Published in final edited form as:

Clin Auton Res. 2011 February ; 21(1): 3–10. doi:10.1007/s10286-010-0078-2.

HEMODYNAMICS FOLLOWING ENDOSCOPIC THORACIC SYMPATHOTOMY FOR PALMAR HYPERHIDROSIS

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Abstract

Purpose—We studied patients with palmar hyperhidrosis before and after endoscopic thoracic sympathectomy (ETS) to determine the effect of chronic sympathetic denervation on 1) forearm blood flow (FBF) response to mental stress and 2) exercise tolerance.

Methods and Results—22 healthy patients were evaluated before ETS, and 17 returned after surgery (11 F; 19–32 yr). We measured heart rate (HR; 12-lead), blood pressure, and FBF (plethysmography, ml/100ml forearm volume/min). Supine HR tended to decrease after ETS (69 ± 10 vs 66 ± 6 , $p=0.2$). Mental stress FBF was recorded during baseline, 3 min Stroop Color Word test, and 2 min recovery. Mental stress responses were unaffected by ETS. However during post-mental stress recovery period, ETS resulted in a significant elevation in FBF (2 ± 1 vs 3 ± 1), FVC (3 ± 1 vs 4 ± 2), and a decrease in FVR (52 ± 22 vs 32 ± 16 , $p < 0.01$ for all). ETS resulted in a reduction in pre-exercise seated baseline HR (94 ± 2.5 beats/min preoperatively vs 84 ± 4.3 beats/min post-operatively, $p < 0.05$), maximal HR response to cycle exercise, and exercise systolic blood pressure (172 ± 5.2 mmHg pre-op vs 158 ± 5.9 mmHg postop, $p < 0.05$) but not mean or diastolic pressure. VO_2 max and exercise duration determined by cycle ergometry was unchanged.

Conclusions—Functional evidence of upper limb denervation is observed during the FBF recovery period from mental stress and hemodynamic alterations associated with upright cycle exercise. However, the sustained exercise capacity suggests modest clinical consequences.

Keywords

hyperhidrosis; mental stress; exercise testing; sympathectomy

Introduction

Palmar hyperhidrosis is an idiopathic phenomenon characterized by excessive sweating of the palms. Severe cases result in physical, professional, and social debilitation. The eccrine sweat glands in the palms are innervated by sympathetic cholinergic fibers from the

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Disclosures: none

sympathetic chain. The T-2 sympathetic ganglia provide the largest proportion of post-ganglionic input to the upper extremities. Therefore, surgical sympathectomy for treatment of palmar hyperhidrosis have traditionally consisted of excision or electrocautery ablation of the thoracic T-2 and T-3 sympathetic ganglia [1]. While this upper extremity denervation is effective at reducing palmar sweating, there are concerns about excessive compensatory hyperhidrosis of the trunk observed in 10–40% of cases. Since there are also cardio-acceleratory fibers in the upper thoracic sympathetic chain, sympathectomy results in a “beta blocker” effect on the heart as observed by a reduction in resting heart rate (HR) and maximal HR achieved with exercise [2].

Recently, our institution has modified this technique by preserving the ganglia and performing a simple chain disconnection between the T-2 ganglion and the stellate ganglion [3]. Termed “endoscopic thoracic sympathectomy” (ETS), the sympathetic chain disruption to the upper extremity has minimal perioperative morbidity and immediate postoperative results [3]. Importantly, this surgical technique minimizes postoperative compensatory hyperhidrosis [3]. This technique results in a more selective denervation in the *distal* extremities and lesser area of anhidrosis; therefore there is less compensatory sweating as compared with the traditional sympathectomy which can result in denervation of the entire arm and some of the upper chest.

While more is known about the traditional sympathectomy procedure, there is limited information available regarding the long-term cardio-circulatory effects of the ETS procedure related to physiological stressors. We used two types of laboratory stressors, mental stress and exercise testing, to examine the function of the cardiovascular systems in palmar hyperhidrosis patients pre- and post-ETS. Our laboratory has shown that mental stress increases forearm blood flow (FBF) and decreases forearm vascular resistance (FVR) and upper extremity muscle sympathetic nerve activity [4].

The purpose of this study was to compare the forearm vasodilator responses to mental stress and the hemodynamic response to exercise in patients with palmar hyperhidrosis before and after ETS. A related study on baroreflex sensitivity and heart rate variability is reported in a companion submission by Schmidt et al.

