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Allergy International

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Letter to the Editor

## Health-related quality of life and drug treatment satisfaction were low and correlated negatively with symptoms in patients having severe refractory chronic rhinosinusitis with nasal polyps

Dear Editor,

Chronic rhinosinusitis with nasal polyps (CRSwNP) places a substantial burden on patients and can significantly decrease health-related quality of life (HRQoL).<sup>1,2</sup> The patient-centered care model encourages physicians to view patient disease burden as a measure of treatment efficacy and to focus more on patient-reported outcomes (PROs), particularly for chronic disorders, including each patient's experience of HRQoL.<sup>3</sup> Questionnaires have been developed for this purpose and studies have reported changes in patient disease burden and HRQoL after sinus surgery,<sup>4–6</sup> but changes in HRQoL from drug therapy in real-world treatment of CRSwNP remain unproven, and few reports are available on patient satisfaction. Clarifying the effects of symptom-related disease burden on HRQoL and treatment satisfaction could help physicians identify unmet medical needs, provide better treatment strategies for CRSwNP, and improve HRQoL and treatment satisfaction among CRSwNP patients. We used a non-interventional questionnaire survey to evaluate the disease burden of symptoms (SNOT-22),<sup>7</sup> assessed the relationship between disease burden and general HRQoL (SF-36)<sup>8</sup> and treatment satisfaction regarding medication (TSQM-9),<sup>9</sup> and analyzed the effects of specific patient characteristics on both HRQoL and treatment satisfaction.

Participants were eligible patients who lived in Japan, were over 20 years old at participation, met diagnostic criteria for CRSwNP<sup>10</sup> and were recommended for nasal polyps surgery by their physician, visited clinics or hospitals for chronic rhinosinusitis treatment within 3 months prior to study initiation, experienced typical symptoms of chronic rhinosinusitis (including nasal blockage, runny nose, decreased sense of smell) for more than 3 months, and could give informed consent. The primary outcome measures were the relationships between SNOT-22 and SF-36 scores and between SNOT-22 and TSQM-9 scores. Detailed methods of this study are summarized in the Supplementary Methods.

The survey was conducted from July 10, 2019 to August 8, 2019 and the analysis population was the first 300 eligible patients completing the survey (Supplementary Fig. 1). Median age was 42 years, and 63.0% were male. The median duration of disease was 10 years. Of the 300 patients, 48.7% had bilateral nasal polyps and

46.7% had a history of surgery. The average total score for SNOT-22 was  $40.1 \pm 20.9$ . In the category “The most important items affecting your health,” 63.0% of participants selected nasal blockage, 37.3% selected runny nose, and 29.7% selected decreased sense of smell/taste (Supplementary Table 1), suggesting that these three are the top 3 symptoms in this survey.

In the total group of participants, SF-36 scores for 6 of the 8 domains were significantly lower than population norms (Japanese version, 2017) (Supplementary Fig. 2). Of the 3 component summary scores, the mental component summary (MCS) and role/social component summary (RCS) scores of SF-36 were significantly lower than the population norms (Fig. 1A). The 3 component summary scores were stratified by quartile of the SNOT-22 total score (Fig. 1B, C, D) and by scores for each of the top 3 symptoms from SNOT-22 (Supplementary Fig. 3). We found a significant association between higher SNOT-22 scores, and lower SF-36 scores. The summary score for the MCS correlated negatively with the scores for the top 3 symptoms in the SNOT-22 items and most negatively with the score for decreased sense of smell/taste (Supplementary Table 2).

For the TSQM-9, the mean  $\pm$  SD effectiveness domain score was  $54.2 \pm 16.0$ , convenience domain score was  $62.9 \pm 15.7$ , and global satisfaction domain score was  $57.5 \pm 15.4$  (Fig. 2A). In groups with a higher SNOT-22 total score, we found a significant trend toward lower scores for all 3 TSQM-9 domains (Fig. 2B, C, D). Scores for the top 3 SNOT-22 symptoms ranged between 1 and 5, and higher scores were negatively associated with satisfaction regarding treatment effectiveness (Supplementary Fig. 4). Correlation analysis of the 3 domains showed the highest correlation between the effectiveness domain score and the SNOT-22 total score. There were also particularly strong correlations between the effectiveness domain score and symptoms of nasal blockage and decreased sense of smell/taste (Supplementary Table 3).

