

Short-term outcomes of tonsillectomy in adult patients with recurrent pharyngitis: a randomized controlled trial

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ABSTRACT

Background: Limited evidence exists as to the benefit of tonsillectomy in adult patients. We sought to determine the short-term efficacy of tonsillectomy for recurrent pharyngitis in adults.

Methods: We conducted a randomized, controlled, parallel-group trial at a tertiary care ear, throat and nose centre in Oulu, Finland, between October 2007 and December 2010. Adult patients with recurrent pharyngitis were randomly assigned to the control group (watchful waiting) or the tonsillectomy group. Our primary outcome was the difference in the proportion of patients with severe pharyngitis (severe symptoms and C-reactive protein level > 40 mg/L) within 5 months. Our secondary outcomes included differences between groups in proportions of patients who had episodes of pharyngitis with or without medical consultation, rates of pharyngitis and numbers of days with symptoms.

Results: Of 260 patients referred for tonsillectomy because of recurrent pharyngitis, we recruited 86 participants for our study. Of these, 40 patients were randomly allocated to the control group, and 46 were randomly allo-

cated to the tonsillectomy group. One patient in the control group and no patients in the tonsillectomy group had a severe episode of pharyngitis (difference 3%, 95% confidence interval [CI] -2% to 7%). Seventeen patients in the control group (43%) and 2 patients in the tonsillectomy group (4%) consulted a physician for pharyngitis (difference 38%, 95% CI 22% to 55%). Overall, 32 patients in the control group (80%) and 18 patients in the tonsillectomy group (39%) had an episode of pharyngitis during the 5-month follow-up (difference 41%, 95% CI 22% to 60%). The rate of pharyngitis and number of symptomatic days were significantly lower in the tonsillectomy group than in the control group.

Interpretation: There was no significant difference in the number of episodes of severe pharyngitis between the control and treatment groups, and episodes were rare. However, tonsillectomy resulted in fewer symptoms of pharyngitis, consequently decreasing the number of medical visits and days absent from school or work. For this reason, surgery may benefit some patients. Trial registration: ClinicalTrials.gov, no. NCT00547391.

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Recurrent pharyngitis is a common health problem causing repeated use of antibiotic agents and absences from school or work. The condition has often been treated with tonsillectomy.¹ According to a recent Cochrane review, tonsillectomy or adenotonsillectomy reduces the number of episodes and days with sore throat in children.² However, the same review found limited evidence of benefit of tonsillectomy in adults.

Alho and colleagues have previously shown that adults with severe recurrent streptococcal pharyngitis received substantial benefit from tonsillectomy over a short period.³ However, some guidelines suggest that throat swabs should not be done routinely in primary care management of acute pharyngitis,^{4,5} raising the question of how to treat recurrent episodes of pharyngitis when the cause is

unknown. Thus, we sought to determine the effectiveness of tonsillectomy in reducing the number of episodes of severe pharyngitis among adult patients with recurrent pharyngitis of any origin.

Methods

Study design

We conducted a randomized, controlled, parallel-group trial in a tertiary care ear, nose and throat centre. All patients provided written informed consent. The study protocol was approved by the Oulu University Hospital ethics committee.

Participants

We selected participants from consecutive patients referred for tonsillectomy because of recurrent pharyngitis from Oct. 29, 2007, to June 30, 2010.

The clinical criterion for entry to the study was 3 or more episodes of pharyngitis within the previous 12 months. These episodes had to be disabling, prevent normal functioning, be severe enough for the patient to seek medical attention and be thought to involve the palatine tonsils. It was not necessary for culture or antigen tests to have shown infection with group A streptococcus. Our exclusion criteria were age less than 13 years, history of peritonsillar abscess, chronic tonsillitis, ongoing use of antibiotic agents, residence outside of the Oulu region, pregnancy or previous illness making same-day surgery unfeasible.

Intervention

We assigned patients to the control group or the tonsillectomy group using simple randomization. The allocation sequence was concealed from the investigators using sequentially numbered, opaque, sealed envelopes (Appendix 1, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121852/-/DC1).