Methods

Subjects

We prospectively enrolled 22 patients with palmar hyperhidrosis (mean age=25.5, sd=7.0, 77% female). Data was collected on 22 patients before surgery and due to geographic constraints in 5 patients, 17 (77%) were able to repeat the protocol 1 to 12 months following surgery. Post-ETS, all patients were interviewed by one investigator (JE) to assess perceived effectiveness of surgical procedures on symptom presentation (the 5 absent patients received a phone interview). A comprehensive neurologic evaluation was performed in the autonomic laboratory and all patients elected to proceed with ETS prior to enrollment. Patients were generally healthy and excluded if they had a history of any cardiovascular disorders or take medications that may prohibit exercise testing or affect baroreflex sensitivity. Any patient diagnosed with (or taking medication for) hypertension, heart disease, diabetes, hyperlipidemia, on pulmonary diseases such as asthma or chronic obstructive pulmonary disease was excluded. Patients were instructed to abstain from food or beverage for 6 hours prior to study, and abstain from alcohol or exercise within 24 hours of study. We also completed a post-hoc comparison on pre-and post-ETS surgery resting and mental stress data to a matched sample of healthy controls who have undergone the identical mental stress protocol in our laboratory [5]. Healthy controls were matched on age and sex to patients, and were non-obese, normotensive, non-smokers, and not taking any medications except oral

contraceptives in females. There was no significant difference in age between the patient and healthy control groups (24.4 vs. 25.2, $p=.650$).

Preoperative and postoperative study day procedures

This study involves 2 identical experimental visits: a preoperative (1 – 6 mo before ETS) and postoperative (1 – 12 mo after ETS). Supine resting blood pressure (finometer), heart rate (HR, 12-lead ECG), and FBF (venous occlusion plethysmography) were assessed in all subjects on both study days. In addition to resting measures, there were two interventions performed on each day: mental stress and cycle ergometer exercise for determination of incremental cardiovascular responses and maximal oxygen consumption (stressors described below).

Postoperative study day scheduling

The post-operative follow up interval (1–12 mo) was chosen for several reasons. First, in other studies, the cardiovascular adaptations to sympathectomy are complete by 30 days following surgery, and have remained unchanged in studies examining cardiovascular function for up to 2 years postoperatively [2,6,7]. Second, the generally accepted recovery duration following surgery is 30 days. Third, a wide postoperative interval was necessary for patient convenience, as many of the patients did not reside near our institution.

Mental Stress Protocol

A computerized version of the Stroop colored word conflict test [8] lasting 3 minutes was administered to induce mental stress similar to the protocol used previously in our laboratory [9,10],[4]. To maximize the stress induced, one investigator used an ordered script of phrases in consistent time increments to minimize variation in the “dose” of mental stress urging each subject to respond faster and to concentrate fully throughout the test. Following two minutes of baseline, printed instructions were read aloud to each subject. The instructions remind subjects that best effort is required and that their performance on the test will be compared to the other subjects. Data were obtained continuously and averaged by minute of the protocol.

Whole-body maximal O₂ uptake (VO₂) bicycle test)

HR was recorded by 5-lead ECG and blood pressure was measured with manual sphygmomanometry prior to and during exercise while the subject was seated on the bicycle. VO₂ was measured by using a breath-by-breath mass spectrometry system previously validated against the Douglas bag collection technique across a broad range of breathing frequencies [11]. Subjects performed a standard incremental bicycle exercise test to exhaustion to determine peak O₂ uptake [12]. After a 5 min warm-up period of light cycling, the workload was increased by 20, 25 or 30 W every minute. All subjects were expected to reach subjective exhaustion (rating of perceived exertion = 19–20) within 8–12 min, and achieve a respiratory exchange ratio (rate of CO₂ production/VO₂) > 1.15, as well as a peak HR within 10 % of the age-predicted maximum. In order to reach exhaustion, each subject had a different total time of cycling and data are reported as a percentage time to completion of the test with 0% being the onset of exercise and 100% being cessation of cycling due to exhaustion.

Statistical analysis

Pre- and post-operative average measurements at baseline, during mental stress, and recovery, and exercise testing hemodynamic variables were analyzed by a repeated measures ANOVA with Tukey's post-hoc analysis. Significance was determined if $p<0.05$.

Only data from subjects who completed both pre and post operative studies was analyzed in the repeated measures ANOVA (n=17).

