen, Non-Steroidal Anti Inflammatory drugs (NSAIDs), and occasionally opioids.[20] Good oral hygiene and lifestyle rules, such as avoiding alcohol, smoking, and certain foods can help reduce recurrent tonsillitis and tonsil stones.[22,23] Antibiotics are generally ineffective for chronic tonsillitis, in part because chronic tonsillitis leads to an impenetrable biofilm on the tonsil surface with high levels of antibiotic resistance.[12] Antiviral drugs such as acyclovir are not effective.[10]

In OSAS related to enlarged tonsils, lifestyle interventions including weight loss, avoiding alcohol and sedatives, and side sleeping can reduce symptoms. A continuous positive airway pressure device or a mandibular repositioning device may also be recommended.[21]

Surgical management

When conservative measures fail to provide sufficient relief, surgery may be necessary. Extracapsular dissection TE, which involves the complete removal of the tonsil and its capsule has been the traditional approach.

TE has a long history dating back to the Roman Empire, where the physician Cornelius Celsus (circa 40 AD) described removing the tonsils with his fingers. This method briefly resurfaced in the 20th century but was discontinued for safety reasons.[24] Over time, surgical techniques evolved, from knives in the Middle Ages to more modern methods like the guillotine, harmonic scalpel, electrocautery, radiofrequency ablation, coblation, microdebrider, and various lasers. Despite these developments, classic cold steel dissection TE under general anaesthesia remains the most performed method due to its established outcomes and familiarity.[25]

Effectiveness of tonsillectomy

Classic dissection TE is an effective treatment for conditions such as recurrent tonsillitis and OSAS.[26,27] The effectiveness of this procedure depends on patient characteristics and surgical indication.

For *recurrent tonsillitis*, previous studies demonstrate significant improvement in quality of life in adults. Douglas reported a reduction of the Health Impact of Throat Problems quality of life score from a median of 47 (out of 100) preoperatively to 4 six months post-operatively.[26] Senska saw a reduction in annual sore throat episodes from 10 before surgery to 2 at seven years post-operatively, along with decreases in doctor visits, analgesic use, antibiotic consumption, and work absences.[28] Alho found fewer throat infections and healthcare visits after TE compared to patients treated conservatively.[29]

Despite its extirpative nature, TE does not always cure complaints attributed to recurrent tonsillitis. However, it generally improves quality of life by reducing the frequency and severity of these conditions.[30]

In adult *OSAS,* a systematic review and meta-analysis by Camacho analyzed 17 studies involving 216 patients, demonstrating a significantly improved sleep parameters after TE with a 65.2% decrease in the Apnea-Hypopnea Index (AHI) from 40.5/hour to 14.1/

hour, improved oxygen saturation (from 77.7% to 85.5%), and a reduction in the Epworth Sleepiness Scale score from 11.6 to 6.1. TE showed an successful reduction of AHI in 85.2% of patients and resolution of OSAS in 57.4%. Treatment success was especially high in patients with hypertrophic tonsils and mild to moderate OSAS by reducing airway obstruction.[16]

Halitosis is considered a relative indication for TE when alternative causes have been excluded, symptoms persistent despite appropriate interventions and malodorous substrates are present within the tonsillar crypts. Although data are limited some studies show up to 100% resolution of symptoms after TE.[31] TE is however often viewed as an excessively invasive, risky, and costly option when performed solely for halitosis.[31]

While studies suggest that TE can be effective for many tonsil-related afflictions, it is crucial to weigh the potential benefits against the risks and downsides of this intervention in adults.

Is classic dissection tonsillectomy in adults safe and patient-friendly?

TE is associated with considerable *postoperative pain, long recovery,* and *complications*.

Postoperative pain is more severe and prolonged in adults than in children, often requiring increased analgesic use.[32] The pain can last up to two weeks and is caused by exposed muscle fibers and nerve endings, specifically the glossopharyngeal and vagus nerves, leading to inflammation and muscle spasms. [33, 34] The pharyngeal constrictor muscles, essential in swallowing, become a major pain source, making swallowing uncomfortable and complicating recovery.[35]

Postoperative hemorrhage is a serious and potentially life-threatening complication, with an incidence in adults around 5%–10%.[36–38] However, when postoperative hemorrhages are actively assessed postoperatively in the context of clinical research, instead of relying solely on chart reviews, this rate increases to approximately 16%.[36] Bleeding can be categorized as primary (within the first 24 hours) and secondary (24 hours to 14 days post-surgery). Primary hemorrhages are generally due to insufficient hemostasis during surgery, while secondary hemorrhages are caused by the dissolution of blood clots, infection, or the exfoliation of necrotic tissue at the wound.[37] Bleeding usually stems from the external palatine vein or, less often, from arteries such as the tonsillar artery.[1] Mild bleeding can be managed conservatively, but more severe cases require surgical intervention and possibly blood transfusions. The mortality risk is 1 in 20,000 procedures in adults.[38,39] An expected 30% of these deaths are due to injury to the internal carotid artery (ICA), the external carotid artery (ECA), or their branches.[40]

Infection is the most common postoperative complication, increasing pain, secondary hemorrhage risks and delaying recovery. Patients can also develop pneumonia and urinary tract infections postoperatively.[41]

Other possible complications are dehydration from pain-induced difficulties with fluid intake, damage to adjacent anatomical structures, and velopharyngeal insufficiency.

These risks and the significant postoperative pain underscore the need for alternative procedures that reduce pain, recovery time, and complication rates while remaining effective in the treatment of tonsil-related conditions.

Are there feasible surgical alternatives for classic dissection tonsillectomy?

Less invasive alternatives to TE aim to reduce the size of the tonsils rather than removing them completely to reduce patient burden and improve recovery time.

Tonsillotomy (TO) constitutes the partial and intra-capsular removal of tonsil tissue. Even though TO is a century-old concept, it only regained clinically significant interest in the last decades.[42] TO can be performed under either local or general anesthesia and is mostly used for treating pediatric obstructive sleep apnea syndrome, offering comparable efficacy to TE but fewer complications compared.[43] In Sweden, TO is now more commonly performed than TE for treating obstructive tonsil symptoms in children. Both procedures lead to high patient satisfaction, but TO is associated with fewer postoperative hemorrhages and a shorter recovery with less pain medication use.[44]

There are a wide variety of surgical techniques available to perform a tonsillotomy including: microdebrider, coblation, CO_2-laser, electrocautery, cold steel, and bipolar scissors with each presenting unique advantages and disadvantages.

In c*old steel tonsillotomy* scalpels and scissors are used for the partial removal of the tonsil. Surgery is usually performed under general anesthesia. It offers precise control over tissue excision but carries a higher risk of intraoperative blood loss, postoperative hemorrhage when performed under local anesthesia compared to laser or coblation methods.[45]

Coblation tonsillotomy uses low-temperature radiofrequency energy with saline to remove tonsil tissue, causing less thermal damage to surrounding tissues compared to electrosurgery. This results in reduced postoperative pain and faster recovery compared to electrosurgery. However, there is a higher risk of saline aspiration and an increased

incidence of postoperative hemorrhage when the procedure is performed under local anaesthesia.[36,46]

Bipolar scissor diathermy tonsillotomy uses bipolar electrical energy through scissor-like instruments to cut and coagulate simultaneously. This technique offers precise tissue removal and effective hemostasis with limited intraoperative blood loss. There is a higher risk of postoperative hemorrhage, thermal damage, increased pain, and longer recovery times compared to other methods.[47]

Microdebrider tonsillotomy utilizes a rotary cutting tool to shave down the tonsil tissue. This allows for precise tissue removal and is effective in preserving the underlying tonsillar capsule, reducing postoperative pain. The mechanical action of the microdebrider can lead to more significant tissue disruption[47] and microdebrider tonsillotomy is associated with increased perioperative blood loss and longer recovery times compared to other tonsillotomy methods.

CO_2-laser tonsillotomy evaporates tonsil tissue without direct tissue contact while simultaneously coagulating vessels, improving intraoperative hemostasis, reducing blood loss and improving the visual clarity of the surgical field. The CO_2-laser operates at a specific wavelength (10.6nm) with high water absorption characteristics, which helps with hemostasis and regulation of thermal diffusion, limiting unintentional damage to surrounding tissue.[49,50] Current literature does not report any CO_2-laser specific complications, indicating a favorable safety profile. Previous research has also shown less intraoperative blood loss and fewer postoperative hemorrhages compared to cold dissection, diathermy, and coblation.[51]

While the various techniques described each offer unique advantages, CO_2-laser tonsillotomy stands out for its precise tissue ablation and minimal collateral damage. This thesis therefore evaluates whether CO_2-laser TO provides a safe and effective alternative to classic dissection TE in adults.

Aims of this thesis

The studies in this thesis aim to evaluate the effectiveness, safety, and cost-effectiveness of CO_2-laser TO compared to TE in adults with tonsil-related conditions, addressing key gaps in current research.

To assess differences in surgical outcomes between TO and TE, **Chapter 2** presents a systematic review highlighting the need for high-quality studies due to inconsistent evidence and varying methodologies. **Chapter 3** builds on this with a prospective non-randomized cohort study comparing short-term outcomes, including postoperative pain, recovery time, and complication rates.

To ensure procedural consistency, **Chapter 4** outlines a detailed CO_2-laser TO protocol under local anesthesia to standardize practice and reduce clinical variability. Given the lack of national data on adult tonsil-related conditions, **Chapter 5** analyzes Dutch healthcare data to quantify the burden and support the need for less invasive treatments.

Chapter 6 reports the TOMTOM study's short-term outcomes, comparing recovery time, symptom resolution, and patient satisfaction between CO_2-laser TO and TE. **Chapter 7** extends this to long-term outcomes and cost-effectiveness, considering direct medical and societal costs.

Chapters 8 and 9 conclude with recommendations for clinical practice, surgical training, and future research.

Collectively, these studies aim to advance our understanding of CO_2-laser TO as a potentially safer, more cost-effective alternative to TE in adults.

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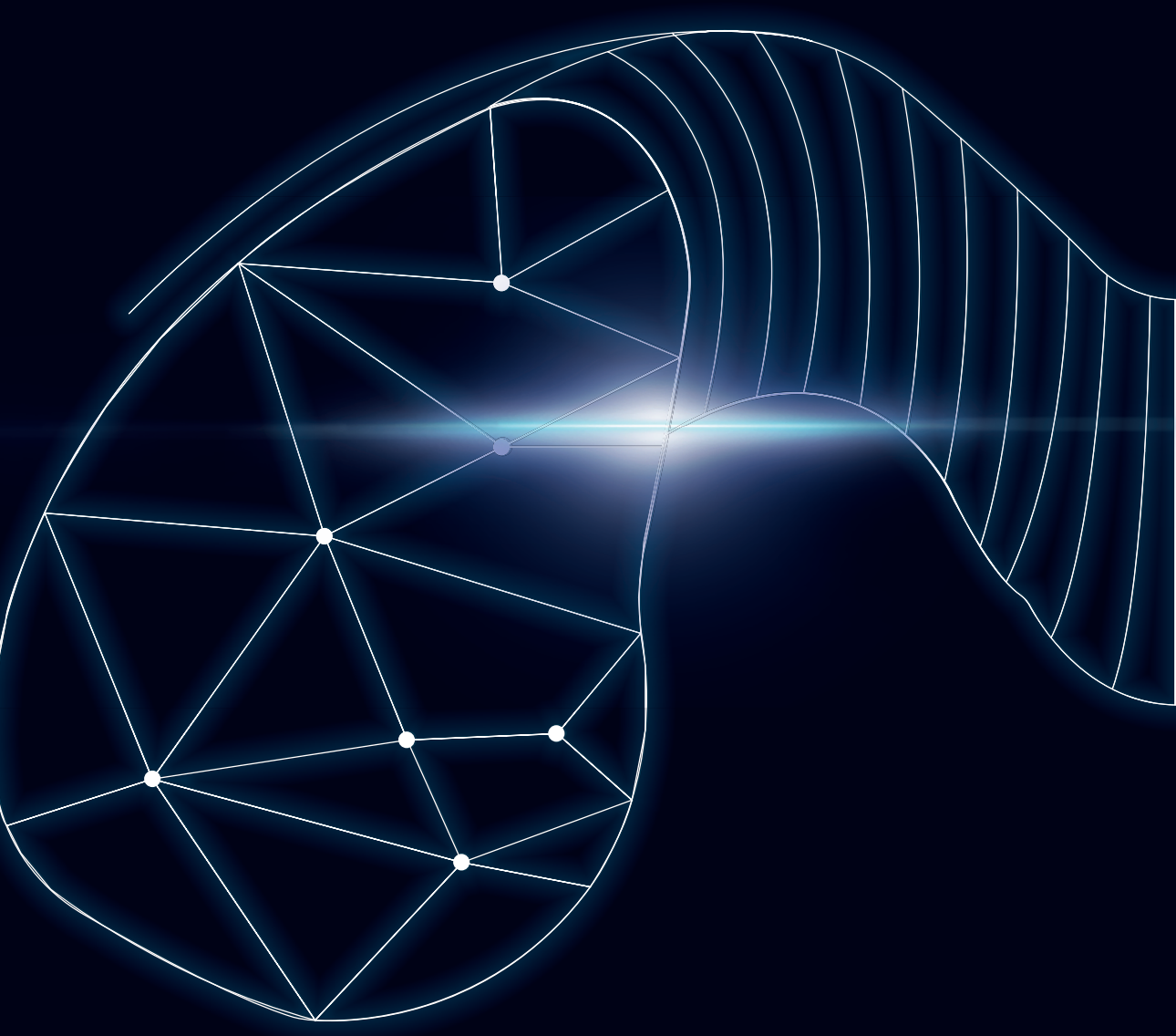

CHAPTER 2

Tonsillotomy versus tonsillectomy in adults suffering from tonsil-related afflictions: a systematic review

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Abstract

Objective: Tonsillotomy has emerged as an alternative for tonsillectomy in treating patients with tonsil-related afflictions. Tonsillotomy provides favorable outcomes in children, but treatment of choice in adults remains unclear. This systematic review sought to evaluate the current literature on the efficacy and adverse events of tonsillotomy compared to tonsillectomy in adults.

Methods: A Medline and Cochrane search was conducted for randomized clinical trials (RCTs) and cohort studies comparing tonsillotomy to tonsillectomy in adults. Risk of bias was assessed. Outcome measures were efficacy of the procedure in resolving the initial tonsil-related symptoms (tonsillitis, obstructive sleep apnea, tonsil stones, halitosis, dysphagia), procedure-related complications, recovery time, post-operative use of analgesics, patient satisfaction, and operating time.

Results: In total nine papers were included. These trials had a high risk of bias and the inter-comparability of results was poor. The reported studies found generally a similar efficacy for both interventions. With regard to pain, the use of analgesics, patient satisfaction and operation time, the results were generally in favor of tonsillotomy. Post-operative hemorrhages were more frequent after tonsillectomy.

Conclusion: Current evidence suggests an equal efficacy of tonsillotomy and tonsillectomy in adults and a preference for tonsillotomy in terms of pain, analgesics use, patient-satisfaction, operation time and post-operative complications.

Introduction

Classic tonsillectomy, the surgical removal of the palatine tonsils, is one of the most performed surgical interventions in the head-and-neck area. Within the United States alone, over half a million tonsillectomies are performed every year.

Tonsillectomies have been performed for over 3 millennia and even though different tonsillectomy methods have been developed over time, the traditional cold dissection tonsillectomy is still regarded as the gold standard.

The function of the palatine tonsils is related to the immune system, but their exact role in the immune response is under debate, especially since studies have shown that the function of the immune system was not compromised in early nor in late childhood in children that had undergone tonsillectomy compared to their age-matched healthy con-trols.[1]

Indications for tonsillectomy vary between the pediatric and adult population. In the adult population, tonsillectomy is mainly performed for chronic or recurrent tonsillar infections rather than for tonsillar hypertrophy with obstructive symptoms. Other indications for tonsillectomy in both adults and children include established or suspected tonsil-related malignancies and dysphagia related to the tonsils. Tonsil-related symptoms, such as halitosis, dysphagia and detritus (tonsil stones) are rarely an indication for tonsillectomy. The median recovery-duration after tonsillectomy is around 10 d for adults and 7 d for children. Post-operative hemorrhage rates after adult tonsillectomy are reported to be around 5% and post-operative infection rates around1–7%.[2]

Adult patients suffering from tonsillitis are reported to both miss around 9 days of work and use antibiotics for 6 weeks on a yearly basis. Altogether, these data underline the fact that the burden of tonsillectomy for patients is not to be underestimated.

An alternative surgical intervention for tonsillectomy is tonsillotomy. Although first described more than a century ago, tonsillotomy has only become a regular intervention in several areas around the world since its r-introduction in the 1990s. Tonsillotomy is defined as the partial, intracapsular removal of tonsil tissue, as opposed to the total, extra-capsular removal performed during tonsillectomy. Different synonyms are used in literature for the partial removal of tonsils, including tonsillotomy, partial tonsillectomy, tonsil ablation, intra-capsular tonsillectomy, radiofrequency-induced thermotherapy (RFITT) of the tonsils and subtotal tonsillectomy.[3]

Moreover, a wide variety of different surgical instruments have been used for tonsillotomy, including CO2-Laser, diathermy, radiofrequency, microdebrider coblation, bipolar and cold-steel tonsillotomy. Tonsillotomy is mostly performed under general anesthesia, but it can also be executed under local aanesthesia [4]

Tonsillotomy is currently mostly used in children with pediatric obstructive sleep apnea syndrome (pOSAS) and performed under general anesthesia. A recent systematic review by Wood et al. showed a comparable effect of tonsillotomy versus tonsillectomy on improving sleep disordered breathing, whereas tonsillotomy was associated with fewer post-operative complications.[5] However, there is insufficient data to show that a single technique for surgical tonsillotomy is superior to others, or to indisputably determine whether tonsillotomy can replace tonsillectomy.[6]

Moreover, currently available study reports do not allow fora reliable estimation of the chance of infection of tonsil remnants after tonsillotomy, which might lead to recurrent tonsillitis, but studies on children have reported a median recurrent tonsillitis rate following tonsillotomy of 3.9%.[6]

In adult patients, tonsillotomy is also increasingly performed, but not yet as frequently as in children. A well-designed overview of current literature comparing the efficacy and safety of tonsillotomy and tonsillectomy in adults is currently lacking. Therefore, the aim of this literature review was to evaluate the current literature on the efficacy and adverse events of tonsillotomy compared to tonsillectomy in adults suffering from tonsil-related diseases and afflictions and identify the knowledge gaps.

Materials and methods

We performed a systematic review following the Cochrane guidelines to assess the efficacy and safety in tonsillotomy versus tonsillectomy in adults suffering from a tonsil-related disease. This study was exempt from institutional board approval as it is a review of previously published data.

Study groups (tonsillotomy)

Our predefined study group of interest consisted of adults or adolescent patients aged over 15 who had been treated with any technique of tonsillotomy for tonsil-related diseases. We used the system of Windfuhr and Werner to classify tonsillotomy interventions into two classes: tonsillotomy procedures in which only the protruding part of the tonsil, the part medial to the faucal pillars, is removed (class I), and tonsillotomy procedures in

which only the inner surface of the tonsil-capsule is preserved and approximately 90% of the tonsil is removed (class 2).[3]

Control group (tonsillectomy)

Our predefined control group consisted of adult patients with tonsil-related diseases who had undergone conventional tonsillectomy. Tonsillectomy was defined as the complete removal of the tonsil, including its complete capsule.

Tonsil-related diseases and afflictions

We included studies comparing the outcomes of tonsillotomy and tonsillectomy for the following tonsil-related diseases and afflictions: (recurrent) tonsillitis, peritonsillar abscess, obstructive symptoms including OSAS, dysphagia, halitosis and tonsil stones.

Outcome measures

Our predefined outcome measures of interest were efficacy of the procedure in terms of resolution of the initial tonsil-related symptoms that lead to surgery ([recurrent] tonsillitis, peritonsillar abscess, obstructive symptoms including OSAS, dysphagia, halitosis and tonsil stones), complications related to surgery, operating time, recovery time, postoperative pain and use of analgesics, and patient satisfaction.

Literature search

The predefined selection criteria were randomized controlled trials (RCT) and cohort studies comparing tonsillotomy to tonsillectomy in adult or adolescent (>15 y) patients, written in English, Dutch, French or German and published after 1960. We included studies with internal controls (one tonsil removed with tonsillotomy and the other with tonsillectomy in the same patient) and studies with external controls, which are patients undergoing classic tonsillectomies.

A three-step search strategy was executed. First, an initial limited search of MEDLINE and Cochrane collaboration databases was conducted, followed by an analysis of the wording used in the titles and abstracts, and of the index terms used to categorize the articles. Second, a search was performed using all the identified keywords and index terms across the MEDLINE and Cochrane databases. The following keywords and index terms were used: 'tonsillotomy', 'partial tonsillectomy', 'subtotal tonsillectomy', 'intracapsular tonsillectomy', 'hot tonsillectomy', 'radiofrequency induced thermotherapy tonsil', 'RFITT' and 'tonsil ablation'. Third, the reference lists of all the identified reports and articles were searched for additional studies.

Risk of bias

Prior to inclusion, all papers selected for retrieval were assessed by two independent reviewers (J. W. C. and H. B.) for methodological validity using the Cochrane Risk of Bias Tool. This tool addresses possible bias, more specifically selection bias, performance bias, detection bias, attribution bias and reporting bias. Any disagreements that arose between the reviewers were resolved through discussion between the two reviewers or in consultation with a third reviewer (P. P. v. B.).

Results

Literature search

Our search and selection process are shown in **Figure 1**. The initial search performed on 1 April 2017 identified 512 articles. Of these, the majority focused on pediatric patients and had study designs other than RCT. Based on title and abstract, we further excluded papers that did not match the objective of this study (e.g. studies that only examined extracapsular tonsillectomies). Of a total of 20 articles eligible for full-text review, 3 studies were excluded because they only focused on extracapsular removal of the tonsils (tonsillectomy), and 7 studies were excluded for reporting on pediatric or pediatric and adult patients, and 1 study did not specify the age group. No additional articles were included after cross-reference checking of the included studies and reviews on tonsillotomies. This resulted in a total of nine RCT and cohort studies eligible for inclusion **(Table 1).**

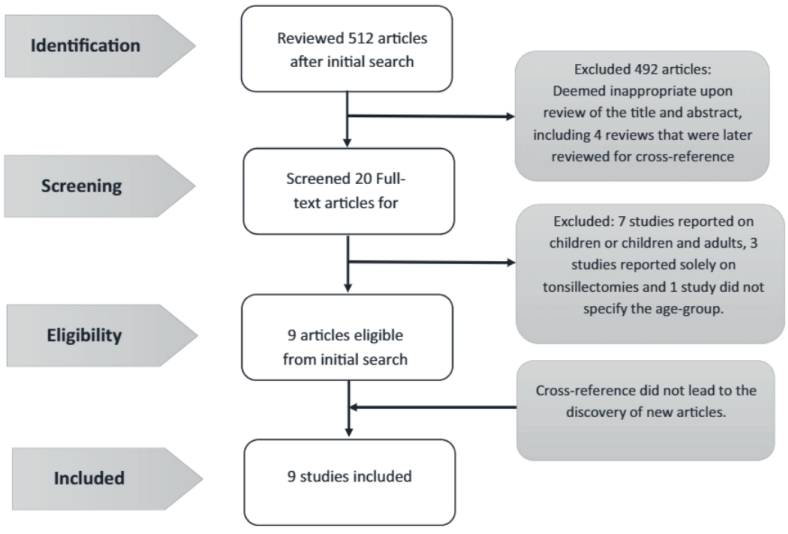

FIGURE 1. SELECTION PROCESS OF ELIGIBLE STUDIES.

Table 1. Characteristics of included studies.

Reference	Study design	Publ. year	Country	Indication	Age (years)	Follow-up	Technique	Patients per tech	Blinding	Lost to follow-up
Bender B [13]	RCT	2014	Austria	Tonsillitis	18–65	6 months	1 ICTE (class I) 2 Cold dissection tonsillectomy	1 50 2 54	Double blinded	10 patients (10%) 5 per group
Nemati S [14]	RCT	2010	Iran	Tonsillitis	15–65	12–24 months	1 RFITT (Class I) 2 Cold dissection tonsillectomy	1 38 2 24	Not stated	None
Arya A [10]	RCT	2003	United Kingdom	Tonsillitis	17–57	24 h	1 Coblation tonsillotomy (Class II) 2 Coblation tonsillectomy	1 14 2 14	Double blinded	None
Ericsson E [7]	RCT	2007	Sweden	Obstruction with or without recurrent tonsillitis	16–25	Until end of post-operative pain (up to 3 weeks)	1 RFITT (Class I) 2 Cold dissection tonsillectomy	1 32 2 44	Not blinded	None
Ericsson E [8]	RCT	2007	Sweden	Obstruction with or without recurrent tonsillitis	16–25	1 year	1 RFITT (Class I) 2 Cold dissection tonsillectomy	1 31 2 43	Not blinded	1 patient (1%)
Wireklint S [9]	RCT	2012	Sweden	Obstruction with or without recurrent tonsillitis	16–25	6 years	1 RFITT (Class I) 2 Cold dissection	1 29 2 39	Not blinded	7 patients (10%)
Hall [11]	RCT	2004	Hawaii	Obstructive hypertrophy or recurrent tonsillitis	adult	14 d	1 Coblation tonsillotomy (Class II) 2 electrocautery tonsillectomy	1 28 2 28	Double blinded	4 patients (7%)
Lourijssen [4]	Prospective follow-up non-randomized non-blinded cohort study	2016	Netherlands	Tonsillitis, halitosis, tonsilloliths, obstructing tonsillar hyperplasia or dysphagia	≥18	1 year	1 Outclinic CO2-laserton-sillotomy (Class II) 2 Cold dissection	1 61 2 46	Not blinded	27 patients (25%)
Johnston [12]	Retrospective cohort study	2010	USA	Chronic tonsillitis, tonsillar hypertrophy	Teens (12–19), Adults (>19)	32 months	1 Powered intra-capsular tonsillectomy (PIT) (Class II) 2 monopolar electro-cautery tonsillotomy (MET)	1 117 adults 2 262 adults	Retrospective	None

ICTE: intra-capsular tonsillectomy; RFITT: radiofrequency-induced thermotherapy.

The nine included RCTs and cohort studies reported on a total of 770 (284 in RCTs and 486 in cohort studies) adult patients. The term used most frequently for describing tonsillotomy was *partial tonsillectomy*. **Table 2** shows the distribution of the terms used for tonsillotomy in the literature.

Table 2. Terminology use in current literature for discribing tonsillotomy.

Term	Number of articles
Tonsillotomy	134
Partial tonsillectomy	35
Subtotal tonsillectomy	13
Intra-capsular tonsillectomy	81
Hot tonsillectomy	46
Radiofrequency-induced thermotherapy tonsil	3
RFITT	23
Tonsil ablation	83

The papers by Ericsson and Hultcrantz[7], Ericsson and Ledin[8], and Wireklint and Ericsson[9] reported on the same cohort of patients in Linköping, Sweden, using a consecutively longer follow-up period. From here on, we will refer to this cohort as 'the Swedish cohort'.

Of all 770 patients, 485 (63%) underwent a tonsillotomy intervention and 327 (42%) underwent tonsillectomy. In the 42 patients included in the studies by Arya et al.[10] and Hall et al.[11], tonsillotomy was performed on one tonsil and tonsillectomy on the contralateral tonsil. We included these patients in both arms of our review, and outcome measures were included for the respective treatment.

The included papers studied different age ranges. The study by Bender et al. considered patients between 18 and 65 years as adults. Nemati et al. included all patients between 15 and 65 years, and Arya et al. reported on adults aged between 17 and 57. The Swedish cohort focused on 'young adults' aged 16 to 25[7–9], Hall et al. did not specify age other than 'adults'.[11] Lourijsen et al. included all patients aged 18 and above and Johnston made a subdivision between teens (12–19 years old) and adults (>18 years old).[4,12] We included results from the adult patient group of Johnston et al.

Indication for surgery

Primary indications for surgery were tonsillitis in five studies[4,10,12–14], obstructive symptoms with or without tonsillitis in five studies[4,7–9,12], obstructive symptoms or recurrent tonsillitis in two studies[4,11], and halitosis, tonsilloliths, and dysphagia in one study.[4]

Surgical technique

The surgical methods used for tonsillotomy were RFITT[7–9,11,14], coblation tonsillotomy[10,11], CO2 laser tonsillotomy[4], power-assisted tonsillotomy[12], and scissor-assisted dissection of the tonsil part medial to the palatine arches followed by the removal of remnants with a microdebrider[13] (**Table 1**). The surgical method for tonsillectomy was standard cold knife dissection in all studies except for the study by Arya et al.[10], in which coblation was used for both tonsillotomy and tonsillectomy, and for the studies by Johnston et al. and Hall et al., which used electrosurgery[11,12].

The number of surgeons performing the surgical interventions was specified in five of nine studied populations. In the studies by Nemati et al. and Arya et al., operations were performed by a single surgeon[10,14]. The Swedish cohort was operated on by three surgeons, and in the study by Hall et al., the interventions were performed by six surgeons, four of whom had no prior experience with coblation tonsillotomy.

RFITT was performed differently in the study by Nemati et al. and in the Swedish cohort. In the study by Nemati et al., the bipolar linear RFITT probe was introduced into the crypts of the tonsils at five up to nine locations, depending on the size of the tonsils, and the tonsil tissue was vaporized with the power set at 7 watts to perform complete cryptolysis. Afterwards, probable bleeding sites were coagulated.[14] In the Swedish cohort, the RF probe was used to cut the tonsil parallel to the anterior pillar, followed by coagulation of bleeding vessels if necessary.[8]

Five studies performed a Class I tonsillotomy, and four studies performed a Class II tonsillotomy (Table 1). Arya et al. and Hall et al. removed all tonsil tissue, except the tonsillar capsule, during coblation tonsillotomy.[10,11]

Follow-up

Follow-up varied between all the included studies. Follow-up was 1 day in the study by Arya et al.[10], 14 days in the study by Hall et al.[11], 6 months in the study by Bender et al.[13], 1 year in the study by Lourijsen et al.[4], and 12 to 24 months in the study by Nemati et al.[14] and 32 months in the study by Johnston et al.[12]. In the consecutive papers on the Swedish cohort, follow-up was 3 weeks, 1 and 6 years.[7–9]

Risk of bias

Apart from the studies by Lourijsen et al.[4] (prospective follow-up non-randomized cohort study) and Johnston et al. (retrospective study)[12], all included studies were RCTs. Risk of bias is summarized in **Table 3**. Studies by Bender et al.[13] and Arya et al.[10] had low risks of bias. The study by Nemati et al. had a medium risk of bias for blinding, the studies

on the Swedish cohort[7–9], the study by Lourijsen et al.[4], Johnston et al.[12], and the study by Hall et al.[11] had medium and high risk of bias. Possible bias will be further debated in the discussion section of this review.

Table 3. Risk of bias of included studies (Cochrane risk of bias tool).

Article	Bias	Authors' judgement		Support for judgement
Bender B [13]	Random sequence generation	Low risk		Randomization plan by Department of Medical statistics
	Allocation concealment	Low risk		Randomization plan by Department of Medical statistics
	Blinding? All outcomes	Low risk		Patients and examiners were blinded to the surgical procedure
	Incomplete outcome data *addressed? All outcomes*	Low risk		Per protocol analysis
	Selective reporting	Low risk		None
	Other sources of bias	Low risk		None
Nemati S [14]	Random sequence generation	Low risk		Block randomization
	Allocation concealment	Low risk		Block randomization
	Blinding? *All outcomes*	Medium risk		Not stated
	Incomplete outcome data *addressed? All outcomes*	Low risk		One case could not visit clinic but was questioned over the telephone
	Selective reporting	Low risk		None
	Other sources of bias	Low risk		None
Arya A [10]	Random sequence generation	Low risk		Sealed envelope allocation
	Allocation concealment	Low risk		Sealed envelope allocation
	Blinding? *All outcomes*	Low risk		Only operating surgeon would know type of intervention. PI was a different person.
	Incomplete outcome data *addressed? All outcomes*	Low risk		Complete data
	Selective reporting	Low risk		None
	Other sources of bias	Low risk		None
Ericsson E [7] Ericsson E [8] Wireklint S [9] (Same cohort)	Random sequence generation	Medium risk		Not stated
	Allocation concealment	High risk		Invitation for participation and written consent to the randomized choice after randomization
	Blinding? *All outcomes*	High risk		Written consent to the randomized choice after randomization
	Incomplete outcome data *addressed? All outcomes*	Ericsson E [7]	Low risk	Complete data
		Ericsson E [8]	Medium risk	1 missing -> excluded
		Wireklint S [9]	Medium risk	7 missing -> excluded
	Selective reporting	Low risk		None
	Other sources of bias	Low risk		None
Hall D [11]	Random sequence generation	Medium risk		Counterbalanced by order of presentation
	Allocation concealment	High risk		Invitation for participation after randomization
	Blinding? *All outcomes*	Medium risk		Patients and primary investigator (PI) were blinded except for 2 surgeries performed by the PI.
	Incomplete outcome data *addressed? All outcomes*	Medium risk		Incomplete follow-up (4 patients) was reported but no statistical analysis was performed on missing data
	Selective reporting	Low risk		None
	Other sources of bias	Low risk		None
Johnston [12]	Random sequence generation	High Risk		Retrospective chart review
	Allocation concealment	High risk		Retrospective chart review
	Blinding? *All outcomes*	High risk		Retrospective chart review
	Incomplete outcome data *addressed? All outcomes*	High risk		Incomplete follow-up (4 patients) was reported but no statistical Completeness of chart data not reported
	Selective reporting	Low risk		None
	Other sources of bias	Low risk		None
Lourijssen [4]	Random sequence generation	High risk		Non-randomized
	Allocation concealment	High risk		Freedom of choice
	Blinding? *All outcomes*	High risk		None
	Incomplete outcome data *addressed? All outcomes*	High risk		Incomplete follow-up (32%) was reported and addressed with best and worse cast scenarios.
	Selective reporting	Low risk		None
	Other sources of bias	Medium risk		Inclusion bias, most patients were redirected especially for the laser treatment and therefor highly motivated

Outcome measures (Table 4)

Efficacy (primary outcome)

Efficacy of the surgical intervention in resolving the initial tonsil-related symptoms was reported in six of nine papers and was evaluated differently between studies. Eight of nine studies showed no difference in efficacy between tonsillotomy and tonsillectomy, while the study by Lourijsen et al. showed significantly better efficacy in favor of tonsillectomy. Bender et al.[13] scored efficacy with the Tonsil and Adenoid Health Status Instrument (TAHSI). The TAHSI is a questionnaire for tonsil disease with a score ranging from 0 to 64, with a higher score indicating more severe tonsil-related morbidity. The TAHSI score in the study by Bender et al. did change significantly after surgery, and there were no differences between the two treatment groups.

Nemati et al.[14] did not find a difference between the two treatment groups in controlling recurrent tonsillitis in 12 to 24 months follow-up. In the Swedish cohort, efficacy was studied using the Short Form 36 Health Survey to evaluate Health-Related Quality of Life (HRQoL) and the EuroQol five dimensions questionnaire (EQ-5D VAS) scales to evaluate the self-rated overall health. The HRQoL and EQ-5D VAS scales did improve significantly after both interventions. No significant difference was found between the treatment groups at 1-year and 6-year follow-up. A significant decrease in ENT infections was seen following both interventions at 1-year and 6-year follow-up, without any difference between treatment groups. Furthermore, the snoring intensity decreased in both treatment groups without a difference between treatments.

In the study by Lourijsen et al., 72.5% of patients were complaint-free 1 year after tonsillotomy compared to 97.2% of patients after tonsillectomy ($p < .001$).[4]

The study by Johnston et al. showed a difference in persistence of tonsillitis after both interventions in favor of tonsillectomy, but no statistical analyses had been performed between both groups.[12]

Complications

Complications were reported in all papers. Bender et al.[13] reported post-tonsillectomy hemorrhage (PTH) in 16 of 54 patients (29.6%) after tonsillectomy and in 6 of 50 patients (12%) after tonsillotomy ($p = .03$). Furthermore, PTH was more severe and recurrent PTH was more frequent after tonsillectomy. In the Swedish cohort, six patients in the tonsillectomy group had a PTH (two primary, four secondary).[7–9] Hall et al. found two minor PTHs on the coblation tonsillotomy side and one on the electrosurgery tonsillectomy side. None of the patients required transfusion or a return to the operating theatre.[11]

There were no primary or secondary hemorrhages in the tonsillotomy group, but in one patient there were difficulties in maintaining intracapsular hemostasis during the tonsillotomy intervention and therefore surgery was converted to tonsillectomy. In the cohort studied by Arya et al., in which patients underwent tonsillotomy as well as tonsillectomy, PTH occurred in one patient, but the type of intervention causing the complication was not mentioned.[10] No PTH occurred in the study by Nemati et al.[14] Lourijsen et al. reported a significant difference in PTH in favor of tonsillotomy: three (3%) PTHs were seen after tonsillectomy, two requiring intervention, and two (1%) PTHs were seen after tonsillotomy, none requiring intervention.[4] Johnston reported a PTH rate of 1.7% after tonsillotomy and 2.7% after tonsillectomy; no statistical analysis was performed.[12]

In addition, Lourijsen et al. reported four post-operative infections after tonsillectomy, none after tonsillotomy.[4] Bender et al. reported more vomiting after tonsillectomy[13], and Nemati et al. reported dysphagia in one patient after tonsillotomy caused by loose tonsil tissue in the throat post-operatively.[14] No deaths occurred in any of the studies.

Pain

Post-operative pain or the use of pain medication was registered in all studies except in the study by Johnston et al.[12] Arya et al. did not find a difference in 24-hour post-operative pain scores between the sides operated with tonsillotomy and the tonsillectomy sides.[10] This finding does not come unexpectedly since significant relief of post-operative pain is not expected within 24 hours. All other studies reported a difference in pain scores or analgesic medication use in favor of tonsillotomy. Bender et al. found that the tonsillotomy group used less and milder pain medication (only paracetamol and NSAID, instead of hydromorphone) than the tonsillectomy group.[13] Hall et al. found less pain after tonsil ablation than after electrosurgical tonsillectomy.[11] Nemati et al. found a lower pain score on days 1, 3, 5, and 10 after tonsillotomy.[14] The differences in pain scores were significant after day 1 and day 3. In the Swedish cohort, patients who had undergone tonsillotomy recorded less pain from the first day onwards, required less analgesics, and were pain-free 4 days earlier than the tonsillectomy group.[7–9] In the study by Lourijsen et al., both overall pain scores (5.4 after tonsillotomy and 7.7 after tonsillectomy) and analgesic use (median of 5.4 days after tonsillotomy and 9.6 days after tonsillectomy) were significantly different in favor of tonsillotomy. The days until resumption of daily activities were significantly different (4.8 days after tonsillotomy and 9.6 days after tonsillectomy).[4]

Duration of surgery

Four studies reported on the duration of surgery. Bender et al. concluded that tonsillectomy prolonged the duration of surgery compared to microdebrider-assisted tonsil-

lotomy.[13] Arya et al. concluded that the duration of coblation-assisted tonsillectomy was longer than the duration of coblation-assisted tonsillotomy.[10] Hall et al. concluded that electrosurgical tonsillectomy took longer than coblation tonsillotomy[11], and Lourijsen et al. found a shorter operation time after CO2 laser tonsillotomy compared to cold dissection tonsillectomy. [4]

Table 4. Summary of outcomes.

Outcome reference	Efficacy	Complications	Operating time	Pain	Recovery time	Analgesics	Patient satisfaction
Bender B [13]	Median of 32.7 point improvement on TAHSI score, no significant differences between groups.	PTH after ICTE in 12% and after ECTE in 29.6% ($p = .03$).	Shorter for ICTE	Not stated	Not stated	Fewer and less intense analgesics in ICTE group ($p = .049$).	Not stated
Nemati S [14]	Significant decrease of tonsillitis, no significant differences between groups.	Remnant of tonsil tissue after RFITT causing dysphagia in one patient.	Shorter for RFITT	Lower mean post-operative pain day 1 & 3 after RFITT ($p < .001$). No significant differences on day 5 and 10.	1.8 d until return to normal diet after RFITT vs. 3.61 d after cold dissection (CD) ($p < .004$)	Not stated	Not stated
Arya A [10]	Not stated.	1 PTH, intervention not stated.	Tonsillectomy took 5–6 min, tonsillotomy took 15 min.	24-h VAS pain score: area under curve of 60.9 for tonsillotomy and 82.5 for tonsillectomy ($p = .13$).	Not stated	Not stated	Not stated
Ericsson E [7]	Not stated.	2 primary bleedings and 4 secondary bleedings after CD.	29.1 min for RFITT and 29.8 min for CD, difference was not significant.	First pain-free day after RFITT on day 8.6, after RFITT on day 12.8 ($p < .001$)	Days to normal eating: TT 7.9 TE 12.0 ($p < .001$). Days to normal activity: TT 6.1 TE 10.6 ($p < .001$)	Fewer analgesics in RFITT group for a shorter period of time. More NSAID use after TE.	Not stated
Ericsson E [8]	Significant HRQoL improvement, decrease in snoring intensity and decrease in number of ENT-infections. No significant differences between groups.	None	See article by Ericsson et al. [7]	See article by Ericsson et al. [7]	See article by Ericsson et al. [7]	See article by Ericsson et al. [7]	Higher satisfaction after cold dissections tonsillectomy
Wireklint S [9]	Significant HRQoL improvement, decrease in snoring intensity and decrease in number of ENT-infections. No significant differences between groups.	None	See article by Ericsson et al. [7]	See article by Ericsson et al. [7]	See article by Ericsson et al. [7]	See article by Ericsson et al. [7]	See article by Ericsson et al. [8]
Hall [11]	Not stated	3 minor PTH: 2 after tonsillotomy, 1 after tonsillectomy.	Shorter for Coblation tonsillotomy ($F = 13.271$ $p < .002$).	VAS score post-operatively significantly lower after tonsillotomy.	Not stated	Not stated	Patients choose coblation tonsillotomy over tonsillectomy ($p < .001$)
Johnston [12]	Recurring tonsillitis: 8.5% after PIT, 2.7% after MET (Statistical analysis not available).	PTH in 1.7% after PIT, 2.7% after MET. Dehydration was seen in 0.9% after PIT and 4.2% after MET. (Statistical analysis not available).	Not stated	Not stated	Not stated	Not stated	Not stated
Lourijssen [4]	72.5% complaint free 1 year after TO. 97.2% complaint free 1 year after CD ($p < .001$).	3 PTH after tonsillectomy, two requiring intervention. 2 PTH after tonsillotomy, none requiring intervention. Four post-operative infections after tonsillectomy.	Shorter for tonsillotomy (17.1 min) compared to tonsillectomy (22.4 min) ($p = .002$)	Post-operative VAS pain score 5.4 after CD and 7.7 after TE ($p < .001$).	Resumption of daily activities on day 4.8 after TO and 9.6 after TE ($p < .001$). Subjective complete recovery on day 9.6 after TO and day 14.7 after TE ($p < .001$).	Analgesics use 5.4 d after TO and 9.9 d after CD ($p < .001$).	Np significant difference on 2 week follow-up

TAHSI: tonsil and adenoid health status instrument; HRQoL: health-related quality of life.

