Does time from previous surgery predict subsequent treatment failure in Chronic Rhinosinusitis with Nasal Polyps?*

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Abstract

Introduction: When considering the introduction of biological treatments for Chronic Rhinosinusitis with nasal polyps (CRSwNP), treatment guidelines must consider not only which patients will best respond to biologicals, but also which patients derive least benefit from current treatment pathways. Using data collected as part of the National Audit of Surgery for Chronic Rhinosinusitis and Nasal Polyps, we sought to evaluate if patients with a history of prior surgery are more likely to need a further revision operation, and whether the interval between surgery may help predict the need for further surgical intervention.

Methods: In the original study, patients were prospectively and consecutively enrolled at the time of sinus surgery in multiple centres in England and Wales. Follow-up captured symptomatic outcomes and revision surgery rates at 3, 12, 36 and 60 months after surgery. Revision surgery rates 5 years after the index procedure, in patients with CRSwNP were analysed with regards to baseline demographics.

Results: Complete data were available for 980 subjects, with a 5 year revision rate of 15.1%. 45.9% had a history of previous surgery before the index procedure, and this group had significantly higher rates of additional surgery compared with those undergoing their first sinus surgery (20.2% versus 9.8%). Patients with an interval of 3 years or less between their previous surgery and the index procedure had the highest rates of further surgery. In a multiple regression, time interval between previous operations was a better prediction of subsequent revision surgery than asthma. Having N-ERD was the strongest predicator of need for further surgery while more extensive surgery was associated with lower revision rates.

Conclusions: Patients presenting with a symptomatic recurrence within 3 years of surgery have a high risk of treatment failure, defined as the need for further surgery. Time to failure after previous surgery may be used to help select patients who may not benefit from current treatment pathways and may be good candidates for alternative strategies, including biologicals

Key words: paranasal sinus disease, nasal polyps, therapeutics, prevention and control

Introduction

Chronic rhinosinusitis with nasal polyps is a prevalent condition characterised by a significant impact on quality of life and productivity, and frequent recurrence after both medical and surgical treatment[(1)]. Oral corticosteroids, while effective at achieving short term symptom improvement[(2, 3)], are limited with regards to repeated use due to the risk of side effects[(4)]. Surgery has been shown to achieve more durable benefits in terms of symptomatic improvement[(5)], but is associated with discomfort or pain, time for recovery and a small but definite risk of serious complications[(6)]. More than one in 6 patients will require another surgery within 5 years of follow-up. Poor disease control is, therefore, commonplace.

Type 2 inflammation is common to the majority of patients with CRSwNP and asthma; biological therapy using monoclonal

antibodies (mab) that block the action of interleukins or other targets central to type 2 inflammation now play an important role in the management of difficult-to-treat asthma and many of these treatments have also been shown to be effective in the management of severe CRSwNP. Dupilumab, an anti IL4/13 receptor mab and omalizumab, an anti-IgE mab have been shown to achieve significant reductions in polyp size and nasal congestion in large phase 3 studies[7, 8]. Both have now been granted FDA and EMA approval for use. Other drugs will likely soon follow, specifically with phase 3 trials completed for mepolizumab[9] and benralizumab, which target IL5.

Although biologicals have been shown to reduce the need for surgical intervention for CRSwNP[9], the high cost associated with biologicals and the need for long term treatment mean that this is unlikely to be the most cost-effective treatment across the whole population with CRSwNP, even if superior in terms of long-term symptom control in the difficult-to-treat group. Scangas et al. undertook a Markov decision tree cost-effectiveness model over 20 years[10], and found, based in US costs which may not be applicable in all healthcare settings, that a strategy of sinus surgery costs circa $50,000 producing 9.80 QALYs while dupilumab treatment costs $535,000 but produced 8.95 QALYS. Surgery was more cost-effective regardless of the frequency of revision surgery. Similarly, in asthma, although the efficacy of biological therapy is well established, none of the currently available drugs have been found to be cost-effective[11].

