Tonsillectomy versus Tonsillotomy in the treatment of Recurrent Acute Tonsillitis: A Randomized Controlled Non-inferiority Trial

TRIAL PROTOCOL

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Principal investigator:
Tejs Ehlers Klug, Consultant, DMSci
Department of Otorhinolaryngology – Head and Neck Surgery
E-mail: tejsklug@rm.dk

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GENERAL INFORMATION

Principal investigator:

Tejs Ehlers Klug (TK) Consultant, DMsci, Department of Otorhinolaryngology – Head and Neck Surgery, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N and Department of Clinical Medicine, Aarhus University, Nordre Ringgade 1, 8000 Aarhus C. Role: Main PhD supervisor.

Investigators:
Hannah Inez Houborg (HH), MD, Department of Otorhinolaryngology – Head and Neck Surgery, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N and Department of Clinical Medicine, Aarhus University, Nordre Ringgade 1, 8000 Aarhus C. Role: PhD student.
Christian Danstrup (CD), MD, Department of Otorhinolaryngology – Head and Neck Surgery, Aalborg University Hospital, Hobrovej 18-22, 9000 Aalborg. Role: PhD co-supervisor.
René Thunberg Svendsen (RS), Consultant, Department of Otorhinolaryngology – Head and Neck Surgery, Aarhus University Hospital, Palle Juul-Jensens Boulevard 99, 8200 Aarhus N. Role: Investigator.

ABBREVIATIONS

AUH: Aarhus University Hospital
AaUH: Aalborg University Hospital
CT: chronic tonsillitis
GBI: Glasgow Benefit Inventory
RT: recurrent acute tonsillitis
TE: tonsillectomy
TH: tonsillar hypertrophy
TO: tonsillotomy
TOI-14: Tonsillectomy Outcome Inventory 14
TR-QOL: throat-related quality of life
QOL: quality of life

BACKGROUND

Recurrent acute tonsillitis (RT) is a frequent condition among teenagers and young adults, especially females[1]. These patients suffer from recurrent episodes of throat pain, odynophagia, fever and malaise with associated absences from work or school, repeated health care visits, and impaired quality of life (QOL)[2]. Tonsillectomy (TE), the complete removal of the tonsils, is the only well-documented treatment of RT[3]. In Denmark, approximately 4,000 patients undergo TE annually for this condition. Patients experience massive improvement after TE with highly reduced frequency of sore throat episodes, days of sick leave, use of medical resources and normalized throat-related quality of life (TR-QOL)[2].

However, TE is associated with significant morbidity and risks[4]. The total removal of the tonsils exposes the pharyngeal constrictor muscle and nearby blood vessels to the airflow and ingested foods for two weeks until the mucosa has healed. In this period, patients experience significant throat pain. In a previous study from our group, RT patients undergoing TE reported high (mean 7.1, CI 6.6-7.7) post-operative discomfort score (scale 1-10)[5]. Nevertheless, 97% of patients expressed satisfaction with their decision of surgery at six months follow up despite the surgical morbidity, thus stressing patients need for treatment. Moreover, approximately 5-10% are admitted because of bleeding, which may, rarely, be life-threatening[6, 7].

Tonsillotomy (TO), the partial removal of the tonsils, has gained increasing popularity in the treatment of tonsillar hypertrophy (TH) among children. TO has been shown to be non-inferior to TE in relieving obstructive symptoms (e.g. sleep apnea), while causing less morbidity (e.g. postoperative pain and time to return to normal diet and activity) and risk (e.g. haemorrhage) compared to TE[8-11]. While TO is comparable to TE in children with tonsillar hypertrophy, the knowledge concerning the use of TO in the treatment of adults is very limited[11-22]. In a systematic review, Wong Chung identified nine studies comparing the outcomes of adults undergoing TE versus TO[21]. Ericsson and colleagues randomized 114 patients to TE or TO for the treatment of obstructive symptoms with or without RT and reported on 76 patients[14, 19]. Significant improvements in QOL at follow up (one and six years after surgery) were found in both groups without significant differences between groups. However, the morbidity associated with surgery was significantly less after TO compared to TE (self-rated health day 7, number of days to normal eating and activity etc.)[14]. Two RCT studies have been conducted comparing the outcomes of TE versus TO in patients with RT[17] or either RT or chronic tonsillitis (CT)[13]. Bender et al reported equal improvement in QOL among 104 patients with RT or CT randomized to TE or TO,

