RESEARCH ARTICLE

Does endoscopic thoracic sympathectomy improve the quality of life of patients with primary hyperhidrosis? A single center retrospective review [version 1; peer review: 1 approved, 1 approved with reservations]

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Abstract

Background: Endoscopic thoracic sympathectomy (ETS) is renowned as an effective surgical treatment for primary hyperhidrosis (PHH) and believed to improve patients' quality of life (QOL). This study aimed to evaluate the quality of life (QOL) of patients with PHH after ETS compared to before ETS, and to determine whether compensatory sweating (CS) affects QOL of patients.

Methods: This is a single-centre retrospective review of patients who had undergone ETS at the National Heart Center [Institut Jantung Negara (IJN)], Malaysia. In total, 62 patients from January 2014 to December 2018 were recruited. Medical records were first reviewed for all relevant data, prior to making telephone interview to administer the questionnaire. A modified questionnaire with validated components was used to assess the patients' QOL. Patient satisfaction, symptom resolution, recurrence and occurrence of CS were also asked during the interview. Data were analysed using IBM SPSS Statistics 25.0.

Results: A total of 46 patients (response rate: 74.2%) completed the questionnaire, with 95.7% reporting improvement in the total QOL score (Mean difference = 113.54, SD=70.79, 95% CI = 95.52 – 134.57, $p < 0.001$). There was remarkable symptom resolution for palmar HH as 97.8% reported dry hands, whereas majority of patients with palmar-plantar HH reported persistent sweating from feet HH. CS rate was 89.1%. In terms of severity of CS, 6 (14.6%) reported mild, 17 (41.5%) moderate, and 18 (43.9%) had severe CS. The severity of CS as well as the number of locations have a significant effect on the QOL reported ($p=0.022$ and $p=0.008$, respectively).

Conclusion: ETS is an effective treatment for PHH in improving the QOL of patients, even long term. The occurrence of CS did not affect

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the QOL, but severity of CS and number of locations involved in CS affect the QOL of patients.

Keywords

primary hyperhidrosis (PHH), endoscopic thoracic sympathectomy (ETS), quality of life (QOL), compensatory sweating (CS)

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Introduction

Primary hyperhidrosis (PHH) is a chronic and distressing condition not caused by a medical condition but thought to be caused by over-stimulation of cholinergic receptors on eccrine glands. An excessive sweating beyond what the body is used for homeostatic temperature regulation remains the main pathologic feature.¹ Since eccrine glands are found commonly at the palms, axilla, face, and soles, these are the areas mainly affected by PHH.² Physiologically, it is thought that the negative feedback loop is impaired in such patients, which also helps to explain how a physiologic response becomes pathologic.³

Different prevalence rates for PHH have been cited around the globe ranging from 0.6% to 16.3%,⁴ and despite the myriad of treatment options, endoscopic thoracic sympathectomy (ETS) is still the most effective with a high rate of patient satisfaction despite the occurrence of compensatory sweating (CS) elsewhere in the body.^{5,6,7,8} Although the pathogenesis of CS remains unknown, it is believed that CS occurs due to an abnormal thermoregulatory response after sympathectomy due to altered feedback mechanism in the hypothalamus, whereby residual sweat glands increase their activity in an attempt to compensate for the loss of neural regulated sweat glands.⁹

Ever since the advent of ETS, CS has become the most feared complication because if severe, will significantly affect the quality of life (QOL) of patients.¹⁰ It is deemed the worst side effect of ETS, which impacts on daily activities.^{11,12,13} However, only a few studies have assessed CS and if its intensity affects the QOL of patients, but the results were inconsistent. Dias *et al*¹⁴ proposed that CS potentially worsens postoperative QOL. Chang and colleagues¹⁵ retrospective review reported that overall satisfaction of patients was inversely correlated with the severity of CS. On the other hand, one study concluded that postoperative QOL did not depend solely on the severity of CS, but also on the ability of patients to tolerate the situation.¹⁶

It is also worth noting that besides traditional outcome data, complication rate and morbidity, as we have presented in our previous research¹⁷, and QOL analyses were also used as benchmarks of the success of such surgical procedure. But it is also noted that some QOL questionnaires are lacking in quality, and in deriving substantive conclusions.¹⁸ Some researchers^{19,20} used generic QOL instruments such as the Short Form 36 (SF36) that would look at all aspects of the patients' health status, but it lacks specificity. These questionnaires might not be able to detect disease-specific changes in the QOL of patients post-surgery²¹. Whereas disease-specific questionnaires might be able to measure the change in the QOL of patients suffering from a specific disease.^{22,23}

We noted that, for assessing the QOL of patients after ETS, two of the most commonly used disease-specific questionnaires are by Keller *et al*²⁴ that assesses the hyperhidrosis scale using 15 questions concerning daily life; and Milanez de Campos *et al*²⁵ that has four different domains with 20 questions that cover sweating symptoms, intimacy, emotional response, and special circumstances.

Aims

The aims of this study are to evaluate the QOL of patients with PHH who had undergone ETS compared to their QOL pre-operatively, and to determine whether CS would affect the QOL of patients post-operatively.

Methods

Study design

This study was conducted from January to July 2019 at the National Heart Institute (IJN) in Kuala Lumpur which was a five-year retrospective review of the QOL of patients who underwent bilateral endoscopic thoracic sympathectomy (BETS) for the treatment of PHH at the National Heart Institute of Malaysia [Institut Jantung Negara (IJN)] from January 2014 to December 2018. With the approval of the IJN Research Ethics Committee (IJNREC), all patients' medical records were screened to ensure the completion of data. A complete medical record would include the proper and adequate documentation of patient's demographics, preoperative consultation record, medical and surgical record, laboratory results and postoperative follow-up notes. All eligible patients were contacted through phone calls for the administration of the questionnaire, which comprises of preoperative and postoperative scoring.

Inclusion criteria: bilateral endoscopic thoracic sympathectomy cases; completed medical records; consented for an interview.

Exclusion criteria: missing data from the medical record; medical condition that resulted in secondary hyperhidrosis; redo endoscopic thoracic sympathectomy; failure to give consent for an interview

This constituted a total of 62 patients who all had moderate to severe PHH prior to surgery, involving more than one location.