It is, therefore, likely that in most healthcare settings, restrictions will be placed on access to biologicals for the treatment of CRSwNP. There have been a number of attempts to define the group of patients most likely to benefit from biological markers of type 2 inflammation [1, 12], however, as yet no biomarker has been shown to predict response rate to biologicals. Perhaps a more important strategy is to identify those that benefit the least from current therapeutic options. The EPOS group recommended that biologicals should be considered primarily in those patients that have a symptomatic recurrence of CRSwNP despite previous surgery. This, in part, acknowledges the potential for long term benefit after surgery in part related to better access to topical steroids after surgery [13].

The aim of this current study utilises data from the National Audit of Surgery for Chronic Rhinosinusitis and Nasal Polyps to evaluate if patients with a history of prior surgery are more likely to need a further revision operation, and whether the interval between surgery may help predict the need for further surgical intervention.

Materials and methods

The full methodology has been previously reported[14]. Baseline clinical data was collected prospectively on 3,128 patients undergoing surgery for CRS (with or without nasal polyps) in NHS Hospitals in England and Wales between April 2000 and May 2001. All patients aged over 16 years of age undergoing surgery for CRS, including nasal polyposis, were eligible for inclusion. The operating surgeon completed a standard form to collect data on patient characteristics, surgical technique, and perioperative complications.

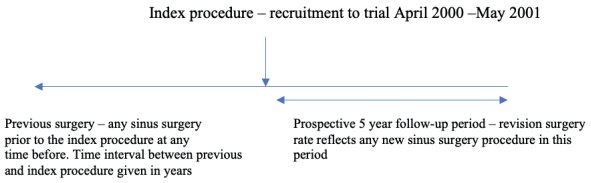

Figure 1. Overview of the timelines and description of surgical procedures captured within the study period.

Patients were asked to complete a preoperative questionnaire about their demographic status and disease history, ENT surgeons recorded data on asthma status and the presence of non-steroidal exacerbated respiratory disease (N-ERD). Patients were sent outcome questionnaires to complete at 3, 12, 36 and 60 months postoperatively and asked to complete the SNOT-22, and to report on their need for further medical and surgical treatment.

Only patients with CRSwNP who completed follow-up to 60 months were considered in this current study. All patients underwent an index sinus surgery procedure at the time of recruitment. They were asked to report on any history of prior sinus surgery and how long before the index operation this had occurred. For analysis, patients were grouped within yearly intervals, except those patients with an interval of 10 years or more who were consolidated in one group, as well as a group who had no history of prior surgery. At each follow-up, respondents were asked to report whether they had undergone any additional sinus surgery after the index procedure (Figure 1). Patients with a history of both surgery prior to, and a revision surgery within 5 years of the index procedure have, therefore, undergone three (or more) surgical procedures.

Revision surgery rates were analysed by time from previous surgery, and a Chi-squared test performed to detect any significant differences in revision surgery rates by time from last surgery. The time interval from previous surgery was categorised as 0 – 3 years, 4-6 years. 7-9 years, 10 years or more, or no previous surgery, and the revision rates reported at 12, 36 and 60 months. Finally, in order to assess whether time from previous surgery is a significant predictor of the need for further surgery within the 5 year follow-up period after the index event, logistic multiple linear regression was performed in order to control for other factors that were considered likely to predict revision surgery

Table 1. Revision surgery rates within 5 years of index procedure, stratified by time interval between index procedure and (most recent) previous surgery.

Time interval between previous surgery and index procedure (years)	Number recruited at baseline	Number completing follow-up at 5 years (%)	Revision surgery within 5 years of index procedure (%)
0	1	0	N/A
1	99	45 (45)	33.3
2	123	61 (50)	36.1
3	79	37 (47)	32.4
4	58	26 (45)	23.2
5	94	48 (51)	18.8
6	65	41 (63)	24.4
7	46	21 (46)	19.1
8	38	20 (53)	25
9	31	20 (65)	15
10 or more	302	117 (39)	9
No previous surgery	1103	484 (44)	9.5

(age, gender, co-morbid asthma, presence of N-ERD, smoking status, polyp extent, baseline SNOT-22 score, radiological extent of disease measured using the Lund-Mackay score and extent of surgery performed at the index procedure). Extent of surgery performed was reported by the operating surgeon, and stratified by each additional sinus group addressed in addition to a baseline polypectomy procedure. Draf 3 frontal sinus procedures, nasalisation or reboot procedures were not considered in this study.

