Quality of life and recurrence of disease in patients with eosinophilic and non-eosinophilic chronic rhinosinusitis with nasal polyposis

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ABSTRACT

Objective: To assess the quality of life (QoL) and recurrence of disease in patients with eosinophilic (ECRSwNP) and non-eosinophilic chronic rhinosinusitis with nasal polyposis (non-ECRSwNP) post endoscopic sinus surgery (ESS).

Methodology: A cross-sectional comparative study was carried out in the Otorhinolaryngology – HNS Department, Universiti Kebangsaan Malaysia Medical Center (UKMMC). Subjective assessments of nasal symptoms and quality of life (QoL) using SNOT-22 and Visual Analogue Scale (VAS) and objective endoscopic assessment was undertaken using a modified Hadley endoscopic examination.

Results: There was no significant statistical difference in the quality of life between the ECRSwNP and non-ECRSwNP groups as evidenced by the SNOT-22 score and the VAS comparison (p>0.05). However, there was a significant difference in terms of recurrence of disease with the presence of nasal polyps on endoscopic examination. (p = 0.016)

Conclusion: In conclusion, we found that there is no significant difference in QoL between ECRSwNP and non-ECRSwNP. There is higher frequency of recurrence of nasal polyps amongst ECRSwNP.

KEY WORDS:
Eosinophilic, CRSwNP, polyps , QoL , SNOT 22

INTRODUCTION

Chronic rhinosinusitis (CRS) is a common disabling illness characterised by mucosal inflammation of the nose and paranasal sinuses with sinonasal symptoms persisting for greater than 12 weeks.[1] According to the EPOS guidelines, CRS is divided into CRS with nasal polyps (CRSwNP) or without polyposis (CRSsNP).[2] It is diagnosed with the presence of anterior or posterior mucopurulent discharge, nasal obstruction and/or facial pain; supported by computed tomography (CT) scan evidence of rhinosinusitis or mucosal disease.

It is one of the most common illnesses worldwide and affects approximately 5% to 15% of the general population in Europe and the United States of America.[2] In Asia, the prevalence in South Korea is 7% while in China is 8%.[3] CRS is known to be responsive to optical medical treatment.[4] However, despite comprehensive medical therapy a subgroup of patients with refractory disease will require surgical treatment in the form of endoscopic sinus surgery (ESS).

CRS is a heterogeneous disease and can be divided into ECRS and non-ECRS based on the histologic subtype.[5,6] ECRS phenotype is clinically characterised by serum eosinophilia, atopy, extensive disease, and poor prognosis compared to the non-ECRS group.[10] Non-eosinophilic CRS is regarded as an extrinsic rhinosinusitis, because the inflammation originates from external stimuli such as bacteria and allergens rather than the intrinsic mucosal abnormalities.[7] In ECRS, eosinophils may contribute to oedema, whereas neutrophilic infiltration has an important role in vigorous glandular hypertrophy. Studies in Japan, South Korea and Malaysia found that CRSwNP patients exhibit non-eosinophilic dominant inflammation, suggesting that the pathophysiological presentation of CRS differs by race, climate, and geographic region.[8,9]

ECRS with nasal polyp patients have pronounced eosinophilic infiltration of nasal polyp tissue compared to neutrophil or lymphocytic infiltration. ECRS patients had more severe endoscopic and CT scores than non-ECRS patients.[11] Additionally, these patients have a strong tendency for the recurrence of nasal polyps after surgery.[10,12,13] Patients with ECRS represent a unique subtype and they especially remain the most resistant to medical and surgical interventions.[14] Zadeh et al., demonstrated that CRS patients with eosinophilia were more likely to have multiple recurrent sinus infections (94% vs 32%), recurrent polyps (35% vs 3%) and required revision surgery (84% vs 24%) despite undergoing endoscopic sinus surgery and the authors advocate that this group of patients be counselled pre-operatively for likelihood of continued symptoms post operatively and the need for revision surgery.[15] Patients with ECRS show a strong possibility of overlapping mechanisms for eosinophilia and have a poor response to medical and surgical management. Therefore, ECRS is considered to be a refractory and intractable disease.