Ethical statement

Ethical approval was obtained from both the IJN Research Ethics Committee (IJNREC/207/2017) and Monash University Human Research Ethics Committee (MUHREC/9214). The study was also registered with the National Medical Research Register (NMRR-17-3133-39469). Verbal consent to participate in the study was obtained over the telephone. This method of consent was approved by the Research Ethics Committees, as set out in the study protocol submitted to them.

All research procedures were done in accordance with the ethical regulations set by the IJN Ethics Committee (IJNEC), Monash University Human Research Ethics Committee (MUHREC) and it abides with the Helsinki Declaration revised in 2013.

Surgical techniques

All patients were assessed for the severity of hyperhidrosis before surgery. Once the anaesthetic assessment is completed, elective surgery of BETS was scheduled. All BETS were performed by two different surgeons with the same level of experience and using similar techniques. All surgeries were performed in a standardized manner using the same equipment under general anaesthesia. None of the surgeries was converted into open surgery. In our institute, BETS was conducted in such a way that two incisions were made for the access of ports and thoracoscope. The first incision was made around the mid-axillary line over the fifth intercostal space. After deflating the lung of the operative side, the pleural space was entered by blunt dissection. Then, a second incision was made around the submammary fold under endoscopic guidance. For each side of the surgery, two ports of either 5mm or 10mm were used with a 30 degree thoracoscope. Once the ganglion was identified, the sympathetic chain would be interrupted using excision method. The same procedure was then repeated on the contralateral side at the same level of interruption in all cases. All specimens excised were sent for histopathology examination for the confirmation of ganglion excision. Patients were hospitalised for a total duration of three to four days to monitor for postoperative complications such as pneumothorax and wound management. All patients were subjected to chest X-rays which were reviewed by surgeons before discharge.

For this study, all surgical and inpatient notes were analysed and recorded including the total operative time, days of hospital stay, pain score, postoperative complications, and medications used.

Follow-up

All except one patient had at least one follow-up after surgery. About 63% of them attended follow-up twice and one of them had it thrice. During follow up, patients were assessed for symptom resolution, occurrence and severity of CS, pain, wound healing as well as other problems resulting from surgery.

Questionnaire

All questionnaires were administered during the period of January until July 2019. The questionnaire used for this study was the validated Health Related Quality of Life (HRQOL) Questionnaire in PHH which is a modified questionnaire based on studies by Milanez de Campos *et al*²⁵ and Keller and colleagues²⁴, which was designed to specifically evaluate preoperative and postoperative improvement of QOL in patients with hyperhidrosis. After obtaining the demographic data from the case records, the patients were interviewed via telephone on the severity of their PHH and also any possible recurrence, and on CS (*Extended data: Appendix 1*⁴⁶). This is followed by the second set of questionnaires that assessed the impact of QOL in four major domains, namely the functional, social, personal and psychological domains (*Extended data: Appendix 2*⁴⁶).

The questionnaire starts with a single question of 'In general, how would you rate your quality of life before and after treatment?', in which patients will be asked to rate from 0 to 10, with 0 being the worst and 10 being excellent. This was followed by a total of 29 questions with 17 questions on functional domain, 3 questions on social domain, 2 for personal domain and 7 questions on psychological domain. Within the functional domain, the questions were further divided into 9 questions that focus on palmar sweating, 5 questions on feet sweating, and 3 questions on axillary sweating. The final total score of QOL can therefore possibly range from 0 to 290. In this study, QOL was assessed in three major forms that are: a) general QOL, b) QOL score as per domain and c) total QOL score of all domains, as illustrated in [Figure 1](#).

Furthermore, patients were asked to rate their overall satisfaction level from 0 being the worst, 5 being neutral, to 10 being excellent, and the score was further categorised into very unsatisfied (0-1), unsatisfied (2-4), neutral (5), satisfied (6-8) and completely satisfied (9-10). For the purpose of this study, there were additional open-ended questions after each section of the domain to address all potential issues that might be missed from the questionnaire. A good mix between closed-ended and limited number of open ended-questions allows for a smooth flow of interview while adequately addressing patients' concern. All questions were asked in a simple and clear manner without medical jargons to avoid

Figure 1. Structure to the interpretation of the Health Related Quality of Life.

ambiguity or misunderstanding. At the end of the interview, we also asked if patients regretted the decision to undergo surgery.

Data collection

All complete patients' medical records were reviewed by a single investigator to record relevant data. Data collection was performed by a single investigator throughout the study in order to reduce potential bias secondary to inconsistent administration of questionnaire and data handling. Prior to interview, a separate reference list with only patients' name and contact details was generated. This ensured the blinding of investigator from the level of interruption that patients had underwent, therefore reducing investigator bias. Before the interview, a template of conversation was created for a good conversation flow. This template included a standard introduction to the identity of investigator, purpose of the project, assurance of patients' confidentiality, and ended by obtaining patients' informed consent. In addition, pilot tests were run with ten volunteers to gain feedback to improve the process of interview. These were patients from our previous cohort of study on ETS¹⁷ and no changes were made to the questionnaire after the pilot study.

Prior to the interview, patients were asked to choose their language of preference, between Malay or English for better communication. This was done on a background of an investigator who is fluent in both languages. Good rapport was built by asking daily questions to make patients feel more at ease in expressing themselves. In order to reduce performance bias, all patients were reassured that there will be no coercion on their response and honest feedback is greatly appreciated for the benefit of scientific research. To reduce recall bias, all patients were informed at the beginning of the phone call that the interview would take an average of 30 minutes; hence, appointment will be made at another time if patients were occupied at that particular moment. Besides, for each of the questions asked, patients were given adequate time to recall without any prompts. This was strictly adhered to across all interviews to minimise recall bias. When asked to rate the QOL from a scale of 0 to 10 with regards to hyperhidrosis, a standard explanation was given to all patients that was: 0 represents the worst QOL you could imagine, while 10 represents excellent QOL, and 5 being a neutral response.

