IQWiG Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen

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Tonsillotomy for recurrent acute tonsillitis and for tonsillar hyperplasia[1]

Extract

1 Translation of Chapters 1 to 6 of the final report *Tonsillotomie bei rezidivierender akuter Tonsillitis und bei Hyperplasie der Tonsillen* (Version 1.0; Status: 6 January 2017). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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[2] Due to legal data protection regulations, employees have the right not to be named.

Key statement

Research question

The aims of the present investigation are

- the benefit assessment of tonsillotomy (TT) in comparison with conservative treatment (e.g. watchful waiting) and
- the benefit assessment of TT in comparison with tonsillectomy (TE)

in each case in patients with recurrent acute tonsillitis and in patients with tonsillar hyperplasia. The focus of the assessment was on patient-relevant outcomes.

Conclusion

Neither relevant nor ongoing studies were identified for the comparison of TT versus conservative treatment.

For short-term effects within 2 weeks after surgery, the data provide a hint of lesser harm with regard to **pain** and an indication of lesser harm with regard to **swallowing and sleeping problems** for TT versus TE. In contrast, the data provide no hint of a greater or lesser benefit or harm of TT versus TE for medium- or long-term effects on these outcomes.

For **recurrent tonsillitis and ears, nose and throat infections**, the data provide a hint of a lesser benefit of TT versus TE. However, due to overall inadequate long-term data it is unclear whether this applies only to the medical indication of tonsillar hyperplasia (recorded after 6 years) or also to that of recurrent acute tonsillitis (recorded after 12 to 24 months). The data on **renewed tonsil surgery** were inadequate for both medical indications, so that these data do not provide a hint of a benefit or harm.

The data provide no hint of a greater or lesser harm or benefit of TT or TE for the other patient-relevant outcomes **postoperative bleeding**, **length of hospitalization and re-hospitalization**, **health-related quality of life,** and **other adverse effects of treatment**. No conclusion could be derived for **mortality**, as no data were available in this regard.

In the weighing of the benefit and harm of TT versus TE, a reduction in procedure-related adverse effects in the short term is opposed by a potential lesser benefit in the long term.

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List of abbreviations

Abbreviation	Meaning
ENT	ears, nose, throat
IQWiG	Institute for Quality and Efficiency in Health Care (Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen)
RCT	randomized controlled trial
TE	tonsillectomy
TT	tonsillotomy
VAS	visual analogue scale

1 Background

The complete surgical removal of the palatine tonsils is referred to as tonsillectomy (TE). Besides TE, tonsillotomy (TT) is available as a second surgical treatment option in which the palatine tonsils are only partially removed. Depending on the extent of resection, the terms partial, intracapsular and subtotal tonsillectomy are also used. A TE and TT can also include an adenoidectomy, i.e. a removal of the adenoids (pharyngeal tonsils) [1].

The most common medical indications for TE in children and adolescents include recurrent acute tonsillitis and tonsillar hyperplasia. Tonsillitis is an inflammation of the palatine tonsils that is caused by viruses or bacteria and can lead to pain, swallowing problems and fever. Tonsillar hyperplasia can lead to airway obstruction and sleep-disordered breathing. A subtype, obstructive sleep apnoea syndrome, is associated with a reduction in quality of life [2,3].

Several techniques for TE and TT are available, among others, these include the use of scalpels, tonsil scissors, microdebriders, coblation, diathermia (coagulation), as well as laser and radiofrequency devices [4-9]. Conservative and pharmaceutical treatment options, such as watchful waiting and antibiotics, represent alternatives to surgery [10,11].

The German guideline "Treatment of inflammatory diseases of the palatine tonsils – tonsillitis" recommends TE as a treatment option if at least 6 episodes of medically diagnosed purulent tonsillitis requiring antibiotics occur within a year. If 3 to 5 episodes occur in the first year, TE is regarded as a potential treatment option if further episodes occur in the next 6 months and the overall number of 6 episodes is reached. No TE is recommended if less than 3 episodes occur in a year. In comparison with the medical indication for a TE, the statements on the medical indication for a TT in children and adolescents with recurrent tonsillitis are identical, except for one further condition: In addition, the oropharynx should be narrowed by at least 25% (corresponding to Brodsky grade 2 to 4) [1].

In Germany, no uniform medical indication for TE and TT has so far been established in patients with recurrent acute tonsillitis or with tonsillar hyperplasia. Depending on the region, the frequency of surgery can vary greatly [2].