but less frequent bleeding (3% vs 12%), less use of pain medication, and more frequent tonsillar remnants in patients undergoing TO[13]. Similarly, Nemati et al reported less morbidity among 38 RT patients undergoing TO compared to 24 patients undergoing TE, with lower pain scores on the first day after surgery (4.0 vs 6.8) and shorter period to normal diet (1.8 vs 3.6 days)[17]. Without further specifying their findings, authors stated that no significant differences were found between groups concerning the number of upper respiratory tract infections at 12 months follow up[17].

To sum up, the literature suggests that the morbidity associated with TO is less than that of TE and outcomes (number of sore throat episodes and TR-QOL) may be equivalent after TO and TE in adults with RT. However, previous studies had questionable quality, the risk of bias was high, and no solid conclusions can be drawn at present[21, 23, 24].

The microbiology associated with RT is unclarified and the pathogenesis of RT is poorly understood. Studies of the tonsillar flora in patients with RT using culture for identification, describe diverse, polymicrobial findings [25-30]. Significant differences in the number and bacterial species are found between the tonsillar surface and core. A few studies suggest that S. aureus may be involved in the pathogenesis of RT. However, S. aureus is part of the normal tonsillar flora, and the role of this pathogen is unclear. A number of studies document that biofilm is present in recurrently infected tonsils, which may be a cornerstone in the pathogenesis of RT.

The current study aims to clarify whether TE is as effective as TO in the treatment of RT, both initially (within the first 6-12 postoperative months) and long term (up to 5 years after surgery), thus decreasing the frequency of sore throat episodes and improving patients' TR-QOL. In addition, we aim to describe the microbiology associated with RT and the possible associations between microbiology and outcomes (the frequency of sore throat episodes and TR-QOL).

HYPOTHESES & AIMS

Hypotheses:

1. The decreased depth of tonsillar crypts from removal of the superficial part of the tonsils in connection to TO decreases the receptivity for infection and other inflammatory processes within the tonsils.
2. Adults with RT experience improved TR-QOL after TE as well as TO.
3. Adults with RT experience decreased frequency of sore throat episodes after TE as well as TO.
4. TO is non-inferior to TE in the treatment of RT in adults, both short (12 months) and long term (5 years).
5. The postoperative morbidity associated with TO is less than TE.
6. TO is non-inferior to TE in the treatment of RT in adults regardless of microbiological findings.
7. The microbiology of the tonsillar bed at follow up (one year after surgery) is equal after TO vs TE.
8. The microbiology of the tonsillar bed at follow up is significantly different from tonsillar surface microbiology at time of surgery.

Aims:

1. Measure TR-QOL in adult patients with RT prior to and after TE vs. TO.
2. Measure the prevalence of sore throat episodes in adult patients with RT after TE vs. TO.
3. Explore patient satisfaction rates in adult patients with RT after TE vs. TO.
4. Explore the prevalence of reoperation (TE) in adult patients with RT after TE vs. TO.
5. Calculate risk factors for persistence of sore throat episodes and decreased TR-QOL.
6. Determine if TO is non-inferior to TE in the treatment of patients with RT (based on outcomes related to aims 1-4).
7. Describe the microbiology associated with RT
8. Explore associations between microbiological findings and outcomes (TE vs. TO, TOI-14 score, number of sore throat episodes after surgery)

METHODS

Study design

This is a two-armed, randomized, controlled, non-blinded trial allocating RT patients for TE or TO. Randomization will be performed using REDCap. This web-based computer randomization will allocate patients to treatment groups in a 1:1 ratio using "*permuted block randomization with random varying block sizes of 4 and 6*".

Study setting

Patients will be recruited from:

1. Aarhus University Hospital, Palle Juul-Jensen Boulevard 99, 8200 Aarhus N (including satellite located in Randers).
2. Aalborg University Hospital, Hobrovej 18-22, 9000 Aalborg.