Statistical analysis

Data entry and analysis were performed using IBM® SPSS Statistics version 25.0. Descriptive statistics were reported as percentages for discrete variables, continuous data were reported as means with standard deviations (SDs) for parametric data and medians with interquartile ranges (IQRs) for non-parametric data. Internal consistency of questions was tested separately for each domains using Cronbach's Alpha reliability test. Questions from each subset of functional domain and psychological domain demonstrate excellent internal consistency. Personal domain demonstrates poor consistency and hence may impose a limitation to our analysis (Table 1). Tested variables were first explored for its normality, outliers and linear relationship and those which met the assumptions will be analysed using parametric analysis whereas those that did not will be analysed using non-parametric analysis. Correlations between factors affecting the occurrence of

Table 1. Cronbach's Alpha reliability test for internal consistency in each domain

Domain	Subset	No. of Items	Cronbach's Alpha	Internal Consistency
Functional	Hands	9	0.937	Excellent
	Feet	5	0.939	Excellent
	Axilla	3	0.960	Excellent
Social		3	0.797	Acceptable
Personal		2	0.582	Poor
Psychological		7	0.940	Excellent

CS were assessed using Spearman's rho or Pearson's correlation. Coefficient of more than 0.7 will be considered significant. Differences between categorical variables were analysed using Fisher's exact test or chi-squared test, depending on the assumptions. Differences for independent continuous variables were analysed using independent *t*-test or Mann-Whitney test for parametric and non-parametric data, respectively. The differences in QOL score rated by patients before and after operation were compared using the paired *t*-tests for normally distributed data, or Wilcoxon signed-rank test for skewed data. As the improvement of QOL in certain domains was not normally distributed, all comparisons of QOL improvement in each domains were done using the Wilcoxon test. The value of significance was taken at $p < 0.05$ for all the analysis.

Results

Number of cases included

A total of 62 patients were included based on the criteria of complete medical records and having BETS done between January 2014 and December 2018. One patient was excluded for having undergone the surgery twice. All relevant medical records were screened thoroughly to ensure that there was no underlying medical condition that may be a confounder to secondary hyperhidrosis such as anxiety disorder, diabetes, or hyperthyroidism. The final diagnosis of PHH in each patient was confirmed through consultation record after the exclusion of possible secondary causes of hyperhidrosis. Thirteen patients were lost to contact, and two patients did not consent to the phone interview for personal reasons. Finally, 46 patients (response rate: 74.2%) consented to the telephone interview, and all of them completed the HRQOL questionnaire (Figure 2).

Demographics

The studied population comprised of 30 (65.2%) and 16 female (34.8%) patients. In total, 36 of patients were ethnic Malays (84.8%), 6 were Chinese (13%) and 1 was Indian (2.2%), which appropriately represented the racial distribution in Malaysia. None of the patients had any medical conditions that might predispose them to secondary hyperhidrosis. Blood tests were done on all patients to ensure there were no cases of thyroid dysfunction, or diabetes. Upon first consultation, no patient reported any anxiety disorder which might worsen the severity of sweating.

The age of the study population ranged from 13 to 55 years old, with 84.8% of the study population being younger than 30 years old. The distribution was positively skewed with a median of 20.5 years old. The BMI of the study population is normally distributed with a mean of 23.02 kg/m² (SD=4.04). When classified into categories, 1 (2.2%) patient was underweight, 25 (54.3%) were normal, 16 (34.8%) were overweight and 4 (8.7%) were obese (Table 2).

Figure 2. Flow chart demonstrating the process of patients' recruitment

Table 2. Characteristics of the study population (N=46)

Parameters		Number (N)	Percentage (%)
Age (years)	10-19	19	41.3
	20-29	20	43.5
	30-39	6	13.0
	>40	1	2.2
Gender	Male	30	65.2
	Female	16	34.8
Ethnicity	Malay	39	84.8
	Chinese	6	13.0
	Indian	1	3.2
BMI (kg/m²)	Underweight (<17.5)	1	2.2
	Normal (17.5 - 22.9)	25	54.3
	Overweight (23.0 - 27.9)	16	34.8
	Obese (≥ 28)	4	8.7
Medical conditions	Diabetes	0	0
	Thyroid dysfunction	0	0
	Anxiety	0	0

Hyperhidrosis profile

Location of hyperhidrosis

Only two patients had sweating from a single location (4.3%), as most of them had hyperhidrosis in two locations (73.9%), with the remaining reported PHH involving more than two locations (21.7%). Combined palmar-plantar hyperhidrosis was present in 73.9% of the study population, with the rest distributed in all different possible combinations, as summarised in [Table 3](#). Broken down to each location and its individual reported frequencies, the palm was the most commonly reported location by all patients (100%), followed by the soles of the feet [43 (93.5%) patients].

Severity

All patients experienced moderate to severe sweating from the palms and soles, which prompted them to seek surgical treatment. Reportedly, 45.7% had moderate palmar hyperhidrosis while 54.3% had severe condition. None had mild sweating prior to surgery. Some described dribbling of sweat from hands and feet, which embarrassed and impaired their daily activities. The majority of patients described worsening of sweating with hot weather and relieved by staying in cool condition. A small proportion of patients described worsening of sweating by stress. In some cases, sweating was persistent even under cool conditions, leading to a very poor QOL before operation.

Level of sympathectomy

In our centre, majority of BETS were performed at a level of T2-T3 (78.3%), the frequency reported is summarised in [Table 3](#). A T2 level has been well recognised to increase the risk of CS and other complications if interrupted^{26,27}. Hence, we further categorise patients into T2-involved and T2-spared group to study the difference between both groups.

Occurrence of compensatory sweating

Although the definition of CS remains vague, it is essentially a condition of increased sweating at a previously normal location, to an extent of being noticed by patients. In our study, CS was reported in up to 41 (89.1%) of patients. We further assessed these patients for the location(s) involved and its severity. Data on the onset of CS first becoming noticeable was also recorded. When assessing the locations involved in CS, every patient was asked regarding the presence of CS at locations such as the face, axilla, trunk, abdomen or groin, and lower limbs. They were then grouped into patients who had CS from one location, two locations and more than two locations. In total, 38 (92.7%) patients

Table 3. Summary of hyperhidrosis profile before surgery (N=46).