Discussion

We conducted a systematic review to assess the value of tonsillotomy versus conventional tonsillectomy for tonsil-related diseases in adults. We identified nine studies comparing the efficacy of tonsillotomy and tonsillectomy. In eight of the nine studies, tonsillotomy was found to be as effective as tonsillectomy, and in all nine studies, it was associated with less pain, a shorter period of recovery, and a shorter duration of surgery.

This systematic review confirms that tonsillotomy versus tonsillectomy in adults has been scarcely studied. Our search only revealed nine papers describing randomized controlled trials or cohort studies comparing intracapsular tonsillotomy with extracapsular tonsillectomy, with a combined population of 770 patients. These studies made use of a variety of tonsillotomy methods, inclusion criteria, and outcome measures, which led to poor inter-comparability and therefore no meta-analysis could be performed. Furthermore, some of the studies were of questionable quality. The study by Bender et al. was the only study of relatively high quality, with a clearly stated randomization and sufficient patients to meet predefined power. Unfortunately, this study had a relatively high percentage of lost-to-follow-up of 16%, and blinding of outcome assessment was not mentioned. A per-protocol analysis was performed, but an intention-to-treat analysis would have been preferred in this study.[13] The study by Nemati et al. had a high dispersion in follow-up time (range 12–24 months) and reported sparse data on group differences. Therefore, possible bias cannot be evaluated thoroughly.[14] Arya et al. chose a very different study design, in which patients were used as their own controls. The number of studied patients was small, with only 14 included patients, and follow-up for pain evaluation was as short as 24 hours. Therefore, no meaningful statements can be made on pain, symptom improvement, and post-operative bleeding. The study reported one complication, a PTH, but it did not state which type of intervention led to this complication. Moreover, patients being their own controls has its limitations in the context of the current interventions, since, for example, it may be hard to distinguish pain or discomfort from one side or the other.[10]

The study on the Swedish cohort reported on a more substantial number of patients (n = 76) with a total follow-up period of 6 years. Unfortunately, patients were not blinded to treatment, and randomization and allocation were not stated. Therefore, subsequent bias cannot be ruled out. Patients lost to follow-up were excluded from the analyses, which may potentially have led to classification bias.[7–9] The study by Hall et al. [11] was, of all RCTs, most prone to bias. Randomization was based on order of presentation and was done before invitation to participate. Also, blinding was not performed correctly

since two patients were operated on by the primary investigator. Besides, there was no statistical correction for missing data during follow-up.

The study by Lourijsen et al. is limited by a non-randomized, non-blinded study design with a high loss-to-follow-up in both treatment groups.[4] A selection bias of highly motivated patients is expected for the tonsillotomy treatment group since most of these were redirected especially to that specific hospital for outpatient laser treatment of their tonsils. The indication for surgery was significantly different between both groups (halitosis and tonsillolithiasis were predominantly treated with tonsillotomy), which makes the suspicion of selection bias stronger. Furthermore, CO2 laser tonsillotomy, an intervention with a clear learning curve, was not solely performed by an experienced laser surgeon but also by less experienced residents. Follow-up was 1 year, but tonsillitis has been shown to recur postoperatively predominantly after 1 year.[15]

The study by Johnston et al. has a retrospective study design with its inherent information bias and patient- and treatment-selection bias. This study sought to evaluate differences between teens and adults treated with powered intracapsular tonsillectomy or monopolar electrocautery tonsillotomy, and all analyses were based on this grouping. Therefore, no analysis was performed between both treatments, and thus nothing can be said about the statistical significance of the reported findings. The sizes of the groups were very disparate, and the indications for intervention varied greatly as well.[12]

In summary, the selected randomized controlled studies and cohort studies on tonsillotomy in adults are very diverse with regard to study population, surgical methods used, and outcomes measured. Thus, they cannot be compared to each other, and therefore the efficacy could not be evaluated by means of a meta-analysis. A better powered, well-designed randomized controlled trial needs to be undertaken to compare the efficacy and safety of tonsillotomy and tonsillectomy in adults and to allow for generalizable conclusions regarding the preferential surgical approach for tonsil surgery in adults. Especially, recovery and complication rates should be evaluated and put in light of socio-economic perspectives. Furthermore, confounding by indication should be assessed beforehand during patient inclusion.

Several procedural differences between tonsillotomy and tonsillectomy may explain the rather positive results that were reported in the few studies that we identified. Compared to tonsillectomy, tonsillotomy entails the removal of a smaller amount of tissue, while the major nerves and vessels running in the tonsillar bed to the tonsillar capsule are retained, and only the smaller nerves and vessels that radiate into the lymphoid outer part of the tonsil are affected. This may limit the risk of PTH and post-operative pain.

This assumption is supported by comparative studies of both interventions in pediatric populations, where this topic has been studied much more thoroughly. However, the anatomy of the palatine tonsillar region is strikingly different in children and adults. In children, the palatine tonsils lay relatively loose in the tonsillar bed and are only loosely connected by the vessel-nerve bundle between the tonsillar bed and tonsillar capsule. In adults, on the other hand, the palatine tonsils are often more rigidly connected to the tonsillar bed, and this connection is often enhanced by recurrent or chronic tonsillar infections. Therefore, tonsillectomy in adults is generally more time-consuming, has a longer post-operative recovery time, and is more frequently accompanied by PTH.[16] Consequently, clinicians are generally much more reticent in performing tonsillectomy in adults than in performing the same operation in children.[13,14]

Different methods for tonsillectomy and tonsillotomy have been described. The literature comprises reports on the use of CO2 laser, coblation, shaver (microdebrider), diode laser, and radiofrequency. All these methods can be used for extracapsular tonsillectomy as well as for intracapsular tonsillotomy. However, regardless of the method used, tonsillotomy will result in less pain and lower post-operative bleeding rates. At present, conclusive evidence supporting the supremacy of any surgical technique is lacking.

Two recent Cochrane reviews on tonsillectomy could not find a difference in morbidity between cold knife dissection and diathermy tonsillectomy, nor could they find a difference in post-operative pain or in the speed and safety of recovery between coblation and other tonsillectomy interventions. Magdy et al. could not find a difference in tonsillar fossa healing when comparing coblation, dissection, and laser-assisted tonsillectomy, but monopolar cautery did show a slower healing process after 7 and 15 days.[17] Coblation was associated with less thermal damage to surrounding tissue, which was presumed to be the result of the relatively low temperatures needed for sustaining the necessary plasma field. Currently, there is no sufficient evidence in favor of any method for tonsillectomy or tonsillotomy, and the choice of a surgical method is, at present, only based on the surgeon's preference and the availability of equipment.

Tonsillotomy as a surgical method for tonsil-related diseases and afflictions is associated with several limitations. First, tonsillotomy is contraindicated when tonsil-related malignancy is suspected. In these cases, the tonsil should be preserved for examination by a pathologist, and tumor spread needs to be prevented. Second, although there is currently no evidence to support transmission of Creutzfeldt–Jakob disease through inhalation of vaporized tissue, some have suggested that this may be a theoretical risk. This risk is thought to be extremely low, but guidelines indicate that there is no hard data available. Third, the possibility of post-operative tonsillitis caused by residual tissue

should be taken into account. Even though tonsillar remnants are also found after tonsillectomy, tonsil residues are always present in tonsillotomy and may (theoretically) lead to post-operative tonsillitis. No increase in post-operative tonsillitis rates was reported in the included studies, but there is no strong evidence that there is no difference in post-operative tonsillitis. Fourth, the possibility of regrowth of tonsils after tonsillotomy is often mentioned. Unfortunately, the risk of regrowth of tonsils in adults after tonsillotomy has not been reported in the literature and is thus a matter of 'expert' opinion. In adults, however, natural involution of the palatine tonsils is seen, and thus significant regrowth of tonsils in adults would be unexpected.[7,18] In children, there are some data on regrowth: Doshi et al. reviewed 636 medical records of children that underwent tonsillotomy and concluded that there is a small risk of tonsillar regrowth and that regrowth is five times more likely at an age <5 years. Their findings were in concordance with the findings of other authors. Patients in the study on the Swedish cohort had surgery primarily for obstructive symptoms. At 6-year follow-up, no differences in snoring index or HRQL were found between the two treatments.[9] This finding was in concordance with the studies by Hultcrantz et al. and Eviatar et al., which found similar effectiveness of tonsillotomy compared to tonsillectomy in children with pOSAS after 10 years of follow-up. Based on these data and on our own clinical experience with tonsillotomy, we expect the need for secondary tonsillotomy caused by regrowth in adults to be low.

As was mentioned before, different surgical methods for tonsillotomy have been put into practice, but the inter-comparability between studies is lacking. The less invasive nature of a tonsillotomy enables surgeons to perform tonsillotomies in an outpatient clinic setting using only local anesthesia without sedation,[4,19,20] thereby reducing the morbidity of tonsil surgery. Tonsillotomy under local anesthesia can drastically reduce the costs of tonsil surgery since the need for general anesthesia and its associated specialty care disappears.

Other cost savings can possibly be found in the change in surgical tools, in the reduction of pain, and in the reduced risk of PTH. A decrease in PTH does not only lead to a significant decrease in morbidity and mortality, but also reduces the costs of in-hospital stay, readmission, and re-intervention. A reduction in pain leads to a decreased use of pain medication, earlier discharge from the hospital, and earlier return to work or school and study, which results in considerable socioeconomic gain.

Conclusion

Current evidence suggests that the efficacy of tonsillotomy and tonsillectomy in adults is equal and that tonsillotomy is preferable in terms of pain, use of analgesics, patient satisfaction, operation time, and post-operative complications. Post-operative hemorrhages were more frequent after tonsillectomy. This review only identified nine randomized controlled trials and cohort studies comparing the efficacy and safety of tonsillotomy and tonsillectomy in adults suffering from tonsil-related diseases and afflictions. An adequately powered, thorough, and well-designed randomized controlled trial should be performed to conclusively bridge the knowledge gap necessary to clinically decide which method should be used in which patient.

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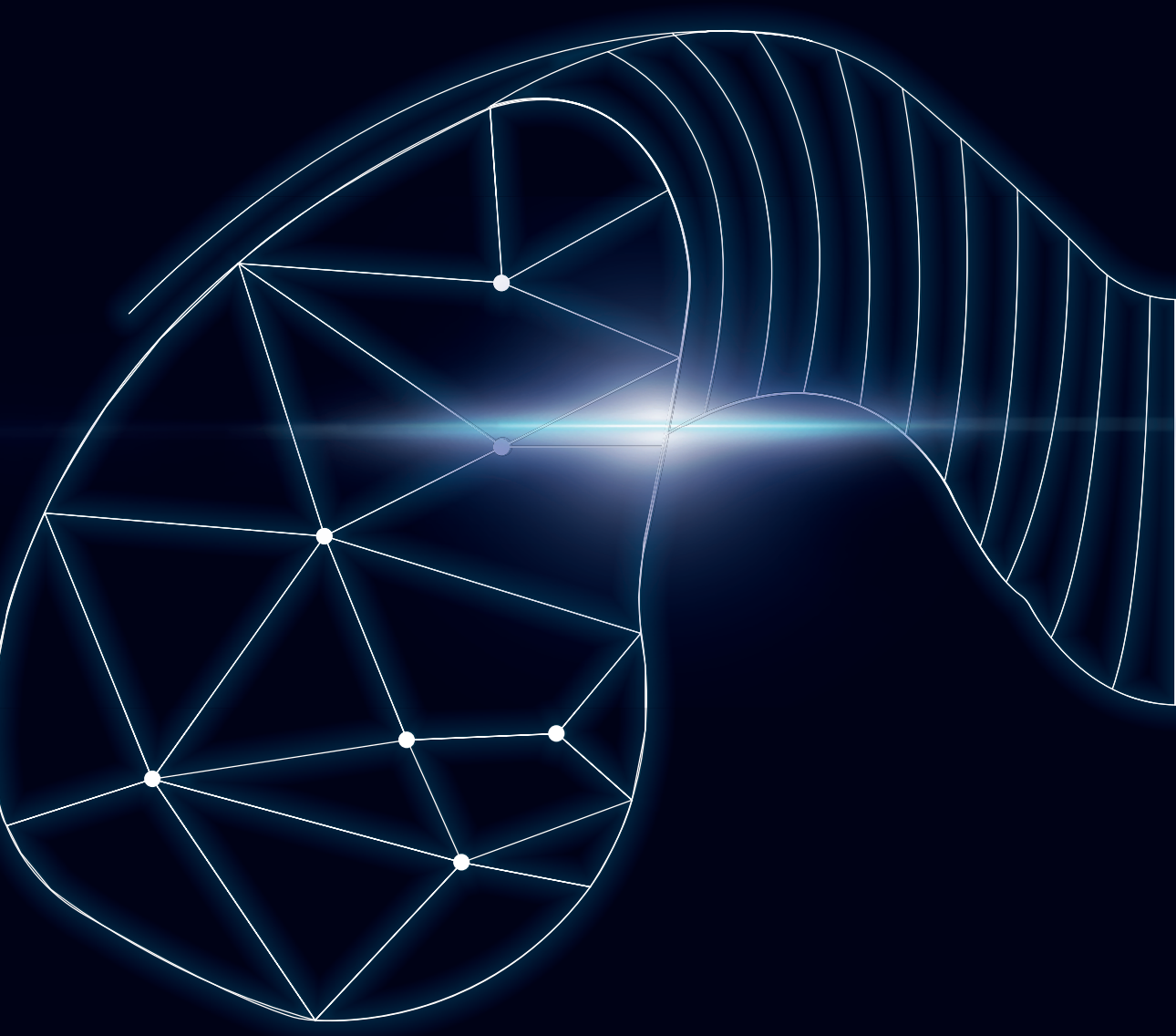

CHAPTER 3

Post-operative morbidity and 1-year outcomes in CO2-laser tonsillotomy versus dissection tonsillectomy

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Abstract

Objective: In this study a type of partial tonsil surgery, CO2-laser tonsillotomy, was compared to regular tonsillectomy. The effectiveness and post-operative recovery rate of both interventions in adult patients was assessed by using a questionnaire.

Study design: Prospective follow-up non-randomized cohort study.

Method: One hundred and seven adults were included; 46 tonsillectomies and 61 tonsillotomies were performed. Patients in the tonsillectomy group underwent general anesthesia, while tonsillotomy was performed in an ambulatory setting with local anesthesia. Post-operative questionnaires were administered by mail after 2 weeks, 6 months, and 1 year to assess recovery rate and symptom recurrence.

Results: In total, 72.5% of patients were cured from their initial symptoms after tonsillotomy. Three patients (7.5%) required re-surgery for their initial complaints. After tonsillectomy, 97.2% of patients were cured. Both groups showed equally high satisfaction scores after treatment. Post-operative evaluation after 2 weeks showed a mean pain-intensity score of 5.4 (Visual Analogue Scale 0–10) after tonsillotomy and a mean pain-intensity score of 7.7 after tonsillectomy. The post-operative use of analgesics was twice as long in the tonsillectomy group compared to the tonsillotomy group and the tonsillectomy group required twice as many days for full recovery. After tonsillectomy a higher rate of major post-operative hemorrhage was seen.

Conclusion: CO2-laser tonsillotomy is associated with a shorter and less painful recovery period. Both surgical methods are equal in terms of long-term satisfaction, although tonsillotomy comes with a higher recurrence rate of mild symptoms. A strict pre-operative patient selection for CO2-laser tonsillotomy is necessary.

Introduction

In the Netherlands, conventional dissection tonsillectomy (TE) is performed when conservative treatment fails in adults with tonsillar disease. After TE, post-operative morbidity remains a major clinical problem.[1,2] The high prevalence of long-lasting post-operative pain and risk of post-operative hemorrhage have made otorhinolaryngologists search for other alternative techniques. New techniques for removing the pharyngeal tonsils are developing and primarily consider partial removal, so-called tonsillotomy. As opposed to TE only the tonsillar crypts, which play a major role in infection, are securely ablated.

A prospective pilot study investigating the effect of CO2- laser tonsillotomy (TO) in adult patients has been initiated at the ENT department in the HagaZiekenhuis, with the first promising results published in 2009 by Datema et al.[3] To assess proper potential of TO, there is need for a comparison with TE. The primary aim of this prospective study is to compare TO and TE with respect to post-operative morbidity and success rates. Initially a prospective randomized trial was started (SMOKE study). Unfortunately, as the Haga-Ziekenhuis was the only centre in the Netherlands performing the outpatient laser tonsillotomy, patients travelled from far to have the TO performed and many could not be motivated to participate in a randomized trial. Therefore, the study design was changed to the next best, which is this cohort study. The goal of this study is to determine the position of TO in the treatment of tonsillar disease in otolaryngological practice in the Netherlands

Materials and Methods

Participants (figure 1)

This study was conducted between September 2012 and January 2014. The study population existed of recruited patients more than 16 years of age suffering from established recurrent tonsillitis (defined as more than five episodes of tonsillitis a year, according to the national guideline[4]), halitosis, tonsilloliths, tonsillar hyperplasia causing partial airway obstruction, or dysphagia. Exclusion criteria for TO were a strong gag reflex, inability to keep the mouth open, and previous tonsillotomy. Specific exclusion criteria for both procedures were a history of peritonsillar abscess and bleeding disorders. In the study period 193 outpatients were diagnosed with any 'adenoid and tonsillar disorder'. Of these patients, 114 were indicated for TE or TO. Seven patients already underwent tonsil surgery once before and were, therefore, excluded from participation in this study. Eventually, 107 patients were included and either allocated to TE or had a freedom of

choice **(Figure 1).** All patients were provided with clear information about both procedures, so a deliberate choice could be made. Thirty-six patients (33.6%) were excluded for TO and were advised to undergo TE. The TE group consisted of 46 patients (n = 46) and TO was performed in 61 patients (n = 61).

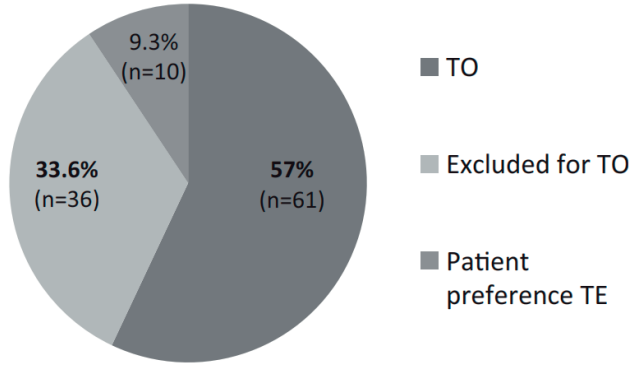

FIGURE 1. DISTRIBUTION OF TONSILLECTOMY (TE) AND TONSILLOTOMY (TO) IN PATIENTS

Table 1. Demographic characteristics for TE and TO after inclusion

Characteristic	TE (n = 46)	TO (n = 59)	Total, n (%)	Level of significance
Gender, n (%)				**NS**
Male	15 (32.6%)	13 (22.0%)	28 (26.7%)	
Female	31 (67.4%)	46 (78.0%)	77 (73.3%)	
Mean age, years (SD)	25.3 (±7.9)	29.7 (±9.6)		**p = 0.014**
Smoking status, n (%)				**NS**
Unknown	3 (6.5%)	5 (8.1%)	8 (7.6%)	
Yes	11 (23.9%)	11 (18.6%)	22 (21.0%)	
No	32 (69.6%)	43 (72.9%)	75 (71.4%)	
Working in environment with children, n (%)				**NS**
Unknown	9 (19.6%)	10 (17.2%)	19 (18.1%)	
Yes	3 (6.5%)	6 (10.2%)	9 (8.6%)	
No	34 (73.9%)	43 (72.9%)	77 (73.3%)	
Ethnicity, n (%)				**NS**
Unknown	6 (13.0%)	2 (3.4%)	8 (7.6%)	
Caucasian	33 (71.7%)	53 (89.8%)	86 (81.9%)	
Asian	—	1 (1.7%)	1 (1.0%)	
East-European	7 (15.2%)	3 (5.1%)	10 (9.5%)	
Indication surgery, n (%)				**p = 0.0012**
Recurrent tonsillitis	41 (89.1%)	40 (67.8%)	81 (77.1%)	
Tonsillolithiasis	3 (6.5%)	13 (22.0%)	16 (15.2%)	
Halitosis	5 (8.5%)	5 (8.5%)	5 (4.8%)	
Partial airway obstruction	2 (4.4%)	—	2 (1.9%)	
Dysphagia	—	1 (1.7%)	1 (1.0%)	
Tonsil size, n (%)				**p = 0.003**
Unknown	13 (28.3%)	2 (3.4%)	15 (14.3%)	
Friedman 1	2 (4.3%)	21 (35.6%)	23 (21.9%)	
Friedman 2	20 (43.5%)	26 (44.1%)	46 (43.8%)	
Friedman 3	10 (21.7%)	8 (13.6%)	18 (17.1%)	
Friedman 4	1 (2.2%)	2 (3.4%)	3 (2.9%)	

Level of sign. = level of significance; NS = Not significant.

Intervention

Trained surgeons performed both procedures. TO was performed as ambulatory surgery in OR, meeting specific criteria for performing laser treatments.[5] Available was a F125 Laser tube by Lumenis, which was set at 25 W in the continuous mode and distributed focused laser energy with a beam diameter of 3 mm. Patients were positioned in a half-supine position, wearing protective glasses and a nose peg. Tonsillar tissue was exposed using a double wooden tongue blade. Local anesthesia was accomplished with Xylocaine 2%/Adrenaline 1:80,000 injected directly into the tonsils and tonsillar pillars. The crypts were evaporated in a sweeping motion until complete cryptolysis was achieved. Patients were instructed to hold their breath during activation of the laser and smoke was evacuated using a smoke evacuator. In case of hemorrhage, hemostasis could be achieved by bipolar coagulation. TE was planned in day care or short clinical stay. Hemostasis was achieved with gauzes or bipolar coagulation if necessary. All patients received standard post-operative care and were discharged with the advice to use paracetamol 1000 mg 4-times a day and diclofenac 50 mg 3-times a day if necessary.

Outcome

Primary outcome variables of the study were post-operative pain scores, using a Visual Analogue Scale (VAS), rate of patient recovery and long-term outcome. A best- and worst case outcome analysis was performed. Secondary outcome variables were per operative results, complications and patient satisfaction. Patients were interviewed at 2 weeks, 6 months, and 1 year post-operatively using a questionnaire that was sent by e-mail after telephone contact **(Appendix).** Any post-operative complications and visits were extracted, if possible, from the patient's medical file.

Statistics

All data were collected in a custom MS-Access database. Statistical analysis was performed with SPSS Statistics for Windows, version 20.0. All statistical significance was set at $p < 0.05$. A descriptive analysis was performed. Quantitative group data differences were analysed using an unpaired t-test or Mann-Whitney U-test, with multiple linear regressions performed to adjust for age and gender. Associations between categorical variables were analysed using a Chi-square-test or Fisher's exact test. Logistic regression was performed if applicable. Missing data were handled by pairwise deletion.

Results

Demographic data is presented in **Table 1**. A follow-up flowchart is presented in **Figure 2**. TO was terminated in two patients due to excessive gag reflexes. These patients were not included in the further post-operative analyses.

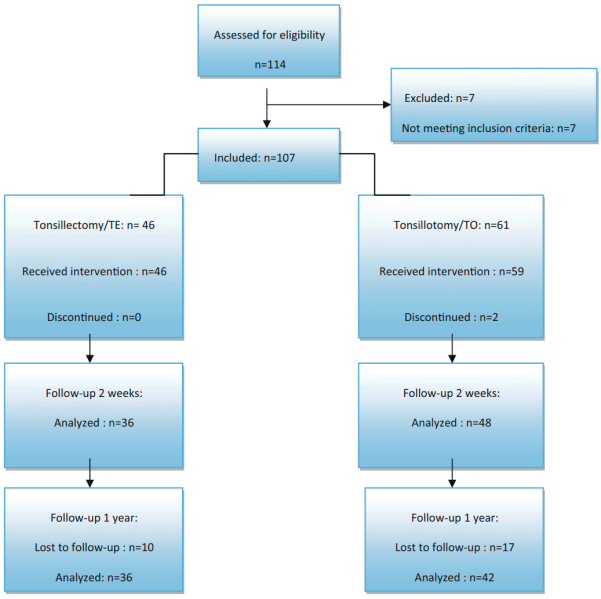

FIGURE 2. FLOWCHART OF TONSILLECTOMY (TE; N = 46) AND TONSILLOTOMY (TO; N = 61) PATIENTS THROUGH STUDY PERIOD.

Per Operative Results

Total operation time was calculated as evaporation time needed in TO and as the time from insertion of the mouth gag until removal in TE. Mean evaporation time in TO was 17.1 ± 6.6 min vs 22.4 ± 6.8 min in TE ($p = 0.002$, Mann-Whitney U-test). Mean blood loss in TE was 177.7 ml (range = 50–500 ml), vs 0 ml in TO ($p < 0.001$, Mann-Whitney U-test). After TO all patients were discharged directly after surgery. After TE the majority of patients were discharged the same day, but eight patients (17.4%) needed an overnight stay ($p < 0.001$, Fisher's exact test).

Post-operative Pain (Figure 3)

Mean pain scores during the first 2 weeks after surgery were based on a Visual Analogue Scale (VAS), ranging from no pain to worst imaginable pain (0–10). TO patients scored 5.4

(range = 0–9) and TE patients scored 7.7 (range = 2–10) ($p < 0.001$, Mann-Whitney U-test). The TO group used analgesics for 5.4 days (95% CI = 4.2–6.5, SE = 0.6), the TE group used analgesics for 9.9 days (95% CI = 8.7–11.2, SE = 0.6) ($p < 0.001$, Mann-Whitney U-test). TE patients predominantly used non-steroidal anti-inflammatory drugs in combination with paracetamol (62.9%). TO patients mainly used paracetamol only (51.1%).

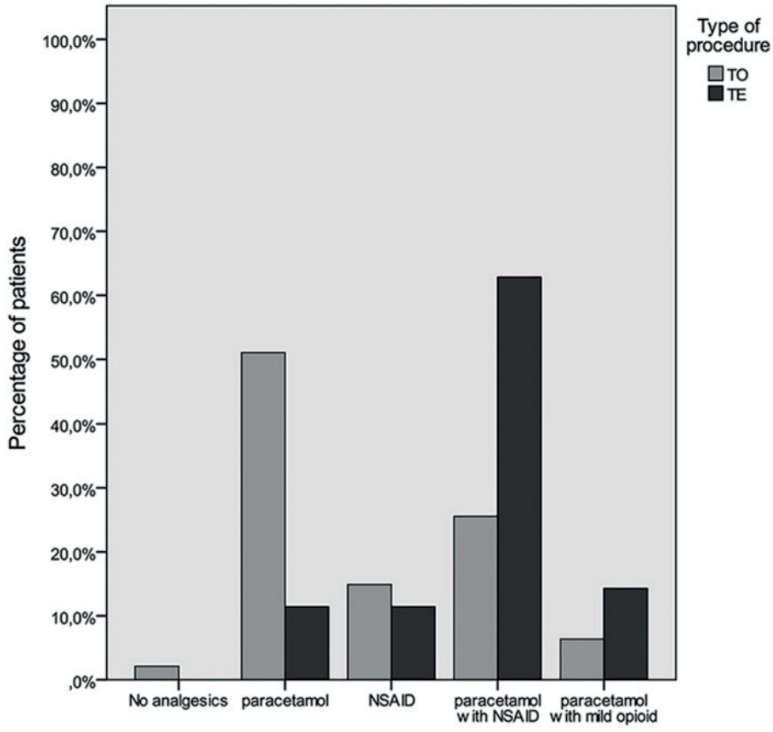

FIGURE 3. DIAGRAM SHOWING THE PERCENTAGE OF PATIENTS IN BOTH TREATMENT GROUPS USING A TYPE OF ANALGESIC DRUG. TE: TONSILLECTOMY; TO: TONSILLOTOMY; NSAID: NON-STEROIDAL ANTI-INFLAMMATORY DRUG (DICLOFENAC 50 MG OR IBUPROFEN 200/400 MG); PARACETAMOL + MILD OPIOÏD (PARACETAMOL 325 MG/ TRAMADOL 37.5 MG OR PARACETAMOL 500 MG/ CODEINE 10–20 MG).

Unscheduled Contact with Physician

Five patients (10.2%, n = 5/49) consulted a physician after TO compared to 14 patients (35.0%, n = 14/40) after TE ($p = 0.005$; 95% CI = 1.53–14.67; Odds ratio = 4.7). These contacts were telephone calls or visits to the outpatient department, general practitioner or emergency department for questions about pain or post-operative bleeding.

Complications

No significant difference in the occurrence of complications between the groups was seen ($p = 0.385$, Fisher's exact test). Three secondary hemorrhages (6.5%) were seen at, respectively, 3, 5, and 7 days post-operatively in the TE group. A severe intake problem (2.2%) was noted to be the reason for re-admission after discharge in one patient who underwent TE. Hemorrhages were managed with bipolar coagulation at the OR in two patients. Other complications after TE included four post-operative infections (8.7%), which were successfully managed with oral antibiotics. In the TO group two patients (4.1%) presented oozing after 6 and 7 days, respectively. Two patients developed an infection (4.1%). All four patients were successfully treated at the outpatient department. No re-admission was required in TO patients.

Patient Recovery Rate (Figure 4)

After 4.8 days (95% CI = 3.6–5.9, SD = 3.0) patients could resume their daily activities or work in the TO group compared to 10.6 days (95% CI = 9.3–11.9, SD = 4.3) after TE ($p < 0.001$, Unpaired t-test). The subjective feeling of complete recovery was 9.6 days (95% CI = 8.2–11.0, SD = 3.7) in TO and 14.7 days (95% CI = 13.2–16.3, SD = 4.9) after TE ($p < 0.001$, Unpaired t-test).

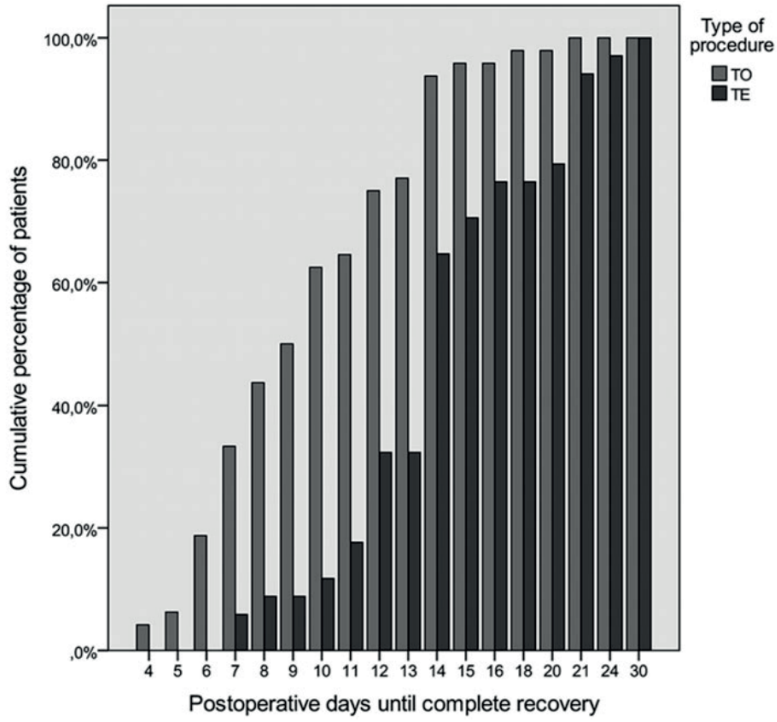

FIGURE 4. DIAGRAM SHOWING THE AMOUNT OF POST-OPERATIVE DAYS AND THE CUMULATIVE PERCENTAGE FOR SUBJECTIVE FEELING OF COMPLETE RECOVERY. TE = TONSILLECTOMY; TO = TONSILLOTOMY;

Satisfaction

After 2 weeks patients were asked to score their feeling of satisfaction about the procedure on a Visual Analogue Scale (VAS), ranging from complete dissatisfaction to high satisfaction (0–10). TO patients scored 8.3 (range = 7–10) and TE patients scored 8.3 (range = 5–10) (p = NS). In 93.6%, patients would recommend the procedure to others after TO, as compared to 73.5% after TE (p = 0.002). Only 57.1% would undergo the procedure again after TE vs 86.8% after TO (p = 0.004).

Success after Procedure (Figure 5)

One year after a first TO procedure, 29 patients (72.5%) were free of their initial complaint compared to 35 patients (97.2%) after TE ($p < 0.001$, Fisher's exact test). A flowchart of treatment courses is shown in Figure 5. Two TO patients with a high peri-operative risk of incomplete cryptolysis, caused by extreme anxiousness, were excluded from this analysis. Eleven TO patients were not free of their complaints. One TE patient suffered from persistent oropharyngeal pain. Both groups were highly satisfied, with a mean of

8.2 (range = 6–10) in TE patients and 8.0 (range = 0–10) in TO patients (NS, Unpaired t-test). After TO 90% would undergo surgery again, in contrast to 27.8% patients after TE (Odds = 27.2).

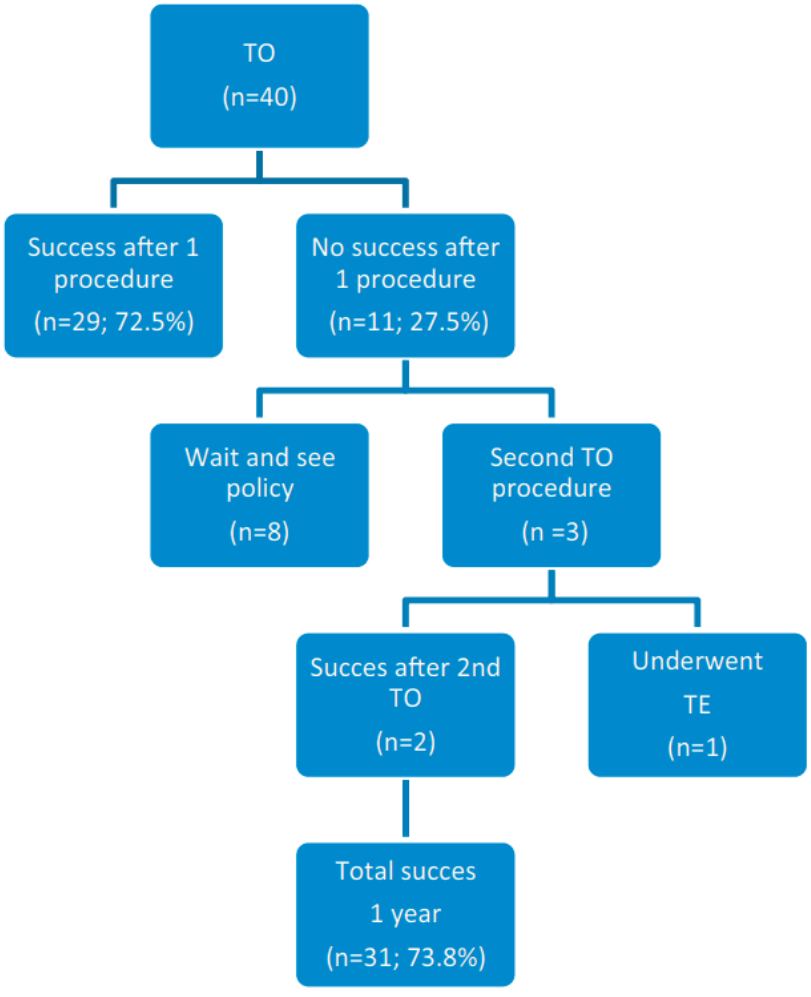

FIGURE 5. FLOWCHART OF COMPLAINTS AND TREATMENT COURSE AFTER TONSILLOTOMY (TO).

Best- and Worst-Case Outcome Analysis (Table 2)

The upper (best case) and lower (worst case) boundaries of the success rates in both groups were established by making missing values positive or negative. In TE patients an interval of 80.7–97.8% for success rate was observed, in comparison to 50.9–76.1%

in TO patients. In both scenarios TE patients had significantly more relief of symptoms. A cross-over analysis was also performed, comparing a best-case scenario in one treatment group with a worst-case scenario in the other treatment group.

TABLE 2. BEST- AND WORST CASE SCENARIO ANALYSIS FOR SUCCESS RATE OF TE AND TO

Scenario	TE (n=46)	TO (n=59)	Level of significance
Best case scenario	97.8%	80.7%	p = 0.011
Worst case scenario	76.1%	50.9%	p = 0.014
Cross-over I[a]	76.1%	80.7%	NS
Cross-over II[b]	97.8%	50.9%	p < 0.000

[a] Cross-over scenario I = best case in TO vs worst case in TE.
[b] Cross-over scenario II = best case in TE vs worst case in TO.

DISCUSSION

To our best knowledge, no studies in adults comparing TE with CO2-laser TO have been performed. Studies that have been published focus on children (mainly for treatment of OSAS) or compare TE with other tonsillotomy procedures (e.g. microdebrider; coblation; radiofrequency ablation)[6–8]. In some countries TO is widely accepted as an alternative for TE and over the last decades a shift towards this technique is noticeable. Recently, even new recommendations were made for tonsil surgery in children in Austria by the Austrian Society of Otorhinolaryngology, aiming to restrict TE to severe cases and to treat all children below the age of 6 years with TO. This new recommendation was preceded by the death of at least five children after post-tonsillectomy hemorrhage in Austrian hospitals in 2006 and 2007.[9]

The CO2-laser used for TO in this study and the preceding pilot study by Datema et al.[3] was chosen, because it was investigated to have potential direct advantages as compared to the dissection technique.[10] Also, no surgical technique has proven superiority in performing partial tonsil resection.[11] The ENT-department of the HagaZiekenhuis decided in 2011 to start a prospective randomized controlled trial, the SMOKE study, to determine the place of TO in tonsil surgery. This study had to be stopped in 2012 due to a lack of patient willingness to participate in randomization. The reason for the impossibility of convincing patients was as follows; our ENT-department located in the HagaZiekenhuis is the only centre in the Netherlands performing TO and, as a result, many patients presenting with tonsil-related complaints are specifically re-directed to our clinic to discuss this laser procedure. A classical TE can be performed in any hospital

in the country. For this reason, the design of the study was changed into a prospective comparative setting.

The initial 193 patients diagnosed with any 'adenoid and tonsillar disorder' during the study period were all patients that were first treated suitably by their general practitioner. In the Dutch national healthcare system patients are referred to the medical specialist in case of major complaints and to discuss surgical options. From this point of view, 114 patients that underwent surgery is within expectations. More females than males undergoing tonsil surgery, which was demonstrated in this study, is in accordance with our National registration centre (CBS).

Less risk of post-operative re-bleeding is observed after TO.[6,12,13] The general reduction in post-operative morbidity in TO patients can be explained by the restricted vaporization of lymphoid tissue and avoidance to damage the tonsilar capsule. All large vessels are packed in the capsule and bottom of the crypts, with only smaller vessels radiating into the lymphoid tissue. This explains why intraoperative bleeding and major post-operative bleeding was not seen during and after TO in this study. Acevedo et al.[8] also support our results by demonstrating a statistically significant lower risk ratio (0.29) of post-operative hemorrhage after TO in comparison to TE, however no differences were seen between intra-operative bleeding. This possibly reflects differences between surgical instrumentation used to perform TO.

Few studies have looked specifically at patients regaining normal activities in the post-operative period comparing TO and TE.[6] However, the study of Ericsson and Hultcrantz supports our findings.[7] Good short- and long-term patient satisfaction after TO procedures is already demonstrated by Krespi et al.[14,15] and Wireklint and Ericsson[16], and these findings are consistent with this study's findings regarding patients prompt resumption of daily activities and self-reported overall high satisfaction. It is surprising though that, after 1-year follow-up, patients were equally satisfied. This suggests that patients with (minor) persisting tonsil related complaints after one or more laser treatments take this for granted.

In 35% of TE patients any physician was contacted with questions regarding discomfort, which was pain mostly. This implies uncertainty about expected symptoms and signs after surgery. TE patients should perhaps be prescribed stronger analgesics (opiates) post-operatively and should be advised to use a strict analgesics regimen.

The shorter period of post-operative pain and earlier return to daily activities after TO yields a potential socioeconomic gain. Also, TO does not require general anesthesia or

hospitalization and this can substantially reduce medical costs. On the other hand, the special equipment purchased for performing TO is currently an investment of at least €60.000 (2014). A proper cost analysis was not conducted alongside this study. In future studies a cost-effectiveness analysis evaluating the socioeconomic costs would be of high value.

Independently of the reduction regarding initial symptoms in the TE patients that were lost to follow-up, effectiveness of surgery after 1 year of follow-up was still equal or better compared to that in TO patients. Opponents of partial tonsillectomy procedures argue the issue of considerable risk of tonsillar regrowth. After TE, success rates of 90%[17,18] compared to 70–93% for TO have been reported.[6,14,19–21] Re-growth of tonsillar tissue has a broad range of 0–26%[6] after TO and few studies report secondary surgery rates in adults.[8] This lack of data highlights the need for more research on this specific topic. The majority of TO patients who were still not free of symptoms in this study chose a wait-and-see policy, while only 7.5% of the total patient group needed revision TO. These results differ from the previously published results by Datema et al.[3], in which 20–25% of patients underwent a second laser session. Krespi and Kizhner[14] describes a second laser session of 16% in 500 reviewed patients with follow-up rates between 1–8 years. This difference in outcomes could reflect an improved TO technique over the years, resulting in less severe complaints after one laser session which could warrant a conservative policy. Another possible factor of influence is the power setting of the laser, which is currently 25 W instead of 18 W, possibly resulting in a more extensive evaporation.[15]

Limitations of the Study

The main limitations of this study are the non-randomized setting and the incomplete follow-up. As a result the current study is prone to bias. The patient group could be biased by highly motivated patients to experience success, after being re-directed especially to our hospital for an intake visit to determine laser TO a suitable treatment option for their complaints. Also, the baseline characteristics for TE and TO patients differed significantly with respect to age, tonsil size, and indication for surgery. First, this difference possibly reflects a surgeons' preference for TE in larger tonsil sizes, considering the higher risk for a second laser session or TE.[3] Second, it is well known that older patients experience more pain after TE[7], which could have been a reason older patients preferred TO. Third, guidelines almost exclusively include recurrent tonsillitis (with a lot of morbidity) as an indication for surgery. Finkelstein et al.[21] and Krespi and Kizhner demonstrated TO a good solution for foetid chronic tonsillitis caused by tonsilloliths.[14] As a result of this finding, tonsillolithiasis was treated predominantly by TO. We, however, believe the study population to be representative for the general patient population presenting with tonsillar problems, because the majority of patients were already indicated for surgery

by other ENT-specialists. Most patients chose to be re-directed to our ENT-department for discussing laser treatment. The best- and worst-case analyses are for the reader to interpret. We believe the patient group that could be followed to be representative for the entire study population as the dropout rate is equal in both groups.

