Remission: Mission Possible in Chronic Rhinosinusitis with Nasal Polyposis?

Yvonne Chan¹, Andrew V. Thamboo², Han Han. J³, and Martin Desrosiers⁴

May 8, 2023

Remission: Mission Possible in Chronic Rhinosinusitis with Nasal Polyposis?

To the Editor,

Remission is emerging as the penultimate goal in the management of several chronic diseases. Recent application of these concepts to the management of inflammatory airway disease has promoted the concept of clinical remission, using a "Treat to Target" approach. The concept of remission, now well-established in Rheumatology as well as Gastroenterology (GI), is emerging in Respiratory Medicine with recent publication of definitions of clinical remission for asthma (1). It is interesting to consider whether the disease remission concept might successfully be applied to Otolaryngology-Head and Neck Surgery (OHNS) in the management of chronic rhinosinusitis with nasal polyposis (CRSwNP).

In the treatment of asthma, 'remission' is defined as the elimination of exacerbations and stabilization of symptoms, with the possibility of normalizing inflammatory markers, which indirectly reflect lung function and inflammation. Guidelines for inflammatory digestive diseases are similar to those in asthma, in terms of their symptomatic endpoints and rigorous control of disease (2). However, for inflammatory bowel disorders unlike in asthma, an additional endoscopic criterion which documents epithelial and mucosal recovery from disease is also included. The nasal endoscope provides similar characterization for the control criteria in CRSwNP, incorporating symptom control signifying clinical remission with endoscopic remission demonstrating normal sinonasal mucosa, which can also incorporate inflammatory markers highlighting biochemical remission.

A consensus statement from tertiary Canadian rhinologists has previously combined symptomatic and endoscopic assessments to define success after endoscopic sinus surgery (ESS), with 'optimal' results reported as absence of symptoms and normal appearance of the sinus mucosa on sinonasal endoscopy (3). However, it was unclear how frequently this 'optimal' outcome could be achieved. An estimate of remission rates in CRS care is now afforded by two recent studies in CRSwNP which employed a clinical endpoint very similar to the remission definition used in GI for inflammatory bowel diseases. The first study, a prospective trial which assessed outcomes after treatment of CRSwNP with endoscopic sinus surgery (4), and the second, a double-blinded, placebo-controlled prospective trial evaluating refractory CRSwNP managed with long-term, low dose azithromycin (5).

After ESS, clinical endpoints resembling remission were attained in 50% of all subjects, but with different rates of remission for different populations distinguished by co-morbidities. At four months after surgery, 72% individuals undergoing primary ESS for CRSwNP attained remission, while those with a history of previous surgery showed lesser response, with a 42% remission rate. Asthmatic subjects did considerably

¹University of Toronto Department of Otolaryngology-Head & Neck Surgery

²The University of British Columbia Department of Surgery

³Eastern Virginia Medical School

⁴Centre Hospitalier de l'Universite de Montreal

worse than non-asthmatic subjects: non-asthmatics attained remission in 60%, while patients with asthma or with aspirin exacerbated respiratory disease (AERD) only showed remission in 23% and 23.5% of cases, respectively. For the azithromycin trial, there was a 54% remission rate overall. Again, asthma was associated with a worse outcome: non-asthmatics had a remission rate of 88%, while asthmatics achieved only 38% remission, and only in 14% of AERD patients. Individuals demonstrating remission were characterized by parameters of epithelial recovery and healing, approaching those of optimal control as suggested for inflammatory digestive diseases (6).

Conclusion: Remission is indeed a concept that can be attained in CRSwNP, even in patients who failed previous surgery, as demonstrated by these findings. Some patient groups apparently have more difficult disease evolution, and asthma emerges as an important treatable trait in patients with CRSwNP. Better defining this outcome through consensus-based definitions will allow for the identification and stratification of clinical scenarios where patients have complete relief from their disease symptomatically in addition to biochemical and endoscopic normalization which penultimately achieving remission.