Statistical analysis was performed using STATA (StataCorp, TX, USA). The study was granted ethical approval by the N Thames Research Ethics Committee

Results

2039 patients with CRSwNP underwent an index surgical procedure in the initial study cohort, of which 980 patients completed 5-year follow-up data (48%). The mean age was 51 years, with a range of 18 – 95 years. 68.8% of participants were male, and 38.2% had asthma. 17.6% were smokers. 5% of the cohort were reported to have N-ERD based on clinical history.

45.9% of participants at baseline had undergone at least one previous sinus surgery prior to the index event. The mean interval between prior surgery and the index event was 8.8 years, with a range of 0 – 60 years. Of the respondents at 5 year follow up, 51% had reported a prior history of surgery.

The 5-year revision rate was 15.1%. The rate was twice as high (20.2%) in patients who reported a history of previous surgery,

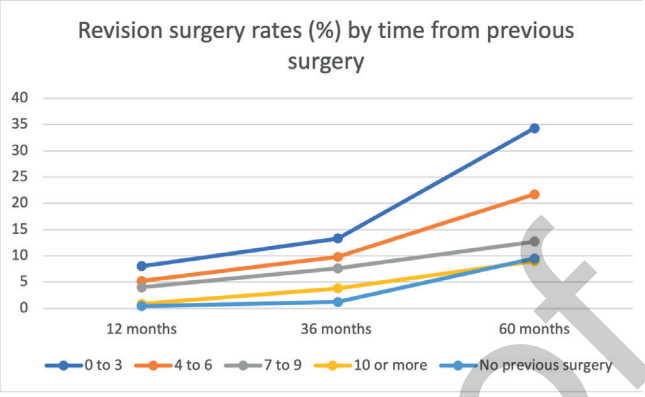

Figure 2. Revision surgery rates within 5 years of index procedure, stratified by time interval in years between index procedure and (most recent) previous surgery.

compared with those who had not undergone any previous surgery (9.8%). Of all respondents to the 5-year follow-up, 102 (10.4%) had a history or surgery prior to the index procedure and an additional sinus surgery within 5 years – that is more than 10% who had undergone at least 3 sinus surgeries for their nasal polyps.

There was a significant association between time from previous surgery and revision surgery rates at 5 years after the index procedure ($p<0.0001$). Patients with no history of prior surgery, and those with an interval of more than 10 years from previous surgery had the lowest 5-year revision rates, with approximately 1 in 10 patients undergoing further surgery after the index procedure (Table 1). 1 in 3 patients with a time interval of 3 years or less from their previous surgery to the index procedure and had undergone a further revision procedure within 5 years of the index operation (i.e. 3 surgeries in an 8 year period or less). The difference became significant as early as 12 months after the index procedure ($p<0.0001$), and at 36 months ($p<0.0001$) (Figure 2).

Of all patients who underwent a revision procedure within 5 years of the index operation, patients with a history of prior surgery with an interval of 3 years or less to the index procedure accounted for 33% of cases. If the prior surgery interval was extended up to 6 years before the index procedure, this included 50% of all those that underwent subsequent revision. 31% of revision surgery cases performed within 5 years of the index procedure captured in the audit had no history of surgery prior to the index procedure.

We looked at the rate of asthma in patients by time interval from pervious surgery. Although the rate of asthma was significantly higher in all CRSwNP patients who had a history of prior surgery compared to those who had not (46.9% versus 29.3%, $p<0.0001$), there was no significant difference in asthma rates in those that had a history of previous surgery with an interval of less than 10 years (Figure 3).