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The aim of this study is to assess the quality of life (QoL) of patients with eosinophilic and non-eosinophilic CRSwNP post ESS subjectively utilising the SNOT-22 and Visual Analogue Scale (VAS) questionnaire; and to assess the frequency of recurrence of disease using a modified Hadley endoscopic examination.

To the best of our knowledge, this is the first study to be conducted in Malaysia to compare surgical outcomes of patients with eosinophilic CRSwNP and non-eosinophilic CRSwNP in our local population.

MATERIALS AND METHODS

This study received ethical committee approval from Universiti Kebangsaaan Malaysia with a project code of FF-2015-135. A cross-sectional comparative study was performed whereby all patients who underwent ESS for CRSwNP between January 2006 and August 2013 who fulfilled both the inclusion and exclusion criteria were included in the study. Informed written consent was obtained. A complete medical history and full ear, nose and throat examination was carried out. Patient's demographic data, SNOT-22 and VAS questionnaire were documented.

Inclusion Criteria

a) Patients aged 18 years old and above
b) Patients diagnosed with CRS with polyposis that underwent ESS between January 2006 and August 2013

Exclusion Criteria

a) Patients with sinonasal tumour
b) Patient who are less than 18 years old
c) Patients without consent for this study
d) Patient diagnosed with inflammatory (e.g. Wegener's granulomatosis, sarcoidosis) nasal pathology
e) Patient diagnosed with systemic conditions affecting the nose e.g. Cystic fibrosis, Kartagener's syndrome

Study tools

a) *Sinonasal Outcome test 22 (SNOT-22) questionnaire*
This is a validated questionnaire that assesses patient's nasal symptoms and also QoL.[9]
b) *VAS scale*
VAS will also be utilized. A score >5 affects QoL.[2] Severity of disease can be divided into Mild = VAS 0-3, Moderate = VAS 4-7, Severe = VAS 8–10
c) *Rigid nasoendoscopy examination*
Polyps were graded using the 0-3 scoring system recommended by the guidelines: score 0, absence of polyps; score 1, polyps in middle meatus only; score 2, polyps beyond the middle meatus but not blocking the nose completely; score 3, polyps completely obstructing the nose.[16] Recurrence of CRS was defined as the presence of nasal polyps detected by nasal endoscopy after 6 months of surgery.

STATISTICAL ANALYSIS

Data was entered and analysed using SPSS 23.0. Mann Whitney U test was employed to analyse the difference between SNOT-22 and VAS scores of the two groups whereas Chi squared test was performed to determine the difference between presence of nasal polyps and revision surgeries. P <0.05 was considered as statistically significant.

RESULTS

A total of 70 patients were included in this study of which 35 patients were in eosinophilic CRSwNP and 35 in the non-eosinophilic group.

In this study the age ranged from 18 to 80 years old. The median age for ECRSwNP is 57 and for non-ECRSwNP was 58. There was no statistical difference between the two groups.

There were a total of 70 patients in this study. In the ECRSwNP group 42.1% and 57.9% were male and female respectively. In the non-ECRSwNPgroup 52.9% and 47.1% were male and female respectively. There was no statistical significant difference between the two groups.

In ECRSwNP groups, the majority of patients were Indian, followed by Chinese and Malay as compared to the non-ECRSwNP group whereby the majority were Malay, followed by Chinese and Indian. Again, there is no statistical difference between the two groups.

There is no statistical difference between these two groups in terms of median score or individual symptom scoring suggesting that there is no significant difference in severity of disease between ECRSwNP and non-ECRSwNP.

In the eosinophilic group, 63% of the eosinophilic CRSwNP group had recurrence of disease evidenced by presence of nasal polyps, compared to 30% in the non-ECRSwNP group. This data is statistically significant, hence recurrence of disease was more frequent in the eosinophilic group.