According to the German Statistical Federal Office, in 2014 a total of 84 332 TEs without adenoidectomy were performed. With about 25 000 cases, the age peak was between 15 and 25 years of age [12]. Especially in children up to 14 years, the complete surgical removal of the palatine tonsils was one of the most common surgical procedures [13,14].

After surgery, besides wound infection and problems with swallowing and sense of taste, bleeding is a common complication. Depending on the definition, bleeding occurs within the first 24 hours after surgery (primary bleeding) in between 0.2% and 2.2% of cases. After 24 hours, the risk of bleeding (secondary bleeding) lies between 0.1 % and 3% [3]. In individual cases, bleeding can be life-threatening, lead to re-hospitalization, and require surgery to stop

the bleeding [3]. Regardless of the medical indication and the procedure used, mortality related to tonsil surgery is very low [15].

Potential advantages of TT over TE mentioned in the literature are that the tonsils with their immunological function are preserved, the rate of postoperative complications is lower, and patients recover faster. However, regrowth of the tonsil tissue is a risk that may lead to symptom recurrence and may require renewed surgery [1,3,16]. Data from Germany, Austria and Sweden show that TT is currently used primarily in younger children [2,17,18].

2 Research question

The aims of the present investigation are

- the benefit assessment of TT in comparison with conservative treatment (e.g. watchful waiting) and
- the benefit assessment of TT in comparison with TE

in each case in patients with recurrent acute tonsillitis and in patients with tonsillar hyperplasia. The focus of the assessment was on patient-relevant outcomes.

3 Methods

The target population of the benefit assessment comprised patients with recurrent tonsillitis and tonsillar hyperplasia. The test intervention was TT. The control interventions were conservative treatment (e.g. watchful waiting) and TE.

The following patient-relevant outcomes were considered for the assessment:

- mortality
- morbidity, especially
  - bleeding
  - pain
  - recurrent tonsillitis and ears, nose and throat (ENT) infections
  - swallowing and sleeping problems
  - length of hospitalization and re-hospitalization
  - renewed tonsil surgery
- health-related quality of life (including activities of daily living)
- other adverse effects of treatment

Only randomized controlled trials (RCTs) were included in the benefit assessment. No limitations applied for study duration. Although a study duration of at least 1 year is required to determine long-term effects of TT, studies of shorter duration were also included so as to record as precisely as possible those outcomes occurring shortly after surgery.

A systematic search for primary literature was conducted in the following databases: MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials. In parallel, a search for relevant systematic reviews was conducted in MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, and the Health Technology Assessment Database.

Publicly accessible trial registries were also searched, and systematic reviews, documents transferred by the Federal Joint Committee (G-BA), and documents provided in the hearing procedure were screened. In addition, the authors of publications of relevant studies were contacted in order to clarify important questions.

The selection of relevant studies was performed by 2 reviewers independently of one another. Data were extracted into standardized tables. To evaluate the qualitative certainty of results, the risk of bias at study and outcome level was assessed and rated as low or high. The results of the individual studies were described, organized by outcomes.

If the studies were comparable regarding the research question and relevant characteristics and no relevant heterogeneity was observed, the individual results were pooled quantitatively by means of meta-analyses.

For each outcome, a conclusion about the evidence base on the (added) benefit and (greater) harm is drawn in 4 degrees regarding the certainty of each conclusion: The data provide either proof (highest certainty of conclusion), an indication (moderate certainty of conclusion), a hint (weakest certainty of conclusion) or none of these 3 situations applies. The latter case applies if no data are available or if the available data do not allow any of the 3 other conclusions. In this case, the conclusion “the data provide no hint of an (added) benefit or (greater) harm” is drawn.

Studies in which the tonsils were randomized (e.g. left tonsil TE, right tonsil TT or vice versa) were included. However, only those outcomes were considered that could clearly be allocated to a procedure. This included bleeding, for instance. In contrast, outcomes such as swallowing problems and pain were not analysed.

If data on the variance of effects were missing, the missing data were calculated from the available data or at least estimated.

If several analysis time points were reported for the outcome of pain, the results from Day 3 were considered in the meta-analysis. If a study did not record data on this day, the closest measurement within the period of Day 1 to 7 was used instead. This approach was to ensure that the analysis across studies covered the time point (under consideration of data availability) at which it could be expected that treatment-related differences were shown, insofar as they existed.