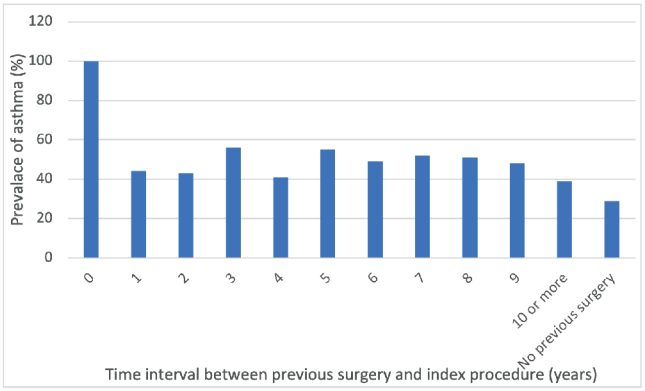

Figure 3. Asthma prevalence, stratified by time interval from (most recent) previous surgery.

With regards to the extent of surgery, this was stratified by the number of sinus groups that were operated on, taking a simple polypectomy as a baseline. The extent of surgery performed within the study was relatively conservative, with half the patients having a simple polypectomy only and the remainder undergoing additional sinus surgery (Table 2).

A significant regression equation was found (LR Chi2 =76.67, p<0.0001). When controlling simultaneously for baseline variables within a regression model, time from previous surgery is significantly and inversely associated with the need for revision surgery – that is the longer the interval between previous surgery and the index procedure, the lower the risk of needing a further revision operation. Asthma (without N-ERD) was not a significant predictor of revision surgery when other variables including N-ERD and time from previous surgery was included, whereas N-ERD itself was a very strong predictor of the need for further surgery. More extensive surgery performed at the time of the index procedure was significantly associated with a reduced risk of subsequent surgery. Increasing age at time of index procedure was inversely associated with risk of revision, although the effect was small. Neither baseline SNOT-22 score, polyp grade nor Lund-Mackay scores were predictive of need for further surgery (Table 3).

The SNOT-22 score at 5-year follow-up in patients who did not require revision surgery at 5 years was significantly lower (24.1, 95%CI 22.7 – 25.5) than the patients who had undergone a revision procedure in the 5 years post-index operation (38.2, 95%CI 36.7 – 39.7).

Patients with N-ERD had both very high rates of previous surgery (84.5% versus 49.9% in those without N-ERD), but also very high revision surgery rates within 5 years (50.9% versus 12.9% in those without N-ERD). This group also had significantly higher SNOT-22 scores at 5 years (40.7, 95% CI 31.2 – 47.3) compared to those without (25.3, 95%CI 23.9 – 26.7).

Table 2. Distribution of surgical procedures, stratified by most distal extent, in patients completing 5-year follow-up.

Most distal extent of surgery	% of patients
Simple polypectomy	49.5
Uncinectomy and antrostomy	9.2
Anterior ethmoidectomy	15.2
Posterior ethmoidectomy	15.2
Frontal sinus surgery	3.7
Sphenoid surgery	4.3
All sinuses	3.0

Table 3. Multivariable logistic regression to identify baseline variables associated with risk of revision surgery within 5 years after index procedure. For time from previous surgery, those with an interval of 10 years or more were assigned a value of 10 years, those with no previous surgery were assigned a value of 11 years. Extent of surgery relates to index procedure, and was categorised with simple polypectomy as the baseline and then increasing extent of surgery to all sinuses opened.

Variable	Odds ratio	p-value
Age	0.95	<0.0001
Male sex	0.75	0.359
Presence of asthma	1.59	0.132
Presence of N-ERD	5.24	<0.0001
Smoker	1.1	0.212
Baseline SNOT-22	1.001	0.559
Baseline polyp grade	0.93	0.710
Baseline Lund-Mackay Score	1.02	0.397
Extent of surgery	0.79	<0.0001
Time from previous surgery	0.89	0.005

Discussion

Our data suggest that approximately 1 in 10 patients with CRSwNP who have primary surgery will develop a symptomatic recurrence such that further surgery is required within a 5-year period. In those with a history of prior surgery, the revision rate is twice as high compared to those undergoing primary surgery. All patients who undergo a second operation within a period of 10 years or less have a significantly higher risk of revision, compared to those presenting for revision more than 10 years after their last operation. Furthermore, we have shown that for those patients who have a symptomatic recurrence sufficient to justify a second surgery within 3 years of the previous procedure have a 1 in 3 risk of requiring a further revision procedure within a short time interval.