Correlations were negative between the SNOT-22 total score and all 3 component summary scores for SF-36. However, only the SF-36 MCS correlated negatively with each of the top 3 SNOT-22 symptoms, suggesting that mental health may be particularly affected by CRSwNP symptoms. The correlation was especially strong between the 3 component summary scores for SF-36 and the score for “decreased sense of smell/taste.” Participating patients reported less impact from that issue than from nasal blockage, but they showed a close association between decreased sense of smell/taste and lower MCS scores.

Peer review under responsibility of Japanese Society of Allergy.

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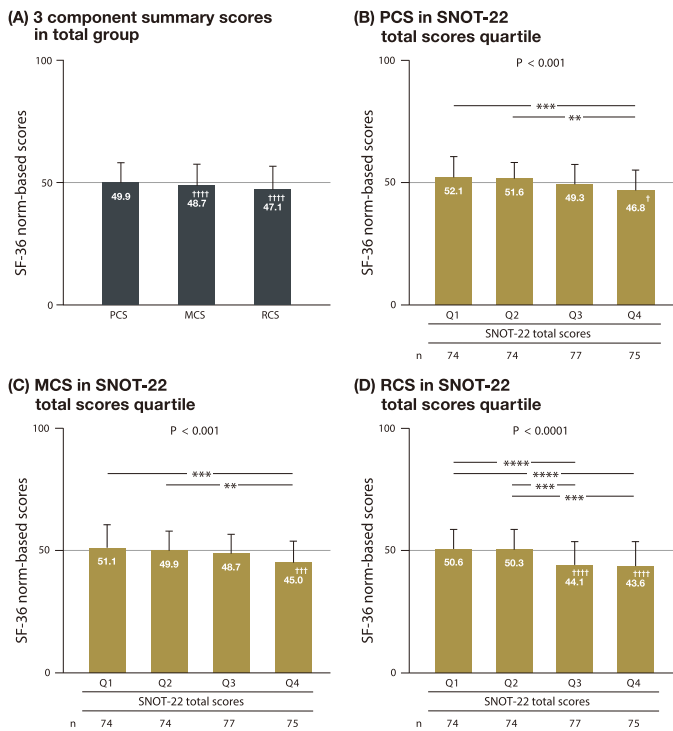


**Fig. 1.** SF-36 component summary scores. (A) 3 component summary scores in total group; (B) PCS in SNOT-22 total scores quartile; (C) MCS in SNOT-22 total scores quartile; (D) RCS in SNOT-22 total scores quartile. Bars indicate mean  $\pm$  SD. The horizontal line at a norm-based score of 50 indicates the population norms (Japanese version, 2017) (with 10 SD). \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ , \*\*\*\* $P < 0.0001$  vs. population norms (Japanese version, 2017), testing the difference between the two population means. P-values in the graph area are for one-way ANOVA. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ , \*\*\*\* $P < 0.0001$ , t-test (Bonferroni correction). Q1, SNOT-22 total score  $\leq 25$ ; Q2, SNOT-22 total score 26–37; Q3, SNOT-22 total score 38–53; Q4, SNOT-22 total score  $\geq 54$ . ANOVA, analysis of variance; MCS, mental component summary; PCS, physical component summary; RCS, role/social component summary; SD, standard deviation; SF-36, 36-item Short-Form health survey; SNOT-22, 22-item Sino-Nasal Outcome Test.

Patients generally reported less satisfaction on the effectiveness domain than on the convenience domain, resulting in a low level of global satisfaction. Satisfaction with drug therapies for CRSwNP was also lower than for a wide variety of other diseases, including serious and potentially life-threatening conditions (Supplementary Table 4). Previous studies have differed in design, so we cannot make detailed comparisons, but broad trends underscore patient dissatisfaction with the effects of current drug therapies for CRSwNP.