The outcome of swallowing and sleeping problems was divided into short-term effects (within 2 weeks after surgery) and medium- to long-term effects (from 3 weeks after surgery). This was to ensure that one could distinguish between postoperative pain-related swallowing and sleeping problems, as well as medium- to long-term recurrence-related swallowing and sleeping problems.

A beta-binomial model was used for the outcome of bleeding in order not to exclude from the analysis the many studies in which no results were observed [19].

4 Results

4.1 Results of information retrieval

The systematic literature search in the bibliographic databases yielded 31 publications on 25 studies that fulfilled the study inclusion criteria defined for this report. The last search was conducted on 2 November 2016.

Two relevant documents on 2 known studies were identified by the search in publicly accessible trial registries.

Four studies were identified whose relevance could not be conclusively clarified.

A total of 25 RCTs (33 documents) were thus identified as relevant for the research question of the present benefit assessment. However, in 6 studies (11 documents) the data could not be used: 2 studies with randomization of the tonsils provided no evaluable results on patient-relevant outcomes (Arya 2003 and Arya 2005). In 3 studies that applied a Zelen randomization design, the proportion of patients not considered in the analysis was greater than 30% or the difference in the proportion of non-considered patients between the groups was greater than 15% (Ericsson 2007, Ericsson 2009 and Hultcrantz 2004). The results of one study could not be used due to inadequate reporting (Densert 2001).

Therefore 19 RCTs (22 documents) were relevant for the research question of the benefit assessment.

4.2 Characteristics of the studies included in the assessment

The medical indication for tonsil surgery was made due to recurrent tonsillitis in 4 studies [20-23] and due to tonsillar hyperplasia in 15 studies [24-38].

In the 19 studies 1590 patients were randomly allocated to the treatment groups. In 2 of these studies [21,31], intra-individual randomization of the tonsils was performed, so that in 125 patients one tonsil was removed by TT and the other by TE. Of the remaining 1465 patients, 814 were randomized to TT and 651 to TE. The number of participants per study varied between 23 and 300. In 8 studies TT was performed via a microdebrider [20,22,29,31,34,36-38], in 4 via coblation [25-27,37], in 3 via radiofrequency [23,28,33], in 2 via a scalpel or scissors [24,35], in 2 via laser [30,38] and in one each via bipolar electrocoagulation [32] and via a guillotine [21].[3] Only 4 authors provided details on the extent of TT. In one study, 40% [33] and in 3 studies 70 to more than 90% of the tonsils were removed [24,25,35]. In 9 studies TE was performed as a cold procedure [20-24,30,33-35] and in 10 studies with an electrosurgical technique [25-29,31,32,36-38].

In 7 studies patients were discharged from hospital within 24 hours after surgery [21,23,24,28,30,32,35]. The other authors did not provide information in this regard. The

[3] The 3-arm studies Kordeluk 2016 and Wilson 2009 both tested 2 variants of TT; this is why the sum here is 21.

follow-up period lasted from 1 week [21,26,27,32,34,38] to 6 years [24,30]. In the other studies the last follow-up visit was after 2 to 4 weeks [29,31,36], after 3 to 6 months [20,22,33], and after 1 to 2 years [23,25,28,35]. In one study, follow-up of patients ended when they returned to their preoperative daily activities [37].

Nine studies were conducted in the USA [25-29,31,32,36,37], 6 in Europe (Germany [33], Greece [24,35], Austria [20], Sweden [30], the United Kingdom [21]) and one each in Egypt [22], Iran [23], Israel [38] and Thailand [34].

Bender 2015 solely recruited adult patients. Frampton 2012 and Lister 2006 did not randomize patients, but tonsils (e.g. left tonsil TE, right tonsil TT or vice versa). Chan 2004 and Coticchia 2006 were the only multi-centre studies.

4.3 Overview of the available outcomes relevant to the assessment

Data on patient-relevant outcomes were extracted from 19 studies. Table 1 shows the overview of available data on patient-relevant outcomes from the studies included. No study reported data on the outcome of mortality.