Eligibility criteria

Inclusion criteria:

- Adults (age ≥15 years) with RT, defined as a minimum of five tonsillitis episodes in one year or a minimum of three tonsillitis episodes per year for two years (Danish National Guidelines criteria[31]).
- The ability to understand Danish orally and in writing.

Exclusion criteria:

- Previous TE or TO.
- Suspected tonsillar malignancy.
- History of malignant tumor in the oral cavity, the pharynx or the larynx.
- Previous radiation therapy on head or neck.
- Hemorrhagic diathesis or anticoagulant therapy.

Reasons for interrupting participation:

- The patient wishes to leave the study.
- No surgery (TE or TO) is performed (for any reason).
- Sponsor and/or investigators decide to terminate participation.

Outcome measures

Primary:

- Efficacy:
    - Number of sore throat episodes 12 months after TE vs TO.
    - QOL measured as postoperative Tonsillectomy Outcome Inventory 14 (TOI-14) score 12 months after TE vs TO.
- Morbidity:
    - Summarized postoperative pain scores (NRS scale 0-10) (days 1-10).
    - Overall postoperative discomfort (day 21).
- Microbiology:
    - Identification of individual bacteria on the tonsillar surface and within the tonsillar crypts and tissue.

Secondary:

- Proportion of patients cured (defined as postoperative TOI-14<15) 12 months after TE vs TO.
- Overall patient satisfaction 12 months after TE vs. TO.
- Postoperative Glasgow Benefit Inventory (GBI) score 12 months after TE vs TO.
- Number of sore throat days 12 months after TE vs TO.
- Prevalence of reoperation 12 months after TE vs. TO.
- All above at 24, 36, and 60 months follow up.

Interventions

Tonsillotomy (TO)

Patients in the TO group undergo bilateral partial removal of the palatine tonsils to a level between the pharyngeal pillars and the tonsillar capsule. Surgery will be performed under general anesthesia using monopolar electrocautery. Bipolar and compression may be used for hemostasis.

Tonsillectomy (TE)
Patients in the TE group will undergo bilateral extracapsular removal of palatine tonsils. Surgery will be performed under general anesthesia using "cold knife" dissection. Bipolar, compression, and tonsil snares may be used for hemostasis.

Additional interventions
Additional adenoidectomy and the use of antibiotics and analgesics are allowed in both groups.

Analgetic medication
Standard analgetic medication (oral Paracetamol 1000 mg x 4 and oral Ibuprofen 400 mg x 3) is prescribed to all patients.

Quality of life questionnaires
Tonsillectomy Outcome Inventory 14:
The Tonsillectomy Outcome Inventory 14 (TOI-14) is originally developed in German in 2012[32] and recently translated and validated in Danish[33] (*Appendix 1)*. The questionnaire is a disease-specific questionnaire for adults with tonsillitis. It is used pre- and postoperatively to detect changes in TR-QOL. It consists of 14 questions that covers four subscales: throat discomfort (question 1-4) general health (question 5-6), resources (question 7-10), and social psychological restrictions (question 11-14). The questionnaire uses a six-point Likert scale with 0 representing "no problem" and 5 representing "couldn't be worse"[34] . The points are summed, divided by the number of questions multiplied by 5, and multiplied by 100, giving scores in the range 0-100, where higher scores reflect poorer TR-QOL[35].

Glasgow Benefit Inventory:
Glasgow Benefit Inventory (GBI) (*Appendix 2)*, originally developed in English in 1996[36], is a validated generic questionnaire for otorhinolaryngological interventions. It is used post-intervention to detect changes in TR-QOL. It consists of 18 questions that covers three subscales: a general health subscale (question 1-6, 9-10, 14, 16-18), a social support subscale (question 7, 11 and 15) and a physical health subscale (question 8, 12-13). The questionnaire uses a five-point Likert scale with 1 representing "worst change of health status" and 5 representing "best change of health status". The points are summed and divided by the number of questions (resulting in average scores), and by subtracting 3 and multiplying by 50, the final scores range from -100 to +100. 0 indicates no change, higher scores reflect better TR-QOL[37].

