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Is an endoscopic thoracic sympathectomy (ETS) at the T2 level effective in resolving palmar hyperhidrosis and resulting in patient satisfaction?

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

December 13, 2019

ABSTRACT

OBJECTIVE: The objective of this selective evidence-based medicine (EBM) review is to determine whether or not “Is an endoscopic thoracic sympathectomy (ETS) at the T2 level effective in resolving palmar hyperhidrosis and resulting in patient satisfaction?”

STUDY DESIGN: Systematic review of three randomized control trials published in 2009, 2016, and 2017, all in the English language. Studies were analyzed and reviewed based on population, intervention, and outcomes measured.

DATA SOURCES: Three randomized controlled trials where all published in peer-reviewed journals and researched using the PubMed and CINAHL databases.

OUTCOMES MEASURED: All three studies measured the presence or absence of palmar hyperhidrosis (PH) and/or compensatory hyperhidrosis (CH) via patient report and physical examination. All studies also measured patient satisfaction through patient questionnaires.

RESULTS: All patients in the studies except one showed immediate anhidrosis postoperatively and no PH recurrence. Despite great initial postoperative results, many patients developed CH symptoms. Patient satisfaction rate was high in all three articles reviewed.

CONCLUSIONS: The results from this systemic review suggest an endoscopic thoracic sympathectomy (ETS) at the T2 level is adequately effective in resolving palmar hyperhidrosis and resulting in patient satisfaction.

KEY WORDS: Sympathectomy, Hyperhidrosis, Randomized Control Trial

INTRODUCTION

Palmar hyperhidrosis (PH) is an excessive, uncontrollable, sweating of the hands. PH occurs equally in both genders and can be present at any age, but tends to affect adolescents and young adults most often due to the increased activation of eccrine sweat glands during puberty.^{1,2} In the US, 15.3 million individuals are estimated to be living with hyperhidrosis on varying bilateral cutaneous body regions, with 0.3-4.5% of the general population having the condition confined to just their palms.^{2,3} There is increasing evidence for a genetic component to the condition since most patients present with a family history.¹ The sweating is thought to be caused by a benign, idiopathic hyperfunctioning of the sympathetic nervous system in thermoregulation of the body in response to normal heat or exercise.¹ The excessive diaphoresis can seriously disrupt a person's daily professional, emotional, and social lives potentially leading to lost opportunities and problems of a psychosocial nature.⁴

Many patients learn to live with their condition despite the effect it has on their quality of life as they do not realize it is treatable. The small group that do seek treatment usually do so through a dermatologist who may initially suggest a number of creams, lotions, or antiperspirants for the patient.⁵ Patients can also receive Botox injections, microwave therapy, or an endoscopic thoracic sympathectomy (ETS).⁴ The total healthcare cost of PH has not been identified since treatments and their expense vary greatly. Certain over the counter options can cost \$8-20, whereas more aggressive treatments, such as surgery, can cost up to \$20,000.³ Additional expenses include frequent new clothing, dry cleaning, and other specific absorbent pads, towels, or fabrics for daily disease management. Many conservative treatments for palmer hyperhidrosis are found to be unsuccessful and unsatisfactory, leading some patients to instead opt for the more definitive solution of surgery.² Currently, the ETS is the most effective and definitive therapeutic

approach to the treatment of PH.¹ The specific neural ganglion level of the ETS performed is still debated by the medical community.⁶

OBJECTIVE

The objective of this selective EBM review is to determine whether or not “Is an endoscopic thoracic sympathectomy (ETS) at the T2 level effective in resolving palmar hyperhidrosis and resulting in patient satisfaction?”

METHODS

In this selective evidence-based medicine (EBM) review, three randomized control studies were analyzed and reviewed based on population, intervention, and outcomes measured. The population includes adults or young adults with palmar hyperhidrosis. Experimental intervention reviewed was an ETS at T2 and compared to ETS at other levels (T3^{1,2}, T2-T3⁶). All patients that participated in the study were blind as to which ganglion level their EST surgery was being performed at. The degree of patient satisfaction with relation to resolution, reoccurrence, incidence, or severity of PH or compensatory hyperhidrosis (CH) were the measured outcomes.