Table 1: Matrix of outcomes

Study	Outcomes									
		Morbidity								
	Mortality	Bleeding	Pain	Recurrent tonsillitis and ENT infections	Swallowing and sleeping problems	Length of hospitalization and re-hospitalization	Renewed tonsil surgery	Health-related quality of life	Other adverse effects of treatment
Bender 2015		●							●
Chaidas 2013		●	●	●	●		●		
Chan 2004			●		●	●			●
Chang 2005		●	●		●	●			●
Chang 2008		●	●		●	●			●
Coticchia 2006			●		●	●			
Derkay 2006					●	●		●	●
Frampton 2012		●							
Gabr 2014		●	●						●
Hultcrantz 1999		●	●	●	●	●	●		
Kordeluk 2016		●							
Lister 2006		●	●[a]						
Nemati 2010			●	●	●	●			
Park 2007		●	●						●
Pfaar 2007		●	●		●				
Pruegsanusak 2010			●		●	●			
Skoulakis 2007		●			●				●
Sobol 2006		●	●		●				
Wilson 2009		●	●		●				●

a: Despite randomization of the tonsils the outcome of otalgia was examined as it can clearly be allocated to a procedure.

4.4 Assessment of the risk of bias at study and outcome level

At study level, the risk of bias was rated as low only for Lister 2006. The risk of bias in all other 18 studies was rated as high. In most cases, the generation of the randomization sequence and/or the methods for allocation concealment were unclear. A blinding of patients was performed only in 11 studies. In addition, study registry entries were only identified for

Frampton 2012 and Kordeluk 2016; however, no detailed description of outcomes was provided. Selective reporting could thus not be excluded for any study.

The risk of bias in the results on bleeding and otalgia was rated as low for Lister 2006. In all other studies, the high risk of bias at study level applied to the risk of bias at outcome level.

4.5 Results on patient-relevant outcomes

No relevant studies and thus no patient-relevant outcomes were identified for the comparison of TT versus conservative treatment (e.g. “watchful waiting”).

For the comparison of TT versus TE, Table 2 provides a summary of results of the 19 studies included for which evaluable data were available.

Table 2: Overview of the results for all patient-relevant outcomes

Patient-relevant outcome	Results
Mortality	No data reported
Morbidity	
Bleeding	The pooled overall effect showed no statistically significant difference between the groups: OR (beta-binomial model) 0.24; 95% CI [0.05; 1.22], p = 0.086
Pain	▪ Days until free of pain: The common effect is not presented due to great heterogeneity. The prediction interval covered the zero effect. 4 out of 5 studies showed a statistically significant effect in favour of TT versus TE. ▪ Pain on Day 3: The common effect is not presented due to great heterogeneity. The prediction interval covered the zero effect. 4 out of 7 studies showed a statistically significant effect in favour of TT versus TE ▪ Otalgia: Only one study reported data. The effect was statistically significant in favour of TT.
Recurrent tonsillitis and ENT infections	▪ Recurrent tonsillitis: ▫ Medical indication of tonsillar hyperplasia: The only study on this outcome found a statistically significant difference to the disadvantage of TT after 6 years (11.6 % vs. 0%, p = 0.016). ▫ Medical indication of tonsillitis: The only study on this outcome found no statistically significant difference after 1 to 2 years, but reported neither the event rates nor the effect measure or p-value. ▪ Reduced rate of ENT infections in the preoperative comparison: The pooled overall effect showed no statistically significant difference between the groups OR 0.70; 95% CI [0.19; 2.56], p = 0.594

(continued)

Table 2: Overview of the results for all patient-relevant outcomes (continued)

Patient-relevant outcome	Results
Swallowing and sleeping problems	**Short-term effects** ▪ Time until first food intake: Data were available from only one study; the difference between treatment groups was not statistically significant. ▪ Time until normal food intake: No common effect is presented due to great heterogeneity. The predication interval covered the zero effect. 6 of the 7 studies showed a statistically significantly effect in favour of TT versus TE. ▪ Percentage of normal amount of food eaten by patients on Day 1 to Day 2: The pooled overall effect was statistically significant in favour of TT MD 17.04; 95% CI [8.17; 25.91], p < 0.001 ▪ Difficulties talking after 1 week: Data were available from only one study; the difference was statistically significant in favour of TT. **Medium- to long-term effects** ▪ Swallowing problems after 3 to 4 weeks: No common effect is presented due to great heterogeneity. The effects were not in the same direction. ▪ Difficulties talking after 24 weeks: Data were available from only one study; the difference between treatment groups was not statistically significant. ▪ Daytime fatigue after 4 weeks: Data were available from only one study; the difference between treatment groups was not statistically significant. ▪ Sleep apnoea after 6 years: The pooled overall effect showed no statistically significant difference between the groups: OR 1.33; 95% CI [0.17; 10.16], p = 0.782
Length of hospitalization and re-hospitalization	▪ Extended period of hospitalization: Data were available from only one study; the difference between treatment groups was not statistically significant. ▪ Re-hospitalization: The pooled overall effect showed no statistically significant difference between the groups: OR 0.87; 95% CI [0.43; 1.78], p = 0.707.
Renewed tonsil surgery	The pooled overall effect showed no statistically significant difference between the groups: OR 4.27; 95% CI [0.46; 39.84], p = 0.202.
Health-related quality of life	Data were available from only one study; the difference between treatment groups was not statistically significant.
Other adverse effects of treatment	No statistically significant difference was shown for any of the other adverse events: ▪ nausea (effects not in the same direction) ▪ vomiting (effects not in the same direction) ▪ allergic rhinitis (1 study with a non-statistically significant difference between the treatment groups) ▪ dehydration (no events), ▪ fever (1 study without events and 1 study with a non-statistically significant difference between the treatment groups), ▪ obstruction of the upper airways (OR 1.69; 95% CI [0.20; 14.04], p = 0.626).
CI: confidence interval; ENT: ears, nose, throat; MD: mean difference; OR: odds ratio; TE: tonsillectomy; TT: tonsillotomy	