Another point that warrants discussion is the time range of follow-up. The conducted 1-year follow-up could be a relatively short period to assess success rates. Windfuhr and Werner showed recurrence of symptoms to be predominantly after 1 year of follow-up. [19]This stresses the need for an extended follow-up period to establish long-term treatment effects with more certainty. It is also recommended to make a strict pre-operative patient selection, because not every patient is suitable to undergo TO.

Conclusion

Total resolution of complaints after CO2-laser tonsillotomy is 72.5% after one laser session. In another 20% of patients a significant improvement is noticed, with only minor complaints left. No adequate improvement of complaints is seen in 7.5% of patients and a second laser session or tonsillectomy is needed. When indicating a patient for tonsil surgery this has to be kept in mind. The success rate of cold dissection tonsillectomy in this study is 97.2%. Tonsillotomy is associated with a significant shorter time to resumption of normal activities and comes with less post-operative pain compared to dissection tonsillectomy. Both types of surgery bring high overall satisfaction in the short-term as well as after 1 year of follow-up. We advise a strict patient selection before TO is performed: our study group exists mainly of patients suffering from chronic recurrent tonsillitis or tonsilloliths with a tonsil size I or II according to the Friedman classification. Long-term follow-up studies should be conducted for further evaluation of the clinical value of CO2-lasertonsillotomy for tonsil related complaints.

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Disclosure statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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Appendix: Questionnaire used for follow-up after tonsil surgery

Questions for 2-Week Follow-Up:

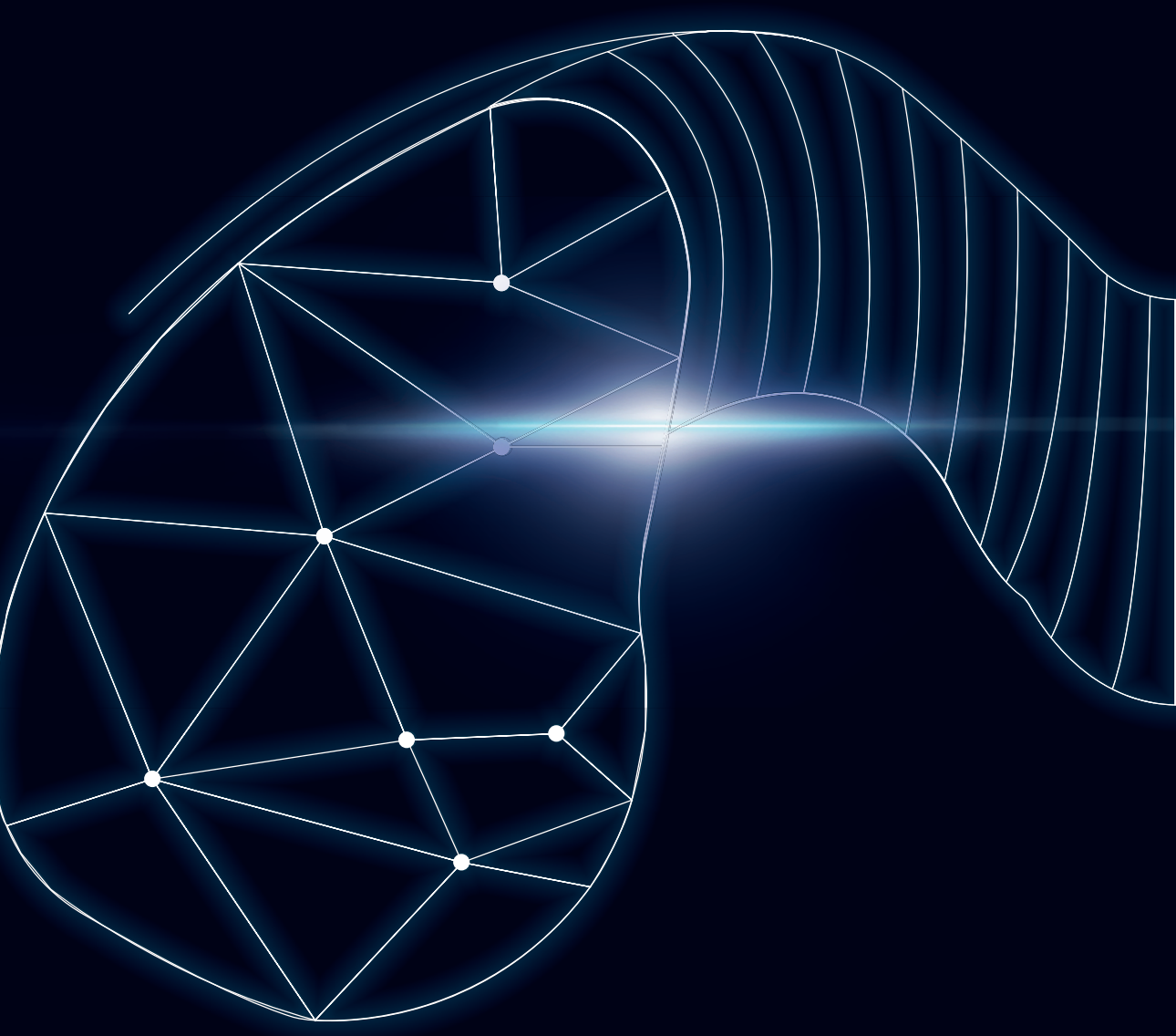
1. Do you work in an environment with children?
2. How intense was your pain?*
3. How many days did you use analgesic drugs?
4. Describe the type(s) of oral analgesics used.
5. After how many days was it possible to resume daily activities?
6. After how many days did you feel completely recovered?
7. Did you visit a GP with complaints related to surgery?
8. If yes, what were your complaints, and was any action needed?
9. Did you visit the First Aid department with complaints related to surgery?
10. If yes, what were your complaints, and was any action needed?
11. Did you receive antibiotics due to a post-operative infection?
12. Would you undergo the same operation again?
13. How satisfied are you in terms of recovery and pain post-operatively?*

*Questions 2 and 13 were based on a Visual Analogue Scale, ranging from 0–10.

Questions for 6-Month and 1-Year Follow-Up:

1. Are you free of the initial complaints?
2. If not, what are your current complaints?
3. For those who had tonsillotomy: how many laser sessions did you have?
4. For those who had tonsillotomy: did you subsequently undergo a tonsillectomy?
5. Would you undergo the same surgery again?
6. How satisfied are you in terms of relief of symptoms?*

*Question 6 was based on a Visual Analogue Scale, ranging from 0–10.



CHAPTER 4

CO2-Lasertonsillotomy Under Local Anesthesia in Adults

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Abstract

Tonsil-related complaints are very common among the adult population. Tonsillectomy under general anesthesia is currently the most performed surgical treatment in adults for such complaints. Unfortunately, tonsillectomy is an invasive treatment associated with a high complication rate and a long recovery time. Complications and a long recovery time are mostly related to removing the vascular and densely innervated capsule of the tonsils.

Recently, CO2-lasertonsillotomy under local anesthesia has been demonstrated to be a viable alternative treatment for tonsil-related disease with a significantly shorter and less painful recovery period. The milder side-effect profile of CO2-lasertonsillotomy is likely related to leaving the tonsil capsule intact.

The aim of the current report is to present a concise protocol detailing the execution of CO2-lasertonsillotomy under local anesthesia. This intervention has been performed successfully in our hospital in more than 1,000 patients and has been found to be safe and to be associated with a steep learning curve.

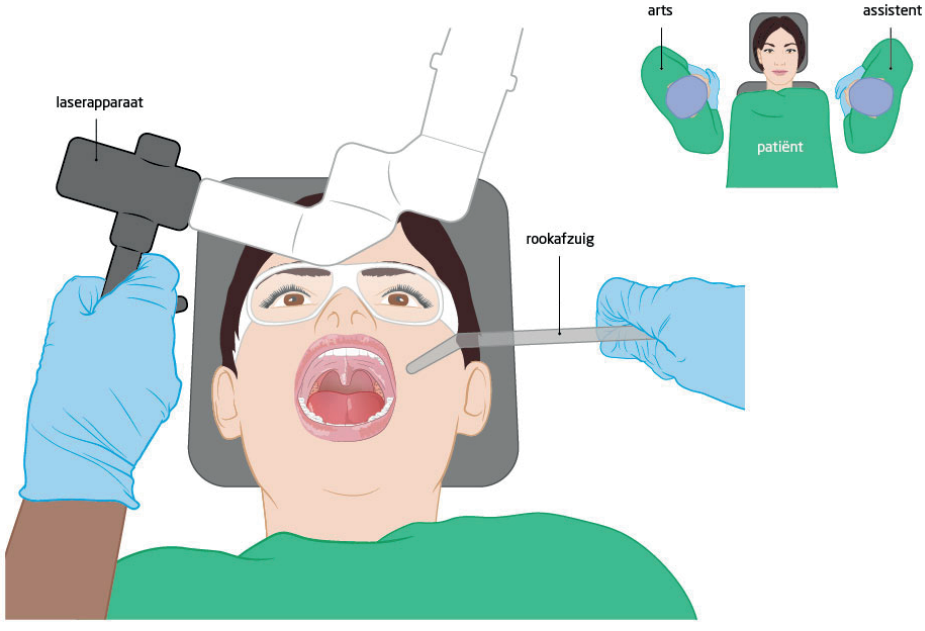

FIGURE 1. OUTPATIENT CLINICAL SETTING OF A CO2 LASERTONSILLOTOMY TREATMENT (UNPUBLISHED IMAGE)

INTRODUCTION

Recurrent tonsil disease is a common health problem resulting in frequent visits to outpatient clinics, antimicrobial treatments, and missed work days.[1] Tonsillectomy is currently the most used surgical intervention for tonsil-related complaints in adults.[2] During a tonsillectomy, the patient is brought under general anesthesia and the entire tonsil, including the tonsil capsule, is removed followed by diathermy coagulation of any bleeding sites. This intervention is rather invasive and associated with significant post-operative morbidity and a long, typically painful, recovery period[3,4]. An alternative to tonsillectomy is tonsillotomy, which is the partial intra-capsular removal of the tonsil tissue.

Both tonsillectomy and tonsillotomy have been performed for millennia.[5,6] The first descriptions of subtotal tonsil removal date back to 1 BC[6]. Since that time many techniques for tonsil removal have been developed including the use of scalpels, microdebriders[7], coblators[8], electrosurgical scissors[9], diode-lasers[10], radiofrequency probes[11] and CO_2-lasers[12].

CO_2-lasertonsillotomy under local anesthesia (CO2LT) for the treatment of tonsil-related complaints is a fairly novel surgical treatment, which is gaining popularity as an alternative for the classic tonsillectomy. Recent studies have shown a shorter and less painful recovery period, but similar overall patient-satisfaction with CO2LT treatment when compared to conventional tonsillectomy.[12,13] During a CO2LT the tonsil is locally anesthetized and only the lobules of lymphatic tonsillar tissue are removed. The tonsillar capsule, through which blood vessels, nerves and lymphatic vessels pass, is left intact. Leaving the tonsillar-capsule intact likely leads to a reduced rate of post-operative bleeding, reduced post-operative pain, and a shorter recovery time[14].

A potential problem with leaving the tonsillar capsule intact can be the incomplete resolution of the tonsil-related complaints, resulting in the need for a secondary CO2LT in a subset of patients[12]. Furthermore, to be eligible for CO2LT treatment patients must be able to remain calm during treatment and their gag reflex intensity should not limit treatment possibilities. The gag reflex is a physiological reflex to protect the airway[15], which can only be partly blunted by local anesthesia in the mouth and pharynx; a particularly strong gag reflex can compromise the safe performance of a CO2LT. To assess the severity of the reflex the Gagging Severity Index (GSI) can be used[15]. The GSI is an index ranging from 1 (very mild) to 5 (very severe) [**Table 1**] and was originally developed in dentistry to classify the intensity of the gagging reflex and its consequences for dental treatments. In any patient with a GSI grade 3 or more the gagging reflex should

first be reduced to increase the odds that the CO2LT procedure will be successful. We advise patients to try to fade out their gag-reflex by "brushing" their tongue-base and tonsils each time they brush their teeth. We have found this exercise to be capable of reducing the gag reflex intensity in most patients by 1-2 GSI points.

TABLE 1: GAGGING SEVERITY INDEX (GSI) SCORE[15]

Dickinson and Fiske Gagging Severity Index grades	**Definition and characteristics of grade of reflex**
Grade I	Very mild, occasional and controlled by the patient.
Grade 2	Moderate, control is required by the patient with reassurance from the dental team.
Grade 3	Moderate, consistent and limits treatment options.
Grade 4	Severe and treatment is impossible.
Grade 5	Very severe, affecting patient behavior and dental attendance and making treatment impossible.

PROTOCOL

1. Patient Selection

1. Consider inclusion of patients with the following tonsil-related diseases: recurrent tonsillitis; dysphagia caused by large tonsils; tonsil stones; obstructive sleep apnea related to tonsils.
2. Include only adult patients.
3. Check for allergies, specifically to local anesthetics.
4. Assess the gag-reflex intensity using the GSI (**Table 1**). For adequate CO2LT treatment, full visualization of the tonsils is required, and patients need to be able to hold their breath for at least 15 s at a time.
5. In patients with a GSI > 2 consider the following exercise to decrease the gag-reflex intensity.
    1. Inform the patient that the gag-reflex can be (partially) faded-out by training.
    2. Explain to the patient that the exercise will be uncomfortable in the first few days to weeks.
    3. Advise the patient to use their toothbrush to gently touch / brush their tongue base and tonsils each time they brush their teeth (preferably twice a day). Instruct the patient to increase pressure when performing this procedure each sequential day.
6. Exclude the following patients: with Friedman grade IV (kissing) tonsils; with undertreated coagulation disorders; using any form of anticoagulants; with an active tonsil infection / peritonsillar abscess; women who are pregnant; those who are uncooperative during tonsil examination.

2. Informed Consent and Pre-operative Instruction Visit

1. Obtain written informed consent including the following.
    1. Explain the intervention to the patient as follows: "The tonsil(s) will be partially evaporated using a laser beam. Local anesthesia will be used to numb the tissue and therefore you will be fully awake and mentally present during treatment. No pain is expected during treatment and low to moderate pain may occur in the first days after treatment. Treatment will take approximately 10-15 min per tonsil. If no complications occur, admission to the floor after treatment is not necessary and you will be able to leave the hospital in 30 min to an hour after treatment, accompanied by a friend or relative that is able to drive you."
    2. Explain alternative treatment options (where applicable: expectant management, conventional tonsillectomy or antibiotics).

3. Explain possible complications of the CO2LT including: per- and post-operative bleeding, infection, incomplete resolution of tonsil disease; need for a second tonsillotomy or a tonsillectomy, pain, allergic reaction to anesthetic, temporary change of taste, (temporary) damage to surrounding structures.

2. Instruct the patient not to eat any heavy meals on the day of treatment.
3. Instruct the patient to take 1,000 mg acetaminophen (paracetamol) 30 min before treatment if acetaminophen is not contraindicated in that specific patient (including, but not limited to active liver disease and liver failure).
4. Ask patients with a troublesome gag-reflex during examination to reduce the gag-reflex by rubbing their tongue base and tonsils with their toothbrush at least twice a day for 1 min, preferably for at least 2 weeks.

3. Preparation of Patient and Equipment

1. Attach the laser pen to the CO_2-laser machine.

FIGURE 2. ATTACHING THE LASER PEN (STILL IMAGE FROM VIDEO PUBLICATION)

2. Make sure that the correct settings are chosen (**Figure 3**) such as (i) continuous laser beam, (ii) 15-30 W intensity depending on the size of the tonsil; generally, start at 18 W and increase the power up to 30 W depending on the size of the tonsils and patient's cooperation, (iii) shape-size of 2-4 mm depending on the size of the (remainder of the) tonsil, (iv) shape: round.

FIGURE 3. PHOTO OF LASER SETTINGS. STANDARD LASER SETTINGS FOR CO2LT ON THE LASER SYSTEM USED.

3. Make sure that the surgeon, the surgical technologist, and the patient are wearing laser safety glasses.

FIGURE 4. LASER SAFETY GLASSES (STILL IMAGE FROM VIDEO PUBLICATION).

4. Make sure that the surgeon and the surgical technologist are wearing appropriate protective surgical masks.

FIGURE 5.PROTECTIVE SURGICAL MASKS (STILL IMAGE FROM VIDEO PUBLICATION).

5. Confirm that the headlight for the surgeon is working.

FIGURE 6. HEAD-LIGHT BEING TESTED (STILL IMAGE FROM VIDEO PUBLICATION).

6. Confirm that a pulse oximeter for patient monitoring is present.

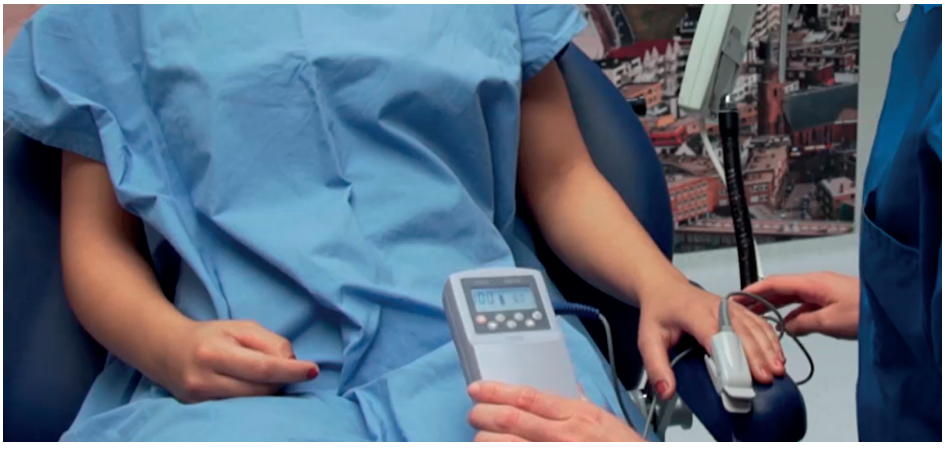

FIGURE 7. PULSE OXIMETER TEST (STILL IMAGE FROM VIDEO PUBLICATION).

7. Confirm that wooden tongue depressors are within reach.

CAUTION: Do not use metal depressors, since they can reflect the laser beam.

4. Time-out Procedure

1. Ask the patient for their name and date of birth.
2. Ask the patient for the intervention that will take place.
3. Ask the patient for the side of treatment.
4. Ask the patient for any allergies, specifically for local anesthetics and medications.
5. Check with the surgical technologist if all equipment is present.
6. Check if the laser-indication light of the operating room is switched on and all windows are covered for laser safety.

5. Patient Instructions Before Surgery

1. Ask the patient to inhale deeply, followed by breathing out slowly during treatment.
2. Explain to the patient that he/she is in control and can signal at any time, which will lead to a pause of the laser-treatment.
3. Instruct the patient to use his/her hand to signal if they wish to pause treatment by tapping the surgeon's leg.
4. Instruct the patient not to swallow any liquids during treatment to prevent aspiration and laryngospasms. Provide a kidney basin to the patient to spit any liquids into when necessary.
5. Reassure the patient not to panic if they experience a feeling as if their airway is blocked, as this is due to local anesthesia of the pharynx region. Remind the patient again that the treatment can be paused at any moment.

6. Positioning the Patient and Inspection of the Tonsils

1. Place the pulse oximeter on the patient's index finger and confirm that it is functioning correctly.
2. Position the patient in an upright position using the chair / table controls.

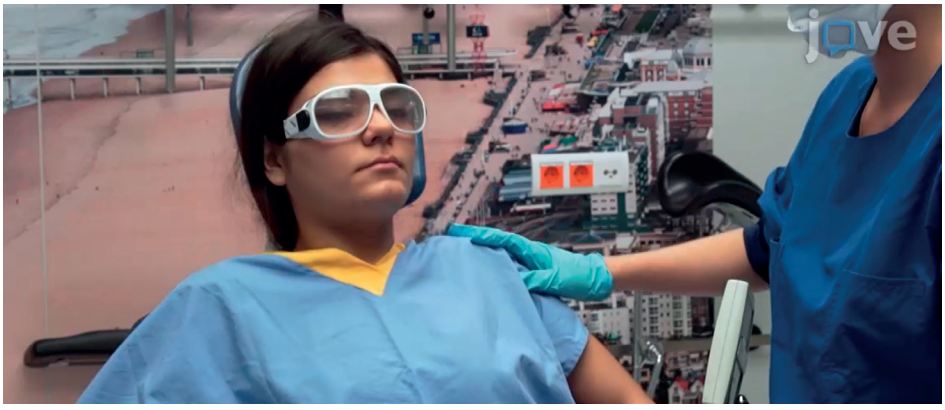

FIGURE 8. POSITIONING THE PATIENT (STILL IMAGE FROM VIDEO PUBLICATION).

3. Set the height of the chair / table so that the surgeon can stand straight comfortably while performing the laser treatment.
4. Ask the patient to make any adjustments to the seating to ensure comfortable and safe positioning.

FIGURE 9. CONFIRMING PATIENT IS SEATED COMFORTABLE AND STABLE (STILL IMAGE FROM VIDEO PUBLICATION).

5. Inspect both tonsils and exclude active inflammation.

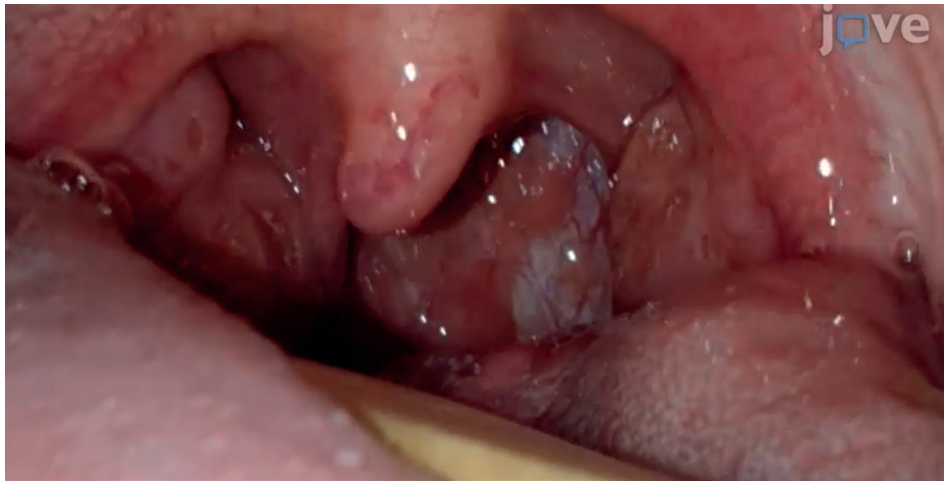

FIGURE 10. INSPECTION OF THE TONSILS (STILL IMAGE FROM VIDEO PUBLICATION).

6. Assess the gag-reflex using the GSI and judge the feasibility of the laser treatment. For adequate CO2LT treatment, the surgeon should be able to fully visualize the tonsils and patients need to be able to hold their breath for at least 15 s.

7. Anesthesia of the Tonsil

1. Tell the patient that the tonsils will be anesthetized one at a time.
2. In case of a significant gag-reflex (GSI grade 2-3) use xylocaine-spray or superficial anesthesia of the tongue-base and pharynx to reduce the gag-reflex.

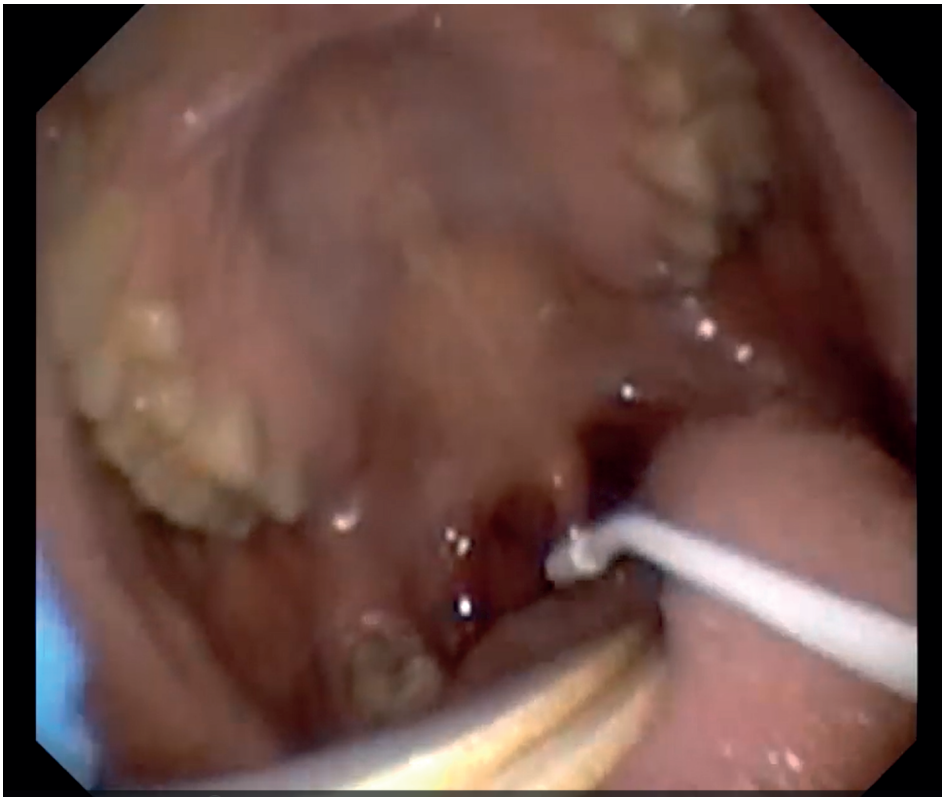

FIGURE 11. LOCAL ANESTHESIA WITH XYLOCAINE SPRAY TO REDUCE THE GAG-REFLEX (STILL IMAGE FROM VIDEO PUBLICATION).

3. Take an ampule with local anesthetic and inject ~0.2 mL slowly into the upper pole, ~0.2 mL into the mid-pole and 0.2 mL into the lower-pole of the tonsil.

NOTE: Optionally, the tonsil-pillars can be infiltrated as well. This is recommended when the tonsils are hidden behind the pillars or to decrease the gag-reflex.

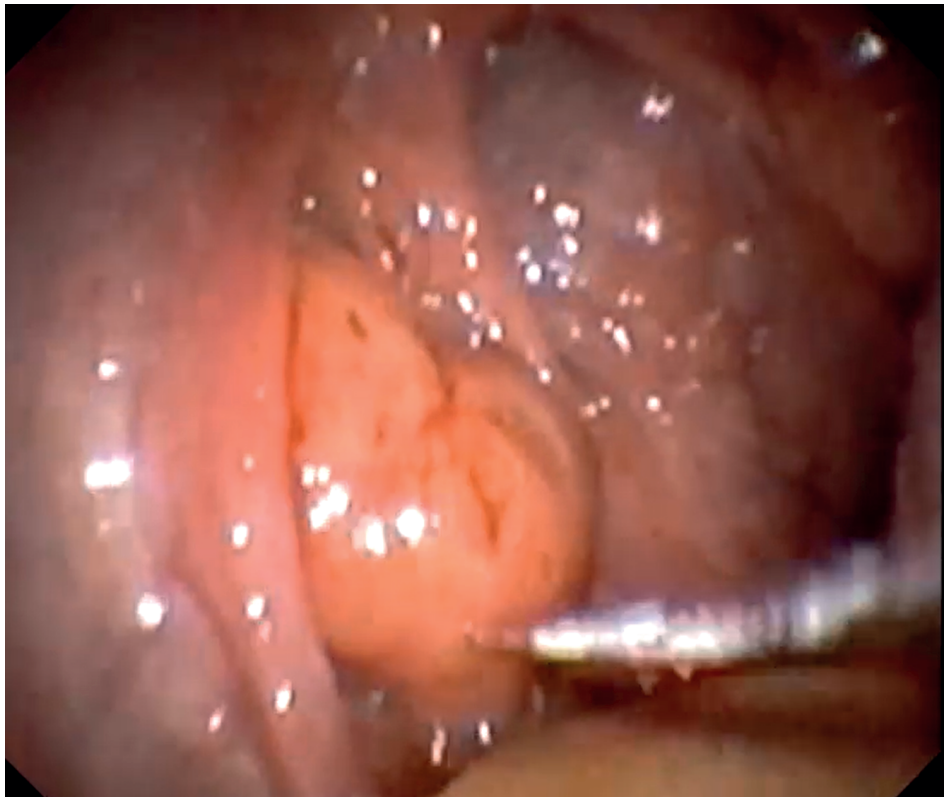

FIGURE 12. LOCAL ANESTHESIA OF THE TONSIL WITH LIDOCAIN-ADRENALINE INJECTIONS (STILL IMAGE FROM VIDEO PUBLICATION).

4. Instruct the patient not to swallow any local anesthetic, but to spit it out.

FIGURE 13. EXPECTORATION OF EXCESS LOCAL ANESTHETIC TO PREVENT UNNECESSARY THROAT TIGHTNESS (STILL IMAGE FROM VIDEO PUBLICATION).

5. Reassure the patient that any feeling of throat tightness is due to the anesthetic; not due to any actual obstruction.

FIGURE 14. EXPLAINING THAT THE SENSATION OF THROAT TIGHTNESS IS CAUSED BY THE ANESTHETIC USED (STILL IMAGE FROM VIDEO PUBLICATION)

8. Laser-treatment of the Tonsil

1. Ask the patient to breathe in deeply and exhale slowly.

FIGURE 15. ASKING THE PATIENT TO BREATHE IN DEEPLY AND EXHALE SLOWLY DURING THE LASER TREATMENT (STILL IMAGE FROM VIDEO PUBLICATION).

2. Have the surgical technologist hold the smoke suction close to the opening of the mouth, without blocking the surgeon's view.

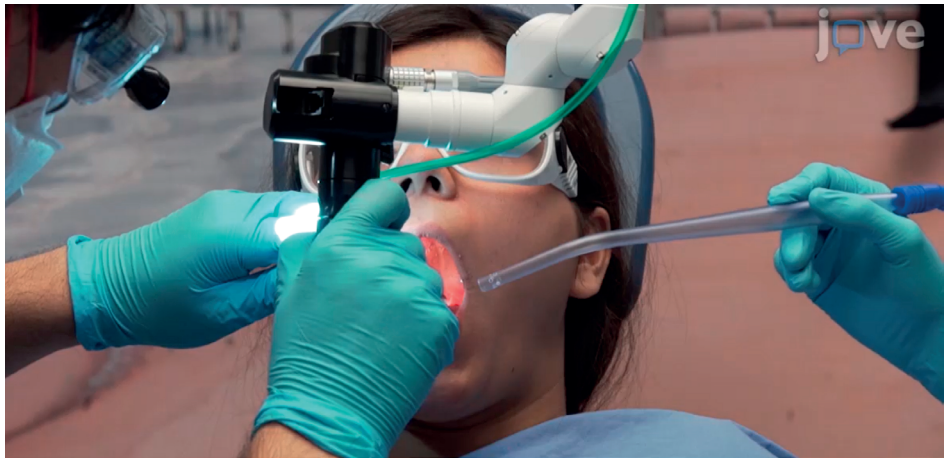

FIGURE 16. SMOKE-SUCTION DEVICE IN PLACE DURING LASER TREATMENT (STILL IMAGE FROM VIDEO PUBLICATION).

3. Use two wooden tongue blades to depress the tongue / tongue-base and expose the tonsil.

FIGURE 17. EXPOSURE OF THE TONSIL WITH LASER PEN READY (STILL IMAGE FROM VIDEO PUBLICATION).

4. During the patient's exhalation, laser the lymphatic tissue of the lobules in a sweeping motion.

FIGURE 18. TONSIL TISSUE BEING EVAPORATED IN A SWEEPING MOTION WITH THE CO2 LASER (STILL IMAGE FROM VIDEO PUBLICATION).

5. Stop when the patient taps your (the surgeon's) leg.

FIGURE 19. PATIENT TAPPING THE SURGEONS LEG TO SIGNAL THE NEED TO CATCH A BREATH (STILL IMAGE FROM VIDEO PUBLICATION).

6. Let the patient catch his/her breath again and repeat steps 8.1–8.4 until complete cryptolysis is accomplished.

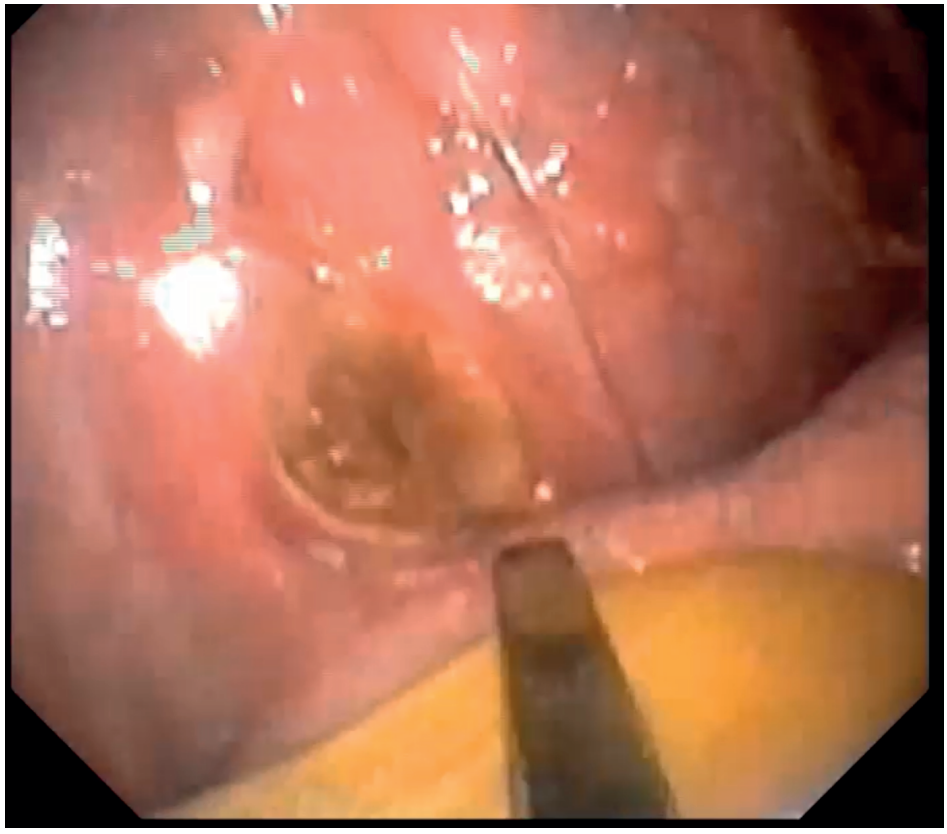

FIGURE 20. TONSIL TISSUE EVAPORATED (STILL IMAGE FROM VIDEO PUBLICATION).

7. If necessary, inject extra local anesthetic (with or without epinephrine).

9. Tips for Laser Treatment

1. In case of peroperative hemorrhage: laser the spot that is bleeding "out of focus". This will lead to burning of the lymphatic tissue with crust formation with a similar effect as coagulation (opposed to evaporation when using the laser 'in focus'). Alternatively, use a (bipolar) coagulation device to stop the bleeding.
2. Use the wooden tongue blades to press against the anterior tonsillar pillar to expose the tonsil further.

FIGURE 21. WOODEN TONGUE DEPRESSOR USED TO MOVE THE ANTERIOR TONSILLAR PILLAR FOR BETTER TONSIL EXPOSURE.

3. Use the wooden tongue blades to press against the upper part of the tonsil pillars to expose the upper lobule of the tonsil.

FIGURE 22. UPPER PART OF THE TONSIL EXPOSED BY MOVING THE ANTERIOR TONSILAR PILLAR OUT OF THE WAY (STILL IMAGE FROM VIDEO PUBLICATION).

4. Use the wooden tongue blades to scoop up the lower tonsil lobule and expose it for laser treatment (one can leave them scooped up on the tongue blades).

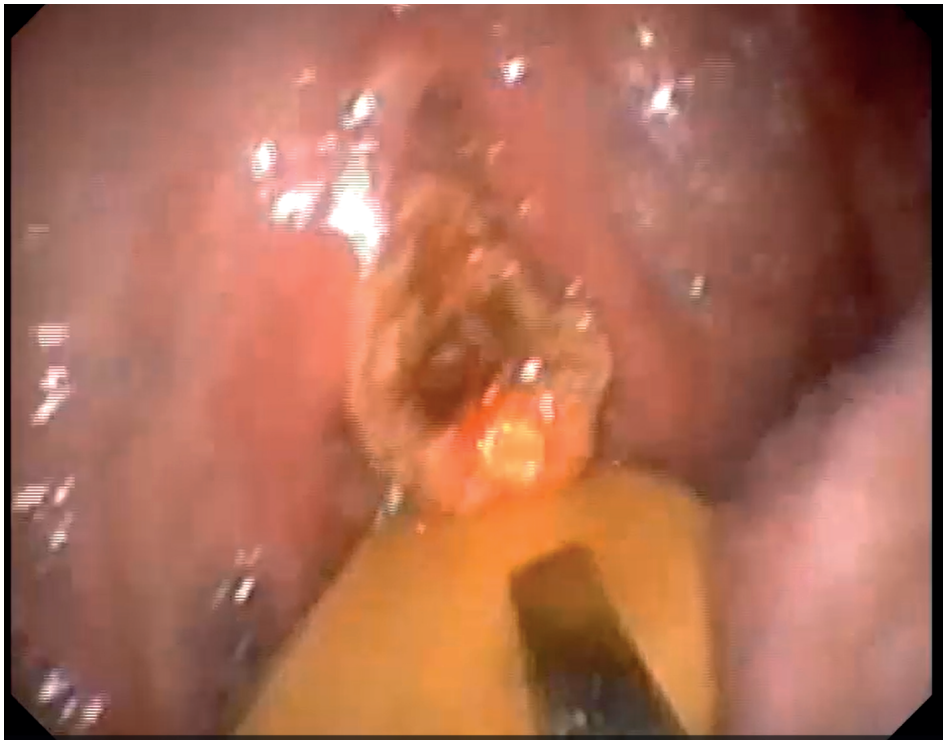

FIGURE 23. "SCOPING UP" THE LOWER TONSILLAR LOBULE WITH THE WOODEN TONGUE DEPRESSOR FOR TREATMENT (STILL IMAGE FROM VIDEO PUBLICATION).

10. Instructions After Treatment

1. Give the patient a popsicle for a minimum of 30 min of postoperative observation.
2. Instruct the patient not to drink or eat anything else for 2 h until the local anesthetic has worn off to prevent aspiration.
3. Instruct the patient not to drink / eat hot (temperature) or spicy drinks/food or food with hard crusts for a week to prevent postoperative bleeding.
4. Tell the patient to take pain medication only if necessary.

NOTE: We advise a maximum of 1,000 mg acetaminophen (paracetamol) 4 times a day, if necessary.

5. Tell the patient to refrain from strenuous physical exercise for a week.
6. Advise the patient to go to the nearest emergency department in case a postoperative bleeding occurs. Advise the patient to contact the ENT department in case of a postoperative infection (e.g. fever).

Representative Results

In a previously published prospective study in 107 patients with one year follow-up, postoperative questionnaires were used to assess recovery rate and recurrence of tonsil-related symptoms for CO2LT compared to conventional tonsillectomy[12]. Forty-six patients underwent conventional tonsillectomy under general anesthesia and 61 patients underwent CO2LT. In total, 72.5% of patients in the CO2LT group were cured from their tonsil-related symptoms. Three patients (7.5%) in the CO2LT group required revision surgery for recurring tonsil complaints. In the tonsillectomy group, 97.2% of patients were cured after initial treatment. The overall satisfaction rate was similar in both treatment groups, but the mean pain intensity scores two weeks post-operatively were 5.4 (out of 10, range 0-9) after tonsillotomy and 7.7 (out of 10, range 2-10) after tonsillectomy leading to longer (9.9 vs. 5.4) use and use of stronger pain medication (NSAIDs / opioids versus acetaminophen) after tonsillectomy. Days to full recovery and number of post-operative bleeding events were both significantly higher in the tonsillectomy group (**Figure 24**).

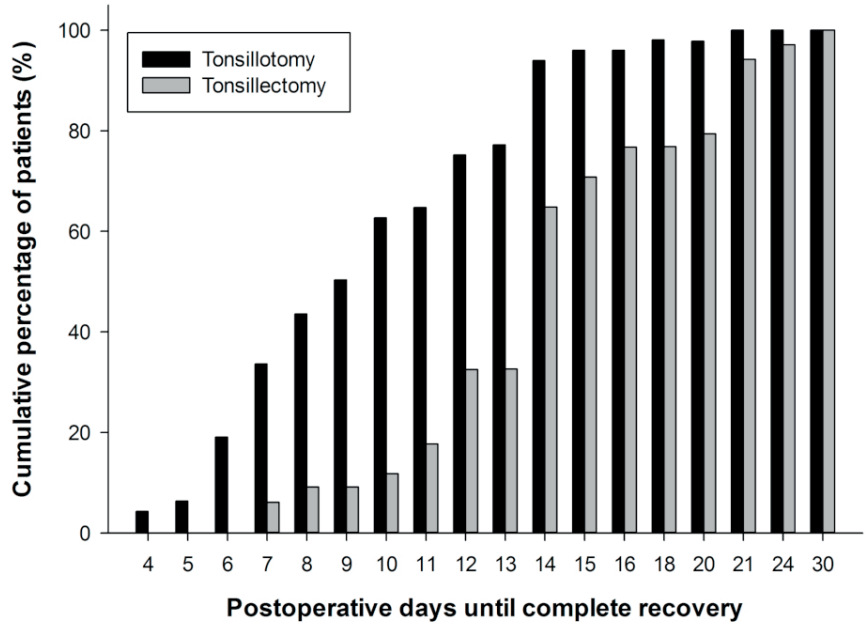

Figure 24. Patient reported recovery after tonsillotomy and tonsillectomy. Cumulative percentage of patients that reported complete recovery postoperatively after tonsillotomy (TO) and tonsillectomy (TE). Data were previously published by Lourijssen et al.[12]

Discussion

This paper describes the steps to perform a CO2LT. To our knowledge, this is the first article to describe this intervention in such detail. Outpatient CO2LT under local anesthesia is a novel surgical method and therefore the presented procedural details have mostly been developed through hands-on experience of the authors.