DISCUSSION

CRS remains to be a challenging disease in terms of treatment and prognosis as a significant proportion of patients are inadequately controlled despite receiving combination of maximal medical therapy and ESS.[1] A wide variety of factors contribute to poor disease control, including patient-related factors such as ECRS.[11]

In our study, recurrence after surgery is higher in the ECRSwNP group as evidenced by the higher proportion of patients who underwent revision ESS ($p<0.05$). This echoes the conclusion of previous studies whereby many studies indicate that ECRSwNP commonly has poorer treatment outcomes compared to non-ECRSwNP. In a study group by Lee et al. 13 of 14 patients (92.9 %) who were treated with multiple courses of oral corticosteroids, revision surgery, or revision surgery together with oral corticosteroids, showed recurrence after six months' follow-up.[6] Lou et al., studied on 387 patients who had CRSwNP.[17] They found that tissue eosinophil accumulation outweighed other parameters as a predictor for recurrence. A cut-off value of 27% for tissue eosinophil percentage was able to predict recurrence with 96.4% sensitivity and 92.7% specificity.[17]

Table I: Frequency and percentages

		Frequency	Percent
Race	Chinese	28	40.0
	Iban	1	1.4
	Indian	12	17.1
	Malay	29	41.4
Age group	≤20	2	2.9
	21-30	4	5.7
	31-40	5	7.1
	41-50	9	12.9
	51-60	23	32.9
	≥61	27	38.6
Operation	Single	56	80.0
	Multiple	14	20.0
Severity polyps	0	38	54.3
	1	22	31.4
	2	8	11.4
	3	2	2.9
Polyps	No	38	54.3
	Yes	32	45.7
Medication	No	28	40.0
	Yes	42	60.0
Subtype Eosinophil	No	35	50.0
Non-eosinophil	Yes	35	50.0
Gender	Female	19	27.1
	Male	51	72.9
Nasal Blockage	Mild	55	78.6
	Moderate	11	15.7
	Severe	4	5.7
Rhinorrhea	Mild	54	77.1
	Moderate	13	18.6
	Severe	3	4.3
Facial pain	Mild	54	77.1
	Moderate	14	20.0
	Severe	2	2.9
Loss of smell	Mild	46	65.7
	Moderate	16	22.9
	Severe	8	11.4
Postnasal drip	Mild	47	67.1
	Moderate	14	20.0
	Severe	9	12.9
Total VAS	Mild	50	71.4
	Moderate	17	24.3
	Severe	3	4.3
	Total	70	100.0

Table II: Descriptive analysis

	N	Mean	Std. Deviation	Minimum	Maximum	Median	Percentiles 25	Percentiles 75	Mode
Years	70	5.94	3.21	1.00	16.00	5.00	4.00	7.00	4
Age	70	56.09	15.44	14.00	86.00	58.00	48.75	67.50	58
TOTAL22	70	22.53	18.44	0.00	74.00	23.00	4.50	32.25	0
Total VAS	70	2.42	2.03	0.00	8.20	2.00	1.00	3.45	0

Fokken et al., concluded that one of the most characteristic clinical features of eosinophilic CRSwNP is a strong tendency for recurrence after ESS.[2] Ferguson et al. postulated that ECRS is a subtype of chronic sinusitis that is considered to occur secondarily to systemic eosinophil deregulation.[18] Therefore, benefit of surgery may be significantly less in these patients. ECRS should be considered a condition to be controlled rather than cured with the use of long-term anti-inflammatory treatment and a maintenance regime achieved. At present, optimal treatment involves regular topical steroid, via nasal irrigation, in the setting of a wide, postsurgical corridor.[19]

The results of our study concluded that that there was no significant difference in terms of symptom severity between ECRSwNP and non-ECRSwNP as evidenced by SNOT-22 and VAS scores.