The patients in the control group were placed on a waiting list for tonsillectomy to undergo surgery after 5 to 6 months (watchful waiting); patients in the tonsillectomy group underwent surgery as soon as possible. Surgery involved total extracapsular removal of both palatine tonsils under general anesthesia. For practical reasons, the median time between the randomization to the tonsillectomy group and surgery was 14 (interquartile range 8–23) days.

Study protocol

Upon assignment to one of the study groups, patients underwent examination, and we collected background data. Both groups were scheduled to be followed for at least 5 months after randomization.

We advised the patients to visit the study physician or their general practitioner whenever they had acute symptoms suggestive of pharyngitis. In addition, we told patients that it was important to seek medical advice for their symptoms during the trial exactly as they had done before. At the acute visit, patients underwent a thorough clinical examination including a throat swab⁶ and a blood test to measure serum levels of C-reactive protein (Appendix 1). The blood test was repeated 3 days later. All laboratory and microbiological analyses were performed by staff blinded to the clinical data.

A study notebook provided to the patients included information about the study and written instructions for their general practitioners, which included information on examining and recording ear, throat and nose status and taking blood samples and throat cultures (Appendix 1). Patients

received treatment as prescribed by a physician (the study physician if available), who recorded the date, location, diagnosis and treatment of acute episodes in the notebook. For patients in the tonsillectomy group, the study notebook also included a Glasgow Benefit Inventory health-related quality-of-life questionnaire⁷ to be answered 6 months after surgery. This instrument has been validated in Finnish by translation, re-orientation, back-translation and pilot testing.⁸

The patients used a symptom diary to record the presence and severity (mild, moderate or severe) of the following acute symptoms: throat pain, cough, rhinitis, fever and absence from school or work. Symptoms lasting more than 30 days were considered chronic and were not included in our analysis.

We collected the study notebooks at the follow-up visit. We checked missing or unreadable information by telephone. We recorded data concerning acute visits and tonsillectomy from patients' charts.

Outcomes

Our primary outcome was the difference in the proportion of patients who had a severe episode of pharyngitis within 5 months. A severe episode had to involve medical consultation registered in the study notebook, and the patient needed to have acute throat pain and signs suggesting the symptoms originated in the pharynx (e.g., edema, erythema, exudative tonsillitis, anterior cervical lymphadenitis). In addition, the serum level of C-reactive protein either on the day of the appointment or 3 days later had to be higher than 40 mg/L.⁹ If a blood sample was not taken, the result of a throat culture had to show other than normal flora, and the patient had to grade the throat pain as severe. Secondary outcomes were differences in proportions of patients with any episode of pharyngitis (sore throat lasting ≥ 2 d) and episodes with medical consultation during the 5-month follow-up, times to pharyngitis episodes, the difference in the mean rates of episodes, the mean number of days absent from school or work and the mean number of symptomatic days during follow-up. We also recorded health-related quality of life and adverse effects related to tonsillectomy.

Statistical analysis

We estimated that 70 patients needed to be enrolled in the study for it to have statistical power of 80% to detect an absolute difference of 25% in the recurrence rates of severe pharyngitis. We determined this estimate using a 5-month recurrence rate of 25% in the control group and 0% in the tonsillectomy group based on the results of the previous trial by Alho and col-

leagues.³ We considered a 2-sided p value of 0.05 to be significant. We analyzed all of the participants on an intention-to-treat basis according to a pre-established plan.

For descriptive data, we calculated means with standard deviations or medians with interquartile ranges. We used the Mann–Whitney U test to compare continuous variables. We constructed survival curves, as they related to the treatment group, using the Kaplan–Meier method, starting from the date of randomization in the control group and from the date of surgery in the tonsillectomy group. We tested differences between the groups using the log-rank test. We calculated the absolute difference and the 95% confidence intervals (CIs) in the proportions of recurrence between the groups at 5 months.

We determined the number of all episodes of pharyngitis, symptomatic days and absences from school or work per person-year using data obtained during follow-up. However, in the tonsillectomy group, we excluded from the risk time the individual recovery times immediately after tonsillectomy during which the patient had continuous throat pain (mean 17 ± 6 d). In scoring the Glasgow Benefit Inventory questionnaire, we averaged the responses to all 18 questions to give each question equal weight. We then transposed the average score onto a continual benefit scale ranging from -100 to 100 ; a score of -100 meant maximal harm, a score of 0 meant no change, and a score of 100 suggested maximal benefit to quality of life.

