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Original article

Proposal for a new diagnostic-therapeutic algorithm in chronic rhinosinusitis with nasal polyps

Matteo Gelardi, Rossana Giancaspro, Giulia Cintoli, Salvatore Simone Minafra, Salvatore Musto, Michele Cassano

Department of Otolaryngology, University Hospital of Foggia, Foggia, Italy

Abstract. Chronic rhinosinusitis with nasal polyps (CRSwNP) is a chronic inflammatory disease of the nose and the paranasal sinuses characterized by the presence of nasal polyps and persistent symptoms of nasal obstruction, anterior or posterior rhinorrhea, facial pain or pressure, and reduction or loss of smell, lasting longer than 12 weeks. Several therapeutic strategies are nowadays available to treat CRSwNP as a function of disease severity. However, a standardized therapeutic algorithm has not yet been proposed. Since CRSwNP severity can be assessed by the Clinical-Cytological Grading (CCG) and the consequent reduction in patients' Quality of Life can be defined with the Sino Nasal Outcome Test-22 (SNOT-22), we aimed to propose a new diagnostic-therapeutic algorithm, that takes into consideration both the characteristics of the patients, including the CCG, nasal obstruction, and SNOT-22, and all the therapies available today. (www.actabiomedica.it)

Key words: Chronic rhinosinusitis with nasal polyps, Clinical-Cytological Grading, SNOT-22, nasal cytology, TNPS

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is defined as an inflammatory disease of the nose and the paranasal sinuses characterized by the presence of nasal polyps and persistent symptoms of nasal obstruction, anterior or posterior rhinorrhea, facial pain or pressure, and reduction or loss of smell, lasting longer than 12 weeks (1).

EPOS 2020 Guidelines define three inflammatory patterns resulting from epithelial barrier damage and tissue remodeling that underlies CRS: type 1 inflammation, targeting viruses; type 2 inflammation, targeting parasites; type 3 inflammation, targeting extracellular bacteria and fungi (2,3). Generally, these inflammatory patterns restore the barrier integrity and eliminate pathogens. However, in CRS, the penetration of exogenous agents through the damaged mucosa leads to a chronic refractory inflammatory response that fails to resolve.

In Western Countries, CRSwNP is considered a type 2 disease, characterized by high levels of type 2 cytokines, such as IL-4, IL-5, and IL-13, as well as T helper polarization and eosinophilic recruitment and activation (4). Indeed, eosinophilic infiltration has been implicated in the severity, and treatment responsiveness of CRSwNP (5).

Another way to define CRSwNP severity is represented by the Clinical-Cytological Grading (CCG), which assesses the severity and the related Prognostic Index of Relapse (PIR), based on the cellular inflammatory infiltrate at nasal cytology and the presence of comorbidities, such as asthma, aspirin intolerance and allergy. The CCG also represents a useful tool to calibrate the medical treatment and optimize the success of the several therapeutic approaches available today, which are not fully standardized yet (6).

Based on this background, we aimed to propose a new diagnostic-therapeutic algorithm, as a function of

CCG and nasal obstruction, defined by Meltzer endoscopic polyp scores (Total Nasal Polyp Score, TNPS) and Sino Nasal Outcome Test-22 (SNOT-22), to guarantee patients effective and tailored treatments.

Nasal cytology and clinical-cytological grading

Nasal cytology is an easy-to apply, non-invasive and painless diagnostic tool that consists of sampling, processing, and microscope reading. Sampling requires the collection of cells from the surface of the middle portion of the inferior turbinate, under anterior rhinoscopy, by a sterile curette (Nasal scaping). The sample is immediately smeared on a glass slide, air-dried, and stained with May-Grünwald-Giemsa (MGG). The stained sample is then read at optical microscopy, with a 100x objective with oil immersion. The minimum number of fields needed to identify enough cells is thought to be fifty (6). Nasal cytology findings allow the identification of the predominant inflammatory cytotypes, which can be neutrophils, eosinophils, mast cells, or both eosinophils and mast cells.

The severity of CRSwNP can be assessed by nasal cytology. Indeed, a CCG has been proposed to estimate patients' PIR based on nasal cytology findings and comorbidities, such as aspirin intolerance, allergy, and asthma. In particular, a score is attributed to each endotype as follows: neutrophilic infiltrate scores as 1; mast cell infiltrate scores as 1; eosinophilic infiltrate scores as 2; mixed eosinophilic and mast cell infiltrate scores as 4. Similarly, a score is attributed to each comorbidity as follows: aspirin intolerance scores as 1; asthma scores as 2; allergy scores as 3; aspirin intolerance associated with asthma scores as 3. The sum of all these scores corresponds to the total CCG score, directly related to the PIR, which ranges from 1 to 10, where a CCG between 1-3 is considered low, 4-6 moderate and ≥ 7 high (7). Moreover, a CCG> 4 is associated with an increased probability of developing olfactory impairment. Indeed, olfactory impairment does not depend on nasal obstruction, measured by the size of the polyps and the restriction of nasal airflow, but rather on the severity of the inflammatory infiltrate (8).