Tonsil size
Preoperatively, tonsil size will be assessed using the Friedman scale[38], and postoperatively, removed tonsillar tissue will be weighed. Analyses will be made on whether tonsillar size and/or the amount of removed tissue affects the efficacy and/or postoperative morbidity of the interventions.

Microbiology and research biobank
Tonsillar surface and crypt swabs (two q-tip sized swabs obtained at time of surgery) and tonsillar bed swabs (one q-tip sized swab obtained at 12 months follow up) and tonsil tissues (approximately 1-4 g; obtained at time of surgery) are transferred to a -80°C freezer within 30 minutes. These materials will be kept and stored in a research biobank at -80°C. Identification of bacteria will be performed using culture, polymerase chain reaction (PCR), and sequencing. The location of the research biobank is AUH, and materials obtained from other locations will be stored at -80°C and transferred to AUH within three months by investigator Hannah Inez Houborg. Materials will be destroyed at time of termination of the project (31 December 2032). Tissue will be destroyed if requested by the patient. The management of the research biobank will comply to Danish legislation ("Databeskyttelsesforordningen" and "Databeskyttelsesloven").

Procedures and investigations
If the patient is eligible for inclusion and signs the informed consent declaration, the followingly procedures and investigations will be performed:

Time	Procedure/investigation
Preoperatively	Data collection: demographic data, number of tonsillitis episodes within the previous 12 and 24 months, preoperative TOI-14 score and tonsil size.
At time of surgery	Specimen collection: bilateral tonsillar surface and crypt swabs. Data collection: weight of removed tonsils.
Day 1-10 postoperatively	Data collection: pain score (NRS scale 0-10).
Day 21 postoperatively	Data collection: postoperative discomfort (NRS scale 0-10).
12 months follow up	Data collection: number and duration (number of days) of tonsillitis episodes after intervention, postoperative TOI-14 score and GBI score, satisfaction with the effects of surgery, tonsil surgery in the follow up period. Specimen collection: bilateral tonsillar surface/bed swabs (consultation).
24, 36 and 60 months follow up	As 12 months follow up (except specimen collection).

All questionnaires will be delivered to the patients by e-mail via REDCap.

Data management
All data are obtained and managed using the REDCap data management system. REDCap is a mature and secure web application for building and managing online surveys and databases. REDCap is supported by Aarhus University, Denmark.

Source data and CRF
The Case Report Form (CRF) will include the following source data:

- In- and exclusion criteria.
- Clinical data: patient age, gender, weight and height, co-morbidities, tonsil size, performed surgery including technical data (date of surgery, surgeon, blood loss etc.), weight of removed tonsils.
- Patient-related data: number of tonsillitis episodes within the last 12 and 24 months, duration of symptoms, number of lip-to-lip kissing partners, use of tobacco, E-cigarettes, vaping, and alcohol, TOI-14 scores, GBI scores, pain scores, discomfort score, patient satisfaction, number and duration of tonsillitis episodes after surgery.
- Incidents/adverse events: admissions related to surgery or the throat (haemorrhage, infections etc.) and reoperation in the follow up period (60 months).
- Microbiological findings.

The following data from the medical journals will be passed on to the investigators prior to signed consent to assess whether the inclusion or exclusion criteria are met: age, reason for surgery, previous tonsillar surgery, and medical history.

The following data from the medical journals will be passed on to the investigators after signed consent to assess information with relevance for the study: CPR, gender, weight and height, co-morbidities, technical data concerning surgery, admissions related to surgery or the throat, and tonsil surgery in the follow up period (60 months).

The informed consent gives the investigators and any control authorities direct access to data from the patients' medical records, including EPJ, in order to assess health data, which is necessary for the study execution as well as the required study control and monitoring Patient data will be protected by Danish legislation ("Databeskyttelsesforordningen" and "Databeskyttelsesloven"). Data will be kept electronically for five years after ending of patient follow up.

Screening log
A screening log of all adult patients undergoing TE because of RT at the participating institutions will be kept. The following data are obtained: gender, age, and date of surgery. Eligible patients denying to participate are asked to answer a questionnaire including the following data: number of sore throats within the last 12 and 24 months, reason(s) for not participating, and the preoperative TOI-14.