Results

Participants and enrolment

The first patient underwent randomization in October 2007, and the last patient completed the study in December 2010. A total of 260 candi-

dates underwent screening, of whom we excluded 132; 42 candidates declined to participate (Figure 1). Most of the patients who were excluded had too few previous episodes of tonsillitis, had chronic tonsillitis or lived outside the study region. Of the 86 remaining patients, we randomly assigned 40 to the control group and 46 to the tonsillectomy group. We saw all of the patients at follow-up (5.7 ± 0.7 mo for the control group, 6.2 ± 0.5 mo for the tonsillectomy group).

Almost all of the patients in the control group underwent surgery on their scheduled date; surgery was done before the limit of 5 months for 3 patients because of severe symptoms.

Two patients, one in each group, lost their symptom diaries but reported not having consulted a physician for throat pain. These patients were assumed to have had no symptoms during the study period. We found no clinically important differences in the baseline characteristics between the 2 groups (Table 1).

Outcomes

At 5 months, 1 patient in the control group and no patients in the tonsillectomy group had experienced an episode of severe pharyngitis (difference 3%, 95% CI -2% to 7%) (Table 2 and Appendix 2, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121852/-/DC1). Seventeen (43%) patients in the control group and 2 (4%) patients in the tonsillectomy group had consulted a physician for pharyngitis (difference 38%, 95% CI 22% to 55%); 32 (80%) patients in the control group and 18 (39%) patients in the tonsillectomy group had experienced an episode of acute pharyngitis (difference 41%, 95% CI 22% to 60%) (Table 2).

During follow-up (6.0 ± 0.7 mo), the overall rate of pharyngitis and number of days with

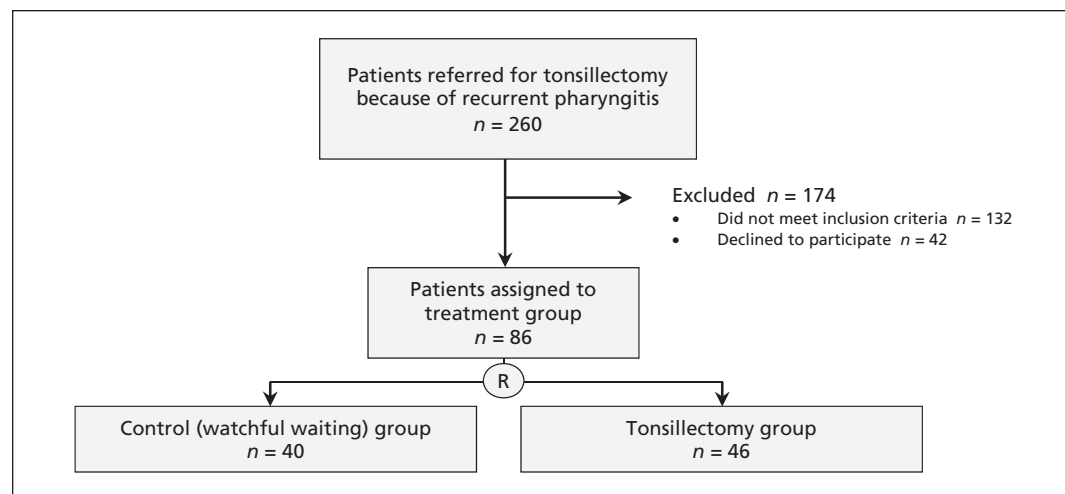


Figure 1: Enrolment of patients in the study.

throat pain, fever, rhinitis and cough were significantly lower in the tonsillectomy group than in the control group (Table 3). Patients in both groups graded most of their throat pain as mild (Appendix 3, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121852/-/DC1). Patients in the tonsillectomy group also had significantly fewer days absent from school or work compared with patients in the control group. According to the postoperative quality-of-life questionnaire, patients in the tonsillectomy group were pleased with their surgeries (Glasgow Benefit Inventory overall score 27 ± 12 , general health subscore 23 ± 15 , social subscore 3 ± 12 and physical subscores 68 ± 28 ; Appendix 4, available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121852/-/DC1).