4.5.1 Results on morbidity

4.5.1.1 Results on bleeding

Information on postoperative bleeding was found in 14 studies. However, events only occurred in 6 studies, all with a moderate qualitative certainty of results (Bender 2015, Chang

2008, Frampton 2012, Kordeluk 2016, Sobol 2006, Wilson 2009). In addition, only Bender 2015 classified the bleeding events that had occurred according to Stammberger.[4] The other authors provided no information in this regard. It is thus unclear whether these events include only blood-tinged sputum or life-threatening bleeding requiring blood transfusions. The calculation of the odds ratio following the beta-binomial model showed a non-statistically significant difference between groups.

Thus for the outcome of bleeding, the data provide no hint of a greater or lesser benefit of TT versus TE.

4.5.1.2 Results on pain

Data from 14 studies, all with a moderate qualitative certainty of results, were available for the outcome of pain; they mostly showed a statistically significant effect in favour of TT. Of these studies, 5 provided information on the number of days until patients were free of pain (Chaidas 2013, Chan 2004, Hultcrantz 1999, Sobol 2006, Wilson 2009) and 9 reported pain scores at different times after surgery (Chang 2005, Chang 2008, Coticchia 2006, Gabr 2014, Nemati 2010, Park 2007, Pfaar 2007, Pruegsanusak 2010, Sobol 2006). For measuring pain, 8 studies used the Wong Baker scale (Chan 2004, Chang 2005, Chang 2008, Gabr 2014, Park 2007, Pruegsanusak 2010, Sobol 2006, Wilson 2009), 4 used a visual analogue scale (VAS) (Chaidas 2013, Hultcrantz 1999, Nemati 2010, Pfaar 2007), and one used a 4-step Likert scale (Coticchia 2006). Lister 2006 recorded the occurrence of otalgia as a dichotomous variable.

Overall, 4 of the 5 studies with information on the number of days until patients were free of pain showed a statistically significant effect in favour of TT. The meta-analysis showed heterogeneity between studies, so that no common effect is presented. The prediction interval covered the zero effect and not all studies showed statistically significant results in the same direction. The effects were moderately in the same direction. It cannot be excluded that single (new) studies show no effect or even an effect to the disadvantage of TT. The certainty of conclusions is therefore downgraded.

The data thus provide a hint of an effect in favour of TT for the number of days until patients are free of pain.

Results from 7 studies were available for the meta-analysis of pain at Day 3 after surgery, of which 4 studies showed a statistically significant effect in favour of TT. No common effect is presented due to the heterogeneity between studies. The prediction interval covered the zero effect and not all studies showed statistically significant results in the same direction of effects. The effects were moderately in the same direction. It cannot be excluded that individual (new) studies will show no effect or even an effect to the disadvantage of TT. The certainty of conclusions is thus downgraded.

[4] Postoperative haemorrhage grades: Grade A: anamnestic recorded blood-tinged sputum; Grade B: bleeding actively under examination; Grade C: haemorrhage needing treatment in general anaesthesia; Grade D: dramatic haemorrhage requiring blood transfusion; Grade E: fatal haemorrhage

The data thus also provide a hint of an effect in favour of TT for pain at Day 3 after surgery; the results of Nemati 2010 and Coticchia 2006 do not contradict this conclusion.