The three articles studied were published in peer reviewed journals, selected using the research databases of PubMed or CINAHL, all written in English, and dated from 2009-2017. Keywords used in the searches included “hyperhidrosis,” “sympathectomy,” and “randomized control trial.” Articles were chosen based on their relevance and inclusion of patient-oriented outcomes (POEMS). Other inclusion criteria were full text RCT studies done on humans published after the year 2008. Exclusion criteria included systematic reviews published before 2008 and any animal studies. These three studies reported statistics as NNT, EER, CER, RBI, ABI, and/or p values. Characteristics of each study are outlined in Table 1.

Table 1. Demographics & Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Yazbek¹ (2009)	RCT	60	16-30	Those with PH, otherwise healthy	“patients with prior thoracic surgery, cardiac diseases, pulmonary infection, neoplasia or pleural or lung diseases that could increase surgical risk, or with a body mass index (BMI) greater than 25” ¹	3	ETS at denervation level of T2 VS. T3 ganglion
Turkyilmaz² (2017)	RCT	50	17-28	Patients who felt handicapped due to PH and in which conservative treatments had failed	Not reported	0	ETS at level of T2 VS. T3
Ong⁶ (2016)	RCT	39	14-58	Patient with PH	Those with secondary causes of PH: hyperthyroidism, chronic infections, malignancy, and immunological disorders ⁶	17	ETS at single level T2 VS. multi-level T2-T3

OUTCOMES MEASURED

The primary outcome measured in all three studies was the presence or absence of PH and/or compensatory hyperhidrosis (CH) via patient report and physical examination of patients who were originally diagnosed with PH. All studies also measured patient satisfaction through questionnaires, though questionnaires varied between the studies.

RESULTS

All three randomized control studies compared two groups that underwent ETS and resulted in no mortality.^{1,2,6} Two studies had one group receive bilateral ETS at ganglion level of T2, while the other group's ETS were completed at the T3 level.^{1,2} In the third study all patients undergoing ETS received a T2 level ablation on one side of the body and a combined T2-T3 level ablation on the other side, with the two groups differing in which side of the body was used for each ETS ganglion level type.⁶ Patients were selected randomly for their group of treatment and all blind to the ETS level performed in all studies. Demographics, inclusion criteria, and exclusion criteria for all the studies can be seen in Table 1.

In the Yazbek et al.¹ study each group equally consisted of 30 patients. Patients had five clinical assessments through the study to assess for palmar anhidrosis, CH, and patient degree of satisfaction using the quality-of-life protocol classifying satisfaction into five levels.¹ Three patients (5%) were lost from the study during follow up and not included in later assessments.¹ The baseline assessment, in the immediate postoperative period, found all patients reported anhidrosis.¹ Only one patient in the T3 group denied anhidrosis at the next assessment 1 week after surgery; they had a second negative outcome following a repeat surgery and was deemed a case of "therapeutic failure."¹ At the subsequent three return assessments at one month, six months, and between 12-34 (mean of 20) months post-surgery all other patients continued to

have no PH recurrence.¹ This study resulted in varying severity of CH for all patients of both groups by the final assessment postoperatively as seen in Table 2. Association between ETS level and surgery results or complications were investigated using the chi-square of Fisher exact test.¹ The patient who experienced a “therapeutic failure,” was not included in the last two assessments for CH due to the timeline coinciding with their repeat surgery.¹ The two compared procedures at T2 or T3 were not statistically significant for either producing a lesser rate of CH presence compared to each other, but the T3 procedure was statistically significant in resulting in a non-severe form of CH instead of severe CH compared to the T2 procedure at all three later postoperative.¹ The quality-of-life protocol measured patient satisfaction by classifying a summed total score of the questionnaire completed by patients into five levels based on “situations in daily life in which hyperhidrosis might interfere,” seen in Table 3.¹ On average, in both groups, all patients’ quality-of-life was considered very poor preoperatively, then improved to excellent in all those still able to be assessed postoperatively. There was no statistically significant improvement in quality of life and therefore patient satisfaction with the procedure done at T2 as compared to T3.¹