As for any surgical intervention, pre-operative patient selection is important. For CO2LT, a relatively calm and cooperative patient without a procedure-restricting gag-reflex is desirable. Therefore, an adequate assessment of limitations due to patient anxiety pertaining to the procedure and gag-reflex are of great importance to reach consistent treatment effects. Furthermore, we advise not to perform CO2LT on patients with grade IV (Friedman grading), or "kissing-tonsils" because of the risks of damaging surrounding tissues with the laser-beam.

In our experience, leaving the tonsil capsule intact and limiting the tissue damage reduces post-operative pain, recovery time and post-operative morbidity compared to tonsillectomy under general anesthesia. This is in agreement with current literature[16–26]. Despite the potential incomplete resolution of tonsil disease with CO2LT, many patients prefer CO2LT over tonsillectomy when informed of their options. This preference has been consistently reported prospectively (pre-surgery) and retrospectively (at follow-up)[12]. We therefore believe that CO2LT fills a gap in treatment options for tonsil-related disease, both from the doctors' and the patients' perspective. Current ongoing studies should provide further insight into the value of CO2LT in adults with tonsil diseases[13].

There is a wide variety of techniques and devices available to perform a tonsillotomy, each with its own potential pros and cons. Utilized surgical devices besides the CO_2-laser include microdebriders, coblators, surgical scissors, radiofrequency ablation probes, interstitial thermal therapy instruments and diode lasers. There is no conclusive evidence favoring any one instrument over another for tonsillotomy in adults[27]. Microdebriders, coblators and CO_2-lasers are among the most frequently used instruments for tonsillotomy[28]. Reports on effectiveness, pain and postoperative complications vary, but current evidence suggests equal efficacy of tonsillotomy compared to tonsillectomy with less postoperative pain and complications[27,28], independent of the method of tonsillotomy.

Even though tonsil-surgery under local anesthesia has been described since decades, it is not performed often in current practice[16,29–31]. Many otolaryngologists are uncomfortable with the idea of tonsil surgery under local anesthesia. This may partly be due to a

lack of experience with this specific form of tonsil surgery as well as due to concerns over the airway and bleeding control[30].

CO2LT has some clear logistical advantages. First, using only local anesthetics obviates the need for an anesthesia team. Second, the operation can be performed in the outpatient setting and there is no need for an operation room. Third, the surgical instruments used with CO2LT are non-disposable and only the laser pen needs to be sterilized after use. Sterilization of the laser pen is a simple procedure for any central sterile services department. These factors all lead to cost-reduction. On the other hand, the use of a laser requires a specialized intervention room meeting the local laser safety standards.

We currently exclude patients with a history of peritonsillar abscess because of the intrinsic risk in those patients of recurrent peritonsillar abscess (14%)[32]. The risk of recurrence is zero in patients after tonsillectomy. In tonsillotomy, residual tissue may lead to a recurrence of an abscess. We also advise to exclude patients on anticoagulants or with bleeding disorders from treatment with CO2LT[33]. Even though our experience is that bleeding sites can easily be managed with the CO_2-laser, or if necessary, with bipolar coagulation. The fact that the patient is conscious and not intubated might complicate per-operative treatment of more profound bleeding due to decreased coagulation. If necessary, the patient can be brought under full anesthesia and the bleeding site can be stopped with diathermy or ligation, similar to postoperative bleeding after tonsillectomy. In our >1,000 patient experience, such an event has never occurred. We estimate the need to use bipolar coagulation under local anesthesia to be around 2% of cases.

Furthermore, as of yet we have never had to stop a CO2LT case early due to an uncooperative patient. Incidentally a strong gag-reflex has led to suboptimal laser-treatment of the lower part of the tonsil. In those cases, sending the patient home with our gag-reflex training scheme led to successful treatment of the remaining tonsil tissue during a subsequent CO2LT procedure. It is important to note that these numbers and procedural characteristics are based on personal experience of the authors at a single center and should be evaluated in further studies.

SUPPLEMENT 1: LIST OF MATERIALS USED DURING CO2LT

Materials

Name	Company	Catalog Number	Comments
Carpule syringe and local anesthetic (e.g., xylocaïne:adrenaline 1:80.000)	n/a	n/a	n/a
CO_2 Laser system	Lumenis	AcuPulse DUO CO2 laser	F125 CO_2 Laser System
Coagulation device	Erbe	Erbe ICC 80 Surgical Generator With Footswitch	n/a
Laser safety goggles	Lumenis	Laservision goggles AX0000068	n/a
Operating chair	n/a	n/a	With possibilities for the patient to sit upright (e.g., opthalmic chair or dental chair)
Operating room which meets the local laser-safety standards	n/a	n/a	n/a
Suction device	TBH	TBH LN 100 or 2000	Air suction and filtration device
Surgical masks	3M	3M 7502 mask with 2138 P3 filters	n/a
Wooden tongue depressor	n/a	n/a	Do not use metal tongue depressors

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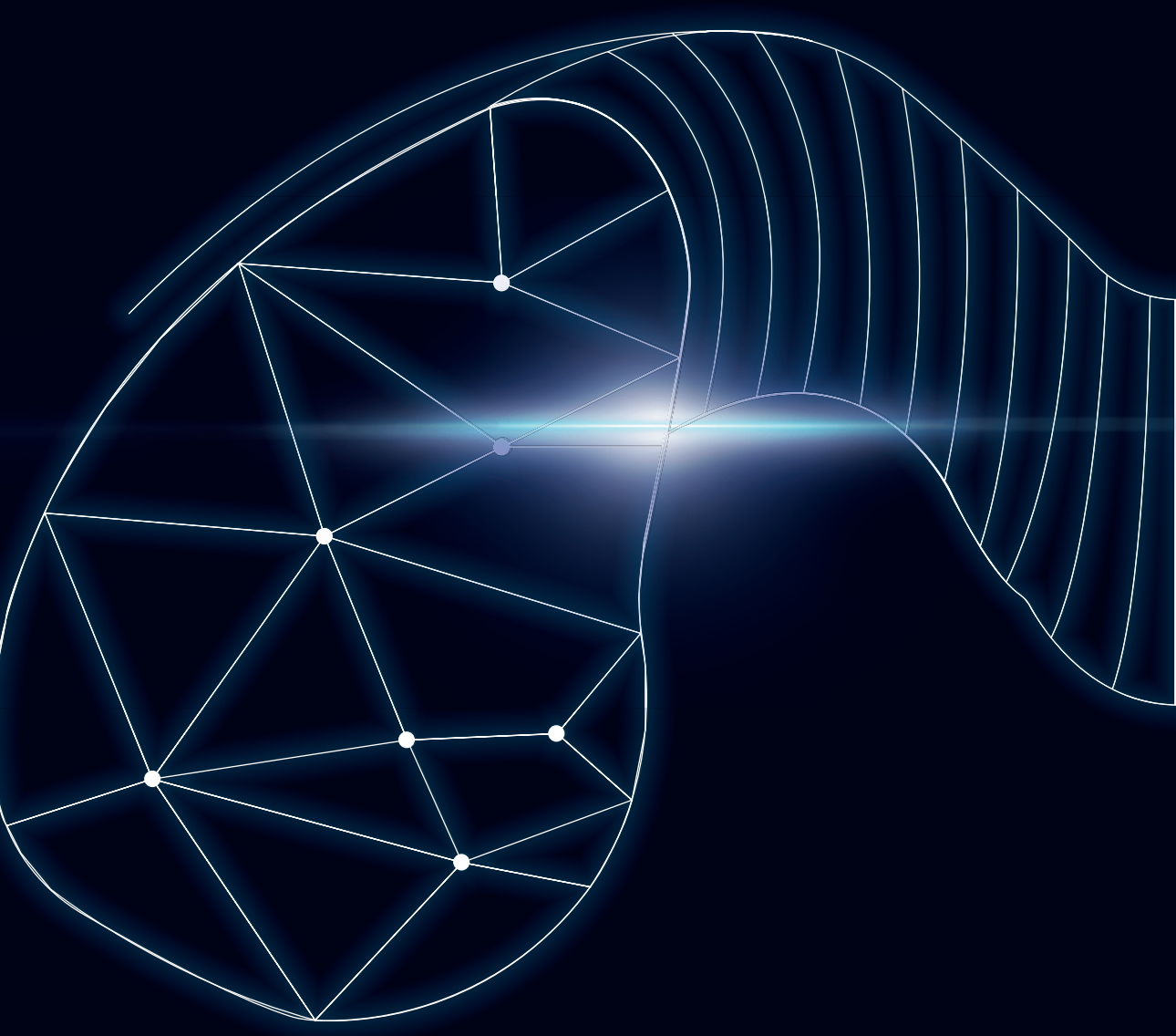

CHAPTER 5

Laser treatment of the tonsils in adults on an outpatient basis

in Dutch

Poliklinische lasertonsillotomie bij volwassenen

Een alternatief voor chirurgische verwijdering van keelamandelen

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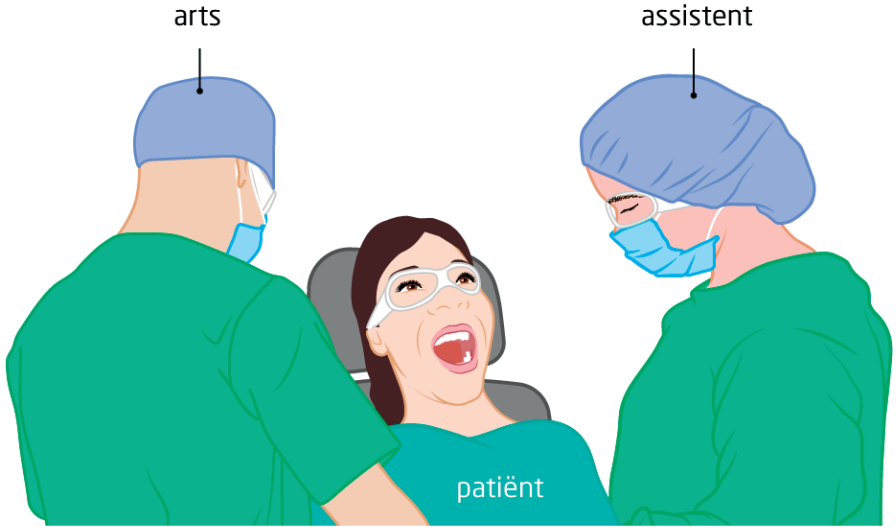
Abstract

Tonsil complaints in adults are common. If conservative treatment fails, there is an indication for surgical removal of the tonsils. The current standard procedure, tonsillectomy under anesthesia, is invasive, painful, and relatively often leads to complications including postoperative bleeding. There is an alternative procedure: the CO2 laser tonsillotomy under local anesthesia. In this procedure, only the lymphatic tissue is removed. As a result, this procedure is associated with significantly less pain, shorter recovery, less postoperative bleeding, and a significant reduction in tonsil complaints.

Samenvatting (Dutch)

Keelamandelklachten bij volwassenen komen veel voor. Als de conservatieve behandeling tekortschiet is er een indicatie voor chirurgische verwijdering van de keelamandelen. De huidige standaardingreep – tonsillectomie onder narcose – is invasief, pijnlijk en leidt relatief vaak tot complicaties, waaronder nabloedingen. Er is een alternatieve ingreep: de CO2-lasertonsillotomie onder plaatselijke verdoving. Bij deze ingreep wordt alleen het lymfeweefsel verwijderd. Hierdoor gaat deze ingreep gepaard met statistisch significant minder pijn, sneller herstel, minder nabloedingen en afname van de keelamandelklachten.



OPSTELLING VAN PATIENT, ARTS EN ASSISTERENDE BIJ EEN POLIKLINISCHE LASERTONSILLOTOMIE BEHANDELIG (NIET GEPUBLICEERDE AFBEELDING, © J.E.R.E. WONG CHUNG)

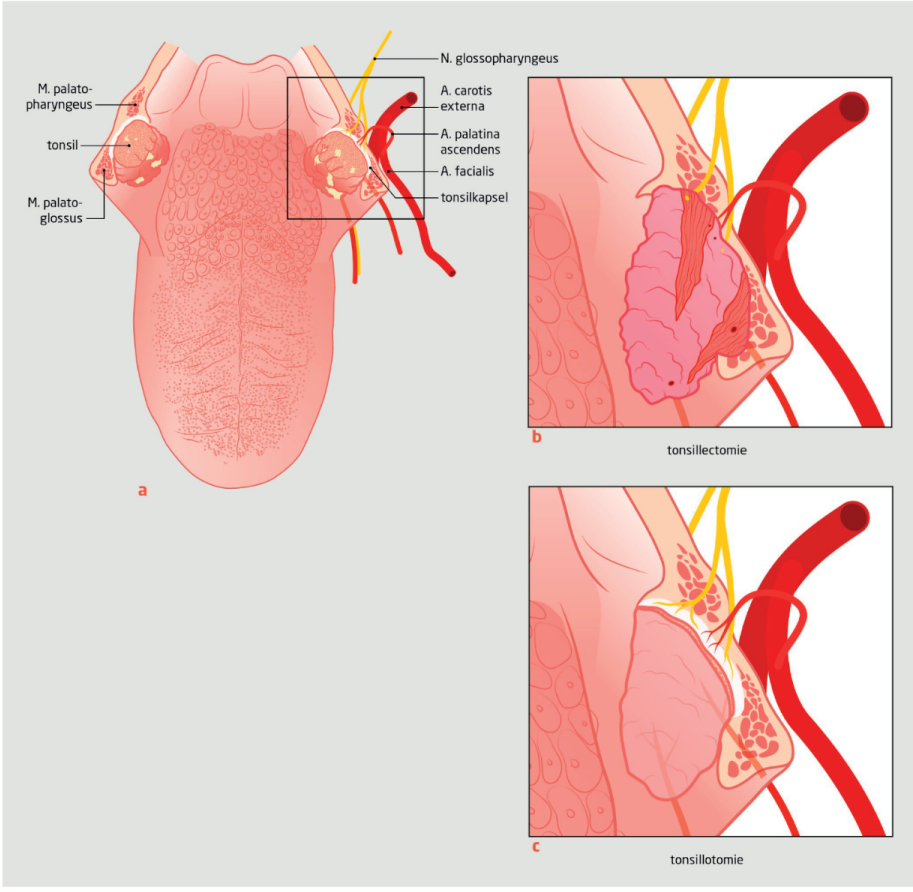
Waarom is er behoefte aan een nieuwe techniek?

Klachten van de keelamandelen komen bij volwassenen frequent voor. Elk jaar worden er in Nederland meer dan 10.000 volwassenen aan hun keelamandelen geopereerd.[1] Een klassieke tonsillectomie onder narcose is de chirurgische standaardbehandeling bij klachten van de keelamandelen. Deze ingreep gaat gepaard met pijn en een risico op wondinfecties, smaakstoornissen en nabloedingen; het herstel duurt gemiddeld meer dan twee weken.[2] Hierdoor zijn de directe en indirecte kosten van tonsillectomie aanzienlijk.[3]

Lasertonsillotomie onder lokale verdoving is een alternatieve ingreep die in dagbehandeling uitgevoerd kan worden. Deze ingreep is minder invasief, kent een sneller herstel en is daardoor naar verwachting goedkoper en laagdrempeliger.

Welke techniek?

CO2-lasertonsillotomie is een chirurgische ingreep van de keelamandelen die wordt uitgevoerd onder lokale verdoving. Dit gebeurt in een poliklinische behandelkamer die voldoet aan de lokale laserveiligheidsvoorschriften. Benodigd zijn een CO2-laserapparaatmet bijbehorende laserveiligheidsbrillen, een luchtafzuiging met filter, mond-neusmaskers en een behandelstoel waarin de patiënt zittend kan plaatsnemen. De patiënt zit rechtop in de behandelstoel. Vervolgens wordt de keelamandel lokaal verdoofd doorinjecties met xylocaïne/adrenaline. Tijdens de uitademing wordt de keelamandel met een laser verdampt tot de tonsilcryptenvolledig zijn verdwenen (figuur). Een protocol waarin de ingreep stap-voor-stap met videobeelden wordt uitgelegd is online beschikbaar.[4] Bij een klassieke tonsillectomie wordt de volledige keelamandel onder narcose verwijderd. Tijdens de complete verwijdering worden grotere zenuwen en bloedvaten doorgenomen en komen de onderliggende spieren bloot te liggen **(Figuur 1)**.



FIGUUR 1. TONSILLECTOMIE EN TONSILLOTOMIE: VERSCHIL IN RESULTAAT

(a) Anatomie van de tonsillen en omliggende structuren. Daarnaast een schematische weergave van **(b)** de situatie na tonsillectomie, en **(c)** de situatie na tonsillotomie. Na tonsillectomie zijn de zenuwen en bloedvaten doorgenomen en ligt het onderliggende spierweefsel bloot. Na lasertonsillotomie blijft het tonsilkapsel en een restant van het lymfeweefsel van de tonsil achter, waardoor grote zenuwen en bloedvaten intact blijven en het onderliggend spierweefsel bedekt blijft.

Welke indicaties?

De indicaties voor tonsillectomie bij volwassenen zijn:[5]

- frequent recidiverende tonsillitiden met ernstige morbiditeit (> 3 per jaar);
- peritonsillair abces waarbij poliklinische punctie met aspiratie niet mogelijk is;
- recidiverend peritonsillair abces;
- obstructieve slaapapneu met obstruerende tonsillen;
- persisterende foetor ex ore op basis van tonsillolithiasis;
- verdenking op een maligniteit van de tonsil.

Deze indicaties gelden ook voor lasertonsillotomie, met uitzondering van het peritonsillair abces (PTA) en de verdenking op een tonsilmaligniteit. Een gecompliceerd PTA kan een dodelijk beloop hebben. Daarom is het niet wenselijk dat na de ingreep nog tonsilweefsel resteert, wat wel het geval is na lasertonsillotomie. Bij een verdenking op een tonsilmaligniteit is aanvullend histopathologisch onderzoek essentieel. Dit is niet mogelijk na de laseringreep, aangezien het tonsilweefsel verdampt.

De keuze tussen lasertonsillotomie of klassieke tonsillectomie voor de genoemde indicaties zal met name afhangen van de ernst van de klachten en de wensen van de patiënt. De narcose en het lange en pijnlijke herstel van een klassieke tonsillectomie werpen een hogere indicatiedrempel op, waardoor patiënten met lichtere klachten minder snel in aanmerking komen voor een klassieke tonsillectomie. Patiënten bij wie een narcose gecontra-indiceerd is zullen alleen in aanmerking komen voor een lasertonsillotomie. In de praktijk blijken patiënten vaak een duidelijke voorkeur te hebben voor de lasertonsillotomie vanwege het snelle postoperatieve herstel en de lokale verdoving óf voor klassieke tonsillectomie vanwege de grotere kans om na de ingreep volledig klachtenvrij te zijn.

Wat is er bekend over effectiviteit?

Lasertonsillotomie is een effectieve behandeling voor keelamandelklachten. In een recent gepubliceerde studie waarin lasertonsillotomie vergeleken werd met klassieke tonsillectomie bij volwassenen, bleken patiënten na beide ingrepen minder last te hebben van hun klachten.[6]

Postoperatief werden er na lasertonsillotomie statistisch significant minder nabloedingen gezien dan na klassieke tonsillectomie (bij 2 vs. 12% van de patiënten). De helft van de patiënten met een nabloeding na tonsillectomie moest opnieuw onder narcose om

de bloeding te stoppen; de nabloedingen na lasertonsillotomie konden zonder narcose gestopt worden.

Het postoperatieve herstel na lasertonsillotomie was aanzienlijk korter en minder pijnlijk. Na lasertonsillotomie hadden patiënten gemiddeld 7,5 dagen nodig voor ze volledig hersteld waren, terwijl het grootste deel van de patiënten twee weken na een klassieke tonsillectomie nog niet hersteld was. Patiënten beoordeelden de postoperatieve pijn gedurende de eerste twee weken met een gemiddelde VAS-score van 42 na lasertonsillotomie en 66 na klassieke tonsillectomie (op een schaal van 0-100).

Zes maanden na een klassieke tonsillectomie waren meer patiënten volledig klachtenvrij dan na een lasertonsillotomie (65 vs. 43%,respectievelijk). Bij 13% van de lasertonsillotomiepatiënten was een tweede lasertonsillotomie nodig om de klachten voldoende weg te nemen. In totaal onderging uiteindelijk 8% van de patiënten na de laseringreep alsnog een klassieke tonsillectomie voordat zijvolledig klachtenvrij waren.

De patiënttevredenheid was iets hoger na klassieke tonsillectomie dan na lasertonsillotomie (VAS: 87 vs. 77, op een schaal van 0-100), maar in beide groepen zouden evenveel patiënten de ingreep aan familie of vrienden aanraden. De significant lagere morbiditeit van lasertonsillotomie lijkt dus op te wegen tegen de lagere effectiviteit als het gaat om volledige klachtreductie.[6] In de studie was het aantal patiënten met het obstructieve-slaapapneusyndroom (OSAS) vrij laag, waardoor er over de effectiviteit van lasertonsillotomie op OSAS geen uitspraken gedaan kunnen worden.

Hoe moeilijk is de techniek te leren?

In principe kan elke kno-arts de techniek van lasertonsillotomie leren. Tijdens het preoperatieve consult is het van belang de kokhalsreflex en de maximale mondopening te beoordelen. In de praktijk blijkt dat de kokhalsreflex voldoende te verminderen is door thuisoefeningen waarbij de patiënt gedurende twee weken met de tandenborstel de tongbasis en tonsillen probeert aan te raken na het tanden poetsen.

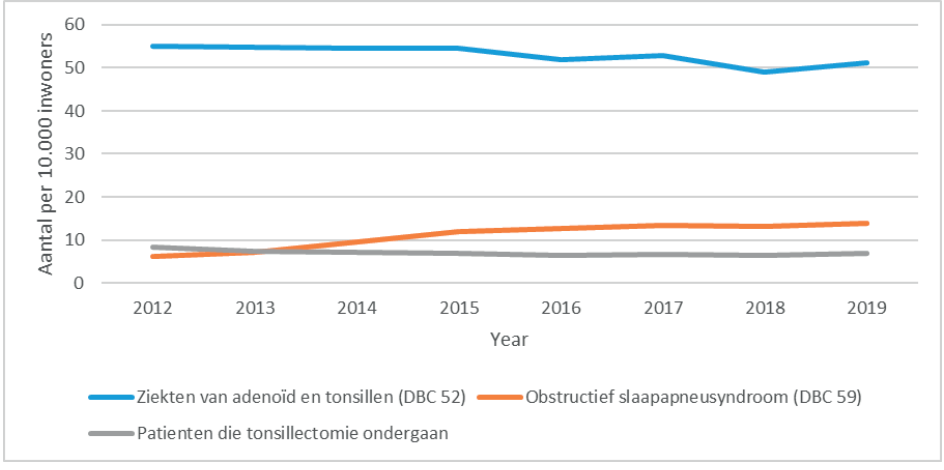
De operateur dient zich een goed beeld te vormen van de bouw, de vorm en de ligging van de keelamandelen voor een veilige en volledige behandeling. Aandacht voor goede expositie van de volledige tonsil verlaagt het risico op resterende tonsilklachten door overgebleven tonsilcrypten. De ingreep kent een steile leercurve waarbij de chirurg na vijf tot tien gezamenlijke operaties met een ervaren operateur in staat is de ingreep zelfstandig uit te voeren.

Toekomstverwachting

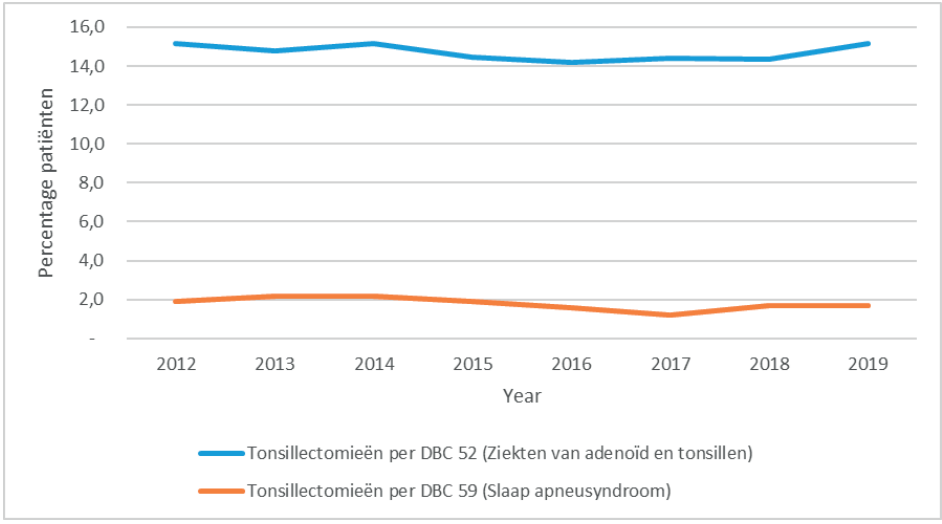
Hoeveel volwassenen met keelamandelklachten zijn er?

De huidige NHG-standaard 'Acute keelpijn' adviseert verwijzing naar de kno-arts bij dreigende luchtwegobstructie, vermoeden vaneen gecompliceerd PTA of peritonsillair infiltraat, lymfadenitis van de hals bij een abces of een ernstig zieke patiënt, ernstig afwijkende infectieparameters in het bloed of vier of meer tonsillitiden in twaalf maanden. In de periode 2012-2019 stelden de kno-artsen in Nederland bij volwassenen (16 jaar en ouder) jaarlijks gemiddeld 73.887 keer de diagnose 'ziekten van het adenoïd of tonsillen' en 15.421 keer de diagnose 'OSAS'. Dit leidde jaarlijks tot gemiddeld 11.130 tonsillectomieën **(figuur 2)**.[7]

In de totale Nederlandse volwassenen populatie resulteert dit in een relatief stabiel gemiddelde van 53 patiënten per 10.000 inwoners (uitersten: 49-55/10.000 inwoners) met adenoïd- en keelamandelaandoeningen die bij de kno-arts komen. Ook is er een toenemend aantal patiënten met OSAS. In 2012 waren dit 6 patiënten per 10.000 inwoners; dit aantal steeg naar 14 per 10.000 inwoners in 2019. Gemiddeld worden er jaarlijks 8 tonsillectomieën per 10.000 volwassenen verricht (uitersten: 7,5-8,7/10.000 inwoners). Deze cijfers zijn door de jaren heen stabiel voor volwassen patiënten met een aandoening van het adenoïd of de tonsillen (15%; uitersten: 14,2-15,2) en patiënten met OSAS (1,8%; uitersten: 1,2-2,2) **(figuur 3)**.



Figuur 2: Aantal diagnoses 'Ziekten van het adenoïd en tonsillen' (DBC 52) of 'Obstructief slaapapneusyndroom' (DBC 59) bij de KNO-arts en het aantal patiënten dat tonsillectomie ondergaat per 10.000 volwassen inwoners in Nederland. *Afbeelding maakt geen deel uit van publicatie in het NTvG*



FIGUUR 3: PERCENTAGE VOLWASSEN PATIËNTEN DAT IN NEDERLAND EEN TONSILLECTOMIE ONDERGAAT VOOR DE DIAGNOSE 'ZIEKTEN VAN HET ADENOÏD EN TONSILLEN' (DBC 52) OF 'OBSTRUCTIEF SLAAPAPNEUSYNDROOM' (DBC 59). *AFBEELDING MAAKT GEEN DEEL UIT VAN PUBLICATIE IN HET NTVG*

TOEKOMSTVERWACHTING LASERTONSILLOTOMIE

Recent onderzoek heeft aangetoond dat poliklinische CO2-lasertonsillotomie onder lokale verdoving een veilige ingreep is met een goede effectiviteit ten aanzien van klachtvermindering na 6 maanden.[6] De ingreep is minder invasief, minder belastend voor de patiënt en naar verwachting goedkoper dan de klassieke tonsillectomie. Soms moet de ingreep 2 keer worden uitgevoerd of moet alsnog een klassieke tonsillectomie worden uitgevoerd.

Toekomstig onderzoek moet uitwijzen wat de effectiviteit en kosteneffectiviteit op lange termijn zijn. Daarna zal de huidige richtlijn voor de behandeling van klachten van de keelamandelen opnieuw geëvalueerd worden. De verwachting is dat de meerderheid van de patiënten ook op de lange termijn voldoende klachtenreductie ervaart na laser-tonsillotomie en dat een minderheid een aanvullende klassieke tonsillectomie nodig heeft. Op dit moment wordt er met de zorgverzekeraars gekeken naar de vergoeding van de laseringreep vanuit het basispakket van de zorgverzekering.

Waar in Nederland is de techniek ontwikkeld?

In het Hagaziekenhuis zijn inmiddels meer dan 1000 patiënten met de laseringreep onder lokale verdoving behandeld. Een aantal kno-artsen uit andere Nederlandse ziekenhuizen heeft inmiddels ervaring opgedaan in Den Haag met de lasertonsillotomie en hopen deze, na opname van de techniek in de richtlijn, elders in Nederland aan te kunnen bieden.

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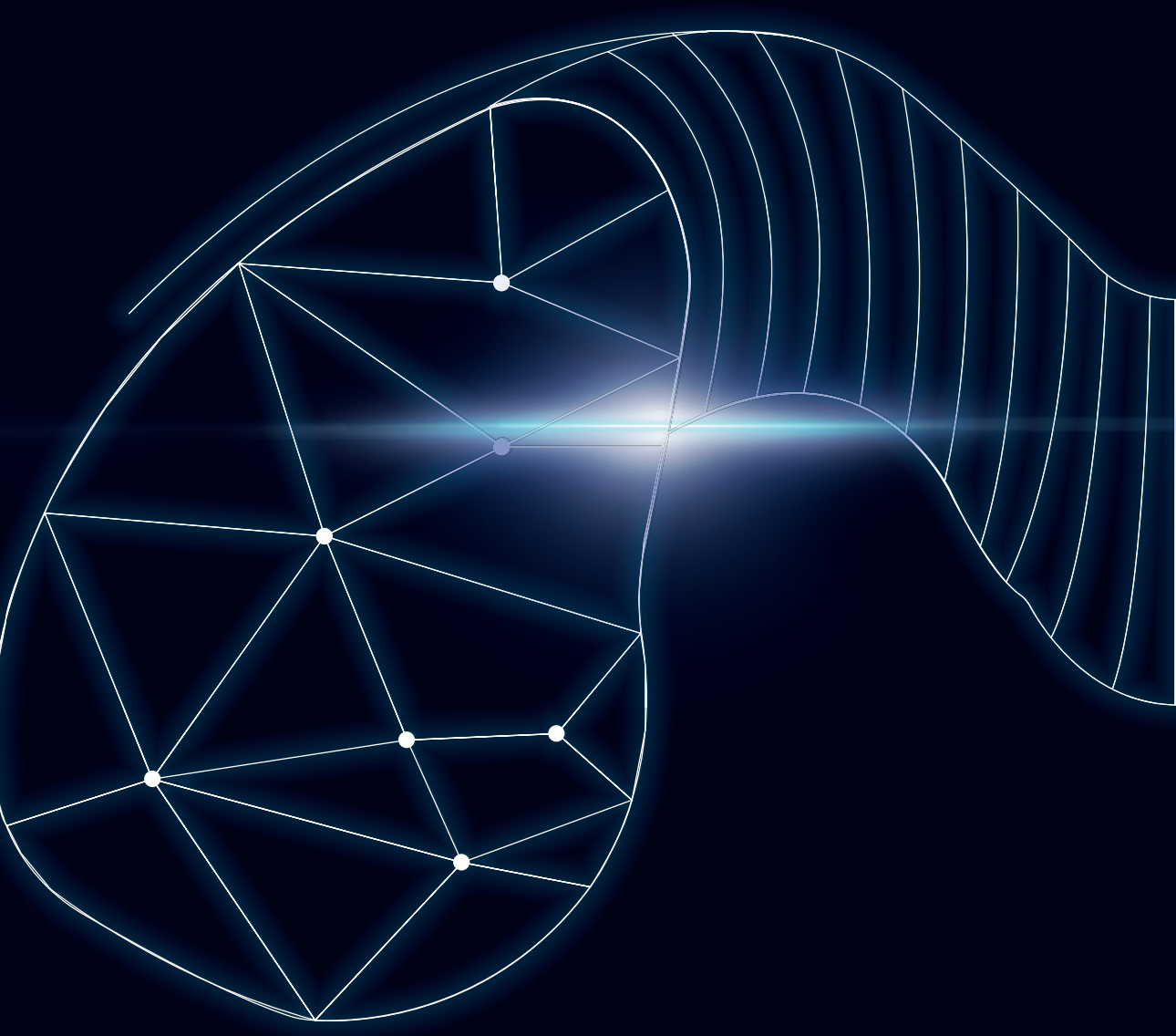

CHAPTER 6

Time to Functional Recovery After Laser Tonsillotomy Performed Under Local Anesthesia vs Conventional Tonsillectomy With General Anesthesia Among Adults

A Randomized Clinical Trial

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Abstract

Importance: Carbon dioxide laser tonsillotomy performed under local anesthesia may be an effective and less invasive alternative than dissection tonsillectomy for treatment of tonsil-related afflictions.

Objective: To compare functional recovery and symptom relief among adults undergoing tonsillectomy or tonsillotomy.

Design, Setting, and Participants: This randomized clinical trial was conducted at 5 secondary and tertiary hospitals in the Netherlands from January 2018 to December 2019. Participants were 199 adult patients with an indication for surgical tonsil removal randomly assigned to either the tonsillectomy or tonsillotomy group.

Interventions: For tonsillotomy, the crypts of the palatine tonsil were evaporated using a carbon dioxide laser under local anesthesia, whereas tonsillectomy consisted of total tonsil removal performed under general anesthesia.

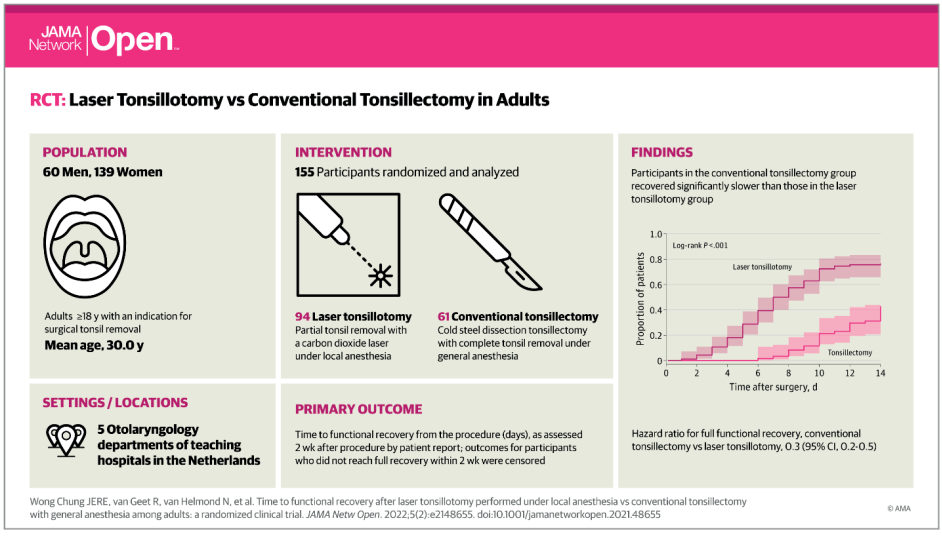
Main Outcomes and Measures: The primary outcome was time to functional recovery measured within 2 weeks after surgery assessed for a modified intention-to-treat population. Secondary outcomes were time to return to work after surgery, resolution of primary symptoms, severity of remaining symptoms, surgical complications, postoperative pain and analgesics use, and overall patient satisfaction assessed for the intention-to-treat population.

Results: Of 199 patients (139 [70%] female; mean [SD] age, 29 [9] years), 98 were randomly assigned to tonsillotomy and 101 were randomly assigned to tonsillectomy. Recovery within 2 weeks after surgery was significantly shorter after tonsillotomy than after tonsillectomy (hazard ratio for recovery after tonsillectomy vs tonsillotomy, 0.3; 95% CI, 0.2-0.5). Two weeks after surgery, 72 (77%) patients in the tonsillotomy group were fully recovered compared with 26 (57%) patients in the tonsillectomy group. Time until return to work within 2 weeks was also shorter after tonsillotomy (median [IQR], 4.5 [3.0-7.0] days vs 12.0 [9.0-14.0] days; hazard ratio for return after tonsillectomy vs tonsillotomy, 0.3; 95% CI, 0.2-0.4.). Postoperative hemorrhage occurred in 2 patients (2%) in the tonsillotomy group and 8 patients (12%) in the tonsillectomy group. At 6 months after surgery, fewer patients in the tonsillectomy group (25; 35%) than in the tonsillotomy group (54; 57%) experienced persistent symptoms (difference of 22%; 95% CI, 7%-37%). Most patients with persistent symptoms in both the tonsillotomy (32 of 54;

59%) and tonsillectomy (16 of 25; 64%) groups reported mild symptoms 6 months after surgery.

Conclusions and Relevance: This randomized clinical trial found that compared with tonsillectomy performed under general anesthesia, laser tonsillotomy performed under local anesthesia had a significantly shorter and less painful recovery period. A higher percentage of patients had persistent symptoms after tonsillotomy, although the intensity of these symptoms was lower than before surgery. These results suggest that laser tonsillotomy performed under local anesthesia may be a feasible alternative to conventional tonsillectomy in this population.

Trial Registration: Netherlands Trial Register Identifier: NL6866 (NTR7044)



INTRODUCTION

Tonsillitis, peritonsillar abscess, tonsillolithiasis, halitosis, dysphagia, and snoring are common tonsil-related conditions in adults. When conservative treatment of these conditions fails, surgery may be indicated.[1]

Classic dissection tonsillectomy with complete tonsil removal under general anesthesia is the most used surgical technique. In the United States and Europe combined, more than 500 000 tonsillectomies are performed in adult patients every year.[2,3] After tonsillectomy, recovery to normal function is typically long. Postoperative complications of tonsillectomy include bleeding, infection, and severe pain, any of which may lead to hospital readmissions and contribute to a protracted recovery.[4] Partial removal of the tonsil, tonsillotomy, has been performed for 3000 years and is increasingly being reexplored to potentially decrease patient burden and risk.[5] During tonsillotomy, only the cryptic lymphatic tissue is removed, and the tonsil capsule that contains larger nerves and blood vessels is left intact.[6,7] This may lead to less postoperative pain and bleeding.[7–9] Tonsillotomy may be performed in adults using different instruments and techniques, including the use of carbon dioxide (CO_2) laser, diathermy, radiofrequency, microdebrider, coblation, bipolar electrosurgical device, and cold steel dissection.[6,10]

The CO_2 laser is the most used laser modality in tonsillotomy and is known for its good ablation and hemorrhage-controlling characteristics.[11,12] An advantage of the CO_2 laser is its ability to perform tonsillotomy under local anesthesia without sedation.[6] General anesthesia has additional effects on postoperative and functional recovery, and obviating the need for general anesthesia may provide additional recovery benefit over tonsillectomy.[13] However, there is a lack of evidence with sufficient quality regarding the clinical usefulness of tonsillotomy compared with tonsillectomy in adults.[5]

We conducted a randomized clinical trial to compare CO_2 laser tonsillotomy performed under local anesthesia to tonsillectomy performed under general anesthesia for tonsil-related concerns in adults. We hypothesized that tonsillotomy would have a shorter functional recovery period. Secondary outcomes included relief 6 months after surgery of the primary concern that led to tonsil removal and tonsil symptom severity.

METHODS

The laser tonsillotomy vs tonsillectomy study (TOMTOM study) is a pragmatic randomized clinical trial (meaning that broad inclusion criteria comparable to a real-world situation were applied) comparing functional recovery time, resolution or reduction of tonsil concerns, and surgical complications between tonsillotomy and tonsillectomy in adults. Patients were recruited from 5 otolaryngology departments of teaching hospitals in the Netherlands from January 2018 to December 2019. This report followed the Consolidated Standards of Reporting Trials (CONSORT) reporting guideline.[14] The study protocol and the statistical analysis plan are available in **Supplement 1** (chapter 10 of this thesis). The study was approved by the Research Ethics Committee of The Hague in the Netherlands. This study adhered to Dutch health care laws and the principles set forth in the Declaration of Helsinki.[15] All patients provided written informed consent. No one received compensation or was offered any incentive for participating in this study.

Patients

Adult patients (age ≥18 years) with tonsil-related concerns that did not resolve sufficiently with conservative management, including antibiotic treatment, were eligible for enrollment in the study. Patients with the following conditions, similar to real-life standard of care practice, were included: chronic or recurrent tonsillitis (indication for surgery was determined following the Dutch guideline of >4 tonsillitis episodes per year not responding sufficiently to antibiotic treatment[16]), tonsil-related halitosis, tonsillolithiasis, dysphagia, and sleep apnea caused by the tonsils. Exclusion criteria were inability to complete all trial procedures and follow-up visits, inability to keep the mouth open for at least 5 seconds continuously, inability to relax the jaw for 30 minutes, a sensitive gag reflex on physical examination, Friedman classification grade 4 tonsil size, insufficient exposure of the entire tonsil on physical examination, history of peritonsillar abscess, coagulation disorders (including the use of anticoagulants), contraindications for local or general anesthesia, evident tonsil asymmetry or other signs of possible malignant or premalignant neoplasm of the oropharynx, immunodeficiency, and pregnancy.

Enrollment and Randomization

Patients were registered in an electronic data capturing system (Castor EDC[17]). Using computer generated random numbers, patients were randomly assigned to tonsillotomy or tonsillectomy treatment using stratified randomization, the strata being type of main tonsil concern. Stratification was used to control the potentially large influence of type of tonsil concern on study outcomes (strata: chronic tonsillitis, halitosis, tonsillolithiasis, dysphagia, and sleep apnea). Considering the different pathophysiological processes

underlying the various concerns, small randomization imbalances could otherwise have a large influence on the analysis of observed treatment outcomes.