	Frequency, N	Percentage, %
Preoperative location(s) of presenting complaint		
Palms	2	4.3
Palms + Soles	34	73.9
Face + Axilla + Palms	1	2.2
Face + Palms + Soles	1	2.2
Axilla + Palms + Soles	7	15.2
Face + Axilla + Palms + Soles	1	2.2
Total	46	100.0
Number of location(s) involved		
Only 1 location	2	4.3
Combined 2 locations	34	73.9
More than 2 locations	10	21.7
Total	46	100.0
Location and its individual reported frequency		
Face	3	6.5
Axilla	9	19.6
Palms	46	100.0
Soles	43	93.5
Severity (Palms)		
Mild	0	0
Moderate	21	45.7
Severe	25	54.3
Total	46	100.0
Severity (Feet)		
Nil	3	6.5
Mild	1	2.2
Moderate	22	47.8
Severe	20	43.5
Total	46	100.0
Level of sympathectomy		
T2-3	36	78.3
T2-4	2	4.3
T2-5	4	8.7
T3-4	2	4.3
T3-5	2	4.3
Total	46	100.0
Category for level of sympathectomy		
T2-involved	42	91.3
T2-spared	4	8.7
Total	46	100.0

reported having CS on the body, followed by lower limbs (48.8%). CS at the abdominal and groin region was reported by 10 (24.4%) patients, and axillary region by 4 (9.8%) patients. We noticed that 64.3% of patients who experienced CS first noticed the sweating within the first month of the surgery. Among these, 31.7% noticed it as early as during the first week of surgery. Less than a quarter (13.0%) noticed CS more than six-months after the surgery. Patients with CS were also asked to rate the severity of sweating as mild, moderate or severe according to the pre-set standard definition (Table 4). The majority of them had moderate CS (41.5%) or severe CS (43.9%). Only 14.6% of them described mild sweating and this information is summarised in Table 4.

Evolution of compensatory sweating

The majority of patients reported no improvement in the intensity of CS. Only four (9.8%) patients reported complete resolution of CS over time, and three (7.3%) reported gradual improvement with time. In those who claimed that CS had resolved, one described having CS on their trunk for around seven-months to a year, before it progressively resolved. The other two patients described having CS for more than a year which slowly improved and then resolved. There was a patient who described having CS at multiple locations including the trunk, abdomen and groin, and thigh but CS from the thigh had resolved after it occurred for a week, even though CS from other locations remained.

Patient satisfaction

In general, there was great satisfaction reported by patients with a median score of 7 (IQR=4). There was an ascending trend of frequency from the worst to excellent as shown below (Table 5). In this study, we took the value of 5 as neutral as explained to all patients before the administration of questionnaire.

Table 4. Summary of compensatory sweating (CS) profile.

Variables		Frequency, N	Percent, %
Occurrence of CS (N=46)	Yes	41	89.1
	No	5	10.9
Time from surgery when CS was first noticed (N=41)	Less than 1 week	13	31.7
	1 to 4 weeks	15	32.6
	1 to 6 months	7	15.2
	More than 6 months	6	13.0
Number of locations (N=41)	1	19	46.3
	2	15	36.6
	More than 2	7	17.1
Severity of CS (N=41)	Mild	6	14.6
	Moderate	17	41.5
	Severe	18	43.9
Evolution of CS (N=41)	Improved	3	7.3
	Resolved	4	9.8
	Same	34	82.9

Table 5. Satisfaction category (N=46).

	Frequency, N	Percent, %
Very unsatisfied (0 - 2)	3	6.5
Unsatisfied (3 - 4)	5	10.9
Neutral (5)	9	19.6
Satisfied (6 - 8)	13	28.3
Completely satisfied (9 - 10)	16	34.8
Total	46	100.0

Compensatory sweating and patient satisfaction

We did not find any significant difference in satisfaction between the group of patients with CS and without CS ($p=0.219$) (Table 6).

We noticed that comparing patients with mild to moderate (non-severe) CS with those who had severe CS, the satisfaction reported was highly and significantly lower in the latter group ($p=0.001$) (Table 7).

Quality of life Improvement

General QOL

In our study, 37 (80.4%) patients reported improvement in the general QOL after surgery, whereas 5 (10.9%) reported no changes with general QOL and 4 (8.7%) reported worse QOL after surgery. All four patients who reported worse general QOL after surgery had severe CS involving more than one location. It was demonstrated in this study that the improvement in the general QOL of patients after surgery was highly statistically significant ($p<0.001$) (Table 8).

QOL improvement by domain

For comparison of QOL improvement in each of the four domains, the mean changes in score were adjusted to give an average improvement of score per question. It can be observed in Figure 3 below that all domains have demonstrated an increment in the median score for postoperative QOL, although it was not prominent in the axilla ($p=0.087$). Besides, the functional domain of hands had shown the greatest improvement as compared to other domains with average increment of 5.86 per question ($p<0.001$). This was followed by the social domain, which also showed substantial improvement with an average increment of 5.12 per question ($p<0.001$).

Table 6. Median of overall satisfaction in patients with compensatory sweating (CS) and without CS (N=46)

		CS, N (%)		<i>p</i> value ^a
		Yes	No	
		41 (89.1)	5 (10.9)	
Overall satisfaction	Median (IQR)	7.0 (10.0)	9.0 (5.0)	0.219

Data is not normally distributed.

^aMann-Whitney test

Table 7. Median satisfaction score between patients with non-severe compensatory sweating (CS) and severe CS (N=41)

		CS severity, N (%)		<i>p</i> value ^a
		Non-severe	Severe	
		23 (56.1)	18 (43.9)	
Overall satisfaction	Median (IQR)	9.0 (8.0)	5.0 (10.0)	0.001*

Data is not normally distributed.

^aMann-Whitney test

*significant difference ($p=0.001$)

Table 8. Median of general quality of life (QOL) of patients for preoperative and postoperative period (N=46)

		Time point		<i>p</i> value ^a
		Preoperative	Postoperative	
General QOL	Median (IQR)	3.0 (9.0)	7.0 (10.0)	<0.001*

Data is not normally distributed.

^aWilcoxon test. IQR: Inter Quartile Range;

*significant difference ($p < 0.001$)

Figure 3. Boxplot illustrating the summation of quality of life score from each domain for both preoperative and postoperative period

Summary of improvement in QOL

Table 9 summarizes the preoperative and postoperative median score for each question with its respective p value. It was noted that all domains had significant improvement in QOL score except for the axillary domain.

Table 10 summarizes the median score for each domain and its respective average increment in score per question and p values. This is followed by **Table 11** that describes the change in QOL in each domain.

Total sum of QOL

We also summed up the total score from all domains to compare the changes before and after surgery. Of all patients, only two (4.3%) had a reduction in the total QOL score, whereby the rest of them (95.7%) reported improvement in total QOL. By comparing the differences between the preoperative and postoperative total QOL score using paired t -test, there was a statistically significant difference ($p < 0.001$), with a mean difference of 113.54 (SD=70.79, 95% CI=95.52 - 134.57) (**Table 12**).