As sinus surgery is a relatively inexpensive procedure in many countries that has durable benefits, it is recommended for patients that derive insufficient benefit from appropriate medical therapy (typically intransal and systemic corticosteroids). Sinus surgery helps to reduce the inflammatory load and by creating a surgical cavity, the access and efficacy of topical corticosteroids is improved in the post-operative period so that their effectiveness is increased [15]. The optimal extent of surgery in patients with CRSwNP remains controversial, but there is some evidence that more extensive surgery may be associated with lower revision surgery rates [16]. Our data support this, with significantly lower revision rates in patients undergoing more extensive surgery at the index procedure. Especially in patients presenting for revision surgery, consideration should, therefore, be given to all measures that minimise the risk of need for further surgery. These include considering the extent of surgery undertaken and optimising post-operative medical treatments, for example by enhancing the delivery of topical steroids such as through the use of steroid irrigations or steroid-eluting stents.

Patients are generally keen to avoid surgery – not only due to concerns about the risk of complications and the perioperative recovery, but also due to concerns regarding the need for revision. A qualitative study looking at views of patients with CRSwNP and non-steroidal exacerbated respiratory disease (N-ERD) highlighted patient frustrations; "surgery, surgery, surgery! I'm tired of this", and "I feel reluctant to be on an endless surgery merry go round if it's such a temporary fix' were amongst the views captured [17]. This analysis has shown that more than 10% of our cohort had undergone at least 3 sinus operations for their CRSwNP, and that patients who underwent a second surgery within 3 years of their last were at high risk of requiring further surgical intervention. This does indeed seem like a surgical merry-go round and a high burden of intervention for such patients. Therefore, patients who present with a significant symptomatic recurrence within 3 years of surgery would seem to be ideal candidates for an alternative strategy. Our data also supports the greater unmet needs of patients with N-ERD as they have much higher rates of repeated surgical intervention; more than 50% patients with N-ERD required revision surgery within 5 years of the index case, and all of these had undergone at least one prior sinus procedures.

Finally, our data suggest that those patients who required revision surgery within the 5-year follow-up had significantly poorer disease-specific quality of life than those that did not require revision – that is, even with revision surgery, this group failed to achieve the same benefit as those that did not require revision. This suggests that these patients likely have prolonged periods of poor disease control both before and after revision surgery and are not adequately treated by the current standard of care.

There is no doubt that for many patients with severe CRSwNP, the use of biological therapies may achieve significant improvements in health related quality of life (HRQOL) [18], and reduce the need for both oral steroids and sinus surgery and their attendant risks. Current evidence supports the efficacy of biological therapies in patients with severe CRSwNP regardless of prior surgical status or co-morbidity [19], and there is no indication to restrict access if the healthcare economy can support widespread use. However, in the current healthcare climate and considering the global economy, the costs of such treatment will undoubtedly mean that their use must be targeted both to those patients most likely to respond, but also to those who will likely derive least benefit from alternative options. When considering where to position biologicals in treatment pathways, our data supports the EPOS recommendation to consider biologicals in patients who have 'failed' primary surgery, as this already identifies patients at higher risk of requiring intervention, and for whom costs of care will be higher. Furthermore, a significant symptomatic recurrence within 3 years of sinus surgery for CRSwNP could be used to help identify those at highest risk of requiring multiple further surgical procedures, and therefore, in whom biologicals will be more cost-effective. Patients with co-morbid N-ERD are least likely to benefit from current standard of care and often require repeated surgery and, therefore, may be considered to be good candidates in whom to target alternative therapies.

This data does not help to identify those patients who will derive the greatest benefit form biological therapies, but may help to identify those most likely to 'fail' current treatment pathways.