All patients randomly allocated to tonsillotomy were advised to start a gag-reflex desensitization training method. Patients were advised to slowly reduce their gag reflex by touching their tongue base and tonsils with a tooth brush each time they brushed their teeth. This method has been previously shown to reduce the gag reflex intensity in most patients within 2 weeks.[6]

Interventions

CO_2 Laser Tonsillotomy With Local Anesthesia

Carbon dioxide laser tonsillotomy was performed by trained surgeons (Justin .E.R.E. Wong Chung, Rozemarie van Geet, Chloe Kastoer, or Henk M. Blom) in ambulatory intervention rooms meeting the standard laser safety guidelines of the Dutch health council.[18] A full operating room was available on-site for safety reasons. Each patient received acetaminophen, 1 g, orally prior to surgery. The patient was seated upright facing the surgeon and local anesthesia of the tonsil was achieved with xylocaine, 2%, containing adrenaline, 1:80 000 units, at a maximum of 5.4 mL. In patients with a substantial residual gag reflex, xylocaine, 10%, was sprayed on the peritonsillar area. After adequate anesthesia was accomplished, the CO_2 laser was set between 25 and 30 W in continuous mode to distribute focused laser energy with a beam diameter of 3 mm. Patients were asked to breath in deeply; during slow exhalations, with the tongue depressed, the crypts of the tonsil were evaporated in a sweeping motion until full cryptolysis was accomplished. A smoke suction device was used to prevent smoke inhalation and to ensure the surgeon's clear vision of the treatment area. In case of bleeding, coagulation was accomplished by pulling the laser out of focus. A step-by-step video protocol of this intervention has been published previously.[6]

All CO_2 laser tonsillotomy procedures were performed in the leading clinical study center. The participating centers were close to the lead center (<2 hours driving time), enabling patients to travel for treatment.

Classic Dissection Tonsillectomy

Classic dissection tonsillectomy procedures were performed in all study centers. The patient was placed in a supine position, and general anesthesia with endotracheal intubation was induced. After applying a McIvor retractor, an Allis clamp was used to grasp the superior pole of the tonsil. Next, an incision was made on the anterior pillar of the tonsil to expose the tonsil. Using a tonsil clamp and scissors, the tonsil was removed.

Hemostasis was ensured with gauze and gentle pressure for 5 minutes. If necessary, additional electrosurgery was performed for full hemostasis. After tonsillectomy, patients were admitted to the postanesthesia care unit and discharged the same day.

Postoperative Pain Medication

Postoperative analgesia for all patients consisted of acetaminophen, 500 mg, given as needed at a maximum of 4 times daily with 1000 mg each time. If acetaminophen was insufficient, diclofenac, 50 mg, was given as needed, with a maximum of 3 times daily for the first 3 days after surgery. If the combination acetaminophen and diclofenac was insufficient, tramadol was prescribed.

Patient Crossover

If deemed clinically necessary, patients could receive additional surgical treatments deviating from the assigned study group after their initial surgical treatment. Those additional tonsillotomy or tonsillectomy treatments were offered in line with the standard of care for symptoms to maintain a pragmatic and ethical randomized clinical trial design. No additional surgical procedures were performed within 6 weeks of the initial study assigned surgery. Patients who were randomized in the study but changed their mind and decided to not undergo their allocated treatment were asked for permission to continue to collect follow-up data on their tonsil symptoms and any surgical procedures they underwent.

Clinical Data Collection

Preoperative Assessment

Before the surgical procedure, we collected demographic and clinical (risk) factors, including the preoperative tonsil-related symptoms and severity, medication use, and tobacco smoking status. Tonsil symptom severity and pain severity were collected both on ordinal (minimal, mild, moderate, and severe) and continuous visual analog scales (VAS) for consistency purposes. General health status was assessed using the 5-level EuroQol 5-Dimensions survey to measure health-related quality of life.[19] To assess the influence of the tonsil-related symptoms on quantitative work productivity and activity impairment, we used the Work Productivity and Activity Impairment questionnaire.[20]

Surgical Complications and Early Postoperative Data Collection

During surgery, the surgeon graded the tonsil size using the Friedman grading scale. Duration of the intervention and any perioperative or postoperative complications were collected.

Data on perioperative and postoperative pain were collected using a 0-100 mm VAS and an ordinal scale (no pain or mild, moderate, or severe pain). Two weeks after surgery, patients reported when they felt fully recovered, when they returned to work, and the duration of analgesic use.

Long-term Follow-up Data Collection

Six months after the surgical procedure, data were collected on the presence of any tonsil-related symptoms, quality of life (5-level EuroQol 5-Dimensions survey), work productivity and activity impairment, and overall satisfaction (0-100 mm VAS). All patient-reported data were collected using digital questionnaires.

Primary and Secondary Outcomes

The primary outcome was functional recovery time from surgery in days until patients reported being fully recovered, up to 2 weeks after surgery. We asked patients directly when they felt fully recovered from surgery. This primary outcome was selected because it is an important patient-centered outcome.[21] Secondary outcomes included return to work within 2 weeks after surgery, postoperative pain scores, the duration of postoperative analgesic medication use, perioperative and postoperative complications, overall satisfaction, resolution of tonsil-related symptoms 6 months after surgery, and general health.

Statistical Analysis

Baseline demographic and clinical characteristics in both groups are presented as means with SDs, medians with IQRs, or as numbers and percentages. Consistent with CONSORT clinical trial reporting guidelines, we did not perform statistical significance testing on the baseline characteristics of the randomized groups.[14] The primary outcome of time to full recovery from surgery was analyzed only in patients who received a surgical intervention (modified intention-to-treat population, ie, by randomly assigned group but only among those with surgery). Functional recovery was not measurable among patients not undergoing surgery. Time was measured from the day of surgery. Time to recovery was graphically depicted in reverse Kaplan-Meier curves with pointwise confidence intervals and was compared using a log-rank test and hazard ratios using Cox regression.[22] The proportional hazards assumption was tested using Schoenfeld residuals.[23] Patients who did not reach full functional recovery within 2 weeks were censored at 2 weeks. Secondary outcomes of return to work within 2 weeks after surgery and duration of analgesic medication use were analyzed in a similar manner. The secondary outcome analyses on patient reported outcomes 6 months after surgery were performed on an intention-to-treat basis (randomized patients analyzed according to randomization). Characteristics 6 months after surgery were compared using χ^2 tests,

Fisher exact tests, Mann-Whitney tests, and unpaired *t* tests depending on the variable and its distribution. Within tonsillotomy and tonsillectomy group changes from baseline were assessed using Wilcoxon signed rank tests, paired *t* tests, and Fisher exact tests. Normality of data was assessed using the Shapiro-Wilk test. Two-sided *P* values were computed, and a significance level of .05 was used for all testing. Statistical analyses were performed using SPSS, version 27 (IBM) and JMP Pro, version 15 (SAS Institute Inc).

Data from a previous nonrandomized prospective study were used for sample size calculation.[24] A 2-sided log-rank test with an overall sample size of 190 patients (95 in the tonsillectomy group and 95 in the tonsillotomy group) achieved 80.2% power at a .05 significance level to detect a tonsillotomy median functional recovery time of 8 days when the tonsillectomy group median survival time was 13.5 days within a 14-day total observation time.[25]

Results

A total of 199 patients were included and randomly allocated to tonsillotomy (98 patients) or tonsillectomy (101 patients). A treatment flowchart is presented in **Figure 1.**

Of 199 patients, 163 (82%) received their allocated treatment. In the tonsillotomy group, 1 patient withdrew from treatment after randomization. A total of 13 patients required a second tonsillotomy treatment within 6 months after the initial study treatment because of residual symptoms in 11 patients or unfinished primary tonsillotomy treatment for 2 patients. Eight patients who initially underwent tonsillotomy later received a tonsillectomy owing to recurrent symptoms. Three of these patients first received additional tonsillotomy. One patient had perioperative bleeding during tonsillotomy and received an elective tonsillectomy later for that reason. In the tonsillectomy group, 35 randomized patients did not receive the tonsillectomy within the study. In total, 23 patients requested withdrawal, 10 patients received tonsillectomy in a nonparticipating center, 1 patient developed back pain for which additional treatment was needed leading to cancellation of the tonsillectomy, and 1 patient became pregnant after randomization. One of the patients who withdrew later received a laser tonsillotomy in a hospital that did not participate in the study. There was no significant difference in baseline characteristics between patients receiving tonsillotomy or tonsillectomy who were treated and those who withdrew from treatment within the study, except for percentage of patients who were employed (127 of 163 [78%] vs 18 of 36 [50%], respectively; difference 95% CI, 5%-51%; $P = .02$).

A total of 94 patients in the tonsillotomy group and 61 patients in the tonsillectomy group were included in the modified intention-to-treat analyses of functional recovery after surgery, return to work after surgery, surgical complications, and early postoperative outcomes. A total of 94 patients in the tonsillotomy group and 71 patients in the tonsillectomy group were included in the long-term follow-up intention-to-treat analyses of symptom resolution (**Figure 1**).

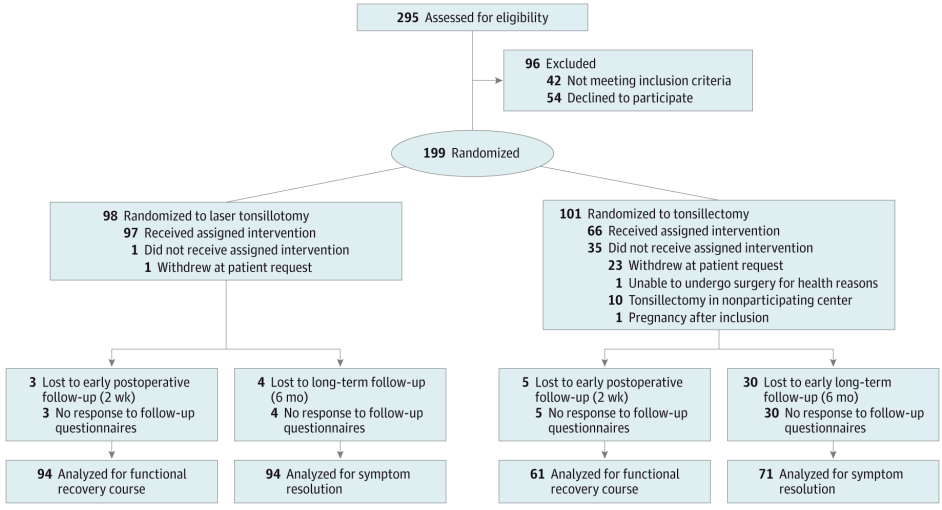


FIGURE 1. PATIENT FLOW DIAGRAM

Baseline Characteristics

Demographic and clinical characteristics were similar between groups (**Table 1**). In both groups, most patients were female (tonsillotomy: of 98 patients, 69 [70%] were female and 29 [30%] were male; tonsillectomy: of 101 patients, 70 [69%] were female and 31 [31%] were male) and most patients reported moderately severe tonsil symptoms (tonsillotomy, 59 [61%]; tonsillectomy, 47 [62%]). The most common indications for surgery were recurrent infections with or without fever (130 of 199 reports [65%]) and tonsillolithiasis (64 of 199 reports [32%]).

Table 1. Baseline Demographic and Clinical Characteristics of Patients in the Tonsillotomy and Tonsillectomy Groups

Variable	No. (%) of patients	
	Tonsillotomy (n = 98)	Tonsillectomy (n = 101)
Demographic characteristic		
Sex		
Male	29 (30)	31 (31)
Female	69 (70)	70 (69)
Age, mean (SD), y	29 (10)	30 (8)
Tobacco smoking status		
Current	17 (18)	14 (18)
Former	24 (25)	16 (21)
Not smoking	56 (58)	46 (61)
Tonsil symptoms		
Chief tonsil concern		
Sore throat without fever	31 (32)	33 (33)
Sore throat with fever	33 (34)	33 (33)
Tonsillolithiasis	32 (33)	32 (32)
Snoring	2 (2)	2 (2)
Dysphagia	0	1 (1)
Self-reported severity of tonsil concerns (ordinal)		
Minimal	1 (1)	1 (1)
Mild	21 (22)	18 (24)
Moderate	59 (61)	47 (62)
Severe	16 (16)	10 (13)
Self-reported severity of tonsil concerns (continuous), mean (SD), mm[a]	57 (19)	59 (17)
QOL and work or activity impairment		
QOL (EQ-5D-5L) index score, median (IQR)[b]	0.87 (0.81-1.00)	0.87 (0.84-1.00)
EQ-5D-5L general health rating, median (IQR)[c]	80 (70-89)	80 (70-89)
Employed	70 (74)	57 (76)
WPAI overall work impairment, median (IQR), %[d]	7 (2-12)	5 (0-11)
WPAI interference with daily activities score, median (IQR)[e]	3 (2-6)	4 (2-6)

Abbreviations: EQ-5D-5L, 5-level EuroQol 5-Dimensions quality of life survey; QOL, quality of life; WPAI, Work Productivity and Activity Impairment questionnaire.

[a] Measured using a 100-mm visual analog scale.

[b] Range of the measurement instrument is −0.329 to 1.00.

[c] Range of the measurement instrument is 0 to 100.

[d] WPAI is evaluated only for patients who are employed.

[e] Range of the measurement instrument is 0 to 10.

Primary Outcome of Functional Recovery After Surgery

Two weeks after surgery, 72 (77%) patients in the tonsillotomy group were fully recovered compared with 26 (57%) patients in the tonsillectomy group. The time to recovery within 2 weeks after surgery was significantly different between the modified intention to treat tonsillotomy and tonsillectomy groups, with patients in the tonsillectomy group recovering substantially slower (hazard ratio for recovery after tonsillectomy vs tonsillotomy, 0.3; 95% CI, 0.2-0.5) **Figure 2A**. Median (IQR) full functional recovery time in the tonsillotomy group was 7.5 (5.0-12.0) days, and 22 patients were censored at 14 days for not reaching full recovery. In the tonsillectomy group, median recovery was not reached within 14 days, and 35 patients were censored at 14 days. At 12 days after surgery, the 25th percentile of full functional recovery was reached.

Secondary Outcomes

Return to Work After Surgery

The time to return to work within 2 weeks was different between the tonsillotomy and tonsillectomy groups, with tonsillectomy patients returning to work later (hazard ratio for return to work for tonsillectomy vs tonsillotomy, 0.3; 95% CI, 0.2-0.4; $P < .001$) **Figure**

2B. Patients in the tonsillotomy group returned to work at a median (IQR) of 4.5 (3.0-7.0) days, whereas patients in the tonsillectomy group returned to work at a median (IQR) of 12.0 (9.0-14.0) days. At 14 days, 8 patients were censored in the tonsillectomy group and 5 patients were censored in the tonsillotomy group because they did not reach full recovery within 2 weeks.

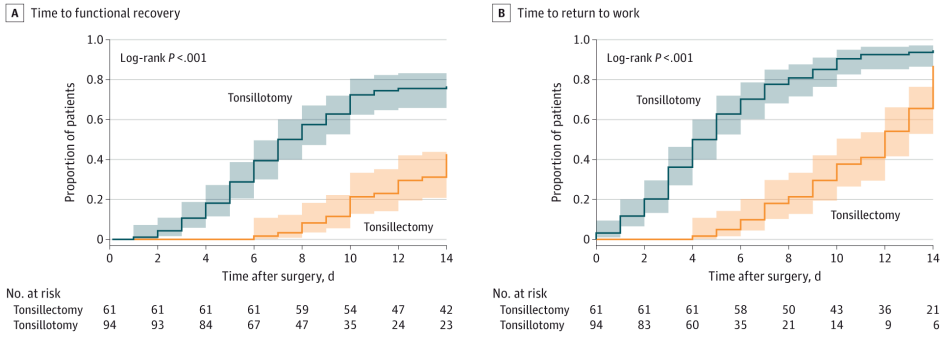


FIGURE 2. REVERSE KAPLAN-MEIER CURVES SHOWING THE PROPORTION OF PATIENTS FUNCTIONALLY RECOVERED AND RETURNED TO WORK UP TO 2 WEEKS AFTER TONSILLECTOMY AND TONSILLOTOMY. SHADED AREAS INDICATE 95% CIS.

Treatment and Surgical Complications

We terminated tonsillotomy treatment early in 3 of 97 patients (3%) because of increased bleeding of the tonsil shortly after initiating tonsillotomy treatment. For 1 of these 3 patients, bleeding was caused by active inflammation. After oral antibiotic treatment, a second tonsillotomy was successfully performed. The second patient crossed over to the tonsillectomy group, with tonsillectomy performed electively later, and the third patient experienced satisfactory symptom reduction after partial tonsillotomy treatment. We stopped 1 tonsillotomy treatment because of insufficient exposure of the tonsils (Mallampati scale class IV). No tonsillotomy treatments were stopped for patient discomfort or anxiety. Postoperative hemorrhage occurred in 2 of 97 patients (2%) in the tonsillotomy group and 8 of 66 patients (12%) in the tonsillectomy group (difference 95% CI, 2%-18%; $P = .02$). One of these patients experienced 2 separate postoperative hemorrhage events after tonsillectomy. The tonsillotomy hemorrhage events were controlled without intervention (n = 1) or with electrosurgery (n = 1). The tonsillectomy hemorrhage events were controlled without intervention (n = 2) or with electrosurgery (n = 6) performed under local anesthesia (n = 2) or general anesthesia (n = 4). After treatment, 2 of 97 (2%) patients in the tonsillotomy group and 1 of 66 patients (2%) in the tonsillectomy group developed wound infection. These infections were managed using oral antibiotics without hospital admission.

Early Postoperative Outcomes

Pain and Analgesic Medication Use

Perioperative pain was significantly lower in the tonsillotomy group compared with the tonsillectomy group (mean [SD] score, 36 [20] vs 58 [25] mm; effect size, 0.97; $P < .001$). Similarly, postoperative pain in the first 2 weeks was significantly lower in the tonsillotomy group (mean [SD] score, 42 [24] vs 66 [21] mm; effect size, 1.06; $P < .001$). More patients in the tonsillectomy group reported moderate (46% vs 30%; difference 95% CI, 1%-31%) and severe pain postoperative pain in the first 2 weeks (30% vs 10%; difference 95% CI, 8%-32%) compared with patients in the tonsillotomy group (both $P < .001$).

Analgesic medications used by patients in the tonsillotomy and tonsillectomy groups consisted of acetaminophen (94% vs 100%, respectively; difference 95% CI, 0% to −11%; $P = .06$), nonsteroidal anti-inflammatory drugs (39% vs 61%; difference 95% CI, −7% to −37%; $P < .001$), and opioid analgesics (1% vs 30%; difference 95% CI, −18% to −40%; $P < .001$). The survival distributions of days until no analgesic medication was required were significantly different between the tonsillotomy and tonsillectomy groups, with patients in the tonsillectomy group requiring analgesics longer (hazard ratio for analgesics no longer needed tonsillectomy vs tonsillotomy, 0.3; 95% CI, 0.2-0.4) (**Figure 3A**). The median (IQR) duration of analgesic medication use was 10 (8-13) days for the tonsillectomy group and 5 (3-7) days for the tonsillotomy group; 14 patients in the tonsillectomy group and 5 patients in the tonsillotomy group were censored for continued analgesic use at day 14. Survival distributions for individual drug classes acetaminophen (hazard ratio, 0.3; 95% CI, 0.2-0.4), nonsteroidal anti-inflammatory (hazard ratio, 0.2; 95% CI, 0.1-0.2), and opioids (hazard ratio, 0.1; 95% CI, 0.0 - 0.2) were also significantly different, with shorter use in the tonsillotomy group (all $P < .001$) **Figure 3B-D**. For the tonsillectomy group, 14, patients were censored at 14 days for the acetaminophen analysis, 2 patients for the nonsteroidal anti-inflammatory analysis, and 0 patients for the opioid use analysis. For the tonsillotomy group, 3 patients were censored at 14 days for the acetaminophen analysis and 0 patients for the nonsteroidal anti-inflammatory and opioid use analyses.

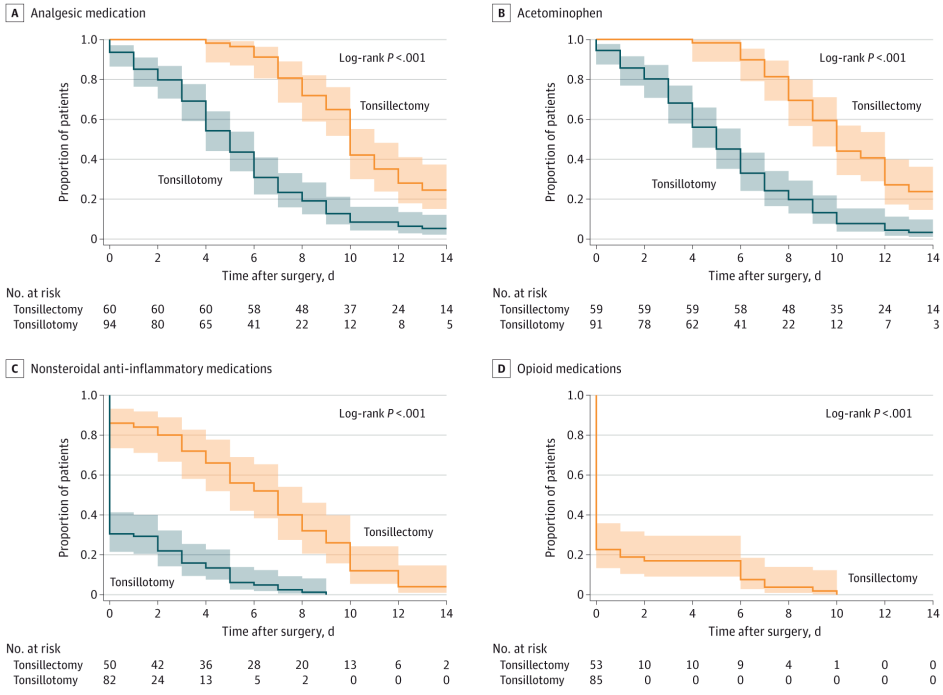


FIGURE 3. USE OF ANALGESIC MEDICATION DURING THE FIRST 2 WEEKS AFTER TONSILLOTOMY AND TONSILLECTOMY.

KAPLAN-MEIER CURVES SHOWING THE PROPORTION OF PATIENTS USING ANY TYPE OF ANALGESIC MEDICATION (A) OR A SPECIFIC TYPE OF ANALGESIC MEDICATION (B-D) DURING THE FIRST 2 WEEKS AFTER SURGERY. SHADED AREAS INDICATE 95% CIS.

Long-term Follow-up

Resolution of Tonsil-Related Symptoms

Six months after randomization to tonsillotomy or tonsillectomy, the chief concern persisted in 54 of 94 patients (57%) after tonsillotomy and in 25 of 71 patients (35%) after tonsillectomy (difference 95% CI, 7%-37%; $P = .005$) (**Table 2**). For patients with remaining concerns, the severity of the chief concern decreased significantly both in the tonsillotomy (mean [SD] baseline, 57.6 [18.1] vs follow-up, 37.6 [22.1]; effect size 0.88; $P = .01$) and tonsillectomy (mean [SD] baseline, 54.4 [13.6] vs 23.9 [11.3] follow-up; effect size 2.24; $P = .01$) groups. Most patients with persistent symptoms in both the tonsillotomy (32 of 54; 59%) and tonsillectomy (16 of 25; 64%) groups reported mild symptoms 6 months after surgery. When measured on a continuous scale of 0 to 100, patients with persistent symptoms in the tonsillotomy group reported slightly higher symptom severity compared with the tonsillectomy group (mean [SD], 38 [22] vs 26 [13] mm; effect size 0.66; $P = .02$). For patients with remaining tonsil concerns, the distribution

of the chief concern leading to surgery was similar to the baseline distribution among patients in the tonsillotomy group (baseline: sore throat without fever, 31 [32%]; sore throat with fever, 33 [34%]; tonsillolithiasis, 32 [33%]; snoring, 2 [2%]; and dysphagia 0 [0%] vs persistent symptoms: sore throat without fever, 16 [30%]; sore throat with fever, 14 [26%]; tonsillolithiasis, 23 [43%]; snoring, 1 [2%]; and dysphagia, 0 [0]%; $P = .64$) and in the tonsillectomy group (baseline: sore throat without fever, 33 [33%]; sore throat with fever, 33 [33%]; tonsillolithiasis, 32 [32%]; snoring, 2 [2%]; and dysphagia, 1 [1%] vs sore throat without fever, 9 [36%]; sore throat with fever, 8 [32%]; tonsillolithiasis, 6 [24%]; snoring, 2 [8%]; and dysphagia, 0 [0%]; $P = .52$), indicating that the type of tonsil concern did not influence treatment success.

Table 2. Characteristics of Patients With Persistent Symptoms After Tonsillotomy and Tonsillectomy as Well as Secondary Outcomes 6 Months After Surgery in All Patients Receiving Tonsillotomy or Tonsillectomy

Variable	No. (%) of patients		*P* value
	Tonsillotomy	Tonsillectomy	
Tonsil symptoms in patients with persisting symptoms			
Persistence of primary symptom that led to surgery[a]	54 (57)	25 (35)	.005
Self-reported severity of tonsil concerns in patients with persisting symptoms[b]			
Minimal	0	0	.46
Mild	32 (59)	16 (64)	
Moderate	13 (24)	8 (32)	
Severe	9 (17)	1 (4)	
Self-reported severity of tonsil concerns in patients with persistent symptoms (continuous), mean (SD), mm[c,d]	38 (22)	26 (13)	.02
Type of chief concern that led to surgery in patients with persistent symptoms[e]			
Sore throat without fever	16 (30)	9 (36)	.25
Sore throat with fever	14 (26)	8 (32)	
Tonsillolithiasis	23 (43)	6 (24)	
Snoring	1 (2)	2 (8)	
Dysphagia	0	0	
Quality of life and work or activity impairment			
No.	94	71	
QOL (EQ-5D-5L) index score, median (IQR)[b,f]	1 (0.85-1.00)	1 (0.87-1.00)	.20
EQ-5D-5L general health rating, median (IQR)[b,g]	80 (74-90)	85 (74-91)	.14
Employed[a]	73 (78)	54 (75)	.69
WPAI overall work impairment, median (IQR), %[b]	0 (0-10)	0 (0-0)	.001
WPAI interference with daily activities score, median (IQR)[b,h]	1 (0-3)	1 (0-2)	.24
Patient satisfaction			
Satisfaction with procedure score, median (IQR)[b,g]	77 (53-97)	87 (67-100)	.02

Abbreviations: EQ-5D-5L, 5-level EuroQol 5-Dimensions survey; QOL, quality of life; WPAI, Work Productivity and Activity Impairment questionnaire.

[a] χ^2 Test.

[b] Mann-Whitney test.

[c] Measured using a 100-mm visual analog scale.

[d] Unpaired *t* test.

[e] Fisher exact test.

[f] Range of the measurement instrument is −0.329 to 1.00.

[g] Range of the measurement instrument is 0 to 100.

[h] Range of the measurement instrument is 0 to 10.

Quality of Life, Work Productivity, and Activity Impairment

At 6 months after surgery, patients in both the tonsillotomy (median [IQR] EQ-5D index, 1.00 [0.85-1.00]) and tonsillectomy (median [IQR] EQ-5D index, 1.00 [0.87-1.00]) groups reported excellent quality of life ($P = .20$). Patients in both the tonsillotomy (median [IQR] EQ-5D index: baseline, 0.87 [0.81-1.00) vs follow-up, 1.00 [0.85-1.00]; effect size, 0.24; $P = .005$) and tonsillectomy (median [IQR] EQ-5D index: baseline, 0.87 [0.84-1.00] vs follow-up, 1.00 [0.87-1.00]; effect size, 0.45; $P = .003$) groups experienced an increase in the quality of life index when compared with baseline. Patients in the both the tonsil-

lotomy (median [IQR] WPAI work impairment at baseline, 7% [2%-12%] vs follow-up, 0% [0%-10%]; effect size, 0.15; $P = .04$) and tonsillectomy (median [IQR] WPAI work impairment at baseline, 5% [0%-11%] vs follow-up, 0% [0%-0%]; effect size, 0.39; $P = .005$) groups experienced improved participation in work and in daily activities compared with baseline (median [IQR] WPAI interference with daily activities at baseline, 3 [2-6] vs follow-up, 1 [0-3]; effect size, 0.65; $P < .001$; and for tonsillectomy at baseline, 4 [2-6] vs follow-up, 1 [0-2]; effect size, 1.19, $P < .001$).

Patient Satisfaction

At 6 months after surgery, overall patient satisfaction with treatment was slightly higher in the tonsillectomy group compared with the tonsillotomy group (median [IQR] score, 87 [67-100] vs 77 [53-97] mm; effect size, 0.35; $P = .02$). Similar percentages of patients in both the tonsillotomy and tonsillectomy groups would recommend the procedure to friends and family (80% vs 83%; difference 95% CI, −15% to 9%; $P = .83$).

Discussion

Consistent with our primary hypothesis, this randomized clinical trial found that recovery, defined as time to both functional recovery and resumption of work, was shorter after tonsillotomy than after tonsillectomy. In addition, patients in the tonsillotomy group had less postoperative pain and shorter use of analgesic medication compared with patients in the tonsillectomy group. The types of analgesics used were also less potent. The tonsillectomy group had more postoperative hemorrhages. After 6 months, the chief concern persisted more often in patients randomized to tonsillotomy. We also found that 13% of patients in the tonsillotomy group required a second tonsillotomy treatment for remaining tonsil concerns. For patients in both the tonsillotomy and tonsillectomy groups who still experienced symptoms after 6 months, the severity of the symptoms decreased.

The shorter functional recovery, lower level of pain, and lower rate of hemorrhaging we found are consistent with previous studies. A prospective observational study by Lourijsen et al[24] comparing laser tonsillotomy performed under local anesthesia to tonsillectomy found a shorter and less painful recovery period after tonsillotomy, lower mean pain 2 weeks after surgery (5.4 vs 7.7 on a 10 cm VAS), and less postoperative hemorrhaging (4.1% vs 6.5%). A randomized clinical trial by Ericcson et al[26] comparing radiofrequency tonsillotomy performed under general anesthesia with tonsillectomy found a significantly faster resumption of normal activities with tonsillotomy (mean [SD], 6.4 [2.3] days) compared with tonsillectomy (10.6 [2.8] days); lower pain on post-

operative days 1, 3, 5, and 10; lower analgesic medication requirements; and fewer postoperative hemorrhage events. Other studies have also found lower bleeding rates with tonsillotomy vs tonsillectomy. [27–30]

On the basis of direct surgical considerations, we believe that the differences in functional recovery, postoperative pain, and complications may be exclusively attributed to the less invasive nature of tonsillotomy. The postoperative wound after tonsillotomy may be comparable to a serious abrasion, whereas after tonsillectomy, tissue damage is more extensive, exposes the underlying constrictor muscle, and includes large blood vessels. This damage increases the risk of more serious postoperative hemorrhage. Similarly, after tonsillectomy, more and larger diameter sensory nerves are damaged, which adds to a significantly longer and more painful functional recovery period.

Eighteen patients who underwent tonsillotomy performed under local anesthesia required additional tonsillotomy or tonsillectomy treatment within 6 months of the initial study treatment because of residual symptoms or unfinished primary tonsillotomy treatment. All patients tolerated tonsillotomy treatment well; however, 3 tonsillotomy treatments were stopped because of increased bleeding. All initial tonsillectomy procedures were performed successfully under general anesthesia. At the 6-month follow-up, persistence of tonsil-related symptoms was significantly higher after tonsillotomy than after tonsillectomy, with 57% of patients in the tonsillotomy group still experiencing some level of symptoms compared with 35% of patients after tonsillectomy. However, patients with persistent tonsil-related concerns reported a significant decrease in symptom severity. Leaving some residual tonsil tissue is part of a successful tonsillotomy treatment. This is most likely the cause of the persistent tonsil-related concerns and may explain the difference found in this study. After the complete removal of the tonsils during tonsillectomy, tonsil symptoms persisting after surgery are unlikely. Throat concerns, however, can be caused by a variety of non–tonsil-related diseases, such as laryngopharyngeal reflux and pharyngitis. In fact, tonsillitis is often accompanied by pharyngitis.[31] The coexistence of multiple anatomical disease generators may explain the persistence of patient-reported concerns after tonsillectomy.[32] Consistent with the improvement in symptoms for patients with persistent symptoms in the tonsillotomy and tonsillectomy groups, both groups showed decreases in work impairment and of impairments in daily activities 6 months after surgery compared with baseline, with both groups reporting excellent quality of life at long-term follow-up. The percentage of patients who would recommend their treatment to others was similarly high for the tonsillectomy and tonsillotomy groups. This is surprising in light of the less effective symptom resolution that was provided by tonsillotomy. Perhaps the risk of needing a

second tonsillotomy treatment for residual symptoms was offset by the benefits of local anesthesia, faster recovery, and overall lower complication rate.

Limitations

This study has limitations. One important limitation is the uneven distribution of patients between the tonsillotomy and tonsillectomy groups who received their randomized treatment. We postulate that the higher patient withdrawal rate in the tonsillectomy group reflected the real-world hesitation to undergo tonsillectomy among patients. We emphasize that this withdrawal is not outcome dependent and therefore should not bias our results unless prognosis of the withdrawn patients differs from the general population. We compared the characteristics listed in **Table 1** between patients who received treatment and patients who withdrew from the randomized surgical treatment and found no significant differences between groups, except for percentage of patients who were employed (78% vs 50%; $P = .02$). Thus, we have no indication that withdrawal biased our results. We also note that our modified intention-to-treat analysis of functional recovery and our intention-to-treat analysis of long-term follow-up symptom resolution represent real-world estimates of patient burden and treatment effect on symptoms.

We found no indication that the type of tonsil concern influenced treatment success. However, our study was likely underpowered to find any difference in specific subgroups. Further research should be conducted to assess potential differences.

The incidence of postoperative hemorrhage in the tonsillectomy group was higher than previously reported from retrospective studies.[32–34] We believe that part of the higher postoperative hemorrhage rate in the present study may be attributed to our strict follow-up, which included questions directly related to complications, including post-operative hemorrhage. Other prospective studies have similar unexpected high rates of postoperative hemorrhages after cold steel dissection tonsillectomy.[35,36]

Finally, in the present study, patients with peritonsillar abscesses and patients with an indication for histopathologic analysis of the excised tonsil tissue (eg, to rule out malignant neoplasm) were excluded, and therefore the results of this trial do not apply to these populations. We recommend that patients with peritonsillar abscess be treated with tonsillectomy owing to the risk of recurrence of abscesses and the potentially lethal complications.[37] Potential residual tonsil tissue after tonsillotomy in those cases is not desirable.[38] Furthermore, when histopathologic analysis is required, laser tonsillotomy is not suitable because all of the tissue is evaporated by laser heating.

Conclusions

This randomized clinical trial found that laser tonsillotomy performed under local anesthesia was a safe alternative to conventional tonsillectomy performed under general anesthesia for tonsil-related conditions among adults and was associated with a significantly shorter and less painful functional recovery period. Six-month follow-up data indicated that more tonsil concerns remained after tonsillotomy than after tonsillectomy, leading to a second tonsillotomy treatment for some patients. Depending on individual patient preferences, laser tonsillotomy performed under local anesthesia may be an alternative for conventional tonsillectomy performed under general anesthesia.

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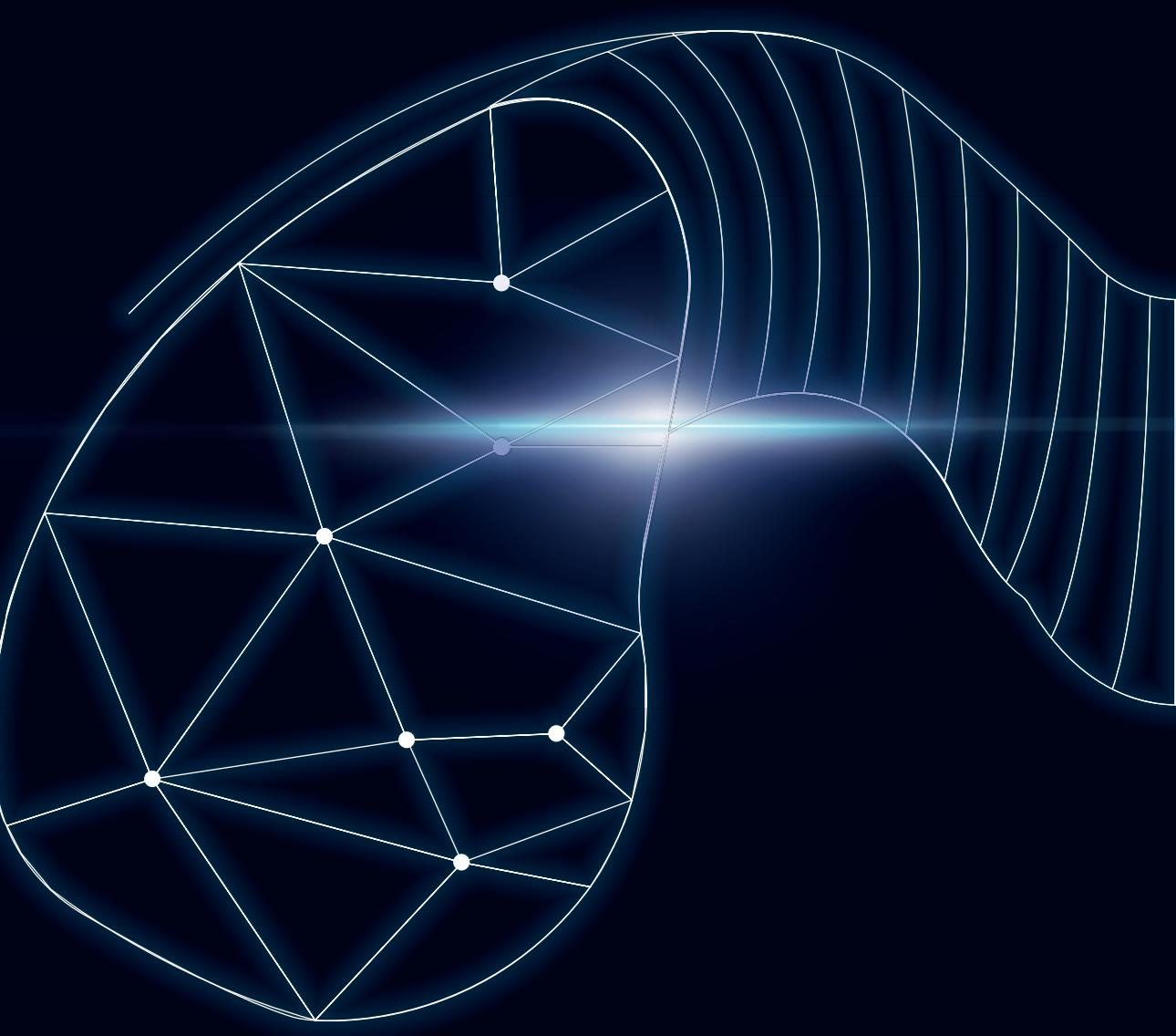

CHAPTER 7

Long-Term Efficacy and Cost-Effectiveness of Laser Tonsillotomy vs Tonsillectomy

A Secondary Analysis of a Randomized Clinical Trial

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Abstract

Importance The current treatment for adult tonsil disease, tonsillectomy (TE), may involve a burdensome recovery.

Objective To evaluate long-term efficacy (1- and 2-year efficacy) and cost-effectiveness of carbon dioxide (CO_2) laser tonsillotomy (TO) vs TE.

Design, Setting, and Participants A prespecified secondary analysis of a randomized clinical trial was conducted in 5 Dutch hospitals. Participants included adults with persistent tonsil-related symptoms enrolled from January 25, 2018, to December 17, 2019. Data analysis was performed from January 5, 2025, to April 9, 2025.

Interventions Tonsillectomy under general anesthesia vs CO_2 laser TO under local anesthesia.

Main Outcomes and Measures Intention-to-treat analysis on primary (persistent symptoms, defined as an answer of yes to the question of whether symptoms were still present, reported at 1 and 2 years) and secondary (symptom severity, patient satisfaction, quality-adjusted life-years [QALYs], and cost-effectiveness) outcomes.

Results In total, 98 patients were assigned to TO and 101 to TE; 98 were analyzed per group. The TO and TE groups were similar (69 [70%] vs 67 [68%] female; mean [SD] age, 29 [10] vs 30 [8] years). The most common symptom was sore throat with fever (34% vs 34%), with a baseline mean (SD) severity score of 57 (19) vs 59 (17) mm. At 1 year, 51.8% of patients assigned to TO had persistent symptoms vs 25.2% assigned to TE (odds ratio [OR], 3.2; 95% CI, 1.6-6.4; $P < .001$); at 2 years, 45.2% vs 19.7% had persistent symptoms (OR, 3.4; 95% CI, 1.7-6.7; $P < .001$). Symptom severity decreased significantly in both groups but was lower after TE at 1 year (14.8 vs 23.0 mm; mean difference, −8.1 mm; 95% CI, −14.8 to −1.5 mm; $P = .02$) and 2 years (10.8 vs 19.6 mm; mean difference, −8.8 mm; 95% CI, −14.7 to −2.9 mm; $P = .001$). Patient satisfaction was similar between groups; mean VAS scores were 79.0 (95% CI, 72.2-85.9) mm for TE and 69.3 (95% CI, 63.4-75.3) mm for TO at 1 year and 64.1 (95% CI, 55.7-72.5) mm and 64.4 (95% CI, 56.9-71.8) mm at 2 years. Similar proportions of participants would recommend the procedure at 1 year (79% TE vs 76% TO) and 2 years (71%, both). Both TE and TO demonstrated high cumulative QALYs at 2 years (EuroQol 5 Dimension: mean, 1.89 vs 1.84; mean difference, 0.05, $P = .06$; EuroQol Visual Analogue Scale: mean, 1.83 vs 1.81, mean difference, 0.02; $P = .38$). Tonsillotomy had lower overall costs ($869 vs $2363 for TE), with societal

cost savings of $1925 ($P = .001$), and a 71% probability of cost-effectiveness at $25 907 per QALY (85%-93% in sensitivity analyses).

Conclusions and Relevance The findings of this trial suggest that both CO_2 laser TO and TE under general anesthesia significantly reduced long-term symptoms, with greater reduction after TE. TO had lower cost and similar patient satisfaction. Based on these findings, CO_2-laser TO appears to be a safe, effective, and cost-effective method for long-term relief of tonsil-related problems with excellent patient satisfaction.