Respectfully submitted,

Yvonne Chan, Andrew Thamboo, Joseph Han, Martin Desrosiers

References

- Busse WW, Melén E, Menzies-Gow AN. Holy Grail: the journey towards disease modification in asthma. Eur Respir Rev. 2022 Feb 22;31(163):210183. Doi: 10.1183/16000617.0183-2021. PMID: 35197266; PMCID: PMC9488532
- 2. Turner D, Ricciuto A, Lewis A, D'Amico F, Dhaliwal J, Griffiths AM, Bettenworth D, Sandborn WJ, Sands BE, Reinisch W, Schölmerich J, Bemelman W, Danese S, Mary JY, Rubin D, Colombel JF, Peyrin-Biroulet L, Dotan I, Abreu MT, Dignass A; International Organization for the Study of IBD. STRIDE-II: An Update on the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) Initiative of the International Organization for the Study of IBD (IOIBD): Determining Therapeutic Goals for Treat-to-Target strategies in IBD. Gastroenterology. 2021 Apr;160(5):1570-1583. doi: 10.1053/j.gastro.2020.12.031. Epub 2021 Feb 19. PMID: 33359090.
- 3. Saydy N, Moubayed SP, Bussières M, Janjua A, Kilty S, Lavigne F, Monteiro E, Nayan S, Piché M, Smith K, Sommer D, Sowerby L, Tewfik MA, Witterick IJ, Wright E, Desrosiers M. What is the optimal outcome after endoscopic sinus surgery in the treatment of chronic rhinosinusitis? A consultation of Canadian experts. J Otolaryngol Head Neck Surg. 2021 Jun 16;50(1):36. doi: 10.1186/s40463-021-00519-9. PMID: 34134762; PMCID: PMC8210358.)
- 4. Maniakas A, Asmar MH, Renteria Flores AE, Nayan S, Alromaih S, Mfuna Endam L, Desrosiers MY. *Staphylococcus aureus* on Sinus Culture Is Associated With Recurrence of Chronic Rhinosinusitis After Endoscopic Sinus Surgery. Front Cell Infect Microbiol. 2018 May 15;8:150.
- Maniakas A, Asmar MH, Renteria AE, Nayan S, Alromaih S, Endam LM, Sampalis JS, Desrosiers M. Azithromycin in high-risk, refractory chronic rhinosinusitus after endoscopic sinus surgery and corticosteroid irrigations: a double-blind, randomized, placebo-controlled trial. Int Forum Allergy Rhinol. 2021 Apr;11(4):747-754. doi: 10.1002/alr.22691. Epub 2020 Sep 15. PMID: 32929891
- 6. Renteria AE, Maniakas A, Pelletier A, Filali-Mouhim A, Brochiero E, Valera CP, Adam D, Mfuna Endam L, Desrosiers M. Successful recovery from ESS is characterised by transcriptomic changes suggesting decreased type 1 inflammation and epithelial restoration. In press, Otolaryngol Head Neck Surg.

Authors:

Yvonne Chan MD FRCSC¹, Andrew V. Thamboo MD MHSc FRCSC², Joseph K. Han MD³, Martin Desrosiers MD FRCSC⁴

Affiliations:

¹Department of Otolaryngology-Head and Neck Surgery, Temerty Faculty of Medicine, University of Toronto, Toronto, ON, Canada

²Division of Otolaryngology-Head and Neck Surgery, Department of Surgery,

University of British Columbia, BC, Canada

³Department of Otolaryngology-Head and Neck Surgery, Eastern Virginia Medical School, Norfolk, VA, USA

⁴Division of Otolaryngology-Head and Neck Surgery, Centre Hospitalier de l'University de Montreal, Montreal, QC, Canada

Corresponding Author: Yvonne Chan, MD FRCSC MSc

Associate Professor, Dept. of Otolaryngology-Head & Neck Surgery, University of Toronto

St. Michael's Hospital, 30 Bond Street, Unit 8-163 CC North

Toronto, ON, Canada M5B 1W8

Phone: 416-864-5279 Fax: 416-864-5367

y.chan@utoronto.ca Word Count: 567

 $\textbf{Key Words:} \ \ \text{Chronic rhinosinusitis with Nasal polyposis; endoscopic sinus surgery; Remission; Asthma;}$

Type 2 inflammation

Abbreviations

AERD: Aspirin exacerbated respiratory disease; CRSwNP: Chronic rhinosinusitis with nasal polyposis; ESS: Endoscopic Sinus Surgery; GI: Gastroenterology; OHNS: Otolaryngology – Head & Neck Surgery

Funding Sources: Not applicable

Disclosure:

This material has never been published and is not currently under evaluation in any other peer-reviewed publication.

Financial disclosure:

YC: Speaker fees: Sanofi, Glaxo Smith Kline (GSK). MD: Research Funding: Pfizer. Clinical trial funding AstraZeneca, GSK, and Sanofi. Equity holder: Probionase Therapies. JKH: Research consultant: Sanofi Regeneron, GSK, AstraZeneca. AVT: Speaker fees: Sanofi, GSK, AstraZeneca, Research funds: GSK