Nasal obstruction and nasal polyps size

CRSwNP symptoms substantially affect patients' quality of life (QoL). In particular, the mucosal inflammation, together with the mechanical obstruction of the nasal cavities caused by nasal polyps, leads to nasal blockage, rhinorrhea, postnasal drip, and hypo/anosmia. Nasal obstruction and hyposmia are the most frequent symptoms, described in 97% and 90% of who underwent surgery, respectively (9). The size of nasal polyps is directly correlated to nasal obstruction and can be assessed according to the endoscopic scoring, known as Melter endoscopic polyp score (Total Nasal Polyp Score, TNPS), which attributes a score to each nasal cavity. In particular, each nostril is scored as follows: no polyps as 0; tiny polyps in the middle meatus that doesn't extend below the inferior border of middle turbinate's inferior border as 1; polyps that extend below the middle turbinate's bottom border as 2; large polyps that extend to the inferior turbinate's lower border or those that are medial to the middle turbinate as 3; large polyps causing complete obstruction of the inferior nasal cavity as 4 (10).

The TNPS is given by the sum of left and right nostril scores and ranges from 0 to 8.

Sino-nasal outcome test -22

SNOT-22 is a validated disease-specific survey that can be routinely used to assess CRSwNP symptoms severity and the consequent patients' Quality of life (QoL). This questionnaire evaluates 22 items concerning non only CRSwNP symptoms but also the social and emotional consequences of the disease. Indeed, the items concern nasal symptoms, sleep quality, otologic symptoms, or emotional symptoms, and each of them is scored from 0 (no problem) to 5 (problem as bad as it can be) (11,12).

Treatment

A medical treatment scheme for CRSwNP on the basis of CCG has already been proposed, to guarantee

patients effective treatments, increase patients' adherence to therapies and define the optimal follow-up as a function of CRSwNP severity (13).

In particular, the appropriate treatment would include nasal saline irrigation added with hyaluronic acid, regardless the CCG score. Moreover, patients with low CCG should use intranasal glucocorticoids, represented by furoate mometasone or budesonide, for 15 days a month. Patients with medium and high CCG, on the other hand, should use intranasal glucocorticoids for 20 days a month in association with oral prednisone (at the dose of 12.5 mg/day for 6 days a month for medium CCG and of 25 mg for three days and 12.5 mg for the other three days a month for CCG) (14). Both patients with medium and high CCG should also use oral antihistamines or undergo allergy immunotherapy (AIT) if allergic and leukotriene antagonists if asthmatic (15). Biological therapy should be recommended in patients with high CCG (16).

Antibiotics should be administered only in the case of active coexisting infections, regardless CCG scores15.

The optimal follow-up would be set up at every 6 months for low CCG, at every 3 months for the first year and then every 6 months for medium CCG, and at every 3 months for the first two years and then every 4 months for high CCG (17).

Despite being a diagnostic-therapeutic scheme tailored to each patient and to the risk of relapse, this algorithm does not consider the degree of nasal obstruction and the quality of life of the patients as well as the surgical therapeutic alternatives. Therefore, we would like to propose a new therapeutic algorithm that takes into consideration all the therapeutic strategies available today, both medical and surgical, in relation to the CCG.

A new therapeutic algorithm in CRSwNP

As a first step, proper diagnostic evaluation of a CRSwNP patient requires a complete medical history, nasal endoscopy, nasal cytology, and SNOT-22.

Once the patients' CCG and TNPS are established, surgery should be considered in case of severe nasal obstruction (TNPS ≥ 7). After surgery, non-surgical maintenance therapy should be recommended according to the CCG and the consequent PIR: conventional medical therapy for CCG ≤ 6 and biological therapy for CCG ≥ 7. For patients inoperable due to anesthetic contraindications, polypectomy with suction debriders, under local anesthesia, should be recommended to resolve nasal obstruction, followed by medical or biological therapy depending on CCG as above. Patients under biological therapy should be re-evaluated after 6 months and continue the treatment in case of reduction of TNPS and SNOT-22 scores, or possibly change the biological agent, in case of no improvements. In the latter case, conventional therapy and surgery should also be reconsidered.

On the other hand, in case of non-severe nasal obstruction (TNPS ≤ 6) associated with CCG ≤ 6, conventional medical therapy should be recommended. Then, after 3 months of medical treatment, both TNPS and SNOT-22 scores should be evaluated: patients with TNPS ≤ 6 and SNOT-22 ≤ 50 should continue conventional therapy; on the contrary, patients with increased nasal polyps (TNPS ≥ 7) after 3 months of medical therapy should undergo surgery to resolve nasal obstruction and then continue with medical therapy. Biological therapy should be considered when unable to continue conventional medical therapy.