Lister 2006, which showed a high qualitative certainty of results, recorded the occurrence of otalgia and reported a statistically significant effect in favour of TT versus TE. The data thus provide an indication of an effect in favour of TT.

In summary, for the outcome of pain the data provide a hint of a greater benefit of TT versus TE.

4.5.1.3 Results on recurrent tonsillitis and ENT infections

Only 2 of 19 studies reported results on recurrent tonsillitis (Chaidas 2013, Nemati 2010). Nemati 2010, which included patients with recurrent acute tonsillitis, showed no statistically significant difference between treatment groups; however, the number of events after 12 to 24 months was unclear. Patients with tonsillar hyperplasia were recruited for Chaidas 2013. After 6 years, recurrent tonsillitis occurred only in 5 of the 43 patients in the TT group. The difference between groups was statistically significant to the disadvantage of TT. Due to inadequate reporting, a common effect for the 2 studies could not be calculated.

Chaidas 2013 and Hultcrantz 1999, as well as their common effect, showed no statistically significant difference between treatments for reduced rates of ENT infections after 6 years. For reduced rates of ENT infections, the data thus provide no hint of an effect of TT versus TE.

The data thus provide a hint of lesser benefit of TT versus TE for the outcome of recurrent tonsillitis and ENT infections. However, it is unclear whether this applies only to the medical indication of tonsillar hyperplasia or also to that of recurrent acute tonsillitis.

4.5.1.4 Results on swallowing and sleeping problems

In 13 studies, information on the outcome of swallowing and sleeping problems was provided; this was divided into short-term (within 2 weeks after surgery) and medium- to long-term effects (from 3 weeks after surgery). First, the individual operationalizations of the outcome are presented; these provide the basis for the derivation of the evidence base for the outcome of swallowing and sleeping problems (short-, medium- to long-term effects).

Short-term effects

The number of days until patients completely resume their normal eating habits was reported in 7 studies (Chaidas 2013, Chan 2004, Derkay 2006, Nemati 2010, Skoulakis 2007, Sobol 2006, Wilson 2009). Heterogeneity between studies was shown, so that no common effect is presented. The prediction interval covered the zero effect and not all studies showed statistically significant results. The effects were moderately in the same direction. It cannot be excluded that individual (new) studies will show no effect or even an effect to the disadvantage of TT. The certainty of conclusions is therefore downgraded.

The data thus provide a hint of an effect in favour of TT versus TE. The results of Pruegsanusak 2010 and Coticchia 2006, who recorded the number of hours until first food intake and until patients resumed their normal eating habits, do not contradict this conclusion.

Two studies (Chang 2005, Chang 2008) with a moderate qualitative certainty of results measured the percentage of the normal amount of food patients ate after 1 to 2 days. The pooled overall effect was statistically significant. The data thus provide an indication of an effect in favour of TT.

The authors of Pfaar 2007, a study with a moderate qualitative certainty of results, investigated problems talking using a VAS. After one week, a statistically significant effect was shown in favour of TT.

The data thus provide an indication of a greater benefit of TT versus TE for the outcome of swallowing and sleeping problems (short-term effects).

Medium- to long-term effects

Two studies with a moderate qualitative certainty of results (Coticchia 2006, Pfaar 2007) provided results on swallowing problems using a VAS for recording data after 3 to 4 weeks. No common effect is presented due to the heterogeneity between studies. The effects of the studies are not in the same direction. The data thus provide no hint of an effect of TT versus TE.

Chaidas 2013 and Hultcrantz 1999 investigated the reoccurrence of sleep apnoea after 6 years. The common effect was not statistically significant. The data thus provide no hint of an effect of TT versus TE.

Only Coticchia 2006 recorded daytime fatigue using a VAS. However, no statistically significant effect between groups was shown after one month. The data thus provide no hint of an effect of TT versus TE.

Pfaar 2007, a study with a moderate qualitative certainty of results, investigated problems talking using a VAS. However, no statistically significant effect between groups was shown after 24 weeks.

In contrast to short-term effects, for medium- to long-term effects from 3 weeks onwards the data provide no hint of a greater or lesser benefit of TT versus TE for the outcome of swallowing and sleeping disorders.

4.5.1.5 Results on length of hospitalization and re-hospitalization

Hultcrantz 1999 showed no statistically significant effect between groups for extended hospitalization.

