Effectiveness of septoplasty compared to medical management in adults with obstruction associated with a deviated nasal septum: the NAIROS RCT

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Scientific summary

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Scientific summary

Background

The indications for septoplasty are practice-based, rather than evidence-based. In addition, internationally accepted guidelines for the management of nasal obstruction associated with nasal septal deviation are lacking.

Objectives

The study objectives are split into three different aspects: clinical effectiveness, economic evaluation and mixed-methods process evaluation.

Objective 1 was to measure clinical effectiveness according to:

- subjective self-reported rating of nasal airway obstruction
- heterogeneity of estimated treatment effect, specifically according to severity of obstruction and gender
- objective measures of nasal patency
- number of adverse events (AEs) and additional interventions required
- technical failure in the surgical arm
- how well those agreeing to enter the trial reflect those screened for eligibility.

Objective 2 was to conduct an economic evaluation from the perspective of the NHS and Personal Social Services. This entailed the following processes:

- conducting a cost-effectiveness analysis, with outcomes reported as incremental cost per ≥ 9-point improvement in the Sino-nasal Outcome Test-22 items (SNOT-22) scores and number of AEs
- conducting a cost–utility analysis, with outcomes reported as incremental cost per quality-adjusted life-year (QALY) gained
- designing a longer-term economic model to assess costs and health consequences beyond the 12-month follow-up period.

Objective 3 was to conduct a mixed-methods process evaluation of the trial and interventions, to understand:

- barriers to optimal recruitment, and potential solutions to address these, through integration of the Qualitative research integrated within Trials (QuinteT) Recruitment Intervention (QRI)
- participants' and healthcare professionals' experiences of trial participation and the interventions, and perceived factors likely to influence wider implementation of trial findings.

Methods

The Nasal AIRway Obstruction Study (NAIROS) was a multicentre, non-blinded randomised controlled trial comparing the effectiveness of septoplasty, with or without turbinate surgery, with a standardised medical management package of 6 months of intranasal steroid spray and saline spray. Participants were randomised on a 1 : 1 basis between the septoplasty (within 8 weeks) and medical management arms. The trial included an integrated health economic evaluation and a mixed-methods process evaluation incorporating a QRI.

The target sample size of 378 participants allowed for 20% dropout to deliver 90% power for detecting a minimal clinically important difference of 9 points in SNOT-22 scores. This assumed a two-sided type error rate of 5% and a standard deviation of 24 points in SNOT-22 scores at 6 months.

Interventions

The two interventions being compared were as follows.

1. Septoplasty, with or without inferior turbinate reduction in the contralateral nostril, performed at the discretion of the investigating clinician, preferably performed within 8 weeks of randomisation or, if not, by 12 weeks.
2. Medical management with 6 months of mometasone furoate 50 µg per dose nasal steroid spray, suspension (Nasonex®; Merck Sharp & Dohme Limited, Hoddesdon, UK), and isotonic nasal saline spray. Participants had the option of deferred surgery after 6 or 12 months post randomisation.

Setting and participants

We recruited 378 patients to the main trial from 17 NHS hospitals in Great Britain. Eligible patients were identified from general ear, nose and throat referrals. Of those recruited, 188 were randomised to septoplasty and 190 were randomised to medical management.

Inclusion criteria

- Adults aged ≥ 18 years.
- Baseline Nasal Obstruction Symptom Evaluation (NOSE) scale score of ≥ 30.
- Septal deflection visible via nasoendoscopy.
- Capacity to provide informed consent/complete trial questionnaires.

Exclusion criteria

- Prior septal surgery.
- Systemic inflammatory disease/use of oral steroid treatment in the previous 2 weeks.
- Granulomatosis with polyangiitis.
- Nasoendoscopic evidence of unrelated associated pathology.
- Intranasal recreational drug use in the previous 6 months.
- Breastfeeding, pregnancy or intended pregnancy for duration of involvement in the trial.
- Bleeding diathesis.
- Therapeutic anticoagulation.
- Contraindication to general anaesthesia.
- Immunocompromised.
- External bony deformity.

Measurement of clinical outcomes

Primary outcome

The primary outcome was patient-reported assessment of nasal and general symptoms, using the SNOT-22 questionnaire, at 6 months (−2 weeks/+4 weeks). The SNOT-22 was also assessed at baseline and 12 months (± 2 weeks).

Secondary outcomes

- Objective measures: peak nasal inspiratory flow and rhinospirometry (maximal inhalation volume and tidal breathing) at baseline and at 6 and 12 months.
- Patient-reported outcomes: SNOT-22 subscales at 12 months, NOSE score and Double Ordinal Airway Subjective Scale at baseline and at 6 and 12 months.

- Safety measures: number and characteristics of any AEs, surgical complications and reinterventions within 12 months.
- Quality of life, measured using the Short Form questionnaire-36 items (SF-36) at baseline and at 6 and 12 months.
- Healthcare utilisation questionnaire at baseline and at 6 and 12 months.
- Time and travel questionnaire at 12 months.