The mean duration of postoperative throat pain was 17 days. Details of the surgeries and adverse effects are shown in Appendices 5, 6 and 7 (available at www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.121852/-/DC1).

Interpretation

Adult patients with recurrent pharyngitis of any origin had very few severe episodes of pharyngitis (as determined by the presence of severe symptoms and serum levels of C-reactive protein), regardless of whether they underwent tonsillectomy. However, patients who did undergo surgery had fewer episodes of pharyngitis overall and less frequent throat pain than did patients in the control group. These reductions resulted in fewer medical visits and fewer absences from

Table 1: Demographic and baseline characteristics of adults with recurrent pharyngitis, by study group

Characteristic	Study group, no. (%)*	
	Control <i>n</i> = 40	Tonsillectomy <i>n</i> = 46
Age, yr, mean \pm SD	27 \pm 11	26 \pm 8
Female sex	28 (70)	30 (65)
Tobacco use		
By patient	15 (38)	19 (41)
By family member	11 (28)	13 (28)
History of allergy	14 (35)	20 (44)
Risk factors for pharyngitis		
More than 4 people in the family	2 (5)	10 (22)
Similar infections in the family	6 (15)	8 (17)
Untreated dental caries	3 (8)	7 (15)
Symptoms of gingivitis	4 (10)	7 (15)
Use of the same toothbrush > 3 mo	7 (18)	7 (15)
No. of previous episodes of acute pharyngitis diagnosed by a physician, mean \pm SD		
During the past 6 mo	3.1 \pm 1.3	3.2 \pm 1.5
During the past 12 mo	5.0 \pm 2.1	5.0 \pm 2.1
Group A streptococcal pharyngitis diagnosed by a physician		
During the past 6 mo	22 (55)	32 (70)
Ever	22 (55)	38 (83)
Frequent throat pain	14 (35)	23 (50)
Complications of pharyngitis		
Joint symptoms	4 (10)	3 (7)
Tonsils at baseline according to clinical assessment†		
Enlarged	17 (43)	22 (48)
Chronically infected	5 (13)	4 (9)
Scarred	25 (63)	28 (61)
Carrier of group A streptococcus	3 (8)	1 (2)

Note: SD = standard deviation.
*Unless otherwise indicated.
†More than 1 clinical feature possible.

school or work. Patients who underwent surgery also felt that their quality of life improved. The most important morbidities related to surgery were postoperative throat pain and a small risk of postoperative bleeding.

The recent Cochrane review on tonsillectomy for recurrent tonsillitis found only a single trial involving adults, done by our research team, which included adults severely affected by recurrent group A streptococcal pharyngitis.^{2,3} In the current trial, we enrolled adults with recurrent pharyngitis of any origin, about half of whom had a streptococcal episode in the 6 months before randomization.

In both trials, patients showed similar benefit from tonsillectomy. In the previous trial, Alho and colleagues found an absolute difference of 30% in the proportion of patients who had pharyngitis with medical consultation and 25% in the proportion of patients who had pharyngitis without medical consultation between the surgical and control groups.³ In the current trial, these differences were 38% and 41%, respectively. The results are remarkably similar, considering that the observation period was 5 months in the current trial, and only 3 months in the previous trial. Adult patients with recurrent pharyngitis seem to consult a physician similarly regardless of the cause of previous episodes.

Finally, the improved quality of life our patients reported after tonsillectomy is in agreement with the results of several previous studies.¹⁰⁻¹⁴

Limitations

Because we used an open trial design, the placebo effect may explain part of the subjective benefit after surgery, as suggested by the slight beneficial effect of tonsillectomy on cough and rhinitis.

The effect of surgery on pharyngeal symptoms was very good, and we believe this result cannot be due to expectation alone. Sham tonsillectomy has been suggested to control for this potential bias,¹⁵ but this suggestion seems naive. In our experience, patients know what the palatine tonsils are and describe their appearance when presenting with a sore throat. Thus, patients would undoubtedly know whether their tonsils had been removed, as would the physicians who assessed them during consultations for pharyngitis.