Factors affecting QOL

To study the factors associated with QOL after surgery, selected variables were initially tested for their correlation with general and total QOL score using Spearman's and Pearson's correlation. It was noted that the severity of CS and number of location(s) involved in CS were significantly associated with both general and total QOL (**Table 13**).

It is interesting to note that when comparing the postoperative general QOL and total QOL between patients with CS and without CS, no significant difference was noted ($p = 0.303$ and $p = 0.167$ respectively) (**Table 14**). However, when we compared the general QOL reported by patients with non-severe CS and those with severe CS, there was a significantly lower general QOL reported by the latter ($p < 0.001$) (**Table 15**). We also performed an analysis between the severity of CS with the total QOL score. By running an independent t -test, the results were consistent with the above analysis in which the mean total QOL score was noted to be significantly lower in the group with severe CS (Mean=217.17 vs 184.22, $p = 0.008$) (**Table 15**).

Post-hoc Bonferroni was performed to improve the accuracy of such comparison. It was found that there was still a significant association between two factors ($p = 0.022$) with a significant difference in mean total QOL reported between patients with moderate and severe CS ($p = 0.019$) (**Table 16**).

Table 9. Summary for improvement of quality of life (QOL) score in each domain according to Health Related QOL in primary hyperhidrosis^a.

Functional domain	Preoperative score	Postoperative score	<i>p</i> value ^b
	Median (IQR)	Median (IQR)	
Palmar domain			
Writing?	2.0 (6)	10.0 (4)	<0.001*
Typing on keyboard?	2.0 (8)	10.0 (5)	<0.001*
Turning knobs or faucets?	3.0 (10)	9.0 (5)	<0.001*
Driving car?	3.5 (7)	9.5 (5)	<0.001*
Eating with fork and spoon?	5.0 (10)	9.0 (6)	<0.001*
Wearing gloves?	2.5 (6)	9.0 (5)	<0.001*
Grasping objects?	2.0 (6)	9.0 (5)	<0.001*
Performing tasks?	2.0 (6)	9.0 (4)	<0.001*
Engaging in sports?	3.0 (7)	9.0 (5)	<0.001*
Soles domain			
Putting on socks/ stockings?	2.0 (7)	5.0 (10)	<0.001*
Walking barefoot?	2.0 (10)	4.5 (10)	0.008*
Wearing sandals/ shoes?	2.0 (10)	4.0 (10)	0.004*
Performing tasks?	3.0 (10)	5.0 (10)	<0.001*
Engaging in sports?	3.0 (10)	5.0 (10)	0.001*
Axilla domain			
Sweating from axilla?	5.0 (10)	5.0 (10)	0.086
Changing clothes?	5.0 (10)	6.0 (10)	0.253
Performing tasks?	5.0 (10)	6.0 (10)	0.065
Social domain			
Shaking hands?	1.0 (6)	10.0 (3)	<0.001*
Socialising in public?	2.0 (10)	8.0 (10)	<0.001*
Hugging others?	4.0 (10)	7.0 (10)	0.003*
Personal domain			
Holding hands with partner?	3.0 (9)	9.0 (6)	<0.001*
Attempts to initiate intimate contact?	5.0 (10)	6.0 (10)	<0.001*
Psychological domain			
Body image?	4.0 (9)	6.0 (10)	0.001*
People acceptance?	4.5 (10)	7.0 (8)	<0.001*
Confidence?	3.0 (6)	8.0 (10)	<0.001*
Happiness?	4.0 (10)	8.0 (10)	<0.001*
Satisfaction in daily activities?	3.0 (10)	7.0 (10)	<0.001*
General well-being?	4.0 (9)	7.0 (8)	<0.001*
Confidence to socialise?	3.0 (7)	8.0 (8)	<0.001*

^aQuestionnaire in *Extended data*: Appendix 2, adapted from Milanez de Campos *et al*²⁵ and Keller *et al*²⁴;^bWilcoxon-test. Data is not normally distributed;*significant difference (postoperative-preoperative) (*p* <0.001).

Another significant finding is with regard to the number of locations of CS. By using Kruskal-Wallis test, we noticed a significantly lower general QOL reported in patients with CS involving more than two locations, as compared with those involving one location or two locations (*p*=0.008). Post-hoc Dunn test had demonstrated, in particular, a significant

Table 10. Summary of median postoperative quality of life (QOL) score from each domain (N=46)

		Time point		p value ^a
		Preoperative	Postoperative	
QOL_Hands	Median (IQR)	26.5 (53)	81.0 (37)	<0.001**
QOL_Soles	Median (IQR)	11.0 (40)	24.5 (50)	<0.001**
QOL_Axilla	Median (IQR)	15.0 (30)	17.5 (20)	0.087
QOL_Social	Median (IQR)	8.0 (20)	24.0 (20)	<0.001**
QOL_Personal	Median (IQR)	7.5 (18)	14.5 (15)	<0.001**
QOL_Psychological	Median (IQR)	25.0 (54)	50.0 (53)	<0.001**

^aWilcoxon-signed rank test. Data is not normally distributed;**significant difference ($p < 0.001$)**Table 11.** Summary for the descriptives of quality of life (QOL) improvement in each domain (N=46)

Domain	Postoperative QOL	N (%)	Average increment per question
Hands	Improved	46 (100)	5.86
	Same	-	
	Worsened	-	
Soles	Improved	24 (52.2)	1.97
	Same	16 (34.8)	
	Worsened	6 (13.0)	
Axilla	Improved	22 (47.8)	1.05
	Same	14 (30.4)	
	Worsened	10 (21.8)	
Social	Improved	44 (95.7)	5.12
	Same	-	
	Worsened	2 (4.3)	
Personal	Improved	33 (71.7)	3.82
	Same	9 (19.6)	
	Worsened	2 (4.3)	
Psychological	Improved	40 (87.0)	3.43
	Same	1 (2.2)	
	Worsened	5 (10.8)	

Table 12. Mean increment in total quality of life (QOL) score (N=46)

		Period		p value ^a	Mean difference (95% CI)
		Preoperative	Postoperative		
Total QOL Score	Mean (SD)	92.02 (52.13)	205.57 (39.96)	<0.001*	113.54 (92.52 - 134.57)

^aPaired *t*-test. Data is normally distributed. Assumptions were fulfilled;**significant at $p < 0.0001$

difference in median score between patients with one location and more than two locations ($p=0.024$) (Table 17). As illustrated in Figure 4, we can see an obvious downward trend of the median general QOL score from 'one location' box to 'two locations' and to 'more than two locations'.