Table 2. CH Presence and Severity After ETS as Measured by Yazbek et al.¹ 2009

	1 month		6 months		20 months	
	T2:T3	p value	T2:T3	p value	T2:T3	p value
Without CH	4:3	>0.999	0:1	NA	0:0	NA
With CH total	26:27		30:29		28:29	
Non-severe CH	16:27	<0.001	20:26	=0.033	15:25	=0.007
Severe CH	10:0		10:3		13:4	

NA: couldn't evaluate; CH compensatory hyperhidrosis; p-value <0.05 statistically significant

Table 3. Patient Satisfaction Total Scores of Quality-of-Life Protocol by Yazbek et al.¹ 2009

	T2	T3	p value
1 week preop (median)	92 (67-100) Very Poor	87.5 (75-100) Very Poor	0.3052
1 month postop (median)	23 (20-47) Excellent	23 (20-42) Excellent	0.8423
6 month postop (median)	24 (20-56) Excellent	24 (19-52) Excellent	0.3905
20 month postop (median)	26 (20-52) Excellent	29 (21-43) Excellent	0.7609

Total score range of 20-100; Score >84 as Very Poor, 69-84 as Poor, 52-68 as Good, 36-51 as Very Good, and 20-35 as Excellent; p-value <0.05 statistically significant

In the Turkyilmaz et al.² study, each group equally consisted of 25 patients. All patients in both groups presented with palmar anhidrosis immediately after surgery.² All subjects were interviewed, assessed, and physically examined for PH recurrence, CH, and patient satisfaction postoperatively at 1 month and 10-16 months (median 13) with no loss to follow up.² No recurrence of PH occurred to any subjects during this study, nor any CH within the first month.² At one year follow up, three patients in the group T2 ETS and two from the T3 ETS group exhibited signs of CH on the back or abdomen, though only one subject from group T2 found their symptoms to be severe leading to dissatisfaction of the procedure performed.² Overall both groups experienced high patient satisfaction rates throughout the study with their specific scoring found in Table 4. Using the chi-square test comparisons, neither CH or patient satisfaction rates were found to be statistically significant between the two ETS ablation level groups (p values: 0.637 and 0.203 respectively; p-value <0.05 statistically significant).²

Table 4. Patient Satisfaction Scoring by Turkyilmaz et al.² 2017

	Satisfaction:	Excellent	Satisfactory	Unsatisfactory	Total Patient Satisfaction	Total Patient Dissatisfaction
1 month	T2 (n=25)	25 (100%)	0	0	100%	0
	T3 (n=25)	25 (100%)	0	0	100%	0
Median 13 months	T2 (n=25)	22 (88%)	2 (8%)	1 (4%)	96%	4%
	T3 (n=25)	23 (92%)	2 (8%)	0	100%	0

In the long-term Ong et al.⁶ study 25 of the 39 patients had their combined T2-T3 ETS on the right side and the single T2 ETS on their left side of the body. The other 14 patients had the same procedures performed on opposite sides. Immediately after surgery, all 39 patients exhibited anhidrosis of the palms bilaterally.⁶ Twelve patients (43.6%) were lost in the years following procedure.⁶ An observer, who was also blind to the ganglion level of each patient's procedure, assessed all the remaining patients via telephone interview for any PH recurrence, CH, and patient satisfaction.⁶ To compare T2 single level verse T2-T3 multi-level ablation, "the

level of sympathectomy on one side was matched to the ipsilateral recurrence of palmar hyperhidrosis, the site and the severity of compensatory sweating for body parts that were not found in the midline (axilla and lower limbs specifically).⁶ This study followed the International Hyperhidrosis Society's disease severity scale but used a grade system instead of points.⁶ Four of the 22 patients successfully contacted later in the study had developed a recurrence of PH bilaterally, though it was milder than their preoperative symptoms.⁶ Twenty patients experienced some bilateral CH in varying forms and found the most common site of CH to be the trunk.⁶ For patients experiencing PH and/or CH there was, "no absolute difference in the severity of sweating," between the two ETS group levels.⁶ Overall, 16 of the 22 final study participants were satisfied with their ETS results.⁶ Those that were not satisfied in the Ong et al.⁶ study reported it being due to forms of PH recurrence in 2 patients or CH in 4 patients. Similarly, patient satisfaction was also not found to be significantly higher in one ETS group than the other. All results for Ong et al.⁶ found in Table 5.