Introduction

Tonsillectomy (TE) is a widely performed surgery under general anesthesia for adults with tonsil-related conditions such as recurrent tonsillitis, tonsillolithiasis, and airway obstruction, particularly when conservative treatment is ineffective. While TE is effective, it is invasive and associated with complications such as postoperative bleeding, infection, and substantial pain.[1,2] Given its invasive nature, there is growing interest in less-invasive alternatives, such as carbon dioxide (CO_2) laser tonsillotomy (TO), which can be performed under local anesthesia.[3]

Short-term studies suggest that CO_2 laser TO offers safer, faster recovery and reduced postoperative pain compared with TE.[4,5] The short-term results of the TOMTOM trial suggest that 77% of patients who underwent CO_2 laser TO fully recovered within 2 weeks, compared with 57% of those who underwent TE, with a median time to return to work of 4.5 vs 12.0 days. Postoperative complications were also lower, with hemorrhage rates of 2% for CO_2 laser TO compared with 12% for TE.[4] Although tonsil-related symptoms persisted more frequently after CO_2 laser TO (57% TO vs 35% TE), symptom severity was greatly reduced and patients report similarly high satisfaction in both study arms.[5] Limited data on long-term outcomes and cost-effectiveness of CO_2 laser TO leave uncertainty about the role of CO_2 laser TO in clinical practice. This study compares the 1- and 2-year efficacy and cost-effectiveness of CO_2 laser TO and TE under general anesthesia in adults in the TOMTOM study.

Methods

Study design and patients

This prespecified secondary analysis of original data examines a randomized clinical trial (TOMTOM study) that was conducted in 5 Dutch teaching hospitals. The present study adheres to the Consolidated Standards of Reporting Trials (**CONSORT**) reporting guideline. Results for the primary outcome of the TOMTOM trial have been previously reported.[5] Approval by the local medical ethics committee (METC Zuid-West Holland) was obtained. Patients were recruited from January 25, 2018, to December 17, 2019. All patients provided written informed consent; no financial compensation was provided. Adults with chronic or recurrent tonsillitis, halitosis, tonsillolithiasis, dysphagia, and sleep apnea were included if their symptoms were unresponsive to conservative treatments. Key exclusion criteria included Friedman grade 4 tonsil size, contraindications to anesthesia, and pregnancy. Full patient inclusion and exclusion details are provided in the trial protocol (**Supplement 1**) and in eMethods in **Supplement 2**.

Randomization

Patients were randomized to either CO_2 laser TO or TE using computer-generated stratification based on primary tonsil concern. Patients could undergo additional surgical treatments if clinically necessary for a pragmatic and ethical trial design. Data collection continued even if patients opted out of their assigned treatment.

Procedures

The CO_2 laser TO procedure was performed under local anesthesia with xylocaine and adrenaline, following standard safety protocols. A step-by-step video protocol for this intervention has been previously published.[6] Classic TE was performed under general anesthesia using standard dissection and electrosurgical techniques. Procedure protocols and postoperative pain medication details can be found in **Supplement 1** (Chapter 10 of this thesis).

Data collection

Outcomes were collected via digital questionnaires at 1 and 2 years post surgery, measuring tonsil-related symptoms, quality of life (EuroQol 5 Dimension [EQ-5D], range 1 [representing full health] to 0 [representing death]; EuroQol Visual Analogue Scale [EQ-VAS], vertical visual analogue scale with values between 1 [best imaginable health] and 0 [worst imaginable health]),[7] health care use, Work Productivity and Activity Impairment,[8] and patient satisfaction with treatment (visual analog scale [VAS], range 0-100 mm, with higher scores indicating greater satisfaction). Recovery times were collected at 2 and 6 weeks. Missing data were handled using multiple imputation. More details can be found in eMethods in **Supplement 2.**

Economic evaluation

A cost-utility analysis was conducted from a societal perspective, at 2023 price levels, with a 2-year horizon. Utility reflects the value of quality of life (scale 0-1) and was calculated using the Dutch tariff for the EQ-5D[9] and EQ-VAS data.[10] A cost-price analysis was performed for both procedures. All costs were analyzed in euros and subsequently converted to US dollars using the 2024 Organisation for Economic Co-operation and Development Purchasing Power Parity for gross domestic product (€0.772=$1). Quality-adjusted life years (QALYs) were derived from the area under the utility curves over the follow-up period. EQ5-VAS scores were analyzed as 0-1 scores. Other tonsil-related health care, absenteeism, and presenteeism at work were patient-reported. Three sensitivity analyses were performed in which costs were limited to health care costs (instead of societal costs), patients without registered TE or CO_2 laser TO were assumed to have had TE (instead of assuming no procedure), and QALYs were calculated from the EQ-

VAS (instead of the EQ-5D index score). Full economic evaluation details are available in eMethods in **Supplement 2**.

Statistical analysis

Data analysis was conducted from January 5, 2025, to April 9, 2025. The target sample size was determined for previously published short-term outcomes of this study.[5] Based on prior short-term outcomes,[4] the target sample size was 190 patients (95 per group) to achieve 80.2% power at a .05 significance level. This allowed for the detection of a median recovery time of 8.0 days for CO_2 laser TO, compared with 13.5 days for TE, with a 14-day observation period.

Baseline characteristics were summarized as means (SDs) or counts (percentages). Long-term outcomes were analyzed on an intention-to-treat basis, using unpaired *t* tests for pooled means and logistic regression for binary outcomes. Changes from baseline were assessed with paired *t* tests. All tests were 2-sided, with a significance level of $P < .05$. Analyses were conducted using SPSS, version 27 (IBM Corp), with annual external data monitoring ensuring data quality. Additional statistical methods are presented in the protocol in Supplement 1.

Results

Patient inclusion and disposition

Of the 199 patients randomized, 98 were assigned to CO2 laser TO and 101 to TE. After excluding 3 patients in the TE group due to informed consent discrepancies, 196 patients were included in the final analysis (**Figure 1**). The CO2 laser TO and TE groups were similar (TO: 69 [70%] female, 29 [30%] male vs TE: 67 [68%] female, 31 [32%] male; mean [SD] age, 29 [10] vs 30 [8] years).

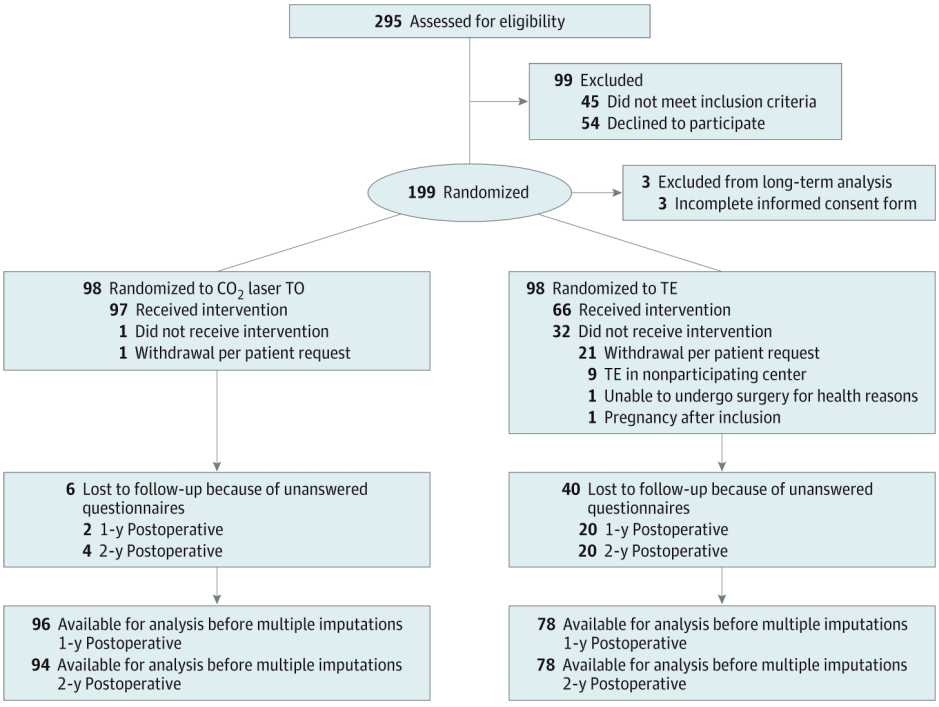


FIGURE 1. TRIAL FLOW DIAGRAM. CO_2 INDICATES CARBON DIOXIDE; TE TONSILLECTOMY; AND TO, TONSILLOTOMY.

Baseline characteristics were comparable between the TO and TE groups in terms of chief tonsil symptoms, with sore throat with (34% vs 34%) and without fever (32% vs 32%) being the most common, followed by tonsillolithiasis (33% vs 32%). The self-reported severity of tonsil symptoms (mean [SD] severity score) was similar between groups (mean [SD], 57 [19] mm for TO vs 59 [17] mm for TE), and most patients rated their symptoms as moderate or severe. Smoking status also showed a similar distribution between groups, with approximately 18% to 14% current smokers, 25% to 16% former smokers, and 58% to 47% never smokers for CO2 laser TO vs TE (**eTable 1** in **Supplement 2**). A total of 163 patients (82%) received their assigned treatment.

	Tonsillotomy (n = 98)	Tonsillectomy (n = 98)
Demographic characteristics		
Sex: M/F n (%)		
Male	29 (30)	31 (32)
Female	69 (70)	67 (68)
Age in years, mean ± SD	29 ± 10	30 ± 8
Smoking status, n (%)		
Current	17 (18)	14 (14)
Former	24 (25)	16 (16)
Never smoked	56 (58)	46 (47)
Tonsil symptoms		
Chief tonsil complaint, n (%)		
Sore throat without fever	31 (32)	31 (32)
Sore throat with fever	33 (34)	33 (34)
Tonsillolithiasis	32 (33)	31 (32)
Snoring	2 (2)	2 (2)
Dysphagia	0 (0)	1 (1)
Self-reported severity of tonsil complaints (ordinal), n (%)		
Minimal	1 (1)	1 (1)
Mild	21 (22)	18 (18)
Moderate	59 (61)	47 (48)
Severe	16 (16)	10 (10)
Self-reported severity of tonsil complaints (continuous) in mm, mean ± SD	57 ± 19	59 ± 17
Quality of life and work/activity impairment		
QoL (EQ-5D-5L) index score, median (IQR)	0.87 (0.81 – 1.00)	0.87 (0.84 – 1.00)
EQ-5D-5L general health rating, median (IQR)	80 (70 – 89)	80 (70 – 89)
Employed, n (%)	70 (74)	57 (58)
WPAI overall work impairment in %, median (IQR) [a]	7 (2 – 12)	5 (0 – 11)
WPAI interference with daily activities (0-10), median (IQR)	3 (2 – 6)	4 (2 – 6)
EQ-5D-5L = Euroqol 5 dimensions quality of life (QoL) survey WPAI = Work Productivity and Activity Impairment Questionnaire		

eTable 1. Baseline demographic and clinical characteristics in tonsillotomy and tonsillectomy groups.

In the CO2 laser TO group, 17 patients required a second treatment for residual symptoms, 9 switched to TE for recurrent symptoms. In the TE group, 32 did not undergo the assigned procedure, and 9 patients reported to have received TE at nonparticipating centers. The primary reason for withdrawal in the TE group was patients opting out after randomization (**Figure 1**). More censored patients were noted in the TE vs TO group for full recovery (35 vs 22), return to work (8 vs 5), and analgesic use (16 vs 3).

In the CO_2-laser TO group, 17 required a second treatment for residual symptoms, nine switched to TE for recurrent symptoms. In the TE group, 32 did not undergo the assigned procedure, and 9 patients reported to have received TE non-participating centers. The primary reason for withdrawal in the TE group was patients opting out after randomization **(Figure 1).** More censored patients were noted in the TE group for full recovery (35 vs. 22), return to work (8 vs. 5), and analgesic use (16 vs. 3).

Efficacy

One year after surgery, 25.2% of TE patients reported persistent symptoms compared to 51.8% in the CO_2-laser TO group (odds ratio [OR] [95% CI] 3.2 [1.6 to 6.4], $P < .001$) **(Figure 2)**. At two years, 19.7% of TE patients versus 45.2% of CO_2-laser TO patients reported persistent symptoms (OR 3.4 [1.7 to 6.7], $P<.001$).

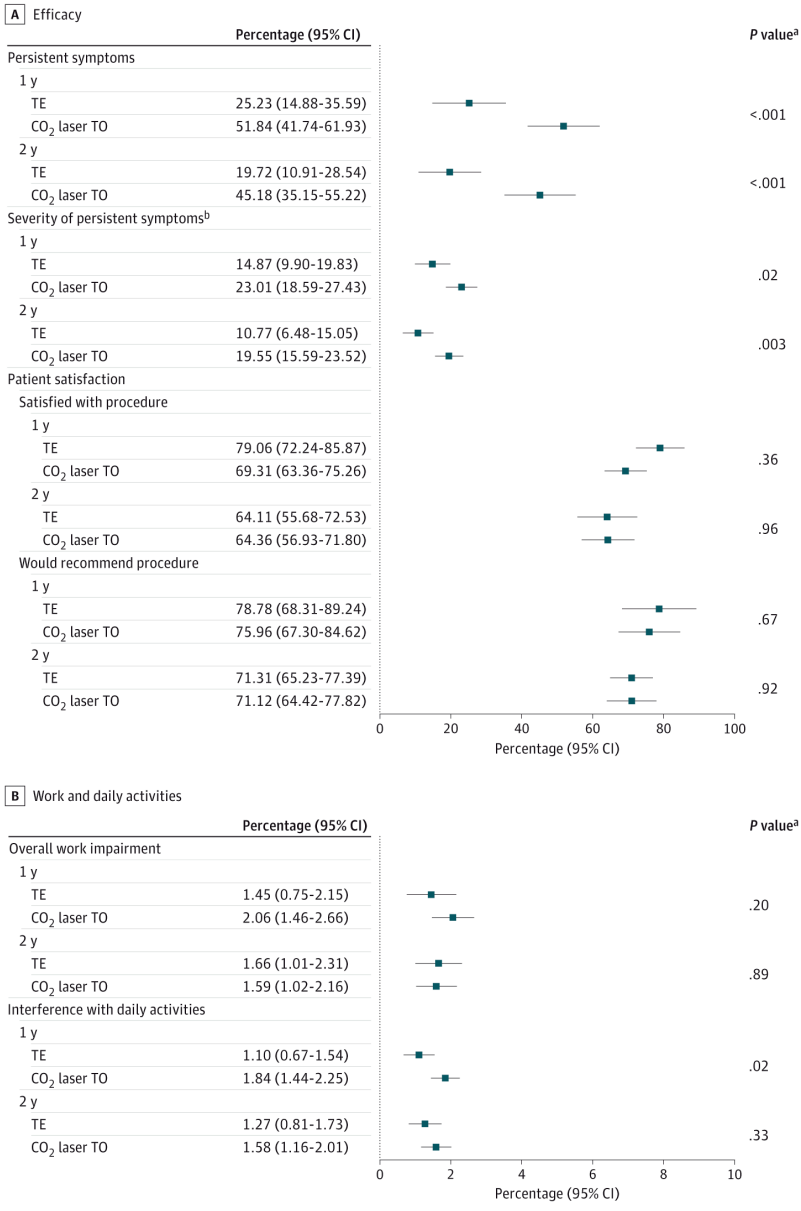


FIGURE 2. LONG-TERM OUTCOME MEASURES.

ONE- AND 2-YEAR MEASURES OF EFFICACY (A) AND WORK AND DAILY ACTIVITIES (B). WORK IMPAIRMENT WAS ASSESSED ONLY IN EMPLOYED PATIENTS. TE, TONSILLECTOMY; TO, TONSILLOTOMY.

[A] *P* VALUES ARE BASED ON INDEPENDENT *T* TESTS FOR CONTINUOUS VARIABLES AND LOGISTIC REGRESSION FOR BINARY OUTCOME VARIABLES.

[B] MEASURED ON A VERTICAL VISUAL ANALOGUE SCALE WITH VALUES BETWEEN 100 (BEST IMAGINABLE HEALTH) AND 0 (WORST IMAGINABLE HEALTH).

Symptom severity in patients with remaining symptoms decreased significantly in both groups, but remained lower after TE at both 1 year (mean VAS score, 14.8; 95% CI, 9.9-19.8 vs mean, 23.0; 95% CI, 18.6-27.4 mm; mean difference, −8.1; 95% CI, −14.8 to −1.5 mm; P = .02) and 2 years (mean VAS score, 10.8; 95% CI, 6.5-15.1 vs mean, 19.6; 95% CI, 15.6-23.5 mm; mean difference, −8.8; 95% CI, −14.7 to −2.9 mm; P = .001). Symptom severity significantly decreased from baseline after 1 year in both the CO2 laser TO group (mean baseline, 56.6 vs 1 year, 23.0 mm; mean difference, 33.6; 95% CI, 28.5-38.7 mm; P < .001) and the TE group (mean baseline, 59.2 vs 1 year, 14.9 mm; mean difference, 44.3; 95% CI, 38.1-50.5 mm; P < .001). Among patients with persistent symptoms at 1 year, self-reported severity shifted toward mild and moderate after CO2 laser TO (mild 26.4%, moderate 22.0%, severe 3.5%) and TE (mild 18.0%, moderate 4.7%, severe 2.5%).

At 2 years, symptom severity continued to decrease in both groups: CO2 laser TO (mean baseline, 56.6 vs 2 years, 19.6 mm; mean difference, 37.1; 95% CI, 31.2-43.0 mm; P < .001) and TE (mean baseline, 59.2 vs 2 years, 10.8 mm, mean difference, 48.4; 95% CI, 42.8-54.0 mm; P < .001). Patients with persistent symptoms after 2 years experienced mostly mild and moderate symptoms in both the CO2 laser TO (mild 28.4%, moderate 14.7%, severe 2.1%) and TE (mild 9.0%, moderate 9.4%, severe 1.4%) groups.

Patient satisfaction

There was no significant difference 1 year after surgery in patient satisfaction (mean score, 79.0; 95% CI, 72.2-85.9 mm for TE and mean, 69.3; 95% CI, 63.4-75.3 mm for TO; P = .36) and 2 years post surgery (mean VAS score, 64.1; 95% CI, 55.7-72.5 mm for TE and mean, 64.4; 95% CI, 56.9-71.8 mm for TO; P = .96). Almost equal percentages of patients would recommend their surgery to others at both 1 year (TE, 79% vs TO, 76%; OR, 0.8; 95% CI, 0.4-1.9; P = .67) and 2 years (both 71%; OR, 1.0; 95% CI, 0.5-2.1; P = .92).

Work and daily activities

Work impairment was minimal in both the CO2 laser TO and TE groups at 1 year (TO: mean, 2.1%; 95% CI, 1.5%-2.7%; vs TE: mean, 1.5%; 95% CI, 0.8%-2.2%; mean difference, −0.6%; 95% CI, −1.5%-0.5%; P = .20) and 2 years (TO: mean, 1.6%; 95% CI, 1.0%-2.2% vs TE: 1.7%; 95% CI, 1.0%-2.3%; mean difference, 0.1%; 95% CI, −0.8% to 0.9%; P = .93). Absolute interference with daily activities was similarly low in both groups at long-term follow-up, but was statistically lower in the TE group at 1 year (TE: mean, 1.1%; 95% CI, 0.7%-1.5% vs TO: mean, 1.8%; 95% CI, 1.4%-2.2%; mean difference, −0.7%; 95% CI, −1.3% to −0.1%; P = .02) but not 2 years postoperatively (mean, 1.3; 95% CI, 0.8-1.7 mm after TE vs 1.6; 95% CI, 1.2-2.0 mm after TO; mean difference, −0.3; 95% CI, −0.9 to 0.3 mm; P = .33).

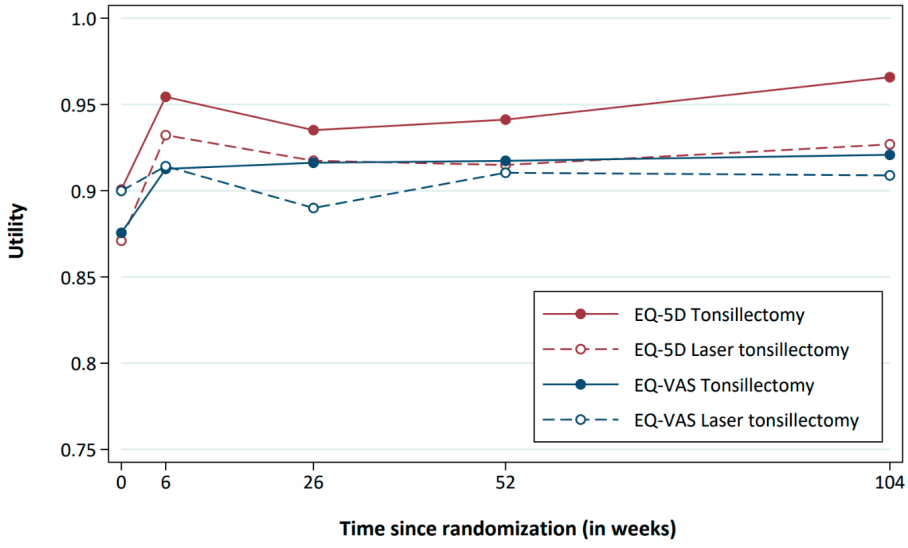
Utilities and QALYs

All postbaseline health-related quality of life utility measures showed small differences between the TE and CO2 laser TO groups (**Table 1; eFigure in Supplement 2**), mostly without statistical significance. Over 2 years, the cumulative QALY difference was 0.05 according to the EQ-5D (TO vs TE: means, 1.89 vs 1.84; P = .06; mean difference, 0.05; 95% CI, −0.00 to 0.11) and 0.02 according to the cumulative EQ-VAS (TO vs TE: means, 1.83 vs 1.81; P = .38; mean difference, 0.02; 95% CI, −0.03 to 0.07).

Table 1. Utilities and QALYs, Over Time and by Randomization Group

Characteristic	Utility measures		Difference (95% CI)	*P* value
	Tonsillotomy (n = 98)	Tonsillectomy (n = 98)		
EQ-5D utilities				
Baseline	0.87	0.90	0.03 (−0.01 to 0.07)	.15
6 wk	0.93	0.95	0.02 (−0.01 to 0.05)	.17
6 mo	0.92	0.94	0.02 (−0.02 to 0.06)	.36
12 mo	0.91	0.94	0.03 (−0.01 to 0.07)	.21
24 mo	0.93	0.97	0.04 (−0.00 to 0.07)	.03
EQ-5D QALYs				
Year 1	0.92	0.94	0.02 (−0.01 to 0.05)	.14
Year 2	0.92	0.95	0.03 (0.00 to 0.06)	.05
Both	1.84	1.89	0.05 (−0.00 to 0.11)	.06
EQ-VAS utilities				
Baseline	0.90	0.87	−0.02 (−0.06 to 0.01)	.21
6 wk	0.91	0.91	0.00 (−0.04 to 0.04)	.94
6 mo	0.89	0.92	0.03 (−0.01 to 0.07)	.20
12 mo	0.91	0.92	0.01 (−0.02 to 0.04)	.65
24 mo	0.91	0.92	0.01 (−0.01 to 0.04)	.36
EQ-VAS QALYs				
Year 1	0.90	0.91	0.01 (−0.02 to 0.04)	.40
Year 2	0.91	0.92	0.01 (−0.01 to 0.03)	.44
Both	1.81	1.83	0.02 (−0.03 to 0.07)	.38

Abbreviations: EQ-5D, EuroQol 5 Dimension; EQ-VAS, EuroQol Visual Analogue Scale; QALYs, quality-adjusted life-years.



eFIGURE. UTILITIES OVER TIME, BY RANDOMIZATION GROUP.

Costs

Costs per CO2 laser TO procedure were estimated at less than half the costs of the TE procedure ($869 vs $2363) (**eTable 2 in Supplement 2**). The difference in average surgery costs per patient was estimated at $304 (95% CI, $74-$534) (**Table 2**). This relatively small

difference was due both to untreated patients in the TE group and repeated treatment in the CO2 laser TO group.

eTABLE 2: COST PRICE OF THE TONSILLECTOMY AND CO_2-LASER TONSILLOTOMY PROCEDURES (IN €)

	Tonsillectomy	Laser tonsillotomy
Pre-procedure 10-minute outpatient visit[1]	197	197
Pre-operative anesthetic assessment	89	
Operating room[2] **- 60 minutes**	841	
Day-care admission - bed occupancy 120 minutes	585	
Outpatient personnel[3] **– 45 minutes**		136
Alterations to the outpatient treatment room[4]		15
Laser equipment[5]		123
Laser maintenance[6]		29
Laser materials		59
Post-procedure 10-minute outpatient visit	112	112
Total costs per procedure	1824	671

1. A pre-procedure outpatient visit was also counted for patients who did not undergo either procedure, but not for repeat CO_2-laser tonsillotomy
2. Including personnel
3. Physician plus an assistant
4. Assuming 25,000 euro, distributed over 2000 patients during 20 year
5. Assuming 105,000 euro, distributed over 1000 patients during 10 year
6. Assuming 2,500 euro annually, distributed over 100 patients

Table 2. Average 2-Year Tonsil-Related Health Care and Societal Costs Per Patient, by Randomization Group

	Tonsillotomy (n = 98)			Tonsillectomy (n = 98)			Differences	
Variable	%	Volume	Costs (SD), $	%	Volume	Costs (SD), $	Costs, $	*P* value
Tonsillectomy	9	0.09	185 (580)	76	0.76	1519 (865)	1334	<.001
CO_2-laser tonsillotomy	98	1.19	1030 (472)	0	0.00	0 (0)	−1030	<.001
Total surgery costs	99	1.29	1215 (754)	76	0.76	1519 (865)	304	.01
Pain medication	56	NA	10 (28)	34	NA	9 (31)	−1	.73
Antibiotics	25	NA	9 (25)	6	NA	1 (9)	−8	.01
General practitioner	37	0.94	52 (95)	32	0.71	39 (79)	−13	.38
Speech therapist	5	0.20	10 (47)	2	0.19	9 (82)	0	.96
Alternative care	3	0.09	9 (60)	1	0.02	3 (22)	−6	.27
Company physician	4	0.10	13 (75)	0	0.01	1 (26)	−12	.17
Emergency department	4	0.06	27 (136)	6	0.06	27 (109)	0	.99
Hospitalization[a]	3	0.21	168 (1315)	7	0.13	102 (573)	−65	.67
Total nonsurgery health care	NA	NA	299 (1567)	NA	NA	192 (624)	−106	.55
Total health care costs	NA	NA	1514 (1760)	NA	NA	1711 (1053)	197	.35
Absenteeism from work[b]	73	2.2	810 (1083)	72	5.8	2154 (3163)	1345	.003
Presenteeism at work[b]	56	0.7	254 (636)	47	1.7	637 (1334)	383	.03
Total productivity	76	2.9	1063 (1328)	73	7.5	2791 (3574)	1728	.001
Total societal costs (SD)	NA	NA	2578 (2223)	NA	NA	4503 (3777)	1925	.001

Abbreviation: NA, not applicable.

[a] Volume is in hospital days.

[b] During 6 weeks after the initial procedure. Volume is in working day equivalents.

Other health care costs were consistently higher in the CO2 laser TO group, but these differences were not statistically significant and were limited in size. The difference in total health care costs was estimated at a nonsignificant and small amount of $197 (95% CI, −$223 to $618).

Both absence from work and reduced productivity while at work were significantly higher in the TE group during 6 weeks after the initial procedure, with an estimated combined cost difference of $1728 (95% CI, $766-$2690). As a result, the total societal costs were also significantly higher in the TE group, by $1925 (95% CI, $854-$2997).

Cost-effectiveness

Figure 3 shows the probability that CO2 laser TO is cost-effective compared with TE, depending on the willingness to pay per QALY. For this relatively mild condition, the appropriate cost-effectiveness threshold in the Netherlands is $25 907 per QALY.[11] At that threshold, CO laser TO is 71% likely to be cost-effective compared with TE. The estimated cost-utility ratio is $36 269 per QALY (95% CI, $11 658-infinity), favoring the less-expensive CO2 laser TO.

Three sensitivity analyses were conducted to account for potential biases. In the first sensitivity analysis, only health care costs were considered, excluding productivity costs (**SA1 in Figure 3**). At a threshold of $25 907 per QALY, this reduced the likelihood of CO2 laser TO being cost-effective to 6%, highlighting the importance of productivity costs in cost-effectiveness.

In the TE group, 24% of patients had no registered TE, likely due to dropouts after not being assigned the CO2 laser TO. These patients may have received TE at a more convenient hospital. In the second sensitivity analysis, all unregistered cases were assumed to have received TE, which increased the surgery cost difference by $472, resulting in a total difference of $776 (95% CI, $627-$926). This raised the likelihood of CO2 laser TO being cost-effective from 71% to 85% at a $25 907 per QALY threshold (**SA2 in Figure 3**).

In the third sensitivity analysis (**SA3 in Figure 3**), QALYs were calculated using the EQ-VAS instead of the EQ-5D, reducing the QALY advantage for TE. This increased the probability of CO2 laser TO being cost-effective to 93% at a $25 907 per QALY threshold, with an estimated cost-utility ratio of $91 969 per QALY (95% CI, $24 611-infinity), favoring the less-expensive CO2 laser TO.

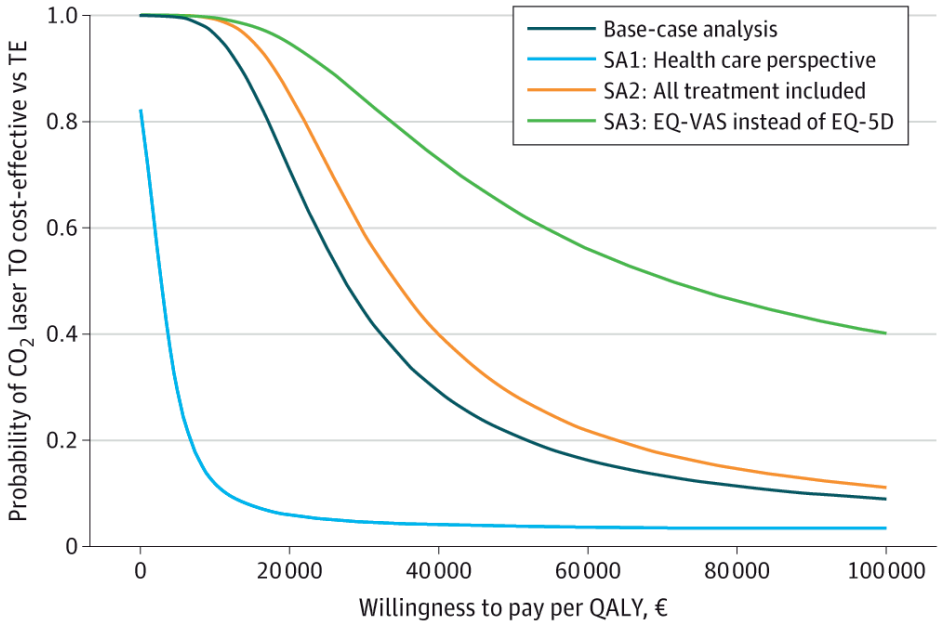


FIGURE 3. COST-EFFECTIVENESS ACCEPTABILITY CURVES

COST-EFFECTIVENESS ACCEPTABILITY CURVES SHOW THE PROBABILITY THAT CARBON DIOXIDE (CO2) LASER TONSILLOTOMY (TO) IS COST-EFFECTIVE COMPARED WITH TONSILLECTOMY (TE), DEPENDING ON THE WILLINGNESS TO PAY PER QUALITY-ADJUSTED LIFE-YEAR (QALY). DIFFERENT CURVES SHOW THE BASE-CASE ANALYSIS AND 3 SENSITIVITY ANALYSES. TO CONVERT EUROS TO US DOLLARS, THE 2024 ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT PURCHASING POWER PARITY FOR GROSS DOMESTIC PRODUCT (€0.772=$1) APPLIES. SA1: ONLY HEALTH CARE COSTS; SA2: ASSUMING UNREGISTERED CASES RECEIVED TE; AND SA3: EUROQOL 5 DIMENSION (EQ-5D) AND EUROQOL VISUAL ANALOGUE SCALE (EQ-VAS).

DISCUSSION

To our knowledge, this secondary analysis of a randomized clinical trial is the largest to compare long-term outcomes of CO2 laser TO and TE in adults. Previous findings reported that CO2 laser TO led to faster, less-painful recovery and lower postoperative hemorrhage compared with TE. Although symptom persistence was higher with CO2 laser TO at 6 months, both groups experienced reduced symptom severity, improved quality of life, and high patient satisfaction.[5] At 1- and 2-year follow-ups, patients who underwent TE reported fewer and milder symptoms than those who received CO2 laser TO. Both groups with residual symptoms experienced significant symptom reduction to clinically nonrelevant levels after 2 years (VAS <20 mm). Satisfaction, willingness to recommend surgery, and work productivity impact were similar across both time points. While CO2 laser TO had slightly lower QALYs, it significantly reduced surgery and productivity costs, with a 71% to 93% likelihood of being cost-effective. These findings are

consistent with the 6-month data, where 57% of patients in the CO2 laser TO group and 35% of those in the TE group had persistent symptoms, with 13% of patients in the CO2 laser TO group needing a second treatment.[5] Both groups showed reduced symptom severity at 6 months, which continued through the 1- and 2-year follow-ups. Quality of life improvements also persisted. Although patients in the TE group had slightly higher satisfaction at 6 months, this difference diminished over time. A similar percentage of patients in both groups would recommend their surgeries. These results address gaps in the literature, which emphasize short-term benefits of TO but with limited evidence on long-term outcomes.[3,12] The higher occurrence of residual symptoms after CO2 laser TO is likely due to incomplete tonsil removal, unlike TE. Retaining the tonsillar bed with major nerves and blood vessels allows CO2 laser TO to be performed under local anesthesia and reduces postoperative bleeding, which lowers the need for surgical revision due to hemorrhage and reduces postoperative pain and recovery time.[5] However, the management of postoperative bleeding may vary across institutions, particularly in the threshold for performing surgical revisions. This highlights the importance of considering institutional practices and patient preferences when counseling on TO vs TE. Some patients required a second procedure within 6 months, resulting in significant and lasting symptom improvement, underscoring the importance of adequate tissue removal for successful CO2 laser TO.

To date, few studies have compared the long-term efficacy of TE and TO in adults. A review reported no significant difference in outcomes over up to 6 years in 5 of 6 studies, although variations in surgical methods, indications, and criteria complicated comparisons, and some studies lacked quality.[3] A previous nonrandomized cohort study reported 72.5% of patients were symptom-free 1 year after CO2 laser TO vs 97.2% after TE, with similar satisfaction.[4] Outside the adult context, longer-term follow-up in children support the durability of TO. A 12-year follow-up study in children found no significant differences between TO and TE in disease-specific quality of life, throat infections, or satisfaction rates, with most patients free from tonsil-related issues.[13] Similarly, a 6-year randomized study in children comparing CO2 laser TO with TE found equally stable outcomes in snoring, apneas, and infections, with no significant differences between groups. Patient satisfaction and health improvements were high in both study arms.[14]

The cost-effectiveness of TO in adults has been minimally studied, with some research suggesting it may be more cost-effective than TE.[15,16] However, to our knowledge, this study provides the only systematic evaluation of TO cost-effectiveness in adults to date. In contrast, TE vs conservative management for recurrent tonsillitis in adults has been extensively studied, with a large randomized clinical trial showing TE to be both clinically effective and cost-effective compared with conservative management.2 While our

study lacked a conservative management arm, it is plausible that immediate CO2 laser TO is also cost-effective compared with conservative management. In this study, the costs for CO2 laser TO were considerably lower than for TE ($869 vs $2363). However, due to additional surgeries in the TO group, the total cost difference was reduced to $304. This likely underestimates the true cost difference, as some patients in the TE group may have received TE elsewhere during the study period. Given that over 100 000 tonsillectomy procedures are performed annually in the US alone, the potential cost savings demonstrated by CO2 laser TO could have substantial societal and health care system implications.[17] Beyond cost savings from avoiding general anesthesia, CO2 laser TO frees operating rooms for procedures requiring anesthesia. This logistical advantage is useful, especially with the growing global backlog of surgeries.[18] To our knowledge, this is the largest randomized clinical trial and the first to evaluate the cost-effectiveness of CO2 laser TO in adults, showing a 71% likelihood of being cost-effective compared with TE at a $25 907 per QALY threshold. Sensitivity analyses highlight the importance of productivity costs, as focusing solely on health care costs reduces this likelihood to 6%, while accounting for patients with unregistered TE increases it to 85%. These results rely on the EQ-5D tool for health-related quality of life measurement, which may not fully capture tonsil-related issues. The EQ-VAS, reflecting patients' overall health perceptions, could provide a more comprehensive assessment.[19,20] Using the EQ-VAS to calculate QALYs raises the likelihood of CO2 laser TO being cost-effective to 93%.

While there are many different methods used for TO surgeries, we chose to use a CO2 laser. The CO2 laser efficiently cuts and evaporates tissue with photothermal hemostasis, minimizing surrounding tissue damage, edema, and scarring compared with other methods.[21,22]

Limitations

This study has limitations. The TE group had a higher withdrawal rate, but since withdrawals were not based on treatment outcomes, bias is unlikely. Baseline characteristics of treated (both within and outside the study) and withdrawn patients showed no significant differences, suggesting minimal withdrawal bias. The higher TE withdrawal rate may reflect reluctance toward more invasive surgery, and the intention-to-treat analysis mirrors clinical practice patient burden and treatment effect. Sensitivity analysis assuming all withdrawals received TE elsewhere increased the surgical cost difference. Patients were asked about additional treatments during follow-up, but not all who opted out of TE completed questionnaires, potentially missing some TE treatments conducted outside the study. Multiple imputations addressed potential missing data bias. Further limitations are that nonsurgical health care and productivity were patient-reported and could

be subject to bias, as patients were aware of their treatment allocation. The study setting may not reflect other health care systems with different cost-effectiveness thresholds than the $25 907 per QALY used. Dutch postprocedure management practices and costs may not be entirely generalizable internationally due to differences in health care systems and guidelines, although the core findings, such as quicker recovery, reduced need for general anesthesia, and cost-effectiveness, are likely applicable in similar settings. Additionally, we did not specifically analyze the potential impact of procedural timing on absenteeism. While this factor could influence the results, any effect is likely minimal.

Conclusion

Based on results of this randomized clinical trial, CO2 laser TO appears to be ideal for adult patients prioritizing quicker recovery and less postoperative discomfort. It suits those unable or unwilling to undergo general anesthesia, need minimal disruption to daily activities, or are apprehensive about the invasiveness of TE.

In addition, CO2 laser TO is recommended for patients with mild to moderate recurrent tonsil-related symptoms, where full tonsil removal may not always be necessary. Although some residual tissue and symptoms may remain, TO significantly reduces symptom severity to clinically nonrelevant levels, with low postoperative risk and low health care cost. Its reduced need for in-hospital care and preservation of tonsillar structure might align better with health care goals of individual patients.

For patients who wish to avoid the possibility of a secondary procedure, traditional TE may be the more appropriate choice. Careful patient selection and counseling about the potential for residual symptoms and a secondary procedure are essential to optimizing outcomes and satisfaction. This personalized approach, backed by the major economic benefits demonstrated in this study, underscores the value of integrating CO2 laser TO into treatment strategies for persistent tonsil-related afflictions in adults.

This study's long-term follow-up showed that CO2 laser TO was less effective than TE in fully resolving tonsil issues but led to a substantial decrease in symptoms for all patients with residual symptoms, resulting in similar patient satisfaction. A slight advantage in 2-year QALYs was noted with TE, but CO2 laser TO was less costly, with lower societal costs due to reduced work absence and productivity loss. Based on these findings, CO2 laser TO appears to be a safe, effective, and cost-effective method for long-term relief of tonsil-related problems with excellent patient satisfaction.

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eMETHODS IN DETAIL

Study design and participants

The TOMTOM study (Netherlands Trial Register, Identifier: NL6866 [NTR7044]), conducted in 5 Dutch teaching hospitals, adhered to CONSORT guidelines and received approval from The Hague's Research Ethics Committee. Short-term follow-up results of this study were previously published.[1] Patients were recruited from January 2018 to December 2019.

The study included adult patients with chronic or recurrent tonsillitis, halitosis, tonsillolithiasis, dysphagia, and sleep apnea attributed to tonsillar problems. Tonsil symptoms had to be inadequately responsive to conservative treatment methods, necessitating surgical intervention as per the prevailing treatment guidelines in the Netherlands.[2] Exclusion criteria comprised inability to complete all trial procedures and follow-up visits, inability to keep the mouth open continuously for at least 5 seconds or relax the jaw for 30 minutes, Inadequate exposure of the entire tonsil on physical examination, including Friedman grade 4 (kissing) tonsils. With kissing tonsils, the laser must be directed straight toward the back of the throat during the initial phase of the laser treatment, increasing the risk of damaging the posterior pharyngeal wall due to the lack of a protective buffer of tonsil tissue. history of peritonsillar abscess, coagulation disorders (including anticoagulant use), contraindications for local or general anesthesia, evident tonsil asymmetry or signs suggesting potential (pre-)malignant oropharyngeal neoplasms, immunodeficiency, and pregnancy. Patients provided written informed consent.

Randomization

Computer-generated random numbers were used for assigning patients randomly to either CO_2-laser TO or TE, with stratified randomization based on their primary tonsil concern. Patients were allowed to undergo additional surgical treatments if clinically necessary to maintain a pragmatic and ethical randomized clinical trial design, and those who opted out of their assigned treatment were requested to allow continued data collection on tonsil symptoms and subsequent surgeries.

Procedures

CO2 Laser Tonsillotomy under Local Anesthesia

CO_2-laser TO was performed in ambulatory intervention rooms, adhering to standard laser safety guidelines.[3] Prior to surgery, each patient received oral acetaminophen (1 gram). Local anesthesia of the tonsil was achieved with xylocaine (2%) containing adrenaline (1:80,000 units), up to a maximum of 5.4 mL. For patients with a significant residual gag reflex, xylocaine (10%) was sprayed on the peritonsillar area. Patients were

instructed to breathe deeply; during exhalation, with the tongue depressed, the tonsil crypts were evaporated in a sweeping motion until complete cryptolysis was achieved. In case of bleeding, coagulation was performed by adjusting the laser out of focus. A step-by-step video protocol for this intervention has been previously published.[4] All CO_2-laser TO procedures were conducted at the primary clinical study center, with participating centers located within a two-hour driving distance, facilitating patient access to treatment.

Patients assigned to CO_2-laser TO were instructed to gradually diminish their gag reflex by brushing their tongue base and tonsils with a toothbrush during regular teeth brushing two weeks before surgery.