Statistical methods
The statistical software STATA will be used for data analysis. Comparisons will be made using the Student's t-test for normally distributed continuous data, the Kruskal-Wallis test for continuous data not following normal distribution, and the Fisher's exact test for categorical data. Statistical significance will be defined as $p<0.05$.

Two analyses will be performed.
- Primary: intention-to-treat.
- Secondary: per-protocol (excluding patients, whose assigned intervention is discontinued or modified).

Power calculations
Non-inferiority and intention-to-treat analysis. The following sample sizes are needed to show statistically significant differences between groups: Alpha=0.05 and power=90% are used.

Primary outcomes:
- Efficacy:
    - Number of sore throat episodes:
        - Estimates: Mean number of sore throat episodes=0.6 (SD 0.18). Non-inferiority margin=20%
        - N=188
    - Postoperative TR-QOL:
        - Estimates: Mean TOI-14 score=10 (SD 4). Non-inferiority margin=2.0
        - N=200
- Morbidity:
    - Summarized postoperative pain score:
        - Estimates: Mean summarized postoperative pain score: TO: 30 (SD 10) and TE: 50 (SD 12)
        - N=16
    - Morbidity score:
        - Estimates: Mean morbidity score: TO: 5 (SD 2) and TE: 7.7 (SD 2.5)
        - N=32

Secondary outcomes:
- Proportion of patients cured:
    - Estimates: Proportion cured=90%. Non-inferiority margin=15%
    - N=148
- Overall patient satisfaction:
    - Estimates: Proportion satisfied=95%. Non-inferiority margin=15%
    - N=158
- GBI:
    - Estimates: Mean GBI: 35 (SD 4.5). Non-inferiority margin=2.5
    - N=114
- Number of sore throat days:
    - Estimates: Mean number of sore throat days=3 (SD 0.6). Non-inferiority margin=10%
    - N=140

- Prevalence of reoperation:
    - Estimates: Proportion reoperation=10%. Non-inferiority margin=15%
    - N=148

Anticipating that a maximum of 20% of patients are lost to follow up, we will include 250 patients.

Of note, the study is not designed to show statistically significant difference in postoperative haemorrhage rates (estimates: TE: 8%; TO: 2%, using alpha=0.05 and n=250 results in power=81%).

RESEARCH PLAN

Study duration and feasibility

Annual number of adult patients undergoing TE for the treatment of RT: AUH (satellite department at Randers Regional Hospital): 250. AaUH: 150. Anticipating that 60% of patients are included, the duration of inclusion will be 250 / 400*0.60 = 1.04 year.

The research project is at a level and time scale suitable for a PhD project with three years of full-time research. In collaboration with TEK and CD, HH will prepare formalities beforehand.

Time schedule

The study and related activities are planned to be conducted between November 2023 and December 2032.

Time	Activities
November 2023 – October 2024	Approval of study by Ethical Committee Enrollment of PhD student by September 1st 2024 Trial registrations
November 2024 – October 2025	Patient inclusion Study execution
November 2025 – October 2026	Analyses, interpretation and manuscript preparation concerning morbidity outcomes at 12 months follow up
November 2026 – February 2027	Analyses, interpretation and manuscript preparation concerning efficacy outcomes at 12 months follow up
March 2027 – December 2027	Publications and presentations concerning morbidity and efficacy outcomes at 12 months follow up
January 2028 – December 2032	Analyses, publications, and presentations concerning microbiology and morbidity and efficacy outcomes at 24, 36, and 60 months follow up

Budget

The study is initiated by Tejs Ehlers Klug and Hannah Inez Houborg. Hannah Inez Houborg will be paid as PhD student. Investigators will not receive other payments. Patients will not be paid for participation or receive other goods. None of the study participants have financial interests in the study.