Table 13. Correlation between various factors with general and total quality of life (QOL) score

	General QOL ^a r	Total QOL Score ^b r	p value
Occurrence of CS	-0.153	-0.207	0.309 ^a 0.167 ^b
Severity of CS	-0.543	-0.310	<0.001 ^{a ***} 0.048 ^{b *}
Number of locations of CS	-0.465	-0.331	0.002 ^{a **} 0.034 ^{b *}
Long term complications	0.084	-0.126	0.579 ^a 0.403 ^b

^aSpearman's rho correlation.^bPearson's correlation. Assumptions were fulfilled. r = correlation coefficient;*significant ($p < 0.05$);**significant ($p = 0.002$)***significant ($p < 0.001$); CS, compensatory sweating.**Table 14. Mean and median differences in the general and total quality of life (QOL) score between patients with compensatory sweating (CS) and without CS (N=46)**

		Occurrence of CS, N (%)		Mean difference (95% CI)	p value
		Yes 41 (89.1)	No 5 (10.9)		
Postoperative General QOL	Median (IQR)	7 (10)	8 (4)	-	0.303 ^a
Total QOL Score	Mean (SD)	202.71 (40.33)	229.00 (30.36)	29.29 (-11.45 - 64.03)	0.167 ^b

^aMann-Whitney test. Data is not normally distributed.;^bIndependent t-test.

Data is normally distributed. All assumptions were fulfilled.

Table 15. Mean and median differences in the general and total quality of life (QOL) score between patients with non-severe and severe compensatory sweating (CS) (N=41)

		CS severity, N (%)		Mean difference (95% CI)	p value
		Non-severe 24 (58.5)	Severe 17 (41.5)		
Postoperative general QOL	Median (IQR)	8.00 (7)	5.00 (8)	-	0.001 ^{a **}
Total QOL score	Mean (SD)	217.17 (33.47)	184.22 (41.63)	32.95 (9.24 - 56.66)	0.008 ^{a *}

^aMann-Whitney test. Data is not normally distributed.;^bIndependent T-test. Data is normally distributed. All assumptions were fulfilled;*significant ($p = 0.008$);**significant ($p = 0.001$)

Similarly, we also ran a test to study the association between number of CS location(s) and total QOL. By using individual *t*-test, patients with more than two locations of CS reported significantly lower total QOL score as compared to those with one location of CS, with a mean difference of 39.48 (95% CI=4.44 - 74.52, $p=0.029$) (Table 18).

Discussion

Our study has demonstrated a significant improvement in the general QOL of patients postoperatively, which is in keeping with most of the literature that supports the effectiveness of ETS in improving the general QOL of patients with PHH.^{12,13,14,22,28,29,30,31,32,33} By summing up the total QOL score from all domains, we noticed 44 (95.7%) patients had

Table 16. One-way ANOVA test for severity of compensatory sweating and total quality of life (QOL) score (N=41)

Severity, N (%)	Mean total postoperative QOL score	<i>p</i> value ^a	Mean difference (95% CI)
Mild 6 (14.6)	207.00	0.022*	36.54 (4.83 - 68.26) ^b
Moderate 17 (41.5)	220.76		
Severe 18 (43.9)	184.22		

^aOne-way ANOVA test was applied. Assumptions were fulfilled;*significant at $p < 0.05$;^bPost-hoc analysis: Bonferroni test was applied. Significant difference was found between moderate and severe compensatory sweating ($p=0.019$).**Table 17.** Kruskal-Wallis test for number of compensatory sweating location(s) and general quality of life (QOL) (N=41)

Number of location(s), N (%)	Median general QOL (IQR)	<i>p</i> value ^a
1 location 19 (46.3)	8.0 (10.0)	0.008*
2 locations 15 (36.6)	7.0 (6.0)	
More than 2 locations 7 (17.1)	5.0 (6.0)	

^aKruskal-Wallis test was applied. Assumptions were fulfilled;*significant at $p < 0.05$;^bPost-hoc analysis: Dunn test was applied. Significant difference was found between patients with only 1 location and more than 2 locations ($p=0.024$). **Figure 4.** Simple boxplot illustrating the median of general QOL score postoperative as categorised by number of location(s) of CS.

Table 18. Mean difference in total quality of life (QOL) score between patients with compensatory sweating (CS) in one location and CS in more than two locations

		Number of CS Location(s)		p value ^a	Mean difference (95% CI)
		1 location	More than 2		
Total QOL score	Mean (SD)	213.05 (39.97)	173.57 (33.26)	0.029*	39.48 (4.44 - 74.52)

^aIndependent t-test. Data is normally distributed. All assumptions were fulfilled;

*significant at $p < 0.05$

an improvement in the total QOL score with a mean improvement of score of 113.54 (SD=70.79, 95% CI=95.52 - 134.57), supporting the overall effectiveness of ETS in improving QOL ($p < 0.001$) (Table 12).

Among all domains that were asked in the questionnaire, functional domain of hands demonstrated the most profound improvement in QOL after the operation, as all patients (100%) reported an improvement in the QOL score after surgery, with a highest average improvement per question and mean score improvement of 53.48 (95% CI=46.91 - 60.04, $p < 0.001$) (Tables 10 and 11). This further supports the effectiveness of ETS in resolving sweating from palms. Apart from the functional domain, all other domains had also shown significant improvement in the QOL score when compared to the preoperative state. However, for the functional domain of axilla, the improvement was not statistically significant ($p = 0.087$) (Table 10). This can be explained by the majority occurrence of CS on the trunk which also had extended effect to the axillary region, leading to less QOL score given in this domain.

Overall satisfaction score was reported to be a median of 7 (IQR=4), with the most common cause of dissatisfaction being the occurrence of CS. As we compared satisfaction between non-severe CS and severe CS, there was significantly lower overall satisfaction in patients who had severe CS (Median=9.00 vs 5.00, $p = 0.001$) (Table 13). However, the occurrence of CS alone was not found to have a profound impact on overall satisfaction (Table 14). This is because satisfaction also comprises other elements other than the outcome of surgery such as consultation, hospitalisation services and other services provided.