Classic Dissection Tonsillectomy

Classic dissection tonsillectomy procedures were conducted at all study centers. Patients were placed in a supine position and administered general anesthesia with endotracheal intubation. A McIvor retractor was then applied, and the superior pole of the tonsil was grasped using an Allis clamp. To expose the tonsil an incision on the anterior pillar of the tonsil was made and the tonsil was removed using a tonsil clamp and scissors. Hemostasis was achieved with gauze and gentle pressure for 5 minutes. If necessary for complete hemostasis electrosurgery was performed on bleeding vessels. Afterwards, patients were monitored in the postanesthetic care unit and discharged on the same day.

Postoperative Pain Medication

Patients were provided postoperative pain relief with acetaminophen, 500 mg, as needed, up to 4 times daily (max 1000 mg per dose). If required, diclofenac, 50 mg, was also administered up to 3 times daily for the initial 3 days post-surgery. Tramadol was prescribed if acetaminophen and diclofenac did not provide adequate pain control.

Data collection

Data on tonsil-related symptoms, quality of life (measured with the 5-level EuroQol 5-Dimensions survey [EQ-5D] [5] including the visual analogue scale [EQ-VAS]), healthcare use, work productivity and activity impairment (measured with the Work Productivity and Activity Impairment [WPAI] questionnaire[6]), and overall satisfaction with the received treatment (assessed on a 0-100 mm Visual Analog Scale [VAS]) were collected one and two years after surgery through digital questionnaires. In addition, at two and six weeks, patients were asked when they felt fully recovered and when they returned to work. For the effectiveness analysis, patients who had not fully recovered, returned to work, or ceased analgesic medication within 14 days post-surgery were censored at that time

point. This approach ensured that short-term recovery comparisons were limited to the predefined 14-day window. Patients with recovery times longer than 14 days were included in the long-term follow-up analysis, and their economic impact was assessed based on six-week follow-up data to capture extended recovery experiences. To handle missing data, multiple imputation was used to create 100 completed datasets, using logistic, ordered logistic and linear regression models with predictive mean matching.[7] Predictors were randomization, sex, age, EQ-5D utilities over time and the VAS for severity of throat complaints over time. Additionally, for repeated measures, that same measure at other timepoints was used as predictor. In case of insufficient variation in the data, fewer predictors were used.

Economic evaluation

A cost-utility analysis was performed from a societal perspective, at price level 2023, with a two-year time horizon. Utility reflects the value of quality of life, on a scale anchored at 0 (=as bad as death) and 1 (=perfect health). Utility was calculated using the Dutch tariff for the EQ-5D[8] and the EQ-VAS with power transformation.[9] Quality-adjusted life years (QALYs) were calculated by the area under the utility curves over the follow-up period. The frequency of CO_2-laser TO and TE was assessed from the hospital administrations. A cost-price analysis was performed for both procedures. Other tonsil-related healthcare use was reported by patients and valued using Dutch reference prices, without discounting.[10] Absenteeism from work was calculated by the patient-reported time to return to work. Presenteeism at work was calculated by the time between self-reported return to work and return to normal self, multiplied by the degree of impediment to work according to the WPAI. Both absenteeism and presenteeism were valued at €286 per full day.[10] Cost-effectiveness acceptability curves were calculated as the one-sided p-value for the difference in net benefit, depending on the willingness to pay for a QALY ($NB = WTP \times QALY - Costs$). Three sensitivity analyses were performed, in which costs were limited to healthcare costs (instead of societal costs), patients without registered TE or CO_2-laser TO were assumed to have had TE (instead of assuming no procedure), and QALYs were calculated from the EQ-Visual Analog Scale (EQ-VAS, instead of the EQ-5D index score).

Statistical analysis

The target sample size was determined for previously published short-term outcomes of this study.[1] The calculation based on data from a prior non-randomized prospective study.[11] Using a 2-sided log-rank test with a total sample size of 190 patients (95 in each group), the study achieved 80.2% power at a .05 significance level. This allowed for the detection of a CO_2-laser TO median functional recovery time of 8 days, assuming the TE group median survival time was 13.5 days, within a total observation time of 14 days.

Baseline demographic and clinical characteristics are presented as means with SDs, or as counts and percentages. Long-term clinical outcomes at one- and two-year after surgery were performed on an intention-to-treat basis (randomized patients analyzed according to randomization). Pooled means were compared months after surgery were compared using unpaired t-tests and proportions of binary outcomes were compared using logistic regression. Within the CO_2-laser TO and TE groups, changes from baseline were assessed using paired t-tests. Two-sided P values were computed, and a significance level of .05 was used for all testing. Statistical analyses were performed using SPSS, version 27 (IBM). External data monitoring was performed yearly to ensure data quality.

Patient Involvement

Members of the Patient Advisory Board of the Hagaziekenhuis hospital were actively involved in the development of the research questions, questionnaires, and recruitment strategy. They provided valuable feedback on the clarity and relevance of the study materials and consent forms. During data analysis, their perspectives helped interpret the results, ensuring that the findings aligned with patient experiences and priorities.

Role of the funding source

There was no funding source for this study.

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CHAPTER 8

General conclusions and discussion

This thesis explored whether tonsillotomy (TO) could serve as a safe, effective, and cost-efficient alternative to tonsillectomy (TE) for adults with tonsil-related conditions. The following discussion and conclusions evaluate the findings, comparing TO to TE in terms of surgical outcomes, recovery, and complication rates, while considering its potential for routine clinical application. These insights aim to contribute to advancements in understanding, clinical usability, and the development of less invasive, patient-friendly surgical options, as well as their broader availability for managing tonsil-related disorders.

KEY DIFFERENCES IN SURGICAL OUTCOMES RELATED TO CURRENT LITERATURE

In **Chapter 2** we present a systematic review of literature comparing TE and TO in adults with tonsil related afflictions. Based on current literature, TO appears to offer significant advantages including less post-operative pain, shorter recovery times and fewer complications. Eight out of nine studies found TO as effective as TE in tonsil-related symptoms resolution. For example, studies by Bender et al. and Lourijssen et al. (**Chapter 3**) reported lower pain scores and a reduced use of analgesics after TO, suggesting a less burdensome recovery process.[1,2]

While TO shows promising results, concerns remain regarding residual tonsil tissue and potential recurrent symptoms, though these concerns are not substantiated by current evidence. Additionally, the lack of large, high-quality randomized trials and variations in surgical techniques limit definitive conclusions.

These findings indicate that TO could be a first-line treatment for many adults due to its lower morbidity. However, the review concludes that research gaps remain, particularly regarding long-term outcomes, the risk of tonsillar regrowth, and post-operative complications. To address these issues, we conducted the TOMTOM-study, from which the results are presented in **Chapters 6 and 7**.

THE MOST COMMON COMPLICATIONS ASSOCIATED WITH TONSILLOTOMY AND TONSILLECTOMY IN ADULT PATIENTS, BASED ON CURRENT LITERATURE.

In **Chapter 2**, the review highlights common complications of TE and TO, focusing on post-operative hemorrhage, pain, infection, and incomplete symptom resolution or

recurrence. TE is associated with a higher incidence of post-operative hemorrhage, with studies like Bender et al. reporting a 30% hemorrhage rate in TE patients compared to 12% in TO patients, with TE-related bleeding often more severe and recurrent.

Post-operative pain is consistently higher in TE patients, who also require more analgesic medication and experience slower recovery compared to TO patients. Infections, although rare, appear slightly more after TE, suggesting another potential advantage of TO.

Lastly, complications related to incomplete symptom resolution or recurrence, particularly with tonsillotomy, are important to address. Since tonsillotomy preserves some tonsillar tissue, there is a theoretical risk of recurrent or persistent tonsil issues.

However, the review of current literature did not demonstrate a significantly higher rate of persistent tonsil-related complaints after TO, but long-term outcomes of TO were insufficiently studied, which prompted us to further investigate this aspect in our study, as detailed in **Chapters 6 and 7**.

CO_2-LASER TONSILLOTOMY AS A VIABLE ALTERNATIVE TO TRADITIONAL TONSILLECTOMY IN ADULTS: POSTOPERATIVE OUTCOMES, RECOVERY TIME, AND COMPLICATION RATES

Recognizing the need for more evidence on the potential of CO_2-laser TO as an alternative to traditional TE in adults, we first conducted a prospective follow-up non-randomized cohort study, which is presented in **Chapter 3**. This study looked at the efficacy and post-operative outcomes of CO_2-laser TO compared to TE.

The findings of this study provide strong evidence that CO_2-laser TO can serve as a viable alternative to TE for adults, particularly with respect to post-operative recovery.

CO_2-laser TO significantly reduced post-operative pain with mean pain score on a Visual Analogue Scale (0-10) of 5.4 after TO compared to 7.7 in the TE group, and required fewer days for full recovery (4.8 days vs. 10.6 days for TE). TO patients return to daily activities faster, which is another important consideration for patients and clinicians.

However, the lower success rate of symptom resolution (72.5%) compared to TE (97.2%) suggests that CO_2-laser TO might not be universally effective for all patients. The need for re-surgery in a small percentage of cases (7.5%) underscores the importance of

careful patient selection to minimize the risk of recurrence. This indicates that while the procedure offers benefits in terms of recovery, its effectiveness might be limited in certain cases, potentially impacting long-term outcomes.

Compared to the broader literature, the findings presented in **Chapter 3** are consistent with previous reports that suggest a faster recovery with tonsillotomy techniques, though the issue of symptom recurrence has been less consistently reported. This suggests a gap in literature, underlining the need for larger randomized controlled trials with extended follow-up to validate the long-term efficacy of CO_2-laser TO.

These findings laid the groundwork for the systematic review presented in **Chapter 2**, which further explored the current literature and underscored the need for more robust, randomized studies with longer follow-up to fully establish the value of CO_2-laser TO as an alternative to TE.

Critical steps in performing a safe and effective tonsillotomy

In **Chapter 4**, we systematically describe a step-by-step protocol for performing CO_2-laser TO under local anesthesia in adults. A detailed guide is not only essential for standardized and safe outcomes but also fills a gap in the current literature by providing a structured and replicable approach. The inclusion of an online video instruction enhances the educational value, making it a valuable tool for both clinical training and patient safety.

The protocol focuses on patient selection, including assessing the gag reflex with the Gagging Severity Index (GSI), and pre-operative preparations. This helps ensure that patients are suitable candidates for the procedure and minimize intraoperative complications. The anesthesia protocol and laser treatment steps are outlined and emphasis the preservation of the tonsil capsule, which is a significant difference from the more invasive TE.

The importance of this detailed procedural description goes beyond individual clinical practice. The protocol serves as a valuable educational tool for training new surgeons and the video format allows learners to visualize the technique, grasp the importance of each step, and understand the subtleties that can only be conveyed through demonstration. This is especially important for CO_2-laser TO, a relatively novel procedure that

requires precision and familiarity with specific techniques to avoid complications and achieve optimal outcomes.

From a patient safety perspective, the protocol provides a standardized approach to CO_2-laser TO, which is important for reducing variability in surgical outcomes and complications. By following these steps, surgeons can minimize the risks associated with the procedure, such as post-operative bleeding and incomplete symptom resolution. Presenting these steps in a video and text format supports further dissemination of the technique, which could help its adoption in more clinical settings and thereby further contribute to advancements in tonsil surgery and the availability of tonsillotomy worldwide.

Trends in the incidence of tonsil complaints in adults in the Dutch population

In **Chapter 5**, we provide an overview of CO_2-laser TO designed to inform and educate Dutch medical professionals about this innovative surgical technique. Additionally, we examine trends in the incidence of tonsil-related complaints and surgery among adult patients in the Netherlands over the past decade. The data reveals a stable yearly incidence of tonsil complaints, which continues to place a significant burden on healthcare services. Between 2012 and 2019, an average of 73,887 adult cases of "diseases of the adenoid or tonsils" were diagnosed annually, leading to approximately 11,130 TE's per year. This comes down to about 8 TE procedures per 10,000 adults, underscoring that the demand for surgical intervention for tonsil complaints remains substantial.

These trends have significant implications for clinical practice, particularly in the surgical management of tonsil-related conditions. The stable rate of adult tonsillectomies indicates that TE remains a widely used treatment, likely due to its proven effectiveness. However, the ongoing demand for TE, along with its associated post-operative morbidity, prolonged recovery, and healthcare costs, underscores the need to explore alternative surgical options. CO_2-laser TO presents a promising alternative in this context.

Short-term efficacy, recovery and safety outcomes of CO_2-laser tonsillotomy compared to tonsillectomy

In **Chapter 2**, we reviewed existing literature suggesting that TO could be a viable alternative to TE in adults, which included our pilot study presented in **Chapter 3.** This

study indicated that CO_2-laser TO could offer favorable outcomes in terms of recovery, postoperative pain, and complications, with similar short-term effectiveness. However, it became clear that more scientifically robust evidence was necessary. Thus, we initiated the **TOMTOM-study**, a large multicenter randomized controlled trial to compare the recovery, complications, efficacy, and cost-effectiveness of both interventions.

In **Chapter 6**, we present the first results of the TOMTOM-study, which involved 199 adult patients across five hospitals in the Netherlands. The trial compared the efficacy and safety of CO_2-laser TO and traditional TE. The results show that while both procedures are effective, there are notable differences in recovery time, postoperative pain, and symptom persistence.

Patients undergoing TO experience a quicker functional recovery, with 77% fully recovered within two weeks, compared to 57% in the TE group. Additionally, TO patients returned to work sooner, with a median of 4.5 days versus 12.0 days for TE patients. The faster recovery was also accompanied by significantly lower postoperative pain and reduced use of analgesics in the TO group, which is in line with the less invasive nature of the procedure.

However, the study also found that while TO resulted in a quicker and less painful recovery, it was associated with a higher rate of persistent symptoms six months post-surgery. Specifically, 57% of TO patients reported persistent symptoms, compared to 35% in the TE group. The intensity of these persistent symptoms was generally below the clinically relevant threshold, and thus overall patient satisfaction remained high in both groups.

These outcomes suggest that while TO offers significant advantages in terms of recovery and comfort, it may be less effective in fully resolving tonsil-related complaints compared to TE, but the clinical implications of remaining symptoms seem limited.

LONG-TERM EFFECTIVENESS AND COST-EFFECTIVENESS OF TONSILLOTOMY COMPARED TO TONSILLECTOMY

After finding out in **Chapter 6** that CO_2-laser TO is a safe and effective treatment for tonsil complaints in the short term, with fewer complications and quicker recovery compared to TE, the question arises whether CO_2-laser TO is also effective in the long term. Additionally, to determine if CO_2-laser TO has value in the clinic as a viable alternative to TE, its cost-effectiveness is crucial because it influences decision-making in healthcare,

particularly in balancing patient outcomes with the efficient allocation of healthcare resources.

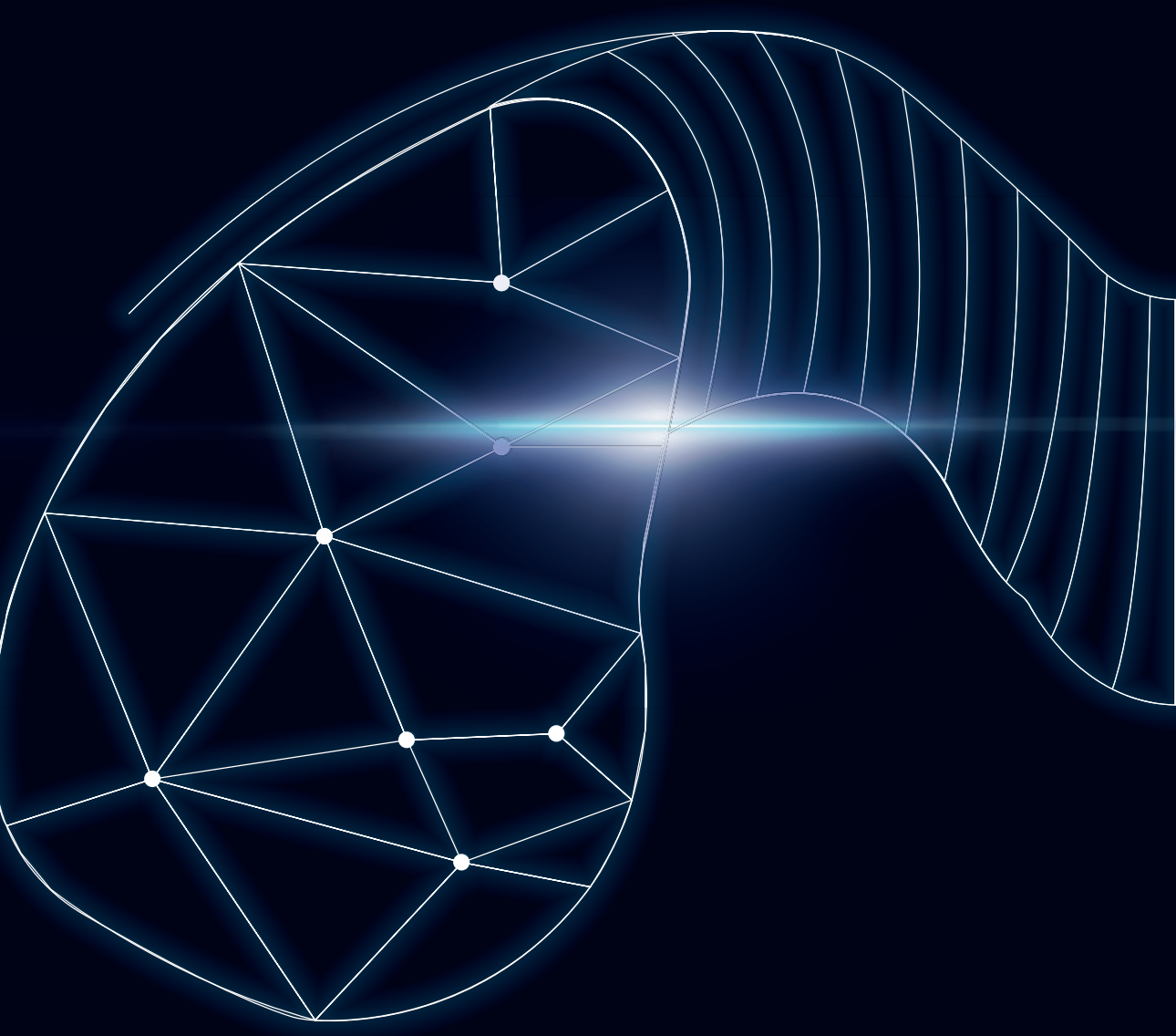
The TOMTOM study therefore extended the investigation into the long-term effectiveness and cost-effectiveness of CO_2-laser TO compared to TE in adults, as presented in **Chapter 7**.

At one year and two years post-surgery, the study found that TE was more effective in resolving the primary tonsil-related complaints than CO_2-laser TO. Specifically, 25.2% of TE patients reported persistent complaints after one year, compared to 51.4% of TO patients. After two years, these figures were 19.7% for TE and 45.2% for TO. However, the severity of these persistent symptoms was significantly reduced in both groups, generally below clinically relevant thresholds. The quality of life improved over time. Interestingly, satisfaction with the procedure and the percentage of patients who would recommend the surgery to others did not differ between the two groups at one- and two-years post-surgery. The substantial symptom reduction, often below clinically relevant thresholds, in patients with remaining symptoms and the faster recovery time after CO_2-laser TO likely compensated for the difference in effectiveness between the procedures.

TO was significantly less costly than TE. The total cost per CO_2-laser TO procedure was less than half that of a TE procedure (€671 vs. €1824). When accounting for additional procedures and other healthcare costs, the total societal costs, including lost productivity, were also significantly lower for TO. This led to a 71% to 93% likelihood that CO_2-laser TO would be considered cost-effective compared to TE at the commonly accepted threshold in the Netherlands.

These findings suggest that while TE may offer slightly better long-term resolution of symptoms, CO_2 laser TO presents a cost-effective alternative with substantial benefits in terms of recovery time, reduced pain, and lower societal costs. The decision between TE and CO_2-laser TO should be based on patient characteristics and preferences. Careful patient selection and preoperative counseling are important to optimize outcomes and patient satisfaction.

This study's findings support the inclusion of CO_2-laser TO as a viable option in the therapeutic arsenal for managing tonsil-related afflictions in adults.



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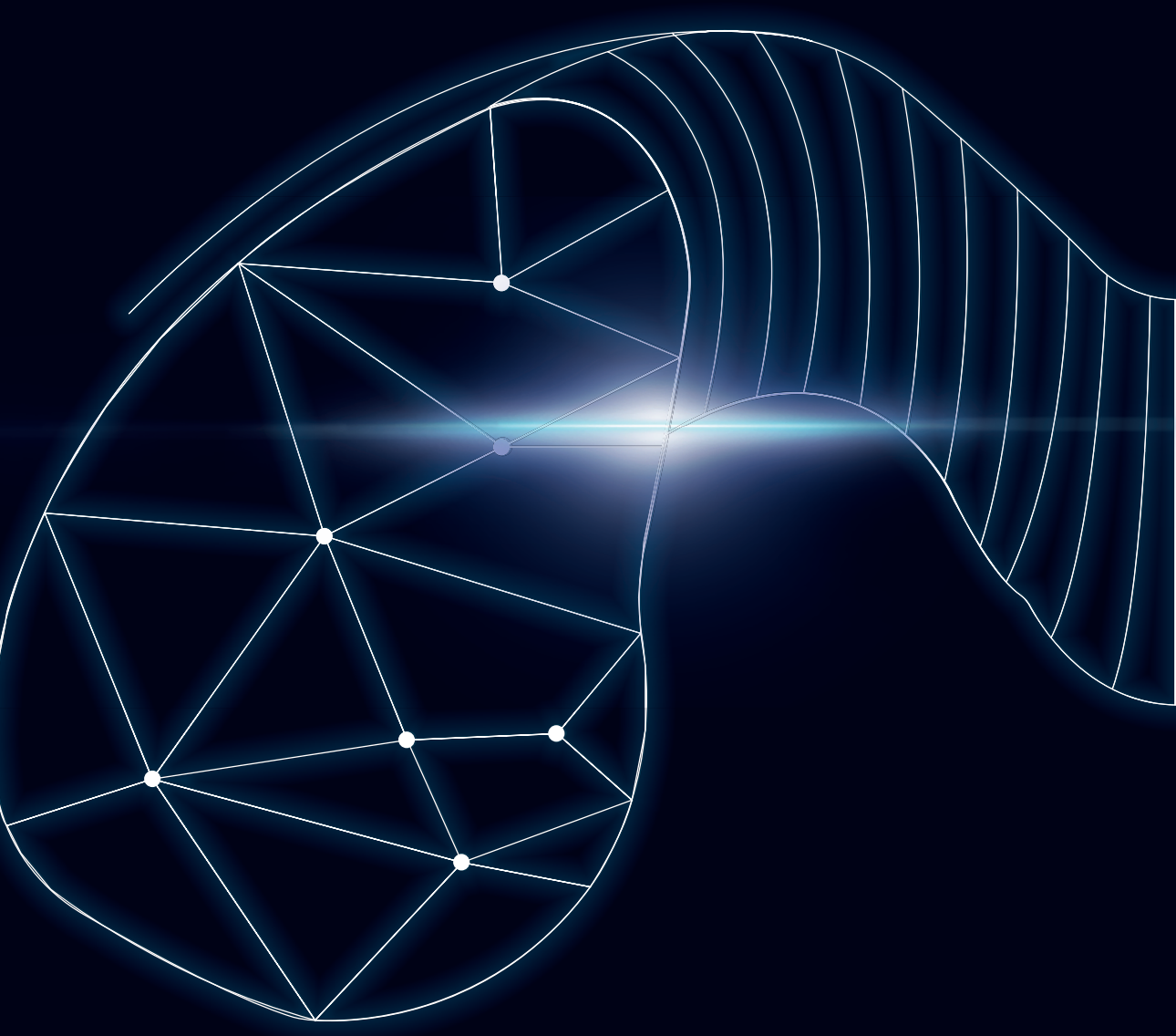

CHAPTER 9

Recommendations for clinical practice, education, future research, and societal impact

This work led to the identification of several recommendations.

Clinical recommendations

***Recommendation**: Consider TO as a first-line surgical option for adults with tonsil-related complaints.*

CO_2-laser TO offers significant advantages over traditional TE including reduced post-operative pain, faster recovery, fewer complications, and lower surgical, medical, and societal costs. This makes it an attractive option for patients seeking a less invasive treatment. Despite concerns about incomplete symptom resolution or recurrence, the current study confirms the long-term (cost-)effectiveness of CO_2-laser TO.

- **Persistent Symptoms**: Patients undergoing TO may report persistent symptoms more often than those undergoing TE, but their symptom severity typically falls below clinically relevant thresholds.
- **Patient Satisfaction**: Both TO and TE show similarly high patient satisfaction in short- and long-term follow-up, thanks to effective symptom reduction and lower morbidity.

***Recommendation:** Select patients carefully to minimize persistent symptoms or re-surgery.*

While many adults with tonsil-related complaints can benefit from a tonsil reduction, CO_2-laser TO may not be suitable for all, as individual factors such as underlying conditions can influence outcomes.

- **Severe tonsillitis**: Individuals with very frequent, severe episodes may be better served by a direct TE to avoid residual, clinically significant symptoms.
- **Patient cooperation**: Non-cooperative patients or those with a significant gag reflex that remains problematic (even after desensitization training as discussed in **Chapter 4**) may require TE under general anesthesia.
- **Malignancy suspicion or peritonsillar abscess**: TO is contraindicated if malignancy is suspected as tissue preservation is necessary for pathological examination. In patients with a history of peritonsillar abscess, TE is given preference over TO, as remaining tissue may lead to recurrence.

Clear information regarding recovery time, risks, and the likelihood of symptom recurrence or need for additional treatment is crucial. The patient's preferences, whether for quicker recovery without general anesthesia with TO, or the higher resolution of symptoms with prolonged and more painful recovery after TE, should guide the discus-

sion. Together, the clinician and patient must weigh the benefits, risks, and individual preferences to reach a shared decision that aligns with the patient's goals.

Recommendation: *Individualize the CO_2-laser TO technique to optimize outcomes.*

Anatomical variability in tonsil size, position and peritonsillar anatomy necessitates precision in treatment to avoid damaging adjacent structures. [1]

- **Complete Tonsillar Exposure**: Use wooden tongue depressors to ensure full visibility, especially important for large lower poles or deeply seated tonsils, to avoid damaging the arches, with subsequent pain and delayed recovery or leaving residual tissue, such as a lower tonsillar pole (**as shown in chapter 4**).
- **Internal carotid artery (ICA) safety margin**: The ICA is normally situated +- 2.5 cm from the base of the tonsils. Anomalies, however, may reduce this distance, increasing the potential for damage and severe arterial bleeding.[2] The tonsillar capsule remains intact in TO, providing an extra protective layer over the internal carotid artery, further reducing bleeding risks.

Recommendations for education

Recommendation: *Include CO_2-laser TO into ENT surgical curriculum.*

Incorporating CO_2-laser TO into the ENT surgical curriculum is important as it provides a valuable alternative to traditional TE. Residents will benefit from learning patient selection criteria, informed consent, and shared decision-making alongside the surgical technique itself for better outcomes and higher patient satisfaction.

- **Informed consent**: Emphasize benefits (lower pain, faster recovery, no general anesthesia, lower overall costs) and risks (persistent complaints, possible retreatment).
- **General knowledge and skills:** Training must emphasize a thorough understanding of tonsil and peritonsillar anatomy for safe and precise CO_2-laser TO. It's essential that training includes proper exposure of the entire tonsil and complete treatment of all lymphatic tonsil tissue to maximize effectiveness and minimize the need for reinterventions.
- **Hands-on training**: Residents should aim to perform at least 15 supervised procedures. Given the steep learning curve, this should ensure sufficient proficiency for safe and effective practice.

Recommendation: *Train current ENT surgeons on diverse tonsillotomy techniques.*

ENT practices use various technologies for local interventions, including CO_2 lasers, blue lasers, diode lasers, KTP lasers, and coblation systems, each with distinct mechanisms of action.

A thorough understanding of their strengths, limitations, and risks is particularly important for tonsillotomy under local anesthesia. For example, CO_2 lasers offer precise control but require more setup and safety measures, while coblation systems are easier to handle but may lack precision and pose risks like fluid or tissue aspiration.

Since many ENT clinics already have these technologies, the initial setup costs and training requirements for implementing tonsillotomy under local anesthesia are lower, making adoption more accessible.

Proper training and familiarity with these systems enable surgeons to make informed, patient-specific choices for safe and effective treatment.

Recommendation: *Develop and disseminate standardized CO_2-laser TO training protocols.*

Structured curricula, including theoretical modules, hands-on workshops, and video tutorials, promote consistent and effective procedures. Given the steep learning curve, structured training will ensure high-quality outcomes across practices.

- **Patient selection:** Emphasize clinical criteria such as frequency and severity of tonsillitis episodes, presence of comorbidities, and patient cooperation. Evaluate gag reflex management, contraindications (e.g., suspected malignancy, peritonsillar abscess), and the likelihood of symptomatic benefit to ensure CO_2-laser TO is appropriate.
- **Procedural Safety**: Thorough practice with tonsil exposure techniques, complete tissue removal, and handling bleeding complications is essential.
- **Video Tutorials**: Resources like the JoVE video protocol (**Chapter 4**) enhance practical learning and support widespread adoption.[3]

RECOMMENDATIONS FOR FUTURE RESEARCH

Recommendation: *Establish a longitudinal tonsil surgery registry.*

By systematically collecting data on long-term outcomes, complications, and surgical techniques, a registry enables evidence-based improvements, validates current findings, and supports their integration into clinical practice, guidelines, and policy decisions.

- **Research Gaps**: Tracking patient data over extended periods helps address questions about symptom recurrence, complications, and comparative effectiveness.

Recommendation: *Conduct large, high-quality randomized controlled trials comparing CO_2-laser TO with other techniques.*

Future research should compare safety, efficacy, and cost-effectiveness across multiple tonsillotomy methods, particularly those feasible under local anesthesia, as they offer a significant advantage over procedures requiring general anesthesia.

- **Existing Infrastructure**: Many clinics already have the necessary equipment, including various laser systems, enabling broader implementation of tonsillotomy without significant new investment. Understanding each device's capabilities and limitations promotes faster, safer, and more cost-effective adoption of TO. The proposed longitudinal registry would further support research comparing outcomes across different tonsillotomy methods.

Recommendation: *Optimize strategies to minimize the gag reflex.*

Enhancing gag-reflex desensitization can improve patient comfort and accessibility for TO under local anesthesia. Our training protocol, involving daily tongue base and tonsil stimulation with a toothbrush for 14 days, shows promise. Future research should refine this method for greater consistency and effectiveness, benefiting TO and other oropharyngeal procedures.

RECOMMENDATIONS FOR SOCIETAL IMPACT

Recommendation: *Advocate for CO_2-laser TO inclusion in national healthcare guidelines and insurance coverage.*

We advocate for CO_2-laser TO in national healthcare guidelines to improve resource allocation. Its cost-effectiveness stems from shorter recovery, fewer complications, and lower surgical and societal costs. Standardizing its use in care guidelines and insurance coverage can reduce healthcare expenses while enhancing patient outcomes. By eliminating general anesthesia and full surgical theater requirements, CO_2-laser TO reduces patient burden, hospital stays, and costs, while freeing up, the often limited, operating rooms and surgical staff for other procedures.

Recommendation: *Increase public awareness of less invasive surgical alternatives like CO_2-laser TO.*

We recommend public education initiatives to raise awareness of less invasive options like CO_2-laser TO, enabling better-informed decisions and shared decision-making between patients and doctors.

Many patients with chronic tonsil diseases potentially remain undertreated due to the invasiveness of TE, leading to high healthcare costs, societal costs and reduced quality of life. Promoting CO_2-laser TO can help address this gap and lower societal costs associated with these chronic and recurrent conditions.

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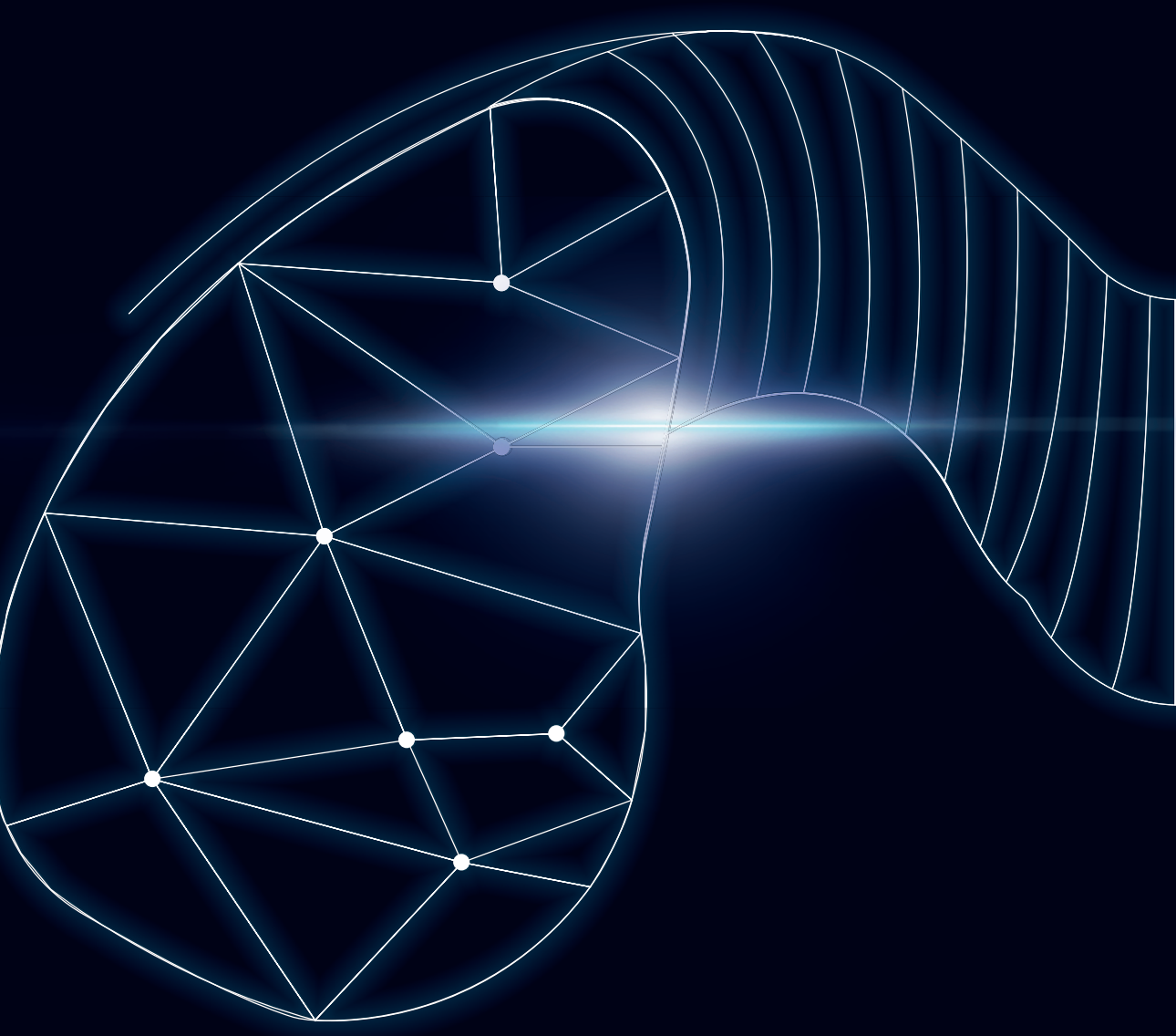


CHAPTER 10

APPENDICES

- General summary
- Nederlandse samenvatting
- Study Protocol
- Curriculum Vitae
- Acknowledgements

GENERAL SUMMARY

The aim of this thesis was to investigate the effectiveness, safety, and cost-effectiveness of CO_2-laser tonsillotomy (CO_2-laser TO) compared to classic dissection tonsillectomy (TE) in adult patients with tonsil-related conditions. Additionally, this thesis aims to contribute to the availability and advancements of tonsillotomy (TO) under local anesthesia for adults.

General introduction

Chapter 1, the introduction, outlines key questions addressed in this thesis to evaluate the potential benefits of CO_2-laser TO. The palatine tonsils, key lymphoid tissues in the human immune system, are the focus of this research. Tonsil diseases such as recurrent tonsillitis, obstructive sleep apnea syndrome (OSAS), and halitosis significantly impact adult patients' quality of life and healthcare systems. Traditional TE remains a common, effective surgical intervention for tonsil-related complaints but carries considerable morbidity and risks. Consequently, there is increasing interest in less invasive alternatives like TO which aims to only remove the part of the tonsil leading to complaints, while preserving the larger nerves and vessels to limit recovery time, pain and complications.

Key differences in surgical outcomes in current literature

In Chapter 2, a systematic review compared TO with TE in adult patients. The review highlighted that TO offers advantages such as reduced postoperative pain, faster recovery, and fewer complications, particularly postoperative hemorrhage. Studies reported TO to be similarly effective as TE in symptom resolution, with lower pain scores and analgesic usage. However, the evidence is of low quality, study designs are incomparable, and studies often lack long-term evaluation. Discussion on residual symptoms after TO remain. For these reasons further investigation through a large, high-quality trial is recommended.

CO_2-laser tonsillotomy as a viable alternative?

A prospective non-randomized cohort study in **Chapter 3** evaluated the outcomes of CO_2-laser TO compared to TE. The findings indicated that CO_2-laser TO reduced postoperative pain, analgesic use and shortened recovery time, enabling faster return to daily activities. However, the slightly lower success rate of symptom resolution and the need for re-surgery in a small percentage of patients underscore the importance of patient selection. While this study concludes that CO_2-laser TO seems to offer substantial benefits, larger, high quality prospective research is necessary to draw more definite conclusions and refine patient selection criteria.

Performing a safe and effective tonsillotomy

Chapter 4 provided a detailed protocol for performing CO_2-laser TO under local anesthesia. This protocol emphasized patient selection, preoperative preparations, and precise surgical steps to minimize complications. The inclusion of an instructional video enhances clinical training and facilitates more standardized surgical outcomes.

Trends in tonsil complaints in the Dutch population

In **Chapter 5**, a review of Dutch healthcare data, revealed a stable incidence of tonsil complaints and a consistent number of annual TE surgeries, indicating a persistent demand for surgical interventions. This underscores the current and future need for viable, less invasive alternatives like CO_2-laser TO.

Short-term outcomes

Chapter 6 presented the first results of the TOMTOM study, which compared the direct surgical safety and recovery between CO_2-laser TO and TE and the six months (short-term) results. TO offered a significantly shorter recovery time and faster return to work, patients experienced less postoperative pain and required fewer and less potent analgesics. The incidence of postoperative hemorrhage was notably lower in the TO group. However, symptom resolution six months after surgery was lower in the TO group, indicating a trade-off between quicker recovery and long-term symptom relief. Patients in both groups who experienced persistent symptoms reported significantly reduced symptom severity compared to baseline, often below clinically relevant scores, with overall quality of life and patient satisfaction remaining equally high in both groups. A small percentage of patients required a second surgery after initial TO. Apparently, the benefits of TO outweigh its lower effectiveness and occasional mild residual symptoms.

Long-term outcomes and cost-effectiveness

Chapter 7 focuses on the long-term effectiveness and cost-effectiveness of CO_2-laser TO and TE. On long term TE was more effective in fully resolving symptoms. However, in patients with remaining symptoms, the severity of symptoms decreased dramatically, often below clinically significant thresholds, leading to an equal patient satisfaction in both groups.

In terms of cost-effectiveness CO_2-laser TO was found to be more cost-effective compared to TE on all 3 dimensions: surgical costs, medical costs and societal costs.

Recommendations for clinical practice, education, and future research

The thesis concludes with a discussion and recommendations for clinical practice, education, and future research in **Chapter 8 and 9**:

Clinical Practice: CO_2-laser TO should be considered a first-line option for adults due to its reduced morbidity, quicker recovery, and lower societal costs. Careful patient selection is crucial to minimize risks of recurrent symptoms.

Education: Incorporate CO_2-laser TO into ENT training curricula, focusing on patient selection, surgical techniques, and informed consent.

Future Research: A longitudinal registry is recommended to track outcomes, improve evidence-based tonsil surgery and compare different TO techniques. Further research is also needed to refine surgical protocols and improve patient outcomes.

These findings and recommendations aim to enhance surgical decision-making and optimize care for adult patients with tonsil-related conditions, establishing CO_2-laser TO as a viable and efficient alternative to traditional TE.

Nederlandse algemene samenvatting

Dit proefschrift onderzoekt de effectiviteit, veiligheid en kosteneffectiviteit van CO_2-laser Tonsillotomie (CO_2-laser TO) en vergelijkt deze met klassieke extracapsulaire dissectie tonsillectomie (TE) bij volwassen patiënten met tonsil gerelateerde aandoeningen. Daarnaast beoogd dit proefschrift een bijdrage te leveren aan de beschikbaarheid en verdere ontwikkeling van tonsillotomie (TO) bij volwassenen.

Algemene Inleiding

De inleiding van dit proefschrift, **Hoofdstuk 1**, identificeert verschillende belangrijke vragen die in deze thesis moeten worden beantwoord om de potentiële waarde van CO_2-laser TO vast te stellen. De palatinale tonsillen (keelamandelen), belangrijke lymfoïde weefsels die onderdeel uitmaken van het immuunsysteem, staan centraal in deze thesis. Tonsil aandoeningen zoals recidiverende tonsillitis, obstructief slaapapneusyndroom (OSAS) en halitose hebben een aanzienlijke impact op de kwaliteit van leven van volwassen patiënten en op de gezondheidszorg. TE is de meest verrichte chirurgische ingreep, maar gaat gepaard met significante risico's en morbiditeit. Hierdoor neemt de interesse in minder invasieve chirurgische alternatieven zoals tonsillotomie (TO) toe. Tijdens TO wordt slechts het deel van de tonsil dat klachten veroorzaakt verwijderd, terwijl het tonsilkapsel inclusief de grotere zenuwen en bloedvaten behouden blijven. Het doel is om daarmee de hersteltijd, pijn en complicaties te verminderen.