Expense type	Description	Amount DKK
PhD salary	PhD salary for 3 years including 3% yearly increase	1.529.965
PhD tuition fee	3 years x 40.000 DKK tuition fee for Aarhus University	120.000
Equipment	Surgical instruments – Monopolar diatermi	5.000
Transportation	Transport expenses for inclusion of patients at Regional Hospital Randers and Aalborg University Hospital	21.500
Microbiology	Cultures	50.000
	PCR	150.000
	Sequencing	250.000
Presentations	Travel expenses, conference fees etc.	50.000
Publication fee	Publication of results in peer-review journals	50.000
Total		**2.226.465**

Funding

Applications have been submitted to public and private foundations (pending). Grants will be administered by Aarhus University and AUH.

PERSPECTIVES

Recruitment

Patients scheduled for TE will be identified from the list of patients planned for pre-operative consultations. We estimate that 70% of eligible patients accept participation in the study. Hence, we estimate to access 400 medical journals to include 250 patients. Patients referred for TE because of RT at the participating institutions, who comply with the inclusion and exclusion criteria, will be asked to participate in the study. The first contact will be in connection to the first consultation at the institution.

Informed consent

Each patient will receive both verbal and written information about the project from one of the investigators in an undisturbed room at the institution, either directly after the first consultation at the institution, or at a subsequent consultation. Patients must give informed consent before being included in the study. Written informed consent will be obtained at the first consultation at the institution or the subsequent consultation. For patients aged 15-17 years, informed consent will be obtained from the patient and all parents with custody.
Consent will be reobtained from minor patients, when they turn 18 years of age.

The patient is informed about the possibility of being assisted by a person of the patient's own choice, as well as the possibility of a reporting period of minimum 24 hours. The patient can withdraw from the project at any time without affecting the relationship with healthcare professionals or the quality of the care and treatment that the patient will receive. If the patient does not wish to participate in the project, they will follow the normal practice regarding care and treatment for RT.

Ethical aspects

Patients are randomized for two different, but both well-described procedures. Hence, we are able to provide a high level of information concerning the benefits and risks associated with both procedures to the patients. Based on previous studies suggesting that patients are likely to experience resolution of symptoms from an alternative procedure (TO) associated with less morbidity and risks compared to the traditional procedure (TE) and a presumed low risk of insufficient treatment, we believe that the benefits of conducting the study weigh heavier than the risks. Patients experiencing an unsatisfying number of sore throats and/or decreased QOL after TO, will be offered TE 12 months postoperatively.

Participants are covered by Patient Insurance Act. The study will be conducted according to the Declaration of Helsinki.

Inclusion of minors

The prevalence of RT peaks in the 15-17 years age group, and the inclusion of patients aged 15-17 years is crucial for the documentation of treatment efficacy in this age group (category iii of the Central Denmark Region Committees on Health Research Ethics criteria for inclusion of minors in research).

To minimize pain, fear and discomfort for minor patients, we will ensure that patients and their parents preoperatively have sufficient information about the project adapted for minors, and that patients postoperatively are treated with sufficient analgesics. In this context it is important to stress that the alternative methods of surgery (TO) is associated with reduced pain, discomfort, and risks compared to the standard method of surgery (TE). The investigators are medical doctors with the necessary pedagogical prerequisites to inform patients aged 15-17 years, as they all frequently work with pediatric patients.

Disadvantages and risks

TE is the current standard treatment for adults suffering from RT, and patients will not be exposed to additional risks in relation to the treatment options currently offered in connection with RT; the only disadvantage for this group is the time used to answer questionnaires, and the time and discomfort associated with swabs at the 12 months follow up.

TO is a commonly used treatment for other tonsil diseases and is associated with less risks and morbidity than TE. As the aim of this study is to evaluate the efficacy of TO vs. TE, inevitably, there is a potential yet presumably small risk of unsatisfyingly relief of symptoms potentially leading to another surgical intervention (TE) for patients randomized to TO. As TE patients, TO patients also has the disadvantage of the time used to answer questionnaires, and the time and discomfort associated with swabs at the 12 months follow up.

The results of the study will primarily benefit future patients, yet the benefit of participating for the individual patient is long-term follow up which is not standard today.

There is no risk for radiation in this study.