Results

Subject Demographics and Surgical Results: Table 1

Individual results are presented in Table 1. All subjects were satisfied with the ETS procedure results. Importantly, all subjects reported a reduction in palmar sweating with minimal or non-bothersome compensatory hyperhidrosis. This relevant data is supportive of the self reported “satisfaction” rating for the procedure. Preoperatively, subjects underwent a thermoregulatory sweat test (TST). TST was how a reduction in compensatory hyperhidrosis was evaluated previously post-operatively [3]. Presently, our postoperative patients are given the option of undergoing a repeat TST and nearly all of them decline due to discomfort (heat stress) in the TST combined with overall reported satisfaction in the outcome of the procedure.

Hemodynamics: Table 2

On the post-op screening visit, supine resting 12-lead ECG tended to decrease HR as compared to the pre-operative visit (69 ± 10 vs 66 ± 6 , $p=0.2$); however, immediately prior to mental stress (in a semi-recumbent chair) the baseline HR recorded over 2 minutes was lower in patients that had undergone ETS ($p<0.01$). In addition, the absolute HR during MS and during recovery was reduced post operatively ($p<0.01$). However, delta HR from baseline to mental stress and during recovery was not affected by ETS. In other words, there was a difference in pre-stress baseline HR related to the ETS procedure but the response to, and recovery from mental stress was unchanged. Also shown in Table 2, ETS did not affect the absolute or delta systolic and mean blood pressures in the mental stress protocol. The absolute diastolic pressure during pre-stress baseline and recovery from MS, but not during MS, was reduced following ETS ($p < 0.05$).

Forearm Vascular Function

As shown in Figure 1, ETS did not change baseline FBF (Figure 1A) or FVC (Figure 1B) at rest; however, baseline FVR (Figure 1C) was decreased following the ETS procedure. During the 3-minute MS protocol there was no difference in pre- vs post-operative values for FBF, FVC, or FVR (MS1, MS2, and MS3; Figure 1A, 1B and 1C). The most striking difference occurred in the 2-minute post-MS recovery period (Rec 1 and Rec 2; Figure 1A, 1B, and 1C) during which there was a significant increase in FBF and FVC and a decrease in FVR post-operatively. In comparison to age- and gender-matched healthy controls, the baseline FBF was not different between hyperhidrosis patients and control subjects (pre-op 2.3 ± 0.3 , post-op 2.9 ± 0.2 , healthy control 2.4 ± 0.2 ml dl⁻¹ min⁻¹, $p=0.22$). Similarly, delta FBF from baseline to 2-min post-mental stress recovery was not different between pre-op condition, post-op condition, and control subjects (-0.2 ± 0.07 , 0.3 ± 0.04 , -0.2 ± 0.04 ml dl⁻¹ min⁻¹), respectively, $p=0.14$). This indicates that the change in FBF from baseline to stress and baseline to recovery was similar when comparing all 3 conditions, but when hyperhidrosis patients served as their own controls, the effect of ETS on absolute FBF, FVC, and FVR was suggestive of upper extremity sympathetic denervation.

Exercise testing: Figures 2 and 3

ETS resulted in a reduction in average maximum HR achieved during cycle ergometry (Figure 2A; 193 ± 3.2 beats/min pre-operative versus 182 ± 3.2 beats/min post-operatively, $p<0.05$). Likewise there was a reduction in average systolic blood pressure achieved at the end of exercise testing post-operatively (Figure 2B; 172 ± 5.2 mmHg pre-op vs 158 ± 5.9

mmHg post-op, $p < 0.05$). Despite a reduction in exercise HR and systolic blood pressure, there was no difference in the estimated maximal oxygen consumption (Figure 2C). HR was tracked over time during exercise and the results are shown in Figure 3. There was a reduction in seated pre-exercise baseline HR on the bike post-operatively (94 ± 2.5 beats/min pre-operatively vs 84 ± 4.3 beats/min post-operatively, $p < 0.05$). This lower HR is observed throughout the entire exercise protocol with significant reductions also observed at 25, 50, and 75% time to completion of testing ($p < 0.05$).