Measurement of health economic outcomes

- To compare costs incurred by the NHS and Personal Social Services (PSS) with those incurred by participants in the management of a deviated septum.
- To compare QALYs, based on responses to the SF-36 administered at baseline and at 6 and 12 months, converted to Short Form questionnaire-6 Dimensions (SF-6D) utility scores, derived using the area under the curve method.
- To compare the cost-effectiveness of septoplasty with that of medical management at 12 months, measured in terms of the incremental:
    - cost per improvement (of ≥ 9 points) in SNOT-22 scores
    - cost per AE avoided
    - cost per QALY gained.
- To compare the cost-effectiveness of septoplasty with that of medical management at 24 and 36 months in terms of the incremental cost per QALY gained (costs and QALYs were extrapolated using an economic model).

Mixed-methods process evaluation outcomes

The objectives for the mixed-methods process evaluation were addressed through observations of training and NAIROS meetings, interviews with health professionals and participants, audio-recording of recruitment discussions and review of screening logs.

The QRI initiated with a 'pre-recruitment' phase to raise awareness about common recruitment issues/solutions learnt from previous trials. Phase 1 of the QRI investigated sources of recruitment difficulty that were specific to the NAIROS, informing 'actions' to optimise recruitment as the trial was under way (phase 2).

Statistical analysis

The primary statistical analysis was carried out on an intention-to-treat (ITT) basis, retaining patients in their randomised treatment groups. Multivariable linear regression models were used to compare the 6-month SNOT-22 scores between the treatment groups, adjusting any treatment effect by baseline SNOT-22 score and stratification factors at randomisation [(1) gender and (2) severity at baseline (according to three NOSE categories reported in the literature: 30–50, moderate; 55–75, severe; and 80–100, extreme)].

Sensitivity analyses, including a per-treatment and a per-protocol analysis, were also undertaken. Secondary outcomes were analysed in a way that was similar to the primary outcome analysis.

Economic analysis

The cost-effectiveness of septoplasty, compared with medical management, was evaluated by estimating the total costs incurred by the NHS and PSS to manage a deviated septum and averaging these costs across participants in each study arm. Both within-trial and model-based analyses were undertaken. The within-trial analysis estimated costs and effects over 12 months. Three different measures of effects were used: improvement (of ≥ 9 points) in SNOT-22 scores, number of AEs and QALYs.

QALYs were derived from responses to the SF-36, which we converted into SF-6D scores (utilities) using a standardised algorithm and the area under the curve approach. An economic model was designed to extrapolate costs and benefits beyond the 12-month study follow-up period.

Mixed-methods process evaluation analysis

QuinteT Recruitment Intervention: thematic and content analyses were undertaken of interviews and audio-recorded consultations, and descriptive analyses of screening log data were undertaken.

Qualitative process evaluation: a thematic analysis was undertaken using a coding framework, informed by normalisation process theory.

Results

Primary outcomes

The ITT analysis found that, at 6 months, participants randomised to the septoplasty arm (n = 152) had SNOT-22 scores that were, on average, 20.0 points lower (i.e. better) than those of participants randomised to medical management (n = 155) [95% confidence interval (CI) −23.6 to −16.4 points; $p < 0.0001$]. This strong signal was confirmed by both sensitivity analyses and analysis of secondary outcomes. The mean SNOT-22 scores at 6 months were 19.9 points for the septoplasty arm and 39.5 points for the medical management arm. At 12 months, the adjusted mean difference for SNOT-22 scores between the two arms had reduced to −10.1 points (95% CI −14.5 to −5.6 points; $p < 0.0001$). This diminished effect at 12 months was predominantly due to SNOT-22 scores tending to reduce over time among those randomised to medical management. Overall, the improvement in SNOT-22 score in the surgical arm was both notably faster and greater, and was sustained over the trial period. Increased baseline severity of nasal obstruction was associated with greater improvements in the primary outcome. Gender had no impact on outcome improvement. Approximately 45 out of 190 (24%) participants discontinued allocated medical management treatment and had non-trial surgery, and 22 out of 188 (12%) of those randomised to septoplasty did not receive the surgical intervention. The per-protocol (treatment effect −19.7, 95% CI −23.4 to −16.0) and per-treatment analyses (treatment effect −19.3, 95% CI −23.3 to −15.3) confirmed a statistically significant greater improvement in the surgical arm.

Secondary outcomes

All secondary outcome measures, both patient-reported and objective measures, showed a greater improvement in the surgical arm. Turbinate reduction did not appear to add additional benefit in comparison with septoplasty alone. At 6 months, 80% of patients reported improvement in nasal breathing (74% at 12 months). Six out of 166 patients undergoing septoplasty were recommended to consider revision septoplasty.

