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Laryngeal reinnervation versus thyroplasty in patients with unilateral vocal fold paralysis

Submission date
16/12/2015

Recruitment status
No longer recruiting

Registration date
16/12/2015

Overall study status
Completed

Last Edited
07/05/2025

Condition category
Ear, Nose and Throat

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The vocal cords, also referred to as vocal folds, are two bands of smooth muscle found in the larynx (voice box). During speech, the vocal folds vibrate to the middle of the larynx producing sounds (voice). Unilateral Vocal Fold Paralysis (UVFP) is a condition where one of the vocal folds does not vibrate as well as it should do, usually due to an injury to the nerve that controls its movement. People suffering from UVFP have a weak or hoarse voice and often suffer from breathing or swallowing problems. Voice therapy is usually the first line of treatment for patients with UVFP, and involves vocal exercises designed to strengthen the weakened vocal fold. If no real improvement is seen however, then surgery is the next logical step. Two of the most promising operations are laryngeal reinnervation (nerve rewiring) and thyroplasty. Laryngeal reinnervation is a procedure in which the weak nerve supplying the voice box is connected to a stronger nerve which supplies one of the muscles on the front of the neck. At the same time, a non-toxic filler called hyaluronic acid is injected into the paralysed vocal fold to temporarily improve the voice while the reinnervation begins to take effect. A thyroplasty is an operation which involves placing a plastic or silicon box (implant) next to the paralysed vocal fold which pushes the vocal cord closer to the middle of the larynx which improves voice quality. Each of these treatments has advantages and disadvantages, and further research is needed to find the most effective technique. The aim of this small study is to compare the effectiveness of these two procedures, and to find out if a larger study looking at these effects would be possible.

Who can participate?
Adult UVFP patients who failed voice therapy.

What does the study involve?
Participants are randomly allocated to one of two groups. Participants in the first group are sedated using a general anaesthetic and then have a laryngeal reinnervation procedure. Participants in the second group are given a local anaesthetic and sedation (which makes them feel sleepy and relaxed) and then have a thyroplasty procedure. Before and after their operations, all patients undergo medical tests to measure voice, swallowing and voice box

muscle movement and strength, so that the effects of the different treatments can be compared. The participants in both groups also are asked to attend follow-up clinic appointments at 6 and 12 months so that the doctor can see how they are getting on.

What are the possible benefits and risks of participating?
Both thyroplasty and erinnervation are safe operations with no significant risk or side effects reported in the literature. Study researchers do not predict any significant disadvantages in taking part in this study. The erinnervation operation is conducted under general anaesthesia and so an anaesthetist will do an assessment to identify any higher risks than normal of having anaesthetic side effects. Reinnervation has a delayed effect because the rewired nerve needs at least three months to regain its function. However, the delay in its effect should not be noticeable as we will also inject a substance to temporarily improve the position of the vocal cord. It may be possible that the effect of the temporary injection will wear off before the nerve has regained its function. Possible side effects of the operations are very similar: swelling of the neck, blood clot accumulation or infection of the wound, and difficulty in breathing may occur. These may occur with any form of surgery in the neck area, and are not uncommon. The chances of these happening are the same whichever operation is received and patients will be closely monitored.

Where is the study run from?
Royal National Throat, Nose and Ear Hospital (UK)

When is the study starting and how long is it expected to run for?
January 2016 to May 2018

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Dr Helen Blackshaw (scientific)
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number
NCT02973152

Secondary identifying numbers
19805

Study information

Scientific Title
Does Laryngeal Reinnervation or Type I Thyroplasty give better voice results for patients with Unilateral Vocal Fold Paralysis (VOCALIST): a feasibility study

Acronym
VOCALIST

Study objectives
The aim of this study is to determine the feasibility of recruiting eligible patients for a randomised single blinded laryngeal reinnervation versus type I thyroplasty surgery in patients with unilateral vocal fold paralysis (UVFP).

Ethics approval required
Old ethics approval format

Ethics approval(s)
London - Bromley Research Ethics Committee, 21/01/2016, ref: 11/LO/0583

Study design
Randomised parallel feasibility study

Primary study design
Interventional

Secondary study design
Randomised parallel trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied

Topic: Ear, Nose and Throat; Subtopic: Ear, Nose and Throat; Disease: Ear, Nose and Throat

Interventions

Interventions as of 08/09/2016:
Participants are randomly allocated to one of two groups.

Group 1: Participants receive laryngeal reinnervation treatment with temporary medialisation (via an injection of hyaluronic acid) of the paralysed vocal fold. Patients will be in supine position, intubated with microlaryngoscopy tube, or placed on suspension laryngoscopy with jet ventilation. Direct laryngoscopy will be performed so vocal folds are visualised. Before the injection, right and left cricoarytenoid joints will be palpated to rule out cricoarytenoid joint fixation. The reinnervation then takes places using the ansa cervicalis and recurrent laryngeal nerve.

Group 2: Participants receive type I thyroplasty surgery. This medialisation/augmentation technique is a static technique, performed under local anaesthesia with sedation that aims to improve the positioning of the paralysed vocal fold. It uses a silastic implant readily available in different sizes according to size of larynx and gender of the patient. The correct size can be determined intraoperatively by using a measuring device while listening and visualising the larynx with flexible fiberoptic scope simultaneously.
All participants have a small size 8 redivac drain inserted into the wound at the end of the surgery.