Discussion

Postoperative compensatory hyperhidrosis is an irreversible, debilitating, and unfortunately widespread consequence of traditional sympathectomy procedures that may cause greater dissatisfaction than the original diagnosis of palmar-plantar hyperhidrosis, and ultimate regret of surgical treatment. ETS surgery at our institution is a simple sympathetic chain disconnection between the stellate and T2 ganglion. The goal of this minimal “sympathotomy” (ETS) is to selectively denervate the distal forearm and hand in order to reduce the severity of post-operative compensatory hyperhidrosis observed with sympathectomy [3]. By conducting a repeated measures comparison before and after ETS in the same patients, this is the first study to determine the effect of chronic sympathetic denervation on cardio-circulatory responses to mental stress and exercise testing. Our findings and those in a companion submission by Schmidt et al. suggest that in the first year following ETS for hyperhidrosis, there are detectable alterations in cardiovascular control, but these differences likely have modest clinical or functional consequences.

Forearm Vascular Function

Our laboratory has demonstrated that resting skin blood flow and forearm vascular function is largely preserved after ETS [12,13]. The present study examined the forearm vasodilator response to mental stress and determined that the known increase in FBF to this emotional stressor was not affected by ETS. Since the sympathetically denervated forearm has a similar vasodilator response to mental stress as the innervated forearm, it suggests a minimal role for upper extremity sympathetic nerve support of vasodilation to mental stress. However, postoperatively there was a significantly higher FBF post-stress during the 2-min recovery period suggesting that there is a role for the sympathetic nerves to return FBF to baseline levels. This is supported by data from Carter et al [14] showing that there is a significant elevation of muscle sympathetic nerve activity during the recovery period in healthy subjects.

From early experiments in the 1940's and 50's until the 1990's it was thought that sympathetic vasodilator nerves existed which caused forearm vasodilation during mental stress. Barcroft and Edholm demonstrated that the normal forearm vasodilator response to vasovagal syncope evoked by progressive blood loss was absent in the sympathectomized forearm [15]. Blair later showed that the normal forearm vasodilator response to mental stress was absent in sympathectomized limbs [16]. However, from a series of studies in our laboratory, we believe that forearm vasodilation during mental stress is due to a combination of local mechanical factors causing nitric oxide release from the vascular endothelium and beta-2 receptor mediated vasodilation from circulating catecholamines [4,17]. Moreover, lower body negative pressure produces a dose-dependent reduction in forearm blood flow due to sympathetic vasoconstriction and this response is absent in patients who have undergone ETS (i.e., confirming sympathetic denervation of forearm vasoconstrictor input) [13]. Our current data may suggest that sympathetic vasodilator nerves do not exist in humans or do not play a role in the response to mental stress.

It is possible that the HR response to mental stress exerts a predominant role in forearm vasodilation to mental stress [5]. Our group has shown that there is a striking correlation between the HR response to mental stress and the extent of vasodilation achieved during the test. The subjects with the largest increase in HR during mental stress have the most substantial vasodilation and increase in FVC. This suggests that the mechanical effects of an increase in HR could cause a flow mediated dilation that is a large contributor to increased FVC observed in mental stress. Although the pre-mental stress semi-recumbent baseline HR was lower in our patients postoperatively, the delta HR response to mental stress was preserved, which may explain why the delta FBF/FVC during mental stress was preserved. The similar HR response to mental stress following surgery is suggestive of intact parasympathetic withdrawal and sympathoadrenal activation. Alternatively, it could be that subjects with more vasodilation have greater compensatory recruitment of sympathetic outflow to the heart, larger adrenomedullary responses, or augmented responses mediated by beta-2 adrenoceptors in the heart and on skeletal vascular smooth muscle cells.

Effect of ETS on exercise capacity, oxygen consumption, heart rate, and blood pressure responses to incremental exercise testing

The effect of our ETS sympathotomy procedure on cardio-circulatory parameters and HR at rest and during incremental exercise was unknown. Since other methods of sympathetic chain surgical therapy for hyperhidrosis destroy at least some of the sympathetic cardiac accelerator fibers in or near the stellate ganglia, it is not surprising that these more destructive sympathectomy procedures have been reported to reduce resting and exercise HR. The following data are examples of results from the traditional sympathectomy procedure. Noppen and colleagues reported that post-sympathectomy HR at rest and exercise is reduced 13% and 7%, respectively [2,18], a finding that is consistent with studies at other institutions [6,19]. Exercise capacity, oxygen consumption, and blood pressure responses during cycling exercise were not affected in two studies by Noppen, [2,18] but Papa and colleagues reported a reduced systolic blood pressure at rest and in response to effort [6].