Selection bias could be a limitation of the study because patients were recruited by their physicians, and patients with a better post-operative course might have been excluded disproportionately. In this study, all participating patients had been recommended for surgery and half had already undergone surgery, indicating that these patients suffered from severe refractory CRSwNP, so our results may not be generalizable to all CRSwNP patients.

This survey focused on the relationship between disease burden and QoL or treatment satisfaction in patients with CRSwNP, to provide real-world evidence on CRSwNP treatment in an ordinary clinical setting. To clarify specific issues, comparative studies are needed between patients with CRSwNP and those with chronic rhinosinusitis without nasal polyps (CRSsNP).

This comprehensive survey showed low levels of HRQoL and treatment satisfaction among CRSwNP patients, and negative correlations with the symptoms of nasal blockage, runny nose, and decreased sense of smell/taste. Improving such symptoms may

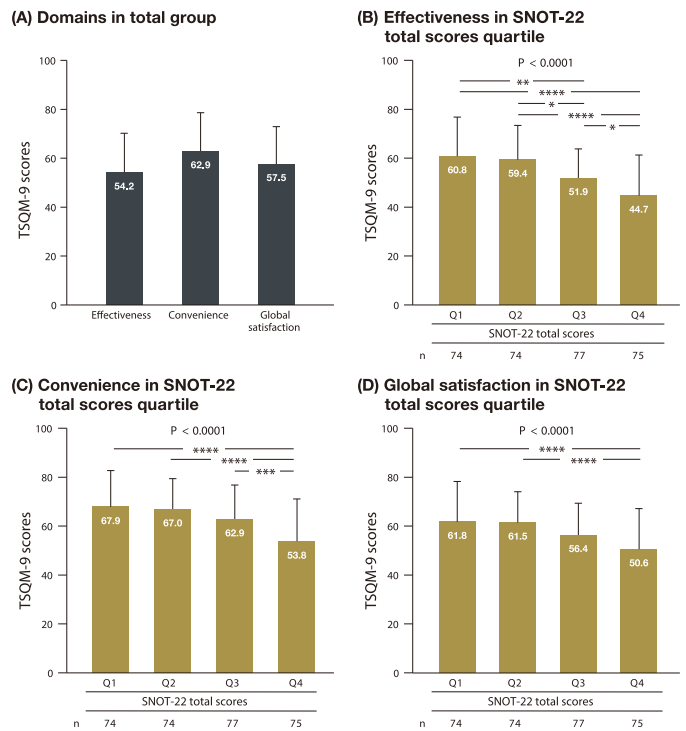


**Fig. 2.** TSQM-9 scores in domains. (A) Domains in total group; (B) Effectiveness in SNOT-22 total scores quartile; (C) Convenience in SNOT-22 total scores quartile; (D) Global satisfaction in SNOT-22 total scores quartile. Bars indicate mean  $\pm$  SD. P-values in the graph area are for one-way ANOVA. \* $P < 0.05$ , \*\* $P < 0.01$ , \*\*\* $P < 0.001$ , \*\*\*\* $P < 0.0001$ , t-test (Bonferroni correction). Q1, SNOT-22 total score  $\leq 25$ ; Q2, SNOT-22 total score 26–37; Q3, SNOT-22 total score 38–53; Q4, SNOT-22 total score  $\geq 54$ . ANOVA, analysis of variance; SD, standard deviation; SNOT-22, 22-item Sino-Nasal Outcome Test; TSQM-9, 9-item Treatment Satisfaction Questionnaire for Medication.

reduce disease burden and increase HRQoL and patient satisfaction. To accomplish this, it is essential to monitor each patient's symptoms and understand individual disease burden.

## Acknowledgements

The study was funded by Sanofi K.K., Japan. Statistical analysis was performed by Shinwa, Inc. and medical writing support was provided by EDIT, Inc., both funded by Sanofi K.K., Japan.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.alit.2020.11.010>.

## Conflict of interest

MO received honoraria from Sanofi K.K. MT, YT and HF are employees of Sanofi K.K. KK has no conflict of interest.

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Received 24 September 2020

Received in revised form 20 November 2020

Accepted 24 November 2020

Available online xxx