Patients with TNPS ≤ 6 but with a completely obstructed nostril, to which an NPS score of 4 is given, deserve a separate mention, since the obstruction of a nostril could also significantly reduce patients' QoL. These patients should undergo surgery despite having a TNPS ≤ 6, followed by medical treatment or biological treatment as a function of CCG. Indeed, in the last decades, office-based polypectomy under local anesthesia in selected patients with obstructive polyposis has become popular, to immediately and safely alleviate nasal obstruction and to improve the access of topical medications (18). This technique could be cost-effective and could fill the therapeutic gap between the standard surgical and medical treatments, offering both patients and clinicians a good alternative to treat obstructive nasal polyps and to reduce waiting list times in saturated healthcare systems (19,20) (Figure 1).

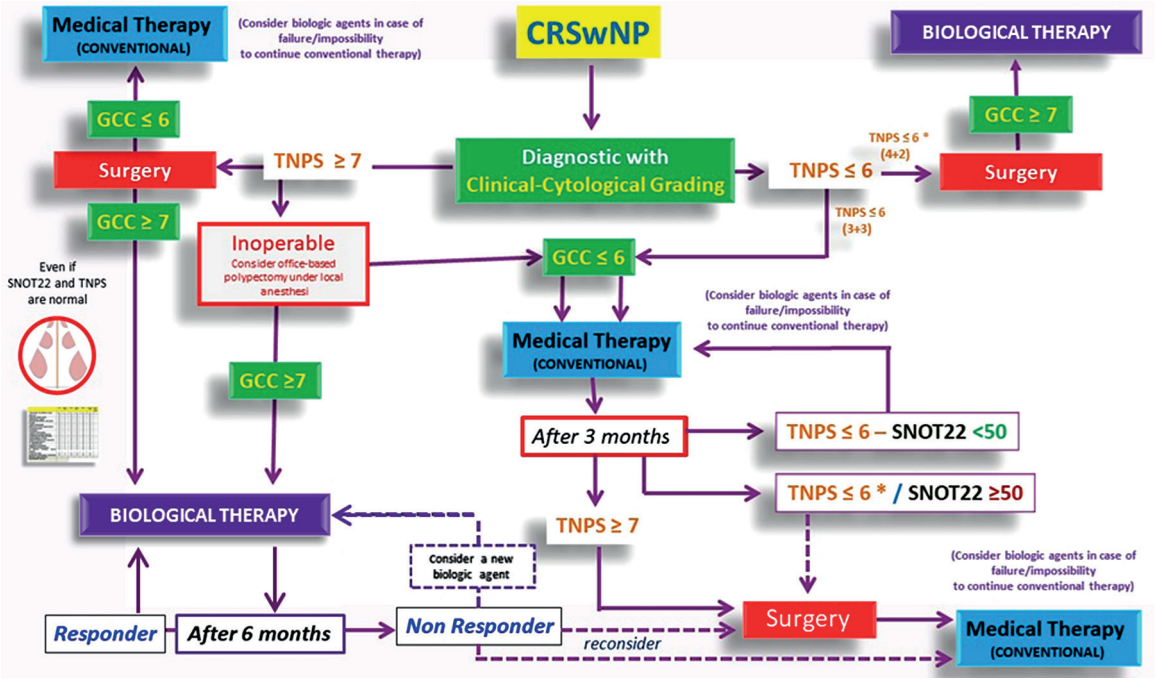

Figure 1. Diagnostic-Therapeutic algorithm. (The figure is an original work of the Authors).

Conclusions

The heterogeneity of medical and surgical therapies currently available to treat CRSwNP requires the creation of diagnostic-therapeutic algorithms that calibrate treatments according to the severity of CRSwNP and to the consequent reduction in patients' QoL (21). As a matter of fact, recent research in Precision Medicine focuses on providing personalized care, based on both patient's phenotypes and endotypes. In this context, the CCG has been proposed to predict the prognosis and the risk of relapse of CRSwNP patients, as well as to guide personalized pharmacotherapy, surgery, and innovative treatments (22). We believe that the proposed algorithm, which is the only one considers both the characteristics of the patients, including the GCC, nasal obstruction and SNOT-22, and all the therapies available today, represents a useful strategy to standardize CRSwNP treatment and to guarantee patients tailored therapies, with greater benefit and fewer side effects. This personalized therapeutic also requires a multidisciplinary approach, to improve CRSwNP diagnosis and management, especially in patients with comorbidities such as asthma (23).

Conflicts of Interest. Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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Correspondence:
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Rossana Giancaspro, MD
Department of Otolaryngology
Viale Pinto, 1 - Foggia, Italy
E-mail: rogianca@live.it