Further limitations of this study are that we do not know if patients who we have identified as being at highest risk of repeated surgery (i.e. those that represent within 3 years of surgery) would avoid the need for further intervention if offered a biological. Currently available data suggests that there is no difference in effectiveness of biologicals on the basis of previous surgery, or number of prior surgeries [19]. Although we know the extent of surgery performed as the index procedure, and we have shown that in patients with nasal polyps, those undergoing more extensive surgery have a lower risk of subsequent revision during the 5 year follow-period, we do not know the extent of any surgery undertaken prior to the index event. With respect to the extent of surgery undertaken as the index procedure, surgeons reported the most distal extent of surgery performed in the study participants, but we were unable to verify the accuracy. Future studies would benefit from using a validated method of assessing the completeness of surgery, such as the recently published ACCESS rating [20]. The numbers of patients undergoing what may be described as 'full-house' ESS was small and therefore firm conclusions cannot be made

regarding the impact of extent of surgery, and further research is required in this area. We also do not know if patients had optimal medical care in addition to their sinus surgery and whether revision surgery could have been otherwise avoided as we do not have robust information on the use of post-operative topical or oral corticosteroids. We are unable to address whether more complete surgery along with more modern techniques to deliver post-operative steroids, such as using steroid irrigations or steroid eluting stents, would reduce the revision rates reported. We do not have data regarding any biomarkers, such as serum or tissue eosinophil levels, and therefore, cannot evaluate if they may act as better predictors of needing revision surgery. Also, we are unable to stratify patients according to the severity of their asthma. Finally, half the original study cohort were unavailable for 5 year follow-up, however, previous analysis has found no responder bias, with no differences at baseline or at other follow-up points [5].

Our data suggest that patients who present with symptoms sufficient to undergo a second surgery within 3 years are at high risk of subsequent revision. It is beyond the remit of this study to consider how a symptomatic recurrence may be adequately defined; Rudmik et al have defined minimum standards for the consideration of sinus surgery [21], suggesting a minimum threshold SNOT-22 score of 20. However, it should be noted that this does not mean that all patients with a score of more than 20 should be considered for surgery or a biological, and further work will be required to refine criteria for treatment.

Conclusion

This study helps to identify those patients with CRSwNP who are less likely to benefit from current standard of care, based on data derived before the advent of biologicals. Patients with N-ERD are at high risk of needing further surgery; patients who represent within 3 years of a previous sinus surgery and those who undergo less extensive surgery are also at a higher risk of revision. This evidence therefore helps to identify patients where surgical techniques and post-operative medical treatments should be optimised. In addition, until we have better evidence to identify those patients who will best respond to a biological, this study may help inform patient selection by identifying those who appear to benefit less from standard treatment pathways.

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Authorship contribution

Both authors were involved in the design, delivery and analysis of both the original study and the current work presented, and have written and edited this manuscript.

Conflict of interest

The authors declare no conflict of interest.