Adverse events

The followingly definitions will be used:

- Adverse event (AE): Any harmful and unintentional incident potentially related to intervention.
- Serious adverse event (SAE): An adverse incident which is life threatening or causes hospitalization, prolonged hospital care, or significant disability.

All AE and SAE will be registered by the sponsors and/or investigators and reported to the Danish Health and Medicines Authority. The study will be terminated if suspicion arises that the risks of participating significantly exceeds the expected.

Potential impact

The current study is an example of investigator-initiated research based on clinical experience and scientific knowledge in an area of limited commercial interest. It approaches a very prevalent condition and prominent clinical problem from a patient point of view using patient-reported data as main outcome measures. Our results may be directly implemented in clinical guidelines and improve/nuance the management of patients with RT. Hence, the current study has the potential to alter the surgical approach to one of the most prevalent diseases in teenagers and young adults in Denmark and globally, reducing the pronounced postoperative pain/discomfort and substantial risk of haemorrhage, without compromising the benefits of intervention. Furthermore, the potentially altered relation between morbidity/risk and efficacy, may open our view on indications as defined in current guidelines for offering TE to patients with RT and, thus, pave the road for less restrictive indications as suggested in our recent publication[5].

Registrations
The study is reported to Region Midt's database of research studies (#1-16-02-303-24), and approved by the Central Denmark Region Committees on Health Research Ethics (#1-10-72-48-24).

Publications
Hannah Inez Houborg, Tejs Ehlers Klug, Christian Danstrup, and René Thunberg Svendsen have the rights to the data and the publication of results. Any reference to or publication of the study results must be accepted by the three. Both positive, negative, and inconclusive findings will be published. Study results will be published in peer-review journals and presented at national and international congresses.
Tentative titles:

1. Efficacy of tonsillectomy versus tonsillotomy in the treatment of recurrent acute tonsillitis: a randomized controlled non-inferiority trial
2. Comparison of morbidity associated with tonsillectomy versus tonsillotomy in the treatment of recurrent acute tonsillitis
3. Prognostic factors for improved quality of life in patients with recurrent acute tonsillitis undergoing tonsil surgery
4. The microbiology of recurrent acute tonsillitis

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APPENDICES

Appendix 1

The Tonsillectomy Outcome Inventory 14 in Danish.

		Intet problem	Meget lille problem	Lille problem	Middelstort problem	Stort problem	Det kan ikke blive værre
1)	Tør hals	○	○	○	○	○	○
2)	Sejt sekret (slim) i halsen	○	○	○	○	○	○
3)	Halssmerter	○	○	○	○	○	○
4)	Synkebesvær	○	○	○	○	○	○
5)	Sygdomsfølelse	○	○	○	○	○	○
6)	Nedsat kropslig arbejdsevne (arbejde/daglige gøremål)	○	○	○	○	○	○
7)	Hyppighed af lægebesøg	○	○	○	○	○	○
8)	Omkostninger ved lægebesøg (transport, mistet arbejde osv.)	○	○	○	○	○	○
9)	Hyppighed af antibiotikum (f.eks. penicillin)	○	○	○	○	○	○
10)	Omkostninger ved medicin	○	○	○	○	○	○
11)	Passe arbejde/skole på grund af halsbetændelser/halsgener	○	○	○	○	○	○
12)	Nedsat deltagelse i begivenheder eller aktiviteter på grund af halsgener	○	○	○	○	○	○
13)	Færre sammenkomster med venner/familie på grund af halsgener	○	○	○	○	○	○
14)	Tristhed på grund af hyppige halsbetændelser/halsgener	○	○	○	○	○	○

Appendix 2

The Glasgow Benefit Inventory in Danish.