Information on re-hospitalization was reported in 7 studies (Chan 2004, Chang 2005, Chang 2008, Coticchia 2006, Derkay 2006, Nemati 2010, Pruegsanusak 2010). In 2 of the 7 studies,

no events occurred (Chang 2008, Coticchia 2006). The study authors named postoperative bleeding and dehydration as reasons for re-hospitalization. The meta-analysis showed no statistically significant effect between groups.

For the outcomes of length of hospitalization and re-hospitalization, the data thus provide no hint of a greater or lesser benefit of TT versus TE.

4.5.1.6 Results on renewed tonsil surgery

Hultcrantz 1999 and Chaidas 2013 reported renewed tonsil surgery after TT. As a reason for renewed surgery both authors noted that sleep-disordered breathing had occurred again. Neither the individual effects nor the common effects were statistically significant.

For this outcome, the data thus provide no hint of a greater or lesser benefit of TT versus TE. However, by and large the data are inadequate, as the overall effect is highly imprecise due to the low number of events and patients and neither a halving nor a doubling of the risk of renewed surgery can be excluded.

4.5.2 Results on health-related quality of life

Derkay 2006 measured the outcome of health-related quality of life after one month using the Obstructive-Sleep-Disorders-6(OSD-6) instrument. The authors found no statistically significant effect between groups. The data thus provide no hint of a greater or lesser benefit of TT versus TE for the outcome of health-related quality of life.

4.5.3 Results on other adverse effects of treatment

Even though only 9 of the 19 studies explicitly reported adverse effects, the other 10 studies at least reported bleeding, pain or re-hospitalization, so that the risk of selective reporting of serious complications seems low. For the other adverse effects of treatment, the data provide no hint of a greater or lesser harm of TT versus TE. The reasons for this are that if homogeneity was present, the common effect was not statistically significant (obstruction of upper airways) and if heterogeneity was present, the effects were not in the same direction (nausea, vomiting). Moreover, for the other adverse events where no meta-analysis was possible (allergic rhinitis, dehydration, fever), the individual studies showed no statistically significant difference between groups.

4.6 Studies of unclear relevance

The search in publicly accessible study registries identified 4 studies of unclear relevance for which no results are yet available. The question as to whether these results will contribute to a benefit assessment of TT versus TE can only be conclusively answered when the data become available. Whether and precisely when these results will be available is currently unclear.

No registry entries were available for the comparison of TT with conservative treatment (e.g. watchful waiting).

4.7 Evidence map

The following Table 3 shows the evidence map in relation to the patient-relevant outcomes.

Table 3: Evidence map in relation to patient-relevant outcomes

	Morbidity							
Mortality	**Bleeding**	**Pain**	**Recurrent tonsillitis and ENT infections**	**Swallowing and sleeping disorders**	**Length of hospitalization and re-hospitalization**	**Renewed tonsil surgery**	**Health-related quality of life**	**Other adverse effects of treatment**
-	⇔	⇗[a]	⇘[b]	⇑[c]	⇔	(⇔)	↔	⇑⇓[d]

⇑: Indication of a greater benefit of TT versus TE.
⇗: Hint of a greater benefit of TT versus TE.
⇘: Hint of a lesser benefit of TT versus TE.
⇔: No hint, indication or proof, homogeneous result.
(⇔): No hint, indication or proof, homogeneous result; the 95% CI for the relative effect is so imprecise that neither a halving nor a doubling of the effect can be excluded.
↔: No statistically significant difference between treatments at the individual study level.
⇑⇓: No hint, indication or proof, heterogeneous result.
-: No data reported.
a: The data provide a hint of an effect in favour of TT for the number of days until patients are free of pain as well as for pain at Day 3. The data provide an indication of an effect in favour of TT for the occurrence of otalgia. Thus for the outcome of pain a hint of a greater benefit of TT versus TE is shown.
b: For the outcome of recurrent tonsillitis and ENT infections, the data provide a hint of a lesser benefit of TT versus TE. However, it is unclear whether this applies only to the medical indication of tonsillar hyperplasia or also to that of recurrent acute tonsillitis.
c: For the outcome of swallowing and sleeping problems, the data provide an indication of a greater benefit of TT only for short-term effects within 2 weeks. In contrast, from 3 weeks onwards after surgery the data provide no hint of a greater or lesser benefit of TT versus TE.
d: For the other adverse effects of treatment, the data provide no hint of a lesser or greater harm of TT versus TE. The reasons for this are that if homogeneity was present, the common effect was not statistically significant (obstruction of upper airways) or if heterogeneity was present, the effects were not in the same direction (nausea, vomiting) or if only one study was available the effect was not statistically significant (allergic rhinitis, dehydration, fever).
ENT: ears, nose, throat; TE: tonsillectomy; TT: tonsillotomy

5 Classification of the work result

This benefit assessment showed a short-term benefit of TT versus TE for effects within 2 weeks after surgery. These include pain as well as swallowing and sleeping disorders. In contrast, no greater or lesser benefit of TT is shown for the outcome of postoperative bleeding.