References

1. Fokkens WJ, Lund VJ, Hopkins C, Hellings PW, Kern R, Reitsma S, et al. European Position Paper on Rhinosinusitis and Nasal Polyps 2020. Rhinology. 2020;58(Suppl S29):1-464.
2. Head K, Chong LY, Hopkins C, Philpott C, Schilder AG, Burton MJ. Short-course oral steroids as an adjunct therapy for chronic rhinosinusitis. Cochrane Database Syst Rev. 2016;4:CD011992.
3. Head K, Chong LY, Hopkins C, Philpott C, Burton MJ, Schilder AG. Short-course oral steroids alone for chronic rhinosinusitis. Cochrane Database Syst Rev. 2016;4:CD011991.
4. Price D, Castro M, Bourdin A, Fucile S, Altman P. Short-course systemic corticosteroids in asthma: striking the balance between efficacy and safety. Eur Resp Rev. 2020;29(155).
5. Hopkins C, Slack R, Lund V, Brown P, Copley L, Browne J. Long-term outcomes from the English national comparative audit of surgery for nasal polyposis and chronic rhinosinusitis. Laryngoscope. 2009;119(12):2459-65.
6. Hopkins C, Browne JP, Slack R, Lund VJ, Topham J, Reeves BC, et al. Complications of surgery for nasal polyposis and chronic rhinosinusitis: the results of a national audit in England and Wales. Laryngoscope. 2006;116(8):1494-9.
7. Bachert C, Han JK, Desrosiers M, Hellings PW, Amin N, Lee SE, et al. Efficacy and safety of dupilumab in patients with severe chronic rhinosinusitis with nasal polyps (LIBERTY NP SINUS-24 and LIBERTY NP SINUS-52): results from two multicentre, randomised, double-blind, placebo-controlled, parallel-group phase 3 trials. Lancet. 2019;394(10209):1638-50.
8. Gevaert P, Omachi TA, Corren J, Mullol J, Han J, Lee SE, et al. Efficacy and safety of omalizumab in nasal polyposis: 2 randomized phase 3 trials. J Allergy Clin Immunol. 2020;146(3):595-605.
9. Bachert C, Sousa AR, Lund VJ, Scadding GK, Gevaert P, Nasser S, et al. Reduced need for surgery in severe nasal polyposis with mepolizumab: Randomized trial. J Allergy Clin Immunol. 2017;140(4):1024-31 e14.
10. Scangas GA, Wu AW, Ting JY, Metson R, Walgama E, Shrime MG, et al. Cost Utility Analysis of Dupilumab Versus Endoscopic Sinus Surgery for Chronic Rhinosinusitis With Nasal Polyps. Laryngoscope. 2021;131(1):E26-E33.
11. Tice JA WJ, Synnott P, Kumar V, Adair E, Rind D, et al. Biologic Therapies for Treatment of Asthma Associated with Type 2 Inflammation. Inst Clin Econ Rev. 2018;1–132.
12. Fokkens WJ, Lund V, Bachert C, Mullol J, Bjermer L, Bousquet J, et al. EUFOREA consensus on biologics for CRSwNP with or without asthma. Allergy. 2019;74(12):2312-9.
13. Kalish L, Snidvongs K, Sivasubramaniam R, Cope D, Harvey RJ. Topical steroids for nasal polyps. Cochrane Database Syst Rev. 2012;12:CD006549.
14. Hopkins C, Browne JP, Slack R, Lund V, Topham J, Reeves B, et al. The national comparative audit of surgery for nasal polyposis and chronic rhinosinusitis. Clin Otolaryngol. 2006;31(5):390-8.
15. Kalish L, Snidvongs K, Sivasubramaniam R, Cope D, Harvey RJ. Topical steroids for nasal polyps. The Cochrane database of systematic reviews. 2012;12:CD006549-CD.
16. Zhang L, Zhang Y, Gao Y, Wang K, Lou H, Meng Y, et al. Long-term outcomes of different endoscopic sinus surgery in recurrent chronic rhinosinusitis with nasal polyps and

asthma. Rhinology. 2020;58(2):126-35.
17. Alanin MC, Laidlaw T, Society TS, Hopkins C. The Burden of Non-steroidal anti-inflammatory exacerbated respiratory disease from the patient's perspective - a qualitative analysis of posts from the Samter's Society. Rhinology. 2020;58(4):333-40.
18. Hellings PW, Verhoeven E, Fokkens WJ. State-of-the-art overview on biological treatment for CRSwNP. Rhinology. 2021;59(2):151-163.
19. Hopkins C WM, Desrosiers M, Bachert C et al. Efficacy of dupilumab in patients with a history of prior sinus surgery for chronic rhinosinusitis with nasal polyps. Int Forum Allergy Rhinol. 2021;In press.
20. Reitsma S, Adriaensen G, Cornet ME, van Haastert RM, Raftopulos MH, Fokkens WJ. The Amsterdam Classification of Completeness of Endoscopic Sinus Surgery (ACCESS): a new CT-based scoring system grading the extent of surgery. Rhinology. 2020;58(6):538-43.
21. Rudmik L, Soler ZM, Hopkins C, Schlosser RJ, Peters A, White AA, et al. Defining appropriateness criteria for endoscopic sinus surgery during management of uncomplicated adult chronic rhinosinusitis: a RAND/UCLA appropriateness study. Rhinology. 2016;54(2):117-28.

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