Follow-up involves pre- and post-operative recording of voice, vocal fold visualisation, electromyography and MRI to measure the size of the vocal folds muscles. Participants attend further follow-up clinic visits at 6 and 12 months.

Original interventions:
Participants are randomly allocated to one of two groups.

Group 1: Participants receive laryngeal reinnervation treatment with temporary medialisation of the paralysed vocal fold. Patients will be in supine position, intubated with microlaryngoscopy tube, or placed on suspension laryngoscopy with jet ventilation. Direct laryngoscopy will be performed so vocal folds are visualised. Before the injection, right and left cricoarytenoid joints will be palpated to rule out cricoarytenoid joint fixation. The patient is kept overnight and discharged the following morning (assuming the drain contains less than 18ml overnight, and that there are no breathing difficulties or other complications). Including the peri-operative dose, three doses of antibiotics are given in all (Amoxicillin or Clarithromycin).

Group 2: Participants receive type I thyroplasty surgery. This medialisation/augmentation technique is a static technique, performed under general local anaesthesia that aims to improve the positioning of the paralysed vocal fold. It uses a silastic implant readily available in different sizes according to size of larynx and gender of the patient. The correct size can be determined intraoperatively by using a measuring device while listening and visualising the larynx with flexible fiberoptic scope simultaneously.

Follow-up involves pre- and post-operative recording of voice, vocal cord visualisation, electromyography and MRI to measure the size of the vocal cords muscles. Participants attend further follow-up clinic visits at 1, 3 and 6 months.

Intervention Type

Other

Phase
Phase II

Primary outcome measure
Recruitment rate.

Secondary outcome measures
Not provided at time of registration

Overall study start date
01/01/2016

Completion date
01/05/2018

Eligibility

Key inclusion criteria
1. UVFP due to unilateral recurrent laryngeal nerve paralysis of traumatic, iatrogenic or idiopathic origin of between 6 and 60 months duration. Or symptoms that have not sufficiently improved with speech therapy alone, as determined by the patient and agreed by a multidisciplinary clinical team, after 6 months and pending a surgical decision.
2. Age from 18 to 70 years old.
3. Male or female
4. Able to provide informed consent
5. A significant voice disorder as measured by perceptual rating (Grade ≥2 GRBAS Scale) and Voice Handicap Index (VHI-10 score >16)
6. Common laryngeal electromyography (EMG, neurophysiological) criteria (Koufman Grades 2-5) in either the thyroarytenoid (TA) or posterior cricoarytenoid (PCA) muscle on the paralysed side

Original inclusion criteria 1-2:
1. UVFP due to unilateral recurrent laryngeal nerve paralysis of traumatic, iatrogenic or idiopathic origin
of between 6 and 36 months duration; or symptoms that have not sufficiently improved with speech therapy alone, as determined by the patient and agreed by a multidisciplinary clinical team, after 6 months and pending a surgical decision
2. Aged between 18 and 60

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 30; UK Sample Size: 30

Key exclusion criteria
1. Impaired vocal fold mobility but a normal EMG (Koufman Grade I)
2. Severe lung disorders
3. Structural vocal fold lesions such as polyp
4. Previous laryngeal framework surgery
5. Cricoarytenoid joint fixation (CAJF)
6. Significant non-laryngeal speech abnormality (severe dysarthria determined by a panel of trained speech therapists)
7. Previous Level 2,3 or 4 thyroid neck dissection
8. Previous ipsilateral surgical neck dissection
9. Previous radiotherapy to the head and neck
10. Laryngeal injection of a rapidly absorbable material in the last 6 months
11. Previous laryngeal injection of a non-rapidly absorbable material (e.g bioplastics, VOX)
12. Neuromuscular disease affecting the larynx or multiple cranial nerve palsies

Date of first enrolment
01/06/2016

Date of final enrolment
31/10/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Royal National Throat, Nose and Ear Hospital (UCLH)
330 Gray's Inn Road
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Sponsor information

Organisation
University College London Hospitals NHS Foundation Trust

Sponsor details

Research & Development Directorate
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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/042fqyp44

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To ensure the results from this feasibility study can be taken forward into a plan for a future large scale RCT, there is a need to engage all those involved in voice health including ENT surgeons, speech therapists, voice and singing teachers, GPs and practice nurses. Therefore results will be disseminated through the publication of articles in peer reviewed medical journals targeted at health professionals involved in the care of patients with voice disorders and presented at national and international scientific meetings. Findings, and future trial plans, will be discussed with relevant professional organisations including the British Laryngological Association (BLA) and Royal Colleges to ensure they are disseminated to their members through

e-newsletters, websites and national meetings. Our PPI representatives will assist in disseminating results in a suitable lay language to relevant journals and patient information sections of health-related websites, ensuring that patients and the publics are both informed and engaged for the future RCT.

Intention to publish date
31/12/2021

Individual participant data (IPD) sharing plan
Participant level data is available on request from the VOCALIST Trial Manager Helen Knowles (helen.knowles@ucl.ac.uk).

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	29/09/2017	30/11/2020	Yes	No
Results article		05/05/2025	07/05/2025	Yes	No