Many studies indicate that ECRS commonly has more severe disease and higher symptom score compared to non-ECRS.[20,21] However, there is conflicting evidence regarding disease severity in association with mucosal eosinophilia. In a recent study Wang et al., showed that in terms of the short-term efficacy of ESS in CRSwNP, both ECRSwNP and non-ECRSwNP patients had significant improvement in symptoms at one-

Table III: Mann-Whitney U test

	EOSINOPHIL	N	Median	Percentile 25	Percentile 75	Mean Rank	Mann-Whitney U	P
Years	No	35	5	4	8	35.06	597.00	0.854
	Yes	35	5	4	7	35.94		
Age	No	35	57	48	65	32.60	511.00	0.233
	Yes	35	58	52	70	38.40		
NEED TO BLOW NOSE	No	35	1	0	2	34.26	569.00	0.594
	Yes	35	1	0	3	36.74		
SNEEZING	No	35	1	0	2	35.11	599.00	0.868
	Yes	35	2	0	2	35.89		
RUNNY NOSE	No	35	1	0	2	33.00	525.00	0.279
	Yes	35	1	0	3	38.00		
COUGH	No	35	0	0	1	34.60	581.00	0.678
	Yes	35	0	0	2	36.40		
PND	No	35	1	0	2	33.93	557.50	0.490
	Yes	35	1	0	2	37.07		
THICK NASAL DISCHARGE	No	35	0	0	2	32.04	491.50	0.135
	Yes	35	1	0	2	38.96		
EAR FULLNESS	No	35	0	0	1	31.80	483.00	0.093
	Yes	35	1	0	2	39.20		
DIZZINESS	No	35	0	0	2	34.20	567.00	0.551
	Yes	35	0	0	2	36.80		
EAR PAIN	No	35	0	0	1	32.06	492.00	0.105
	Yes	35	0	0	2	38.94		
FACIAL PAIN	No	35	0	0	2	34.14	565.00	0.531
	Yes	35	0	0	2	36.86		
DIFFICULTY FALLING ASLEEP	No	35	0	0	2	34.51	578.00	0.658
	Yes	35	1	0	2	36.49		
WAKING UP AT NIGHT	No	35	1	0	2	33.77	552.00	0.456
	Yes	35	1	0	2	37.23		
LACK OF A GOOD NIGHTS SLEEP	No	35	0	0	2	33.44	540.50	0.369
	Yes	35	1	0	2	37.56		
WAKING UP TIRED	No	35	0	0	2	33.56	544.50	0.390
	Yes	35	1	0	2	37.44		
FATIGUE	No	35	0	0	2	34.17	566.00	0.551
	Yes	35	1	0	2	36.83		
REDUCED PRODUCTIVITY	No	35	0	0	1	34.69	584.00	0.713
	Yes	35	0	0	2	36.31		
REDUCED CONCENTRATION	No	35	0	0	1	32.30	500.50	0.148
	Yes	35	1	0	2	38.70		
FRUSTRATED	No	35	0	0	1	34.07	562.50	0.487
	Yes	35	0	0	2	36.93		
SAD	No	35	0	0	0	35.90	598.50	0.823
	Yes	35	0	0	0	35.10		
EMBARRASSED	No	35	0	0	0	33.97	559.00	0.403
	Yes	35	0	0	1	37.03		
SENSE OF TASTE/SMELL	No	35	0	0	3	35.80	602.00	0.893
	Yes	35	0	0	2	35.20		
BLOCKAGE	No	35	0	0	2	32.61	511.50	0.214
	Yes	35	1	0	2	38.39		
TOTAL22	No	35	21	1	28	33.20	532.00	0.343
	Yes	35	24	13	33	37.80		
NASAL BLOCAKGE	No	35	1	0	2	32.19	496.50	0.165
	Yes	35	2	1	4	38.81		
RUNNY NOSE	No	35	2	0	3	33.47	541.50	0.396
	Yes	35	2	1	5	37.53		
FACIAL PAIN	No	35	1	0	2	30.24	428.50	0.026
	Yes	35	2	1	4	40.76		
SENSE OF SMELL	No	35	1	0	4	31.20	462.00	0.072
	Yes	35	3	1	5	39.80		
PND	No	35	2	0	5	34.13	564.50	0.566
	Yes	35	2	1	5	36.87		
Total VAS	No	35	2	0	3	31.73	480.50	0.119
	Yes	35	3	1	4	39.27		