Table 5. Long-term Clinical Outcomes of Both ETS Groups Measured by Ong et al.⁶ 2016

Outcomes	Scale	Results (n=22)	Totals (n=22)	
PH Recurrence	No	18 (81.8%)	No	18 (81.8%)
	Yes (mild)	2 (9.1%)	Yes	4 (18.2%)
	Yes (moderate)	0		
	Yes (severe)	2 (9.1%)		
CH	No	2 (9.1%)	No	2 (9.1%)
	Yes	20 (90.9%)	Yes	20 (90.9%)
Patient Satisfaction	Very Satisfied	13 (59.2%)	Satisfied	16 (72.8%)
	Satisfied	3 (13.6%)		
	Dissatisfied	3 (13.6%)	Dissatisfied	6 (27.2%)
	Very Dissatisfied	3 (13.6%)		

Comparisons of all three studies can be seen in Tables 6 and 7. All but one patient in the three studies experienced immediate postoperative anhidrosis.^{1,2,6} Specifically, for those with the T2 level ETS, the surgery was 100% successful in achieving instant anhidrosis. Out of three, a single study had recurrence and did involve ETS at T2 at a rate of 22%, which was only slightly

higher than the typical report average of 18%.⁶ Despite great initial postoperative results, in each study many patients developed varied CH symptoms across the board with different ranges in comparison to the usual average of 60%.⁶ No specific ETS level reviewed was able to completely avoid the CH effect. Patient satisfaction rate in general and specifically for T2 ETS was high in all three articles reviewed.^{1,2,6}

Table 6. Treatment Effects on Patient Satisfaction of Included Studies

Study	Yazbek et al. ¹	Turkyilmaz et al. ²	Ong et al. ⁶
CER	0.9655	1.0	No data due to study data being presented as combined not compared
EER	1.0	0.92	
RBI	0.0357	0.0417	
ABI	0.0345	-0.04	
NNT	-29	-25	
Treatment effect p-value	0.7609	0.203	No comment

p-value <0.05 statistically significant

Table 7. Comparison of Full Final Results of Included Studies and Their T2 Groups

Study	Avg ETS postop	Yazbek et al. ¹		Turkyilmaz et al. ²		Ong et al. ⁶	
		Full	T2	Full	T2	Full	T2
Initial Anhidrosis		59/60=98%	30/30=100%	50/50=100%	25/25=100%	39/39=100%	All subjects had ETS T2 done bilaterally (with 1 side also T3) Results same as Full study
PH recurrence	18% ⁶	0/59=0%	0/30=0%	0/50=0%	0/25=0%	4/18=22%	
Final CH Values	60% ⁶	57/57=100%	28/28=100%	5/50=20%	3/25=12%	20/22=91%	
Severe CH		17/57=30%	13/28=46%	0/5=0%	1/3=33%		
Final Pt Satisfaction		57/57=100% Excellent	28/28=100% Excellent	49/50=98% Satisfactory	29/50=96% Satisfactory	16/22=73% Satisfied	

DISCUSSION

As stated previously, conservative treatments for PH usually produces unsatisfactory results. In the past however, that was all patients were offered. Today a multitude of conservative and more invasive options are offered, with the most definitive treatment being the ETS.¹ This permanent surgical procedure, performed under anesthesia and lasting less than one hour, attempts to block signals from the sympathetic nerve trunk to sweat glands by destroying their neural pathways through cauterization or ablation.^{3,6} This procedure can be confirmed in the operating

room by an increased temperature reading on a finger prob.⁶ To do this a lung may be temporarily collapsed for access to the nerve pathways in question. At the end of surgery any residing air is evacuated from the pleural space and postoperatively patients undergo routine “chest radiography to exclude pulmonary or pleural abnormalities.”² Thoracic sympathectomies had high morbidity rates in the past, that were improved as videothoracoscopy was developed.¹ Today videothoracoscopic sympathectomy is considered the “surgical technique of choice,” due to success rates, increased safety, further development of the technique, more experienced surgical teams, minimized invasiveness, and the esthetically pleasing result.^{1,2,6} Standardizing as much of the procedure process is important to help prevent adverse outcomes.²