When we examined the relationship between CS and QOL, we noticed that the severity of CS had a significant impact on the general and total QOL score. Comparing patients with non-severe CS, patients with severe CS reported much lower general and total QOL score ($p = 0.001$ and $p = 0.008$ respectively) (Table 15). For greater accuracy, further analysis was run using one-way ANOVA. It was noted that there was still a significant association between the severity of CS and total QOL score after the operation with $p = 0.022$. Patients who reported moderate CS had higher total QOL score than those with severe CS. (Mean difference=36.54, 95% CI=4.83 - 68.26, $p = 0.022$) (Table 16).

Furthermore, patients with a lower number of location(s) involved in CS reported better general and total QOL score. By using the *t*-test, patients who had CS in a single location reported a significantly higher total QOL as compared to patients with more than two locations of CS, with a mean difference of 39.48 (95% CI=4.44 - 74.52, $p = 0.029$) (Table 18). In short, even though we could not comment on the association between the occurrence of CS and QOL, we found significant association between both severity of CS and number of location(s) of CS with QOL score.

We also believe that there is a common assumption that CS will disappear or improve with time. However, Herbst *et al*³⁴ did not agree with this assertion as from their study for over fourteen years, the authors concluded that up to 67% of patients still reported permanent CS without improvement. In our study, the majority of patients (82.9%) with CS had persistent CS without improvement. Only 9.8% of patients reported resolved CS over time, with gradual improvement of CS reported in 7.3% of patients. This is of course a higher rate of CS persistence if compared to the study by Herbst *et al*³⁴ but of a shorter duration. The inconsistency of our data with the current literatures available with the lack of supporting literatures necessitates more studies to validate such assumptions.

One issue that must be discussed here is the relationship between CS and the extent or level of sympathectomy, which has been the subject of intense debate and controversies among surgeons. Although the optimal level of interruption and method of interruption remains debatable, it was suggested by The Society of Thoracic Surgeon expert consensus³⁵ for the surgical treatment of hyperhidrosis that the optimal operation for palmar hyperhidrosis is a T3 interruption with cauterizing or clipping as it has been shown to result in close to 100% symptom resolution. However, it is also reasonable to approach for T4 interruption. The expert consensus³⁵ also mentioned that interruption at T3 as compared with T4, poses a slightly higher risk of CS but provided better symptom resolution. Even though it is impossible to predict the risk

of CS, avoiding interruption at T2 and limiting the extent of interruption are currently the best method to reduce the risk of CS.

We would summarize that studies with high reliability and strength have shown that higher interruption resulted in greater risk of complications³⁶. Our centre, which carried out most surgeries involving T2 level, did not report any case of Horner's syndrome and few cases of gustatory sweating in five (10.9%) patients. Amongst the 8.7% of patients who had T2 spared, all of them experienced CS as well. However, this interpretation is reserved with a marked limitation noted in our study as our centre performed surgical interruption at the level of T2-T3 in the majority of cases (78.3%) with a great portion of patients falling into the T2-involved group (91.3%). Besides, we could not yield a similar finding to those found in our previous study¹⁷ as our sample size is relatively small compared to previous studies. Furthermore, as this study is a continuation of the previous study¹⁷, different study populations used in the different studies may explain variations in the results. However, we believe that more surgeries sparing T2 should be carried out in order for further analysis on such association to be done.

After an extensive literature search, we found that most studies have investigated CS and QOL as two separate entities. Among the few literatures that associated CS with QOL, the findings were inconsistent with one another. And in consonant to what was claimed by Hajjar *et al*²⁸ that there was no relationship between CS and postoperative QOL, our study did not find any significant relationship between the occurrence of CS itself and postoperative QOL as well (Table 14). This finding contradicted Dias *et al*¹⁴ who proposed that CS potentially worsens postoperative QOL. As we explored the effect of CS on QOL on other aspects, we found a significant association between QOL and severity of CS where poorer QOL was reported in patients who experienced severe CS (Tables 15 and 16). It was observed in certain cases that some patients had severe CS but reported a higher QOL than patients who had milder form of CS. This was because patients' ability to tolerate CS is subjective and will affect the QOL that they perceived. This finding was entirely consistent with findings reportedly done by Leiderman *et al*¹² and Wolosker *et al*¹⁶.

To date, we did not find any literature that has clearly demonstrated a relationship between the number of CS location(s) with QOL, not to mention that this factor might not be known to researchers. However, as described previously, we found a significantly lower postoperative QOL reported by patients in our study who had more than two locations involved in CS as compared to those with one location (Tables 17 and 18, and Figure 4). Therefore, we suggest the number of location(s) involved in CS to be considered as a confounder to postoperative QOL for future research. The clinical implication of this study is that with the high incidence of CS reported in this study and our previous study,¹⁷ which can be associated with the involvement of T2 resection, it may be proposed to our institute regarding reducing ETS surgery that involves T2 resection. This suggestion is backed by the literature, which claims that symptom resolution was not significantly different between T2-involved and T2-spared group, but incidence of CS was significantly higher in the T2-involved group^{26,36}. In addition, the expert consensus³⁵ of The Society of Thoracic Surgeons also supported the idea that ETS should avoid involving the T2 level as it may result in more complications and significantly higher risk of CS.

Limitations

Given the relative rarity of this surgery with less than 15 cases performed per year at our institute, we believe a longer duration of such retrospective study is more effective in capturing a higher number of patients. However, there were a few limitations in this study. First of all, the study design requires inclusion of telephonic follow-up. As with any research that involves telephone follow-up, reaching all participants was a difficult and tedious process because of changed or disconnected numbers and hence a few patients were lost. In addition, since the data was pre-recorded, there may be inaccuracy and inadequacy with regards to the history and examination notes. Furthermore, as data was collected from a single centre, this may potentially introduce selection bias. In addition, as the QOL questionnaire was applied postoperatively, there was also a risk of recall bias. We have taken a few steps, as mentioned in Methods, that were carried out and strictly adhered in order to reduce recall bias. Additionally, Cronbach alpha reliability test was run and showed poor internal consistency for the questions in the personal domain, which might affect the analysis that involve total QOL score. Finally, as this study also looked into the occurrence of CS and factors affecting it, a small sample size in the group of patients without CS has limited our analysis related to the occurrence of CS.