The wait-time for tonsillectomy is restricted by law to no more than 6 months, which resulted in a relatively short follow-up. However, we think that the short-term effect of tonsillectomy shows its overall usefulness. Moreover, considering the objective outcomes used in earlier trials, the effect of tonsillectomy does not depend on

the length of follow-up.¹⁶ Any improvement in the pharyngitis rate in the control group during follow-up was likely due to the natural course of the disease. Thus it is unlikely that the patients in the control group reported negatively biased data in their diaries, and the difference between groups was likely due to the benefit of tonsillectomy rather than to any detrimental effect of remaining on the waiting list. Our use of waiting list controls also had advantages. With this

Table 2: Adult patients with recurrent pharyngitis who had an episode of acute pharyngitis within 5 months of enrolment in the study, by treatment group

Outcome	Treatment group, no. (%)		
	Control n = 40	Tonsillectomy n = 46	Difference, % (95% CI)
Objective			
Severe acute pharyngitis*	1 (3)	0 (0)	3 (-2 to 7)
Any pharyngitis with medical consultation†	17 (43)	2 (4)	38 (22 to 55)
Subjective			
Any pharyngitis‡	32 (80)	18 (39)	41 (22 to 60)

Note: CI = confidence interval.
 *Acute sore throat and signs suggesting the pharynx or tonsils as the origin of symptoms (edema, erythema, exudative tonsillitis, anterior cervical lymphadenitis), in addition to serum C-reactive protein level > 40 mg/L either at the appointment or 3 days later.
 †Acute sore throat and signs suggesting the pharynx or tonsils as the origin of symptoms (edema, erythema, exudative tonsillitis, anterior cervical lymphadenitis).
 ‡Two consecutive days of throat pain recorded in symptom diary.

Table 3: Outcomes in adult patients with recurrent pharyngitis, by treatment group

Outcome	Treatment group,* mean ± SD†		
	Control n = 40	Tonsillectomy n = 46	p value‡
Subjective			
Episodes of sore throat, no.	7.4 ± 5.8	1.5 ± 2.4	< 0.01
Throat pain, d	40.2 ± 60.5	5.1 ± 8.7	< 0.01
Fever (> 37.5°C), d	7.8 ± 10.1	2.2 ± 5.2	< 0.01
Rhinitis, d	26.3 ± 28.4	10.2 ± 14.3	< 0.01
Cough, d	16.0 ± 17.7	7.0 ± 14.8	< 0.01
Objective			
Medical consultation for pharyngitis, no.	1.0 ± 1.4§	0.1 ± 0.5	< 0.01
Absence from school or work, d	6.6 ± 11.8	3.3 ± 10.0	0.02

Note: SD = standard deviation.
 *Mean length of follow-up was 5.7 mo for the control group and 6.2 mo for the tonsillectomy group. Patients in the tonsillectomy group had 17 (± 6) d of throat pain and 14 (± 6) d of absence from school or work during the immediate postoperative period. These data are not included in the analysis.
 †Calculated as events per year.
 ‡Mann-Whitney U test.
 §Only 1 episode was due to group A streptococci.

method, the patients in the control group knew they would undergo surgery, and 67% of them agreed to participate. Only 3 patients in the control group asked to undergo surgery before the end of their 5-month wait, because of severe symptoms; no patients were lost to follow-up.

Our criterion for entry to the study was at least 3 disabling clinically significant episodes of pharyngitis per year. However, decisions to perform surgery with so few episodes were exceptions in which the episodes were very severe and prolonged; most patients had about 5 episodes during the previous year. This threshold for tonsillectomy is a bit lower than the criteria presented in certain guidelines.⁵ However, in our experience, these criteria are too strict for adult patients who opt for surgery earlier.

Based on the baseline characteristics of our patients and the high participation rate, we consider our results generalizable to the population of patients seen in otolaryngology outpatient clinics in Finland.¹⁷

Conclusion

Adult patients who had disabling pharyngitis involving the palatine tonsils more than 3 times per year that prevented normal functioning and led to medical consultation benefited from tonsillectomy. After tonsillectomy, patients had fewer episodes of pharyngitis and fewer days with sore throat, resulting in fewer medical visits and absences from school or work. However, pharyngitis and sore throats prevented by surgery were mild and probably of viral origin. The morbidity and complications related to tonsillectomy must be considered when physicians and patients decide whether the clinical benefits outweigh the risks of surgery.¹⁸

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