Adverse events

Overall, there were 227 AEs: 132 in the surgical arm and 95 in the medical management arm. Fourteen serious adverse events occurred in the surgical arm and nine in the medical arm. At 6 months, 7 out of 174 (4%) participants experienced hospital re-admission with nasal bleeding, none of whom required operative reintervention. Twenty out of 172 (12%) participants reported infection requiring antibiotic treatment, 19 out of 171 (11%) participants reported decreased sense of smell, 18 out of 171 (11%) participants reported numbness of the upper teeth and 17 out of 171 (10%) participants reported change in appearance of the nose. Six nasal septal perforations (3%) and seven intranasal adhesions (4%) were noted at 6 and 12 months' follow-up.

Economic evaluation

On average, septoplasty was more costly and more effective in terms of improvements in SNOT-22 score and QALYs than medical management. The incremental cost per improvement (of ≥ 9 points) in SNOT-22 score was £4855. The incremental cost per QALY gained was £27,114 and septoplasty had a

15% probability of being considered cost-effective at a £20,000 willingness-to-pay threshold for an additional QALY. This probability increased to 68% at a £30,000 threshold. Septoplasty was dominated by medical management when AEs were the outcome of interest, as it was more costly and associated with a greater number of AEs. The economic model estimated the incremental cost per QALY gained at 24 months (£13,221) and 36 months (£7368). Septoplasty had a 99% (at 24 months) and a 100% (at 36 months) probability of being considered cost-effective, compared with medical management, at a £20,000 threshold for an additional QALY.

Mixed-methods process evaluation

QuinteT Recruitment Intervention findings

Data sources included 19 interviews with recruiters, 108 audio-recorded discussions and regular scrutiny of screening logs. Despite recruiters' commitment to the NAIROS, there were challenges operationalising recruitment processes into routine clinical care, which restricted identification of potentially eligible patients. Analysis of recorded consultations revealed evidence of recruiters operationalising the pre-recruitment training, but also illuminated unanticipated challenges around explaining the trial arms, which undermined equipoise. Tailored actions were implemented in phase 2 to address these issues, through feedback/training for individuals/groups, 'recruitment workshops' with sites, and written guidance and webinars for professionals who interacted with patients throughout the clinical pathway. The recruitment target was reached successfully without a funding extension and without the need to open additional sites.

Qualitative process evaluation

Nine surgeons and five research nurses working on the NAIROS trial were interviewed and 39 interviews were conducted with 31 participants. Prior to the NAIROS, decisions regarding the appropriateness of surgery for individual patients were made on the basis of a complex and largely subjective combination of symptoms, history and patient anatomy. Surgeons indicated that they would welcome clearer criteria to guide decision-making. However, although some surgeons embraced a role for standardised outcome measures such as the NOSE and the SNOT-22 in decision-making, others were more reluctant; this could be a barrier to the implementation of trial findings.

Although trial findings show that, as a group, participants in the surgical arm experienced more improvement than those in the medical management arm, the qualitative study demonstrated that individual experiences were varied. Although some patients in the medical management arm achieved little or no benefit from treatment, others did report positive effects, with a possible mechanism of action being a reduction in turbinate size. Patients undergoing medical management might benefit from individual advice regarding application of the sprays, taking into account distorted anatomy, to maximise effectiveness and reduce side effects. Although most participants were able to incorporate spray use into their daily routines, long-term spray use was perceived by some to be burdensome.

Despite the large number of participants who perceived septoplasty to be effective in reducing their symptoms, there were still some participants who felt that they received little to no benefit from the operation. Participants reported being underprepared for the immediate post-surgery period.

Limitations

COVID-19 had a major impact on the study, resulting in the cessation of clinical measurements and objective outcomes from March 2020. From that time, all patient-reported outcomes were collected by post or online, or transcribed over the telephone. The ITT analysis is likely to offer an overestimate of the true impact of medical management in improving outcomes as 22% of participants in that arm received septoplasty before the 12-month outcome point.

Conclusions

Septoplasty, with or without turbinate reduction, is a clinically effective intervention. Participants with a deviated nasal septum with a moderate, severe or extreme baseline severity of nasal obstruction symptoms had an improvement in patient-reported outcomes at 6 and 12 months. This improvement surpassed that of standardised medical management. The results suggest that surgery has a low probability of being cost-effective at 12 months but may be considered cost-effective at 24 months.

Impact on health services

The NAIROS clearly demonstrates that adults presenting with nasal obstruction associated with a deviated nasal septum, in the absence of clinical evidence of a coexistent nasal/sinus disease and with a baseline NOSE score of > 30, can reliably be offered surgery in the knowledge that improvements in patient-reported outcomes are superior to improvements when treated with a nasal steroid/saline spray combination.

Recommendations for research

- The most important research priority to emerge from the NAIROS is the need to develop a patient decision aid to explore management of a deviated nasal septum.
- The place of medical treatment in the management of nasal obstruction associated with a deviated nasal septum needs to be explored further.
- A prospective randomised trial would be required to examine the place of turbinate reduction surgery in nasal obstruction.

Study registration

This trial is registered as ISRCTN16168569 and EudraCT 2017-000893-12.

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