In addition, this outcome was defined in detail in only one study, so that the severity of postoperative bleeding cannot be estimated in the other studies. It is thus unclear whether these events include only blood-tinged sputum or life-threatening bleeding requiring blood transfusions.

In contrast, the data show no medium- or long-term benefit of TT versus TE: the data showed no statistically significant effect for the outcome of swallowing and sleep problems from 3 weeks onwards nor for health-related quality of life after 4 weeks. However, overall the reporting on the outcome of quality of life was inadequate, as only 1 of 19 studies reported such results at all.

For the outcome of recurrent tonsillitis and ENT infections, the data provide a hint of a lesser benefit of TT versus TE. However, due to a lack of corresponding data, it is unclear whether this applies only to the medical indication of tonsillar hyperplasia or also to that of recurrent acute tonsillitis.

In the 2 studies that had recorded this outcome, renewed tonsil surgery had been performed only after TT. However, neither the effects of the individual studies nor the common effect were statistically significant. Overall, the data are inadequate as the overall effects are highly imprecise due to the low number of events and patients and neither a halving nor a doubling of the risk of renewed surgery can be excluded.

A registry analysis from Sweden [16] found a more than 7-fold higher risk of renewed tonsil surgery after TT compared with TE (adjusted hazard ratio 7.16; 95% confidence interval [5.52; 9.13], $p < 0.001$). The analysis considered 27 535 children between 1 and 12 years of age who had undergone TE or TT due to an obstruction of the upper airways. The average follow-up period was 2.36 years for the TT group and 3.30 years for the TE group. A renewed surgical intervention was necessary in 609 (3.9%) of 15 794 children after TT and in 75 (0.6%) of 11 741 children after TE. The most common reason for this was obstruction of the upper airways in 504 (82.3%) and 49 (66.2%) patients respectively, followed by infections in 73 (12.0%) and 11 (14.9%) patients, as well as further medical indications in 35 (5.7%) and 14 (18.9 %) patients.

The data on the outcomes relevant to the assessment were overall moderate, as hardly any outcome had complete data from all studies. Only data from 1 to 3 studies were available for some outcomes such as recurrent tonsillitis, ENT infections, renewed tonsil surgery and health-related quality of life. It is unclear to what extent the recording of individual outcomes

in the studies was planned or even took place (without the reporting of results), as this is not replicable on the basis of the documents available. However, there are no indications of systematic bias.

Even if the recovery time is shorter after TT, potential medium- to long-term unfavourable effects of TT should be considered for decision-making.

6 Conclusion

Neither relevant nor ongoing studies were identified for the comparison of TT versus conservative treatment.

For short-term effects within 2 weeks after surgery, the data provide a hint of lesser harm with regard to **pain** and an indication of lesser harm with regard to **swallowing and sleeping problems** for TT versus TE. In contrast, the data provide no hint of a greater or lesser benefit or harm of TT versus TE for medium- or long-term effects on these outcomes.

For **recurrent tonsillitis and ENT infections**, the data provide a hint of a lesser benefit of TT versus TE. However, due to overall inadequate long-term data it is unclear whether this applies only to the medical indication of tonsillar hyperplasia (recorded after 6 years) or also to that of recurrent acute tonsillitis (recorded after 12 to 24 months). The data on **renewed tonsil surgery** were inadequate for both medical indications, so that these data do not provide a hint of a benefit or harm.

The data provide no hint of a greater or lesser harm or benefit of TT or TE for the other patient-relevant outcomes **postoperative bleeding**, **length of hospitalization and re-hospitalization**, **health-related quality of life,** and **other adverse effects of treatment**. No conclusion could be derived for **mortality**, as no data were available in this regard.

In the weighing of the benefit and harm of TT versus TE, a reduction in procedure-related adverse effects in the short term is opposed by a potential lesser benefit in the long term.

References for English extract

Please see full report for full reference list.

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