Belangrijkste verschillen in chirurgische resultaten in de huidige literatuur

In **Hoofdstuk 2** wordt een systematische review gepresenteerd waarin TO wordt vergeleken met TE bij volwassen patiënten. TO blijkt voordelen te bieden zoals minder postoperatieve pijn, sneller herstel en minder complicaties. De gevonden studies tonen een vergelijkbare effectiviteit van TO aan ten aanzien van klachtenverlichting, met lagere pijnscores en minder pijnstillergebruik. De bewijskracht is echter laag van kwaliteit, de studies gebruiken slecht te vergelijken studie-designs en vaak ontbreken lange termijn resultaten. De discussie over eventuele restklachten na TO blijft hierdoor bestaan. Daarom wordt verder onderzoek door middel van een grote kwalitatief hoogwaardige gerandomiseerde trial aanbevolen.

CO2-laser tonsillotomie als een goed alternatief?

De prospectieve niet-gerandomiseerde cohortstudie uit **Hoofdstuk 3** vergelijkt CO_2-laser TO met TE. CO_2-laser TO ging gepaard met minder postoperatieve pijn, minder postoperatieve pijnstillers en een kortere hersteltijd, waardoor patiënten sneller hun dagelijkse activiteiten konden hervatten. De iets lagere klachtenreductie en de

noodzaak tot een tweede ingreep bij een klein percentage van de patiënten die TO ondergingen benadrukken het belang van goede patiëntselectie. Hoewel CO_2-laser TO grote voordelen lijkt te bieden, is grootschaliger, gerandomiseerd onderzoek nodig om meer definitieve conclusies te trekken en de patiëntselectie te verbeteren.

Het verrichten van een veilige en effectieve CO_2-laser Tonsillotomie

Hoofdstuk 4 bestaat uit een gedetailleerd protocol voor de uitvoer van CO_2-laser TO onder lokale anesthesie. In dit protocol wordt er nadruk gelegd op goede patiëntselectie, preoperatieve voorbereidingen en worden de chirurgische stappen in detail beschreven. Het protocol bevat een uitgebreide instructievideo die kan helpen bij de training van (toekomstige) KNO-artsen.

Trends in tonsilklachten in de Nederlandse bevolking

In **hoofdstuk 5** wordt de stabiele incidentie van tonsilklachten en tonsillectomie ingrepen bij volwassenen in Nederland gepresenteerd. Deze trend benadrukt de huidige en toekomstige behoefte aan minder invasieve, effectieve chirurgische alternatieven zoals de CO_2-laser TO.

Korte termijn resultaten

In **hoofdstuk 6** worden de eerste resultaten van de TOMTOM-studie gepresenteerd, waarin de veiligheid, het postoperatieve herstel en de resultaten op korte termijn (zes maanden) werden vergeleken tussen CO_2-laser TO en TE. TO bleek gepaard te gaan met een aanzienlijk kortere hersteltijd en snellere terugkeer naar werk. Patiënten hadden minder postoperatieve pijn en hadden minder én minder sterke pijnstillers nodig. Er waren opvallend minder postoperatieve bloedingen na TO. Patiënten in beide groepen die aanhoudende symptomen hadden rapporteerden aanzienlijk minder hevige klachten vergeleken met vóór de operatie, vaak tot onder de klinische relevante drempelwaardes. De algehele kwaliteit van leven en patiënttevredenheid na de operatie was gelijk in beide groepen. Een klein deel van de patiënten had een tweede ingreep nodig na hun initiële TO-behandeling. Blijkbaar wegen de voordelen van de TO op tegen de lagere effectiviteit met soms milde restklachten.

Lange termijn resultaten en kosteneffectiviteit

Het artikel in **hoofdstuk 7** rapporteert de lange termijn effectiviteit en kosteneffectiviteit van CO_2-laser TO en TE. Op de lange termijn bleek TE effectiever in het volledig verhelpen van de klachten. Bij patiënten met aanhoudende klachten nam de ernst van de symptomen echter significant af in beide groepen, vaak tot onder de klinisch relevante drempelwaardes. Dit leidde tot een even hoge patiënttevredenheid in beide groepen. Wat betreft kosteneffectiviteit bleek CO_2-laser TO significant kosteneffectief

ten opzichte van TE op alle drie de dimensies: chirurgische kosten, medische kosten en maatschappelijke kosten.

Aanbevelingen voor klinische praktijk, onderwijs en toekomstig onderzoek

Het proefschrift sluit af met een conclusie, discussie en aanbevelingen voor de klinische praktijk, onderwijs en toekomstig onderzoek in **hoofdstuk 8 en 9:**

Klinische praktijk: CO_2-laser TO zou als primaire chirurgische optie moeten worden overwogen voor volwassenen vanwege de lagere morbiditeit, het snellere herstel en de lagere kosten. Zorgvuldige patiëntselectie is cruciaal om het risico op aanhoudende klachten te minimaliseren.

Onderwijs: Integreer CO_2-laser TO in het curriculum voor de KNO-opleiding, met de nadruk op patiëntselectie, chirurgische technieken en shared decision-making.

Toekomstig onderzoek: Het opzetten van een longitudinaal register wordt aanbevolen om uitkomsten van operaties te vervolgen, evidence-based tonsilchirurgie te verbeteren en verschillende TO-technieken te vergelijken. Verder onderzoek is nodig om chirurgische technieken te verfijnen en de resultaten van operaties verder te verbeteren.

Deze bevindingen en aanbevelingen helpen in de chirurgische besluitvorming en de zorg voor volwassenen met tonsilklachten te verbeteren, waarbij CO2-laser TO wordt gepresenteerd als een veilig, effectief en efficiënt alternatief voor TE.

STUDY PROTOCOL (IN DUTCH)

TOMTOM-STUDY
LASERTONSILLOTOMY VERSUS TONSILLECTOMY

'TOMTOM-study'- protocol

(summarized for publication in thesis)

CO2-Lasertonsillotomy versus tonsillectomy in adults;

a randomized multicentre study

Keel-, neus- en oorheelkunde HagaZiekenhuis, 's Gravenhage

J.E.R.E. Wong Chung MD, H. M. Blom MD PhD

PROTOCOL ID

Titel: CO_2–lasertonsillotomie versus klassieke tonsillectomie bij volwassenen; een gerandomiseerde multicenter studie

Lijst van afkortingen en relevante definities

CO_2	Koolstofdioxide
KNO	Keel, neus, oor
METC	Medisch Ethische toetsing commissie
POK	Poliklinische operatiekamer
(S)AE	(Serious) Adverse Event
TE	Tonsillectomie
VAS	Visual analogue scale
WMO	Wet Medisch-wetenschappelijk onderzoek met mensen

SAMENVATTING

Achtergrond: Bij volwassenen kan voor tonsil gerelateerde klachten een tonsillectomie uitgevoerd worden volgens de klassieke dissectietechniek onder narcose. Deze ingreep gaat gepaard met een aanzienlijke morbiditeit. Poliklinische CO_2-lasertonsillotomie onder lokale anesthesie lijkt een interessant alternatief voor een geselecteerde groep volwassenen.

Doel: De toegevoegde waarde van CO_2-laser tonsillotomie voor de behandeling van tonsil-gerelateerde klachten evalueren.

Studie opzet: De studie zal worden uitgevoerd als een open multicenter randomized controlled trial. De patiënt zal loten voor een klassieke tonsillectomie of een lasertonsillotomie na informed consent.

Studie populatie: Patiënten ouder dan 18 jaar met tonsil gerelateerde klachten waarvoor interventie geïndiceerd is.

Interventie: Een groep zal een klassieke tonsillectomie onder narcose ondergaan. De andere groep zal een CO_2-lasertonsillotomie ondergaan onder lokale anesthesie.

Uitkomstmaten:
De resultaten zullen gebaseerd zijn op de volgende uitkomstmaten: aantal dagen post-operatief herstel tot hervatting dagelijkse werkzaamheden , aan- of afwezigheid van de preoperatieve tonsil gerelateerde klachten, postoperatieve pijnscores en analgeticage-bruik, ingreep gerelateerde complicaties en patiënttevredenheid.

Complicaties laserbehandeling:
- Ongeveer 10% is niet van de klachten af en heeft zoveel klachten dat hij / zij hiervoor een klassieke operatie ondergaat
- In totaal ondergaat ongeveer 20% van de patiënten meer dan 1 laserbehandeling
- wondinfectie (3,4%)
- Nabloeding waarvoor interventie noodzakelijk (<1%)
- Allergische reactie op de lokale verdoving (<1%)
- Bijwerkingen van de verdoving (xylocaine 2% /adrenaline 1:80.000) zoals beschreven in de bijsluiter (<1%)

Complicaties klassieke ingreep
- Nabloeding waarvoor interventie noodzakelijk (+- 1.4%)
- Wondinfectie (+- 2%)
- Complicaties narcose (<1%)

Inleiding

Bij volwassenen wordt een tonsillectomie uitgevoerd volgens de klassieke dissectietechniek onder algehele anesthesie. Deze ingreep gaat gepaard met een aanzienlijke morbiditeit. Poliklinische CO_2-lasertonsillotomie onder lokale anesthesie lijkt een interessant alternatief voor een geselecteerde groep volwassenen. Eerdere studies naar poliklinische CO_2-lasertonsillotomie laten zien dat deze ingreep met een aanzienlijk mindere postoperatieve morbiditeit gepaard gaat [1-7]. De gedachte achter deze therapie is dat de crypten de bron van infectie zijn [8-9]. In tegenstelling tot een klassieke tonsillectomie, worden bij een lasertonsillotomie de crypten met het tussengelegen lymfatische weefsel oppervlakkig verdampt (cryptolyse). Het tonsilkapsel en de peritonsillaire ruimte blijven onaangetast. Dit laatste verklaart mogelijk waarom er sprake is van minder (na-)bloeding [10, 11, 12] en minder pijn terwijl de beoogde totale cryptolyse herinfectie voorkomt [3-7]. Verder is er geen noodzaak voor algehele anesthesie en ziekenhuisopname. Naast een medisch voordeel kan dit ook vanuit financieel oogpunt voordeel opleveren. Een belangrijke kanttekening bij de beschikbare resultaten van eerder onderzoek is dat de meeste resultaten zijn gebaseerd op kleine patiënten groepen waar veelal de patiëntkarakteristieken ontbreken[14]. Hiervan zijn slechts weinig prospectieve follow-up resultaten bekend. Om deze reden verrichtten wij een follow-up studie met het doel te kijken naar de toepasbaarheid, effectiviteit en complicaties van een CO_2-lasertonsillotomie. Wij kiezen voor een follow-up van 2 jaar, langer dan de huidige studies aangezien er aanwijzingen bestaan dat 1 jaar na tonsillotomie klachten terug zouden kunnen keren [15].

In een periode van viereneenhalf jaar ondergingen 425 patiënten met chronisch recidiverende tonsillitis, foetor ex ore, slikklachten of obstructieve klachten door tonsilhypertrofie na informed consent een CO_2-lasertonsillotomie. Hieruit bleek dat patiënten gemiddeld na 4,2 dagen weer hun dagelijkse activiteiten en werk konden hervatten. Van de 204 patiënten die langdurig konden worden gevolgd (gemiddelde 16,8 maanden, range 1-40) bleek dat uiteindelijk 69,6% geheel klachten vrij werd, bij 19,1% was er sprake van een zodanige reductie van de klachten dat er geen verdere interventie gewenst was, 10,3% was niet klachtenvrij na de behandeling en onderging een klassieke tonsillectomie. Bij 2,6% was er sprake van een minimale nabloeding welke conservatief behandeld kon worden. Bij 8,6 % werd antibiotica kort na de ingreep voorgeschreven, deze getallen komen echter niet geheel overeen met de werkelijkheid. In de beginjaren werd er door de huisarts regelmatig antibiotica voorgeschreven in verband met de witte verkleuring van het wondbed. Na betere informatie verstrekking is dit getal aanzienlijk afgenomen. In 2010 werden 117 patiënten behandeld met de laser en werd er bij 4 patiënten antibiotica voorgeschreven in verband met een wondinfectie (3,4%). Bij twee

patiënten was er sprake van een hevige vagale reactie op de lokale verdoving waardoor de procedure voortijdig werd afgebroken.

Een vergelijking met de klassieke tonsillectomie werd in dit onderzoek niet gemaakt. Vanwege de te verwachten potentie van de CO_2-lasertonsillotomie, voelen wij de noodzaak een gedegen vergelijkend onderzoek met de klassieke tonsillectomie te verrichten. Het doel van dit onderzoek is het geven van meer inzicht in het postoperatief herstel, de effectiviteit, complicaties (zowel op de korte als langere termijn) en de patiënttevredenheid na CO_2-lasertonsillotomie in vergelijking met een klassieke tonsillotomie.

STUDIEDOEL

Het doel van dit onderzoek is het vergelijken van de effectiviteit van CO_2-lasertonsillotomie bij een geselecteerde groep patiënten met een klassieke tonsillectomie. Hypothese is dat het aantal dagen postoperatief herstel na de laseringreep minimaal 3 dagen verschilt met de klassieke tonsillectomie, dat de effectiviteit van de CO_2-lasertonsillotomie niet meer dan 30% verschilt met de klassieke tonsillectomie en er sprake is van significante betere secundaire uitkomstmaten.

3.1 Studie-uitkomsten

3.1.1. Primaire uitkomstmaat

- Aantal dagen postoperatief herstel

3.1.2. Secundaire uitkomstmaten

- Aan / of afwezigheid van de tonsil gerelateerde klacht
- Aantal episodes tonsillitis per jaar geobjectiveerd door de huisarts of KNO-arts
- Aantal keren antibiotica in verband met tonsillitis per jaar
- Gemiddeld aantal dagen per jaar ziekteverzuim t.g.v. de tonsil gerelateerde klachten
- Aan- / afwezigheid van halitose
- Aan- / afwezigheid detritus
- Pijnklachten gedurende / na de procedure
- Complicaties
- Patiënt tevredenheid met betrekking tot de ingreep en reductie van de klachten (m.b.v. VAS)
- Tijdsduur tot werkhervatting/schoolhervatting
- Aantal dagen ziekteverzuim in het jaar na de ingreep
- Kosten Effectiviteit laser tonsollotomie vs klassieke tonsillectomie
- Budget Impact laser tonsollotomie vs klassieke tonsillectomie

STUDIE-OPZET

Studie-opzet

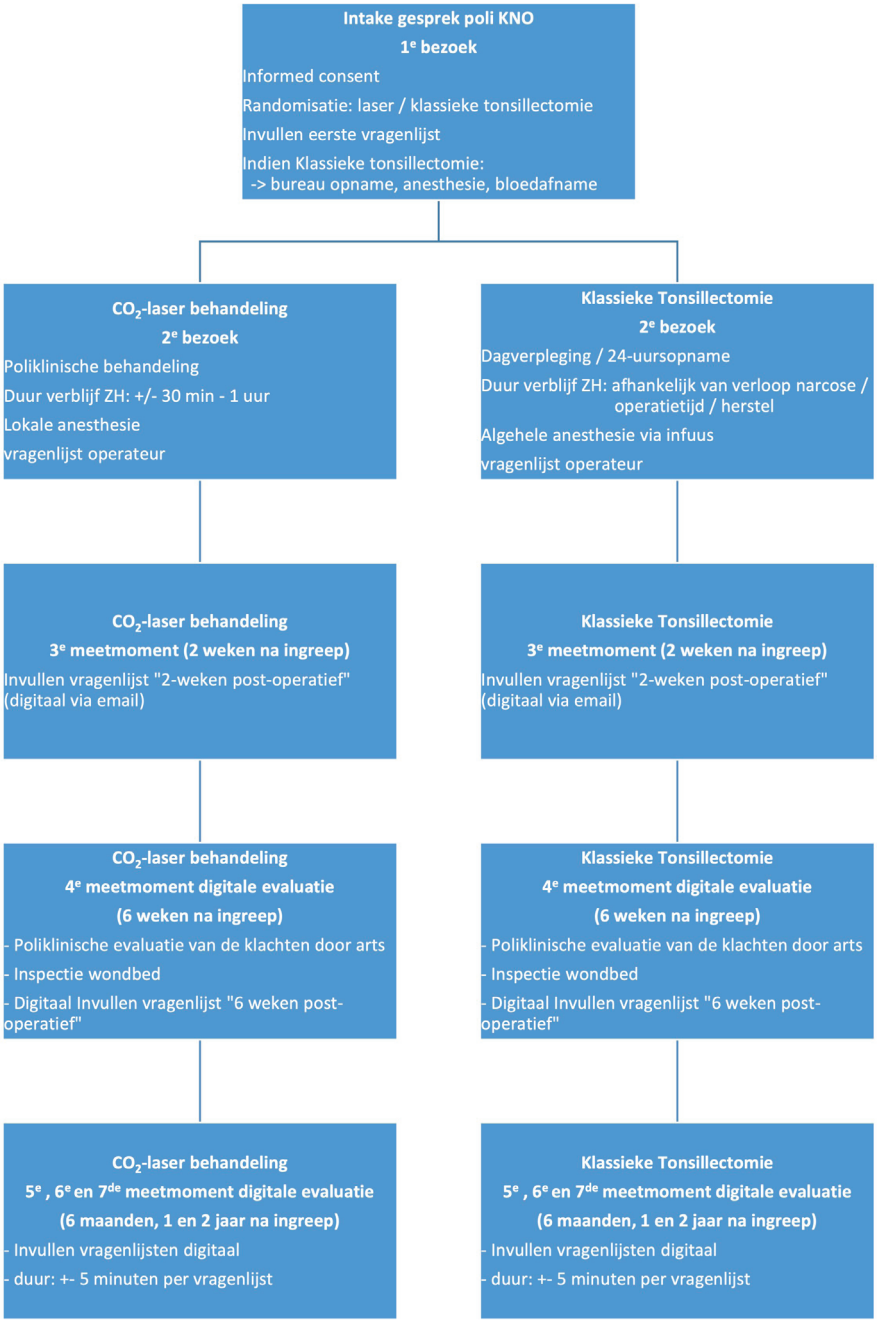
De studie zal worden uitgevoerd als een niet-geblindeerde multicenter gerandomiseerde gecontroleerde trial. De patiënt zal gerandomiseerd ingedeeld worden voor een klassieke tonsillectomie of een lasertonsillotomie.

Organisaties

De patiënten zullen na informed consent in de studie geïncludeerd worden.

De CO_2-lasertonsillotomieën zullen plaatsvinden in een behandelkamer die voldoet aan de lasercriteria op de poliklinische interventiekamer van het HagaZiekenhuis, locatie Sportlaan. De klassieke tonsillectomieën zullen worden uitgevoerd op de operatiekamers van het deelnemende centrum alwaar de patiënt geïncludeerd is.

Het aantal bezoeken van de patiënt aan het ziekenhuis staat weergegeven in bijgevoegde Flow-Chart (figuur 1).



FIGUUR 1. ZIEKENHUISBEZOEKEN EN EVALUATIEMOMENTEN VOOR DE PATIENT

STUDIEPOPULATIE

1. Populatie

De studie populatie zal bestaan uit mannen en vrouwen ouder dan 18 jaar met tonsil gerelateerde klachten zoals nader beschreven onder indicaties. In totaal worden in de klinieken die meedoen aan de studie ongeveer 2000 patiënten per jaar behandeld voor tonsil gerelateerde klachten.

1. Inclusiecriteria

- Patiënten ouder dan 18 jaar
- Indicaties:
- Chronische/recidiverende tonsillitis, > 4 tonsillitiden/jaar (ZATT richtlijn, KNO vereniging [17]) en/of
- Halitosis en/of
- Klachten van tonsillolithiasis en/of
- Dysfagie en/of
- OSAS (bewezen) veroorzaakt door de tonsillen

2. Exclusiecriteria

- Onrustige of niet-coöperatieve patiënt, naar oordeel van de behandelend arts
- Mond niet langdurig kunnen openhouden
- < 5 seconden achtereenvolgens
- < 30 minuten met tussenpozen waarbij de kaak kan worden ontspannen
- Hoge wurgreflex
- Te grote tonsillen (Friedman IV)
- Onvoldoende expositie gehele tonsil
- Peritonsillair abces in de voorgeschiedenis
- Hemorragische diathese / gebruik van bloed verdunnende medicatie
- Allergie voor lokaal anestheticum
- Uitgebreide co-morbiditeit in de voorgeschiedenis waarbij narcose niet wenselijk is dan wel lokale anesthesie niet wenselijk is
- Immuun gecompromitteerde patiënten

SPECIFICATIE BEHANDEL OPTIES (INTERVENTIE)

1. Te onderzoeken behandeling

De CO_2-lasertonsillotomieën zullen worden uitgevoerd op de poliklinische interventiekamer van de keel-, neus- en oorheelkunde van het HagaZiekenhuis, locatie Sportlaan. De behandelkamer voldoet aan de criteria zoals geformuleerd in het boek "laserveiligheid in de gezondheidszorg" (www.laserveiligheidindegezongdheidzorg.nl). Alle aanwezigen dienen een veiligheidsbril te dragen en buiten de kamer zal een waarschuwing zichtbaar zijn. Preoperatief wordt 1000 mg Paracetamol gegeven. De ingreep wordt in half liggende houding uitgevoerd. De tonsil en de superieure, laterale en anterieure zijde van de farynxboog worden geïnfiltreerd met xylocaine 2% en adrenaline 1:80.000. Er wordt ongeveer 10 minuten gewacht om de verdoving in te laten werken. Er wordt gebruikt gemaakt van een F125 laser van Lumenis (Acupulse Surgitouch CO2 laser system) met een beam diameter van 3 mm, met een power van maximaal 29 watt. De tonsil wordt gepresenteerd met een tongspatel waarna laag voor laag met een vegende beweging het oppervlak van de tonsillen wordt verdampt. De patiënt wordt geïnstrueerd diep in te ademen voordat de laser wordt geactiveerd en tijdens het laseren langzaam uit te ademen. De rook die door de verdamping ontstaat wordt continu afgezogen door een afzuiger.

In eerste instantie worden de CO_2-lasertonsillotomieën alleen in het Hagaziekenhuis uitgevoerd. Na training van KNO-artsen uit andere ziekenhuizen, wordt er gekeken of de CO_2-lasertonsillotomieën ook in andere klinieken kunnen plaatsvinden. Indien dit mogelijk blijkt wordt er een amendement ingediend om toestemming van uitbreiding aan te vragen.

2. Controle behandeling

De klassieke tonsillectomie wordt gepland in een dag opname of korte klinische opname in het centrum van inclusie, deze ingreep is mogelijk in alle centra die meewerken aan dit onderzoek. Peroperatief wordt er een perifeer infuus geprikt. De patiënt wordt op de operatiekamer in rugligging geplaatst en onder narcose gebracht waarna de patiënt geïntubeerd wordt. In de mond wordt vervolgens een mondspreider aangebracht. Er wordt een Alyss klem aangebracht op de superior gelegen pool van de tonsil. Vervolgens wordt er een incisie gemaakt door de anterieure pijler van de tonsil om het onderliggende kapsel in beeld te krijgen. De incisie wordt dicht op de anterieure plooi gemaakt en wordt door de mucosa verlengd tot de basis van de tonsil. Met behulp van een tonsiltang wordt vervolgens de tonsil verwijderd. Er worden gazen aangebracht om het bloeden te stelpen. Na het verwijderen van de gazen na 5 minuten wordt er gekeken of het wondbed droog is en wordt er zo nodig gecoaguleerd. De mondspreider wordt

indien het wondbed droog is uitgenomen. Na de operatie wordt de patiënt opgenomen op de afdeling.

Post-operatieve pijnstilling beide ingrepen:

- Recept paracetamol 500mg 4dd2, gebruik zo nodig naar eigen inschatting van de patiënt.
- Recept diclofenac 50mg 3dd1 , gebruik zo nodig de eerste 3 dagen naar eigen inschatting van de patiënt.

METHODE

1. Primaire uitkomstmaat

- Aantal dagen postoperatief herstel tot hervatten dagelijkse activiteiten

2. Secundaire uitkomstmaten

- Aan / of afwezigheid van de tonsil-gerelateerde klacht
- Aantal episodes tonsillitis per jaar geobjectiveerd door de huisarts of KNO-arts
- Aantal keren antibiotica in verband met tonsillitis per jaar
- Gemiddeld aantal dagen per jaar ziekteverzuim t.g.v. de tonsil gerelateerde klachten
- Aan- / afwezigheid van halitose
- Aan- / afwezigheid detritus
- Pijnklachten gedurende / na de procedure
- Complicaties
- Patiënt tevredenheid met betrekking tot de ingreep en reductie van de klachten (m.b.v. VAS)
- Tijdsduur tot werkhervatting/schoolhervatting
- Aantal dagen ziekteverzuim in het jaar na de ingreep
- Kosten Effectiviteit laser tonsollotomie vs klassieke tonsillectomie
- Budget Impact laser tonsollotomie vs klassieke tonsillectomie

3. Randomisatie

Na informed consent zal de patiënt gerandomiseerd worden voor één van beide behandelingen. Het is niet mogelijk de studie geblindeerd uit te voeren. De loting zal gebeuren met behulp van een stratificatie randomisatie waarbij er rekening wordt gehouden met de indicatie. Van de patiëntengroep zal ongeveer 50% gerandomiseerd worden voor een klassieke tonsillectomie en ongeveer 50% van een laser tonsillotomie.

4. Steekproefberekening

We willen een verschil in het aantal dagen postoperatief herstel tussen de beide therapiegroepen van minimaal 3 dagen aan kunnen tonen. Het gemiddeld herstel na een klassieke tonsillectomie is ongeveer 10 dagen (SD 5 dagen). Met een power van 90% en een 2-zijdige alfa van 5% zijn er 59 patiënten per therapiegroep nodig. Wij zullen rekening houden met een maximale uitval van 40%. Daarom willen wij in totaal 198 patiënten includeren.

We verwachten in de secundaire uitkomstmaten grotere verschillen tussen de twee therapiegroepen. Het aantal patiënten om deze grotere verschillen aan te kunnen tonen zal dus ruim voldoende zijn.

5. Studie procedure

Om de primaire en secundaire uitkomstmaten te evalueren zal de patiënt gevraagd worden om 2 weken, 6 weken, 6 maand, 1 jaar en 2 jaar na de ingreep een digitaal evaluatieformulier in te vullen. Deze formulieren zullen per e-mail aangeboden worden. Tevens zal er poliklinische controle van het wondbed plaatsvinden 6 weken na de ingreep. Bij recidiverende klachten na de ingreep wordt de patiënt gevraagd voor beoordeling naar de KNO-arts / huisarts te gaan en dit tevens door te geven aan de onderzoeker (per telefoon / email). Dit zal ook nogmaals geëvalueerd worden in de vaste meetmomenten.

De operateur zal een aantal vragen met betrekking tot de procedure invullen.

Procedure laser:

- Duur van de laser procedure
- Totale duur van poli bezoek
- Hoeveelheid toegediende lokale anesthesie (aantal carpules)
- Pijn gedurende de procedure (VAS score) (beleving patiënt)
- Gebruik van aanvullende verdoving, en de hoeveelheid hiervan
- Gedurende procedure wel / geen coagulatie nodig
- Complicaties gedurende ingreep

Procedure klassieke TE:

- Duur procedure (snijtijd)
- Duur ziekenhuisopname
- Toegediende pijnstilling gedurende operatie (medicijn, dosering)
- Pijn gerelateerd aan procedure (prikken infuus e.d.) (VAS score) (beleving pt)
- Gedurende procedure wel / geen coagulatie nodig
- Complicaties gedurende ingreep

6. Voortijdig uitstappen uit de studie

De patiënt kan zich te allen tijde terug trekken uit de studie. De arts kan te allen tijde de patiënt uit de studie terugtrekken omwille van medische redenen ten behoeve van de patiënt.

7. Interventie voortijdig / tussentijds afbreken

Zowel de arts als de patiënt kan besluiten gedurende de procedure de interventie om medische dan wel andere redenen te beëindigen. Er is in deze studie geen mogelijkheid tot cross over.

VEILIGHEIDSOVERWEGINGEN

1. Sectie 10 WMO

In overeenstemming met sectie 10, subsectie 4 van de Wet Medisch-wetenschappelijk onderzoek met mensen (WMO) zal de verrichter de studie stopzetten indien er, voldoende onderbouwd, verdenking bestaat dat voorzetting van de studie de gezondheid of veiligheid van de patiënt in gevaar brengt. De verrichter zal, zonder onnodige vertraging, de geaccrediteerde METC informeren over het tijdelijk stopzetten en reden van stopzetten van de studie. De studie zal, in afwachting van een toekomstig positief oordeel van de geaccrediteerde METC, worden stopgezet. De onderzoeker zal er voor zorgen dat alle betrokken geïnformeerd zijn.

2. Adverse events (AE)en serious adverse event (SAE)

Bij beide behandelingen bestaat er het risico op een nabloeding gedurende de procedure of postoperatief. Bij de klassieke TE is dat in het HAGA ziekenhuis ongeveer 1.4% (2007) waarbij interventie nodig is, de pilot studie toont bij lasertonsillotomie in 2,6 % van de patiënten een nabloeding waarvoor echter geen interventie noodzakelijk was. Tevens is er bij beide behandelingen een risico op infectie na de behandeling, dit risico is voor beide interventies vergelijkbaar.

Op dit moment is er geen evidence dat er transmissie van 'transmissible spongiform encephalitis' kan ontstaan door inademing van de rook en / of verdampt weefsel. Wel bestaat hiervoor in theorie een risico bij CO_2-lasertonsillotomie. Ondanks dat er geen specifieke richtlijnen zijn voor rookpluimen in relatie met variant Creutzfeld Jacob Disease en het risico voor besmetting van de behandeld arts en operatieassistentes als zeer laag wordt geschat wordt er vanuit de veiligheidsrichtlijnen rondom laserbehandeling geadviseerd om een efficiënt filterend evacuatiesysteem te gebruiken. [14, 16]

Het toedienen van lokale anesthesie kan een anafylactische shock ten gevolg hebben of een systemische reactie zoals beschreven in de bijwerkingen van xylocaine/adrenaline ten gevolg hebben.

In verband met deze mogelijk ongewenste gevolgen / bijwerkingen van de behandeling zullen er verscheidene voorzorgsmaatregelen getroffen worden.

- Er is te allen tijde een dienstdoend KNO-arts beschikbaar wanneer er een complicatie plaatsvind waarvoor opnieuw interventie / beoordeling nodig is.
- Saturatie en hartslag van de patiënt wordt gedurende de gehele ingreep gemonitord.

- De ingrepen zullen plaatsvinden in klinieken waar te allen tijde personeel met BLS certificaten aanwezig zal zijn, tevens is er een anafylactie-set én beademingsapparatuur beschikbaar.
- De behandelkamer waar de laser behandeling plaatsvindt voldoet aan de criteria zoals geformuleerd in het boek "laserveiligheid in de gezondheidszorg" (www.laserveiligheidindegezongdheidzorg.nl).

Wanneer er sprake is van een (S)AE zal dit gerapporteerd worden via het webportaal van ToetsingOnline aan de geaccrediteerde METC dat het protocol heeft goedgekeurd. Wanneer er sprake is van een SAE zal dit binnen 15 dagen aan de geaccrediteerde METC worden gerapporteerd. Wanneer er sprake is van overlijden of een levensbedreigende toestand zal dit binnen 7 dagen aan de medisch ethische commissie worden gerapporteerd, binnen 8 dagen zal de initiële rapportage gecompleteerd worden.

Een jaarlijkse veiligheidsrapportage met overzicht van alle SAE's zal aan de METC worden toegestuurd.

3. Monitoring

Het onderzoek zal volgens het monitorplan van het HagaZiekenhuis door de monitorpool van het Hagaziekenhuis gemonitord worden.

Statistische analyse

1. Beschrijvende statistiek

Deze studie zal verschillende typen data bevatten. Er wordt gebruik gemaakt van zowel kwalitatieve data als kwantitatieve data. De metingen vinden plaats met behulp van vier meetschalen: ordinaal, nominaal, interval en ratio. Welke schaal gebruikt wordt is afhankelijk van de variabele.

In de database zullen de volgende patiënt karakteristieken opgeslagen worden welke later geanalyseerd worden:

- Geboortedatum
- Co-morbiditeit
- Medicatiegebruik
- Wel/niet roken
- Hoofdklacht (Keelpijn met koorts, keelpijn zonder koorts, dysfagie, detritus, halitose, OSAS)

- Aanwezigheid van andere klachten (Keelpijn met koorts, keelpijn zonder koorts, dysfagie, detritus, halitose, OSAS)
- Aantal malen antibiotica gebruik in het afgelopen jaar in verband met tonsil gerelateerde klacht
- Aantal dagen werk verzuim / school verzuim gerelateerd aan tonsil gerelateerde klachten
- VAS score m.b.t. klachten (in te vullen per klacht)
- Friedman classificatie (zie bijlage 1)

De variabelen die worden geanalyseerd gerelateerd aan de ingreep betreffen de volgende:

Procedure laser:
- Duur van de laser procedure
- Totale duur van poli bezoek
- Hoeveelheid toegediende lokale anesthesie (aantal cc)
- Pijn gedurende de procedure, VAS score (beleving pt). Pijnscore afnemen 30 minuten na de ingreep, 1 dag na de ingreep, 2 weken na de ingreep.
- Gebruik van aanvullende verdoving (aantal cc)
- Gedurende procedure wel / geen coagulatie nodig
- Complicaties gedurende ingreep

Procedure klassieke TE:
- Duur procedure (snijtijd)
- Duur ziekenhuisopname
- Toegediende pijnstilling gedurende operatie (medicijn, dosering)
- Pijn gerelateerd aan procedure, VAS score (beleving patiënt). Pijnscore afnemen 30 minuten na de ingreep, 1 dag na de ingreep, 2 weken na de ingreep.
- Gedurende procedure wel / geen coagulatie nodig
- Complicaties gedurende ingreep

De variabelen die worden geanalyseerd om de effectiviteit en patiënt tevredenheid te beoordelen betreffen de volgende:
- Aan- / afwezigheid van de klachten waarvoor de ingreep is ondergaan
- Duur herstelperiode (tijd tot werkhervatting/hervatting dagelijkse activiteiten) in dagen
- Duur gebruik pijnstillers in aantal dagen
- Tevredenheid m.b.t. ingreep (VAS score)
- Klachten na de ingreep (aan/afwezig, VAS score)
- Complicaties op korte en lange termijn (nabloeding, infectie, abces)

- Aantal benodigde lasersessies
- Uiteindelijk wel / geen klassieke tonsillectomie ondergaan
- Aantal malen antibiotica gebruik in de periode na de ingreep in verband met tonsil gerelateerde klacht
- Aantal dagen werk verzuim / school verzuim gerelateerd aan tonsil gerelateerde klachten na de ingreep
- Patiënt zou de ingreep wel / niet aanraden aan anderen
- Patiënt zou de ingreep indien nodig nogmaals ondergaan

2. Analyse

Alle analyses zullen worden uitgevoerd met een intention-to-treat analyse. Eerst zullen univariate analyses worden uitgevoerd, zoals een general linear model voor de continue variabelen en een generalized linear model voor de dichotome variabelen. Er zullen nog secundaire analyses uitgevoerd worden middels geavanceerde regressie technieken als mixed models en Generalized Estimating Equations (GEE). Hierbij zal er gecorrigeerd worden voor mogelijke confounders. Een p-waarde <0,05 zal beschouwd worden als significant.

3. Statische software

De data zullen worden opgeslagen in de databases van het CastorEDC systeem. De statische analyse zal uitgevoerd worden met behulp van het SPSS software pakket.

ETHISCHE ASPECTEN

1. Verordening verklaring

Bij deze studie zullen de principes met betrekking tot de medisch ethische aspecten in acht worden genomen zoals beschreven door de World Medical Association in de 'WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects (2013)' [19] en zoals beschreven in de Wet Medisch-wetenschappelijk onderzoek met mensen (WMO).

2. Informatie verstrekking en informed consent

De patiënten die in aanmerking komen om mee te doen aan de studie zullen door de arts op de hoogte worden gebracht over de voor- en nadelen van de verschillende interventies. Ook zal de mogelijkheid tot een expectatief beleid besproken worden. Na het verstrekken van zowel mondelinge als schriftelijke informatie krijgt de patiënt de mogelijkheid om een keuze te maken of hij deel wil nemen aan de studie. De patiënt kan zelf aangeven welke tijd nodig is om te beslissen wel / niet aan de studie deel te nemen. De maximale bedenktijd is 2 weken. Aanvullende informatie kan de patiënt via onze informatieve website vinden.

3. proefpersonenverzekering

Alle aan dit onderzoek deelnemende proefpersonen in alle deelnemende centra vallen onder de WMO proefpersonenvezekering die door Hagaziekenhuis is afgesloten bij Centramed.

4. Risicoclassificatie

Matig risico, zie bijgevoegd formulier risicoclassificatie.

ADMINISTRATIEVE ASPECTEN EN PUBLICATIE

1. Behandeling en opslag van gegevens en documenten

De gegevens die zijn verkregen tijdens deze studie zullen vertrouwelijk en anoniem worden behandeld. De persoonlijke gegevens zullen worden behandeld volgens de Wet Bescherming Persoonsgegeven (Wbp). De gegevens zullen waar mogelijk worden gecodeerd en een persoons identificatiecode lijst zal worden gegenereerd. De sleutel tot deze code zal worden gewaarborgd door de hoofdonderzoeker. Alleen de hoofdonderzoeker en coördinerend onderzoeker hebben toegang tot de brongegevens. Gegevens worden bewaard gedurende een periode van tien jaar.

2. Wijzigingen

Alle substantiële wijzigingen zullen worden meegedeeld aan de METC en door hen goedgekeurd moeten worden voordat deze wijzigingen in praktijk gebracht kunnen worden.

Een substantiële wijziging wordt gedefinieerd als een wijziging ten opzichte van de aanvraag waarvoor de METC zijn goedkeuring heeft gegeven welke invloed heeft op:

- de veiligheid van de fysieke of mentale integriteit van de deelnemende personen;
- de wetenschappelijke waarde van de studie;
- heb beheer van de studie;
- de kwaliteit of veiligheid van de interventie gebruikt in de studie

Niet substantiële wijzigingen zullen niet aan de METC worden doorgegeven.

3. Jaarlijks voortgangsverslag

De onderzoeker zal eens per jaar een samenvatting van de voortgang van het proces aan de erkende METC sturen. Informatie over het aantal deelnemende personen, aantal deelnemers welke de studie af hebben gerond, (S)AE 's, wijzigingen en problemen worden doorgegeven.

4. Verslag einde van de studie

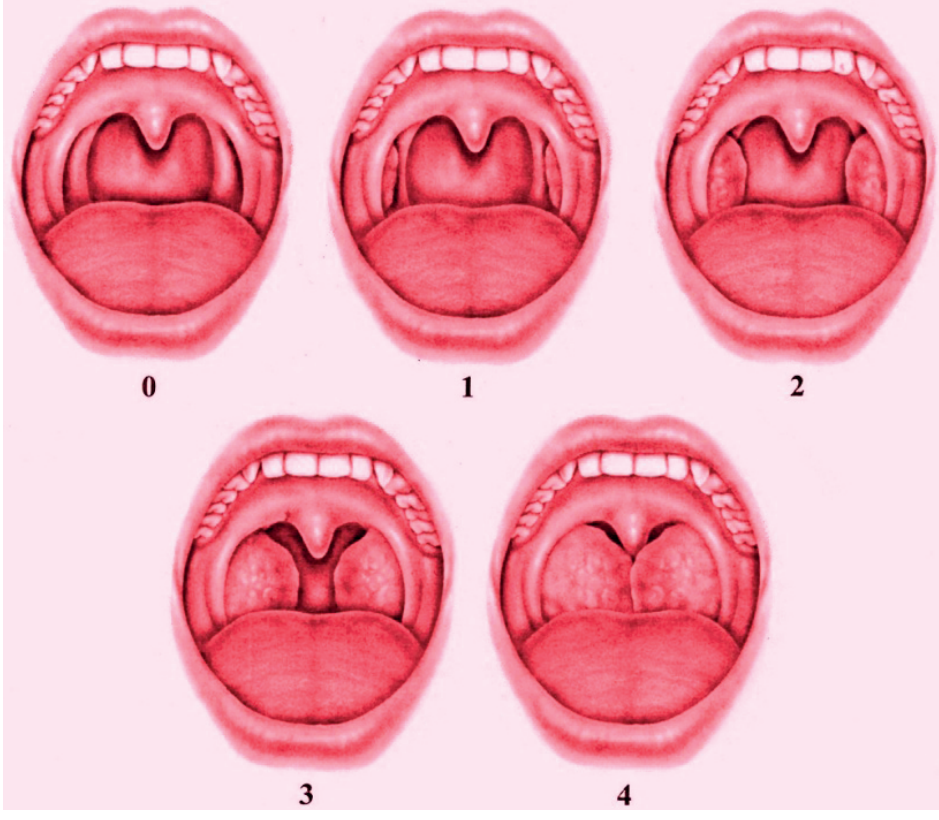
De onderzoeker stelt de erkende METC binnen een termijn van 8 weken na beëindiging van de studie op de hoogte. Het einde van de studie is gedefinieerd als het laatste bezoek van de laatste deelnemer aan de studie. In het geval de studie voortijdig wordt afgebroken zal de onderzoeker de METC hiervan op de hoogte stellen met inbegrip van de redenen hiervoor.

Binnen een jaar na het einde van de studie zal de onderzoeker een eindrapport indienen met de resultaten van het onderzoek. De verwachting is dat er naar aanleiding van dit onderzoek tenminste 2 publicaties in internationale tijdschriften zullen volgen. Deze zullen aan het METC gestuurd worden.

Bijlagen

Figuur 2:. Tonsilgrootte, classificatie volgens Friedman.

0. Status na tonsillectomie 1. Tonsillen verscholen tussen de pharynxbogen 2. Tonsillen komen net buiten de pharynxbogen 3. Tonsillen vergroot tot buiten de pharynxbogen, maar niet over de mediaanlijn 4. tonsillen vergroot tot (over) de mediaanlijn, "Kissing Tonsils"



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Curriculum Vitae

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Work Experience as MD:

2024 – Present:
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2016 – 2017:
Medical Officer in Plastic Surgery, Sanavisie Mill, the Netherlands

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Medical Officer in ENT, Haga Hospital and Juliana Children's Hospital The Hague, the Netherlands

Education:

2007 – 2014 Medicine, Radboud University Nijmegen

- Elective Internship: Plastic Surgery (CWZ, the Netherlands), and Tropical Medicine (Paramaribo, Suriname)
- Senior Internship: ENT Surgery, Radboud University Medical Center Nijmegen

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1. Justin E.R.E. Wong Chung, Wilbert B. van den Hout, Noud van Helmond, Peter Paul G. van Benthem, Henk M Blom. **Long-Term Efficacy and Cost-Effectiveness of Laser Tonsillotomy vs Tonsillectomy A Secondary Analysis of a Randomized Clinical Trial**. *JAMA Network OPEN*. 2025
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