Clinical Benefit and cost effectiveness of endoscopic sinus surgery (ESS) in adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP)

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Current practice variance in adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP) is not efficient. Endoscopicsinus surgery (ESS) is the most common ENT operation in adults in the Netherlands. The objective of the present study is...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Upper respiratory tract disorders (excl infections)
Study type	Interventional

Summary

ID

NL-OMON47166

Source
ToetsingOnline

Brief title
Clinical Benefit of endoscopic sinus surgery in nasal polyps

Condition

- Upper respiratory tract disorders (excl infections)

Synonym
CRSwNP, nasal polyps

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: ZonMw doelmatigheid

Intervention

Keyword: drug treatment, nasal polyps, Rhinosinusitis, surgery

Outcome measures

Primary outcome

The primary clinical endpoint is HRQol in CRSwNP patients, measured by the SNOT-22 at 12 months follow-up. HRQol is a frequently used clinical endpoint in CRS clinical trials.

Secondary outcome

Secondary study parameters/endpoints include

The effectiveness of ESS in addition to drug treatment as compared to drug treatment alone in adults with CRSwNP in the short (3-6 months) and long (12 - 24 months) term, in terms of:

* Generic HRQoL (EQ-5D-5L)

* Disease specific HRQoL and symptoms (SNOT-22)

* Endoscopic assessment of the nose (Endoscopic assessment of the nasal cavity, graded using the Lildholt scale (0 * no polyps, 1-confined to middle meatus, 2-below middle turbinate. 3- massive polyposis)

* Endoscopic assessment of the nose (Lund-Kennedy endoscopy scores and Modified Lund Mackay Postoperative Endoscopy Score)

* Olfactory function (Sniffin Sticks)

* Nasal obstruction (PNIF)

* Daily records cards (DRC) will be provided 2 weeks before until 2 weeks after a visit to the clinic to record daily symptoms, medication use, adverse events, healthcare resource use and related health care costs
* CRS disease control (EPOS CRS control test, NOSE test)
* Asthma control in the subgroup of patients with asthma (Asthma Control Test)
* Symptomatic exacerbations requiring further treatment including ESS identified using diaries and medical notes
* Adverse effects of drug and surgical treatment and readmissions identified using diaries and medical notes
* Healthcare resource use and related health care costs including patient time and travel costs, out-of-pocket expenditure, time off education, work and usual activities using repeated questionnaires and diaries (DRC)

Baseline data collection for the RCT include

Most of the measurements described above. On top of that we will collect the following measurements:

* CT scan (Lund-Mackay score)
* If surgery is performed a surgical report indicating which sinus are opened and what was found there (surgical report with standard items) will be made
* Laboratory results including total IgE and serum eosinophils
* Earlier sinus surgery with dates and estimation of extent (based on CT scan)
* Skin Prick test (if done in the last year, results are recorded)

* Structured history with questions on allergy, smoking, asthma, aspirin

intolerance, other diseases, and occupational

exposure.

* Bodyweight, bloodpressure and heartrate

Study description

Background summary

Given its prevalence (11% in Europe, 14,6% in the Netherlands) and the significant negative effect on quality of life, the diagnosis and treatment of chronic rhinosinusitis (CRS) is associated with a significant medical resource use and societal economic burden (1, 2). CRS has been shown to have a negative impact on most aspects of Health related Quality of Life HRQoL), and has a greater impact on HRQoL than chronic heart failure, angina, diabetes or back pain (1, 3). CRS is the most common reason for surgery (ESS) in adult patients in the otorhinolaryngological practice with around 18,000 ESS performed in The Netherlands yearly (2010 data stichting hospital data (DHD)). CRS can be divided into the more serious disease CRS with nasal polyps (CRSwNP) (prevalence 1-4%) and CRS without nasal polyps (CRSsNP). Around 70% of the ESS is done in patients with CRSwNP.
Surgery requires anaesthesia and convalescence and has a small but relevant risk of serious (intracranial) complications (1). At present it is unknown whether ESS added to drug treatment offers significant benefits over drug treatment alone. Implementation of the results of this study will lead to tailored care for CRS, improvement of clinical pathways for relevant phenotypes and a considerable reduction of the number of ESS in in the Netherlands.
The indications for and timing of ESS in CRS management are mainly practice based. At present it is unknown whether
endoscopic sinus surgery (ESS) added to drug treatment offers significant benefits over drug treatment alone. National and
international clinical guidelines advise to start with drug treatment for at least 1 month before considering surgical intervention
(2, 6, 7). Currently, patients failing drug treatment are offered a choice of surgery on addition to drug treatment or on-going
more intense drug treatment alone. The costs and benefits of ESS over more intensive drug treatment in the treatment of adult
patients with chronic rhinosinusitis with nasal polyps (CRSwNP) are unclear and 50% of the patients with CRSwNP have
multiple (repetitive) surgeries and long time burden of disease. The need for long term health care use (intermittent and

repetitive) can be costly, so tailored-based alternatives should be preferred in CRS disease management.
There is a significant individual practice variance within the Netherlands and also in contrast to other western-countries with more than average surgery in The Netherlands. Scientific evidence for the effectiveness and adequate timing of ESS is scarce and (inter)nationally accepted standardized clinical guidelines are lacking.
The positioning of surgery (ESS) in the treatment of patients with CRSwNP has been acknowledged as one of the most important knowledge gaps for which an RCT is warranted by the Dutch Society of Otolaryngology (top priority pg 17 www.kno.nl/publiek/document/2908), the CBO guideline CRS (6), the EU Pos. paper on CRS (2) and the patient society of CRS-NP (letters of support as addendum). An estimated reduction of 30-50% of performed ESS interventions for CRSwNP (based on percentages in other western countries) would save 15-26 million euros annually without impairment of HRQoL.