If the ETS does not immediately improve the PH it is usually due to sympathetic level incomplete ablation or mistaken anatomic structure cauterization and therefore an “inadequate sympathectomy,” which can lead to more postoperative complications.^{1,6} With a failed result, most providers encourage a repeat procedure, which will usually receive the desired anhidrosis result.^{1,6} Pleural adhesions from the first surgery can make a subsequent procedure difficult and leading to possible “anatomic variations” in the surgeons technique.⁶ If there is still no improvement, as seen in the Yazvek et al.¹ study patient, the subject may have experienced a rare phenomenon called the “neurologic escape route,” where the body’s sympathetic signals to the sweat glands evade blockage.¹ Common complications of ETS include, but are not limited to, PH recurrence, CH, overly dryness to previously hyperhidrosis effected areas, Horner’s syndrome, pneumothorax, subcutaneous emphysema, and/or prolonged hospital stays. All of these potential side effects can in turn effect a patient’s perception of their procedures success. CH is the most frequent ETS complication and the most feared due to its drastic effect on patient satisfaction scores.^{1,6} CH normally occurs in the first 8 weeks to 1 year postoperative, can range from mild to

severe enough to effect activities of daily living(ADLs), can effect multiple body regions such as the face, axillae, trunk, abdomen, back, groin, lower limbs, and feet, and is so significant that it has been named the “quality marker of ETS.”^{1,2,6}

Some limitations of this review or the studies it assess include small sample size, sample population, study length, classification definitions, and geographical location. PH occurs most often in young healthy patients, which can be problematic due to this populations tendency to migrate and thus not follow up with studies.⁶ Longer study length is shown to be more effective in capturing true patient outcomes that may not appear in the initial time frame, but may - No study had standardized terminology for CH, CH severity, or patient satisfaction. Yazbek et al¹ study classified CH as a place of diaphoresis on the body that was not present to surgery but didn't distinguish if this includes only constant sweating or exclude any due to heat or exercise. In comparison, Ong et al⁶ modified an international society scale to define hyperhidrosis and labeled the most severe CH category as symptoms effecting ADLs.⁶ The other two studies arbitrarily granted patient preference for CH symptom severity.^{1,2} All studies focused on different body areas for CH occurrence: Yazbek et al.¹ focused on the feet, legs, back, abdomen, and gluteal region; Turkyilmaz et al.² focused on the back, waist, groin, and legs; Ong et al.⁶ focused on the trunk, axillae, face and groin. Patient satisfaction was also not standardized between questionnaires, which varied from study to study. It was unclear if dissatisfaction included embarrassment, different diaphoresis thresholds such as being visible to others or if frequent changing of clothing was needed. It is theorized that climate could effect CH rates, such as those from the Yazbek et al. study¹ located in Brazil and the Ong et al.⁶ study located in Singapore. Areas with higher year-round temperatures may lead to more sweating in general and thus falsely elevate CH incidences.^{1,6}

CONCLUSION

The results from this systemic review suggest an endoscopic thoracic sympathectomy (ETS) at the T2 level is adequately effective in resolving palmar hyperhidrosis and resulting in patient satisfaction. All patients in the studies except one showed immediate anhidrosis postoperatively and no PH recurrence.^{1,2,6} Longer studies in the future would be even better at observing if PH recurrence is a possibility. Despite great initial results, many patients developed undesirable CH symptoms without much improvement overtime. Despite high rates of CH in the Yazbek et al.¹ and Ong et al.⁶ studies, the overall patient satisfaction rate was high in all three articles reviewed. Future research, on the subject of PH, would benefit and better represent truer patient outcomes and satisfaction levels if gathered over a longer time period, from a larger population, and/or in a less tropical study location climate. Standardizing definitions used in all studies on PH would help to improve the significance of their results and comparisons between similar research. Also, more tangible test results from sweat tests may help in refining the hyperhidrosis terminology.

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