1)	Har resultatet af operationen / indgrebet påvirket, hvad De foretager Dem?	◯ Meget værre ◯ En smule eller lidt værre ◯ Ingen ændring ◯ En smule eller lidt bedre ◯ Meget bedre
2)	Har resultatet af operationen / indgrebet forbedret eller forværret Deres liv i det hele taget?	◯ Meget bedre ◯ En smule eller lidt bedre ◯ Ingen ændring ◯ En smule eller lidt værre ◯ Meget værre
3)	Er De mere eller mindre optimistisk m.h.t. fremtiden efter Deres operation / indgreb?	◯ Langt mere optimistisk ◯ Mere optimistisk ◯ Ingen ændring ◯ Mindre optimistisk ◯ Langt mindre optimistisk
4)	Føler De dem mere eller mindre forlegen efter Deres operation / indgreb, når De er sammen med en gruppe mennesker?	◯ Langt mere forlegen ◯ Mere forlegen ◯ Ingen ændring ◯ Mindre forlegen ◯ Langt mindre forlegen
5)	Har De fået mere eller mindre selvsikkerhed efter Deres operation / indgreb?	◯ Langt mere selvsikker ◯ Mere selvsikker ◯ Ingen ændring ◯ Mindre selvsikker ◯ Langt mindre selvsikker
6)	Har De fundet det nemmere eller vanskeligere at klare selskabelighed efter Deres operation / indgreb?	◯ Langt nemmere ◯ Nemmere ◯ Ingen ændring ◯ Vanskeligere ◯ Langt vanskeligere
7)	Føler De, De får mere eller mindre støtte fra Deres venner efter Deres operation / indgreb?	◯ Langt mere støtte ◯ Mere støtte ◯ Ingen ændring ◯ Mindre støtte ◯ Langt mindre støtte
8)	Har De af den ene eller anden grund været hos Deres familielæge mere eller mindre ofte siden Deres operation / indgreb?	◯ Langt oftere ◯ Oftere ◯ Ingen ændring ◯ Mindre ofte ◯ Langt mindre ofte

9)	Føler De Dem mere eller mindre tillidsfuld m.h.t. jobmuligheder efter Deres operation / indgreb?	◯ Langt mere tillidsfuld ◯ Mere tillidsfuld ◯ Ingen ændring ◯ Mindre tillidsfuld ◯ Langt mindre tillidsfuld
10)	Føler De Dem mere eller mindre genert efter Deres operation / indgreb?	◯ Langt mere genert ◯ Mere genert ◯ Ingen ændring ◯ Mindre genert ◯ Langt mindre genert
11)	Er der flere eller færre mennesker, der virkeligt holder af Dem efter Deres operation / indgreb?	◯ Langt flere mennesker ◯ Flere mennesker ◯ Ingen ændring ◯ Færre mennesker ◯ Langt færre mennesker
12)	Rammes De mere eller mindre ofte af forkølelser eller infektioner efter Deres operation / indgreb?	◯ Langt oftere ◯ Oftere ◯ Ingen ændring ◯ Mindre ofte ◯ Langt mindre ofte
13)	Har De taget mere eller mindre medicin af den ene eller anden grund efter Deres operation / indgreb?	◯ Langt mere medicin ◯ Mere medicin ◯ Ingen ændring ◯ Mindre medicin ◯ Langt mindre medicin
14)	Føler De Dem bedre eller værre tilpas efter Deres operation / indgreb?	◯ Meget bedre ◯ Bedre ◯ Ingen ændring ◯ Værre ◯ Meget værre
15)	Mener De, de har modtaget mere eller mindre støtte fra Deres familie siden Deres operation / indgreb?	◯ Langt mere større ◯ Mere støtte ◯ Ingen ændring ◯ Mindre støtte ◯ Langt mindre støtte
16)	Føler De dem mere eller mindre besværet af Deres helbredsproblemer efter Deres operation / indgreb?	◯ Langt mere besværet ◯ Mere besværet ◯ Ingen ændring ◯ Mindre besværet ◯ Langt mindre besværet
17)	Har De kunnet deltage i flere eller færre selskabelige aktiviteter efter Deres operation / indgreb?	◯ Langt flere aktiviteter ◯ Flere aktiviteter ◯ Ingen ændring ◯ Færre aktiviteter ◯ Langt færre aktiviteter
18)	Har De været mere eller mindre tilbøjelig til at trække Dem tilbage fra selskabelighed efter Deres operation / indgreb?	◯ Langt mere tilbøjelig ◯ Mere tilbøjelig ◯ Ingen ændring ◯ Mindre tilbøjeligt ◯ Langt mindre tilbøjelig