Study objective

Current practice variance in adult patients with chronic rhinosinusitis with nasal polyps (CRSwNP) is not efficient. Endoscopic sinus surgery (ESS) is the most common ENT operation in adults in the Netherlands. The objective of the present study is to investigate whether two regular used strategies (*ESS in addition to drug treatment (usual care)* versus *drug treatment alone*) in adults with CRSwNP differ in improvement in health related quality of life (SNOT-22, EQ-5D-5L) at 12 months follow-up.
Furthermore both strategies will be compared with respect to cost-effectiveness. Secondary outcomes are generic and disease specific HRQOL, cost-effectiveness, endoscopic assessment of the nose, olfactory function, nasal obstruction, asthma control and adverse events, in the short (3-6 months) and long (12 - 24 months) term. Because the average time to revision surgery can be considerable a longer follow-up is advisable.

In this open multi-centre randomized controlled trial in 238 adults with CRSwNP selected for ESS (usual care) are randomized to ESS in addition to drug treatment (usual care) or drug treatment alone. We hypothesize that ESS in addition to drug treatment has no or limited health benefit in terms of HRQoL compared to drug treatment alone in the treatment of CRSwNP.
We expect ESS only to be cost effective in a subgroup of patients.

Our goals in this prospective multicentre study of patient with CRSwNP scheduled for ESS are:
1. To assess the effectiveness of ESS in addition to drug treatment as compared

to drug treatment alone in adults with
CRSwNP in terms of improving patients* health related quality of life, measured by the SNOT-22 (primary endpoint), objective
signs of disease, exacerbation of disease, adverse effects of treatment and associated costs for a period of 12 months.
2. To determine which patient phenotypes within CRSwNP benefit from ESS in addition to drug treatment as compared to drug
treatment alone.
3. To determine the relation between healthcare resource use, patient costs and effects of ESS from a societal point of view.

Study design

We will perform a prospective open multi-center randomized controlled trial in 238 adult patients with CRSwNP selected for
ESS according to current medical practice in the Netherlands. Patients will be randomized to either a) ESS within 6 weeks in
addition to drug treatment, or b) drug treatment alone. Total follow-up will be 24 months. The study will be conducted according
to applicable (inter)national regulatory requirements (WMO, GCP, Declaration of Helsinki 2004).
The study will be performed in at least 11 hospitals: Academic Medical Center, VU Medical Centre Amsterdam, Flevo
Ziekenhuis Almere, Spaarne Ziekenhuis Hoofddorp, Kennemer Gasthuis Haarlem, Ziekenhuis Amstelland Amstelveen,
BovenIJ ziekenhuis Amsterdam, Rijnland Ziekenhuis Leiderdorp en Alphen, Deventer Ziekenhuis, Westfriesgasthuis Hoorn en
het Tergooi ziekenhuizen. When necessary for inclusion, more hospitals will be asked to be involved.

Intervention

Eligible patients will be randomly assigned in a 1:1 ratio to one of both interventions:
1. a surgical strategy consisting of ESS in addition to drug treatment
Those assigned to the surgical strategy will be offered endoscopic sinus surgery within 6 weeks of randomization. In this study
we mean by endoscopic sinus surgery the surgery as done regularly by otorhinolaryngologists in the Netherlands. Usually the
extent of the surgery is tailored to the extent of the disease. We do not standardize surgery. We accept that this introduces a
performance bias (procedures or interventions are not executed in a uniform way * any one surgeon may do the same
procedure in a different way from day to day, and that is even more true between different surgeons) but this is closest to usual
care.

2. a medical strategy consisting of drug treatment alone.
Those assigned to the drug treatment strategy will be seen by the otorhinolaryngologist within 6 weeks of randomization to evaluate the need for additional medical treatment. Drug treatment can be any treatment that is normally given in routine medical practice to treat CRSwNP. We do not standardize drug treatment because we want to stay closest to standard of care.
Moreover patient*s need for drug treatment vary per patient and over time. Finally standardization of treatment will impede inclusion because patients that have a (relative) contraindication for certain medication (e.g. systemic corticosteroids or certain antibiotics) cannot be included in the study. This will reduce diversity and thus the generalization of the results of the study.
The randomization will be website-based, using block randomization and stratified by study centre. Randomization will be performed using a dedicated, password protected, SSL-encrypted website.

Study burden and risks

The burden and risks associated with participation consist of:
- questionaires
- nasal endoscopy (5 times)
- smell test (5 times)
- PNIF (5 times)
- Skin prick test (if not done before)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

* Bilateral CRSwNP (nasal polyps)
* >17 years
* indication for endoscopic sinus surgery (primary or revision) as judged by their ENT surgeon

Exclusion criteria

* pregnancy
* inability to comply with study protocol,
* systemic diseases affecting the nose (e.g., Wegener*s, granulomatosis, sarcoid, primary ciliary dyskinesia, cystic fibrosis,
* antrochoanal polyps (benign polyps originating from the mucosa of the maxillary sinus).
* inverted papilloma and malignant polyps.
* acute upper or lower respiratory tract infections within 2 weeks before the inclusion visit),
* use of systemic corticosteroids within 4 weeks before the inclusion visit
* need of continuous systemic corticosteroids treatment for other disease than CRSwNP
* systemic diseases preventing participation in the study,
* inability to be operated
* medical or surgical treatments influencing the study.

Study design

Design

Study type: Interventional

Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-02-2015
Enrollment:	238
Type:	Actual

Ethics review

Approved WMO Date:	02-09-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-01-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-03-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	18-05-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-08-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	20-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-01-2018
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL48200.018.14