Table IV: Chi Square test based on histology subtypes

		Histology Subtypes					
		Non-eosinophil		Eosinophil			
		N	%	N	%	χ^2	P
Race	Chinese	15	53.6	13	46.4	3.20	0.362
	Others	0	0.0	1	100.0		
	Indian	4	33.3	8	66.7		
	Malay	16	55.2	13	44.8		
Age group	≤20	2	100.0	0	0.0	7.24	0.203
	21-30	3	75.0	1	25.0		
	31-40	2	40.0	3	60.0		
	41-50	6	66.7	3	33.3		
	51-60	8	34.8	15	65.2		
	≥61	14	51.9	13	48.1		
Gender	Female	8	42.1	11	57.9	0.65	0.420
	Male	27	52.9	24	47.1		
Severity polyps	0	24	63.2	14	36.8	10.68	0.014*
	1	10	45.5	12	54.5		
	2	1	12.5	7	87.5		
	3	0	0.0	2	100.0		
Polyps	No	24	63.2	14	36.8	5.76	0.016*
	Yes	11	34.4	21	65.6		
Medication	No	15	53.6	13	46.4	0.24	0.626
	Yes	20	47.6	22	52.4		
Operation	Single	32	57.1	27	42.9	5.71	0.017*
	Multiple	3	21.4	8	78.6		
NASAL BLOCAKGE	Mild	29	52.7	26	47.3	0.99	0.609
	Moderate	4	36.4	7	63.6		
	Severe	2	50.0	2	50.0		
RUNNY NOSE	Mild	29	53.7	25	46.3	1.33	0.513
	Moderate	5	38.5	8	61.5		
	Severe	1	33.3	2	66.7		
FACIAL PAIN	Mild	29	53.7	25	46.3	1.46	0.483
	Moderate	5	35.7	9	64.3		
	Severe	1	50.0	1	50.0		
SENSE OF SMELL	Mild	25	54.3	21	45.7	2.44	0.295
	Moderate	8	50.0	8	50.0		
	Severe	2	25.0	6	75.0		
PND	Mild	24	51.1	23	48.9	0.13	0.936
	Moderate	7	50.0	7	50.0		
	Severe	4	44.4	5	55.6		
Total VAS	Mild	28	56.0	22	44.0	2.55	0.279
	Moderate	6	35.3	11	64.7		
	Severe	1	33.3	2	66.7		

week follow-up after ESS, but there was no significant difference in symptom improvement between the two subgroups.[22] Interestingly, in another study by Browne JP et al., there was no significant difference of SNOT-22 scores of patients who underwent simple polypectomy with that of patients who underwent polypectomy with additional surgery.[23]

Another study by Hu et al. also showed no difference in visual analogue scale (VAS) score or duration of symptoms between ECRSwNP and non-ECRSwNP patients, suggesting that the two subtypes may have an equivalent severity of symptoms.[24] Similarly, ECRSwNP and non-ECRSwNP patients may present with comparable symptom scores which is what was found by Tecimer et al.[25]

In a study by Soler et al., in a study of 147 patients they found that eosinophil levels did not predict significantly worse scores on any objective or QoL measures.[20] Studies by Kountakis and Boudain have similarly failed to show a correlation between symptoms and eosinophil counts.[21,26]

Although the disease severity in our study was worse in the ECRSwNP group, the difference was not statistically significant, possible reasons behind this maybe be due to the varied time frame in the subjective assessment post operatively and adopting a definition of eosinophilia in samples with >5 per HPF compared to other studies which adopt eosinophil count of >10, 25 per HPF.

CONCLUSION

In conclusion, there was no significant difference in the quality of life between the eosinophilic and non-eosinophilic chronic rhinosinusitis patient groups post endoscopic sinus surgery. However, we found statistically significant difference in recurrence of disease. We recommend prospective multi-center studies in the future to further evaluate the difference in clinical features and severity of eosinophilic and non-eosinophilic CRSwNP in our local population in an effort to achieve improved tailored management.

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