Conclusion

This study has managed to answer the pre-set research questions, on the QOL of patients after ETS compared with that before, as well as the secondary question of whether or not CS affects QOL of patients. Our study has proven the effectiveness of ETS in providing sustained improvement of QOL after the surgery, with remarkable resolution of sweating from the palms. Furthermore, overall satisfaction was reportedly high and not affected by the presence of CS or other long-term complications. These findings on the efficacy of ETS is largely in coherence with many other studies^{37,38,39,40,41,42,43,44,45} that recognise ETS as an effective treatment for PHH with a good safety profile. With regards

to CS, our institute reported a relatively high prevalence (89.1%) of the occurrence of CS, which can be attributed to two reasons. Firstly, the majority of our surgeries were performed involving the level of T2, which has been highly regarded by many researchers to increase the risk of CS and other complications. Secondly, as this rate is comparable to a study²⁸ done in a desert climate country of Saudi Arabia which reported prevalence of 92%, hence leading us to think that a hot climate, like in our own country, could be a confounder to CS.

To answer the second research question, we found no significant association between the occurrence of CS and QOL of patients. However, we noticed a significant relationship between severity of CS and QOL. In addition, we discovered a potential relationship between the number of location(s) involved in CS and QOL. It is worth noting that such association has never been clearly described or studied in other research before, to the best of our knowledge. We hope that this study will provide a research background for future researchers to confirm the number of CS locations as a confounder to postoperative QOL. Knowing the inadequacy of our study due to the small sample size, we believe an extension of current study with inclusion of more patients with spared T2 will be able to provide more convincing answers to the many questions that were limited due to its sample size.

Data availability

Harvard Dataverse. Replication Data for: Does endoscopic thoracic sympathectomy improve the quality of life of patients with primary hyperhidrosis? A single center retrospective review, <https://doi.org/10.7910/DVN/REQ7Y7>⁴⁶

This project contains the following underlying data:

- Set 1: Raw Data (.tab)
- Set 2: Output Data (PDF)

Extended data

Harvard Dataverse. Replication Data for: Does endoscopic thoracic sympathectomy improve the quality of life of patients with primary hyperhidrosis? A single center retrospective review, <https://doi.org/10.7910/DVN/REQ7Y7>⁴⁶

This project contains the following extended data:

- Set 3: Appendix 1: Questionnaire - Set 1 (PDF)
- Set 4: Appendix 2: Questionnaire - Set 2 (PDF)

Data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

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Stamatis Gregoriou

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The authors report improvement of QOL in patients with multiple site focal hyperhidrosis undergoing sympathectomy and presenting with compensatory sweating. Data on patients with multiple site focal hyperhidrosis are scarce in the literature so the data presented are of merit. The paper could improve with the following information added:

- According to all guidelines surgical procedures are 3rd line treatment in severe focal hyperhidrosis when other therapies have failed or are contraindicated. In the paragraph describing severity, data of severity in a validated scale such as HDSS would be welcome. Furthermore, data on previous therapies used by the patients should be presented as patients having tried most of the 1st or 2nd line treatments unsuccessfully would be more prone to have no compromise in their QOL even with CS.
- Are there any data on sites of hyperhidrosis not treated with ETS (such as the craniofacial region) developing exacerbation of hyperhidrosis after treatment? This is not included in the strict CS definition but has been mentioned in literature after other therapies (e.g. in my article: Gregoriou S. *et al.* Effects of botulinum toxin-a therapy for palmar hyperhidrosis in plantar sweat production. *Dermatol Surg.* 2010 Apr;36(4):496-8.¹). The article I mention evaluated worsening of hyperhidrosis in sites other than the ones treated. Since compensatory hyperhidrosis is defined as novel appearance of hyperhidrosis in sites that were previously sweating normally, it would be useful to know (if such information is available) if in the patients reporting facial hyperhidrosis (that could not improve after ETS) hyperhidrosis exacerbated after ETS.

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Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 10 June 2021

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Introduction

Musa A *et al.* present their experience with patients operated for hyperhidrosis due to bilateral sympathectomy. Initially, they offer a current review of the characteristics of the disease, its epidemiology, therapeutic alternatives, and forms of evaluation of surgical treatment are presented. The forms of evaluation of the results are exposed, presenting the analysis of quality of life as one of the main methods. The authors analyze the existing questionnaires. This study is based on an analysis of quality of life created by a group of researchers that contemplates the positive characteristics of several previous questionnaires. A retrospective study of 46 patients (initially 62) conducted in Malaysia comprising five years of bilateral sympathectomy between 2014

and 2018.

The failure in the introduction is the lack of a paragraph dedicated to the presentation of the questionnaire created for this study.

Methods

Clear. A retrospective study of 62 patients conducted in Malaysia comprising 5 years of BETS, between 2014 and 2018. The surgical techniques, methodology, and statistical analysis are straightforward.

Surgical techniques

Well described.

Quiz

Well presented.

Statistical analysis

Proper.

Results

Number of cases included. The authors explained in detail why the final number of patients studied has decreased to 46. The demographics of the patients were presented in detail, similar to the literature. They were patients with severe hyperhidrosis who presented the resolution for palmar HH in 97.8% of the patients, and the majority of patients with palmar-plantar HH reported persistent sweating from feet HH. Results consistent with the literature. Compensatory Sudoresis occurred in 89.1% of patients to some degree. Despite this, 95.7% reported improvement in the total QOL.

Demographics

Well presented.

Location of hyperhidrosis

Presented in great detail.

Severity

Clear.

Level of Sympathectomy

Clearly presented.

Compensatory Hyperidrosis

Well presented.

QOL

Well presented and interesting.

Discussion

Proper. The discussion was very appropriate, and once again, it is observed that ETS is a suitable

method for the treatment of palmar hyperhidrosis, despite compensatory hyperhidrosis.

Conclusions

Adequate.

Is the work clearly and accurately presented and does it cite the current literature?

Yes

Is the study design appropriate and is the work technically sound?

Yes

Are sufficient details of methods and analysis provided to allow replication by others?

Yes

If applicable, is the statistical analysis and its interpretation appropriate?

Yes

Are all the source data underlying the results available to ensure full reproducibility?

Yes

Are the conclusions drawn adequately supported by the results?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Hyperhidrosis

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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