There was minimal destruction of cardiac sympathetic fibers during the ETS procedure. Unlike the supine measurements, the pre-mental stress (semi-recumbent) and pre-exercise (seated) baseline HR was significantly reduced following ETS. This reduction in seated HR on the postoperative visit may due be to patient familiarity with the stress protocols on their second visit or could be related to the difference in body positioning during HR measurement (screening ECG is performed supine while mental stress is performed in a semi-recumbent chair and pre-exercise values are performed seated on the bike).

SUMMARY

ETS is highly effective as a treatment for palmar hyperhidrosis with limited post-operative compensatory hyperhidrosis and high satisfaction with the procedure. Patients tolerate the procedure well and have no adverse physiological effects in the context of response to emotional stress and exercise. ETS appears to have only minor hemodynamic consequences during sympathoexcitation with mental stress but this study confirms a significant role for sympathetic control of FBF in the post-mental stress recovery period. There was a reduction in exercise HR and systolic pressure; however, this had minimal functional consequence as it did not impact exercise tolerance.

LIMITATIONS

This study is a descriptive study of the effects of ETS as we did not include a control group of healthy subjects or a comparison traditional sympathectomy group except for the mental stress forearm blood flow. We are unable to separate effects of ETS from an interaction

between ETS and the underlying disorder of palmar hyperhidrosis when it is not feasible to perform this procedure in humans without the disorder. Since all subjects were assessed on two days, one pre- and one post-surgical, it was impossible to blind the researchers or randomize the study days. Also, all subjects received the same surgical treatment which was known to the research group. Parasympathetic, sympathetic noradrenergic, and adrenomedullary activities were not monitored directly in this study. Importantly, some of our results may be explained by augmented adrenomedullary secretion of epinephrine in ETS patients but we did not measure this. Assessments of autonomic function (e.g., plasma levels of norepinephrine and epinephrine, effects of neuropharmacologic probes, or upper extremity muscle sympathetic nerve activity) were not performed in this study.

Acknowledgments

The authors thank Pamela A. Engrav and Nicolee C. Fode Thomas for their recruiting efforts, and all of the patients for their enthusiastic participation. **Grant Support:** NIH HL-089331, NS-32352, NIH-CTSA RR-024150

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Figure 1.

Figure 2.

Table 1

Patient Demographics and Surgical Results

Pt. #	Sex	Age	Pre-op visit			Post-op visit			Post-op clinical sweating				
			BMI	BP	HR	Mo.	BMI	BP	HR	Hands	Ax.	Feet	CH
1	F	22	24.7	112/69	73	3	25.8	121/81	70	↓↓↓	↔	↔	Abs.
2	F	23	20.0	147/92	85	3	20.8	138/67	69	↓↓↓	↓	↓	↑
3	M	27	28.2	136/75	50	4	28.6	131/73	53	↓↓↓ ^a	↔	↓	↑
4	F	30	19.0	98/70	79	6	20.0	84/54	74	↓↓↓	↓	↓	↑
5	M	30	28.2	121/69	66	4	29.4	119/76	64	↓↓↓	↔	↔	↑
6	M	19	22.8	141/76	68	6	23.1	124/80	59	↓↓ ^b	↔	↓↓	Abs.
7	F	20	25.7	119/71	70	2	26.0	114/72	62	↓↓↓	↔	↑	↑
8*	F	20	22.9	117/75	87					↓↓↓	↔	↓	Abs.
9	F	32	23.9	103/62	66	4	24.6	112/80	67	↓↓↓	↓↓	↑	↑
10*	F	41	21.5	114/68	66					↓↓↓	↓	↓↓	↑
11	F	21	21.4	112/66	55	1	21.6	123/66	67	↓↓↓	↓	↓	Abs.
12	F	21	20.6	114/77	71	12	22.8	102/65	68	↓↓↓ ^a	↔	↑	↑↑ ^c
13	F	24	21.8	124/79	89	8	21.7	116/75	74	↓↓↓	↑	↑	↑
14	F	25	34.1	129/73	62	2	30.4	129/68	66	↓↓↓	↔	↔	↑
15	F	25	17.4	100/60	74	3	18.3	100/64	63	↓↓↓	↔	↔	Abs.
16	M	24	22.1	135/72	68	3	22.7	128/65	68	↓↓↓	↓↓	↓	↑
17	F	19	17.2	125/67	65	3	17.8	110/59	65	↓↓↓	↔	↑	Abs.
18*	F	18	23.0	102/64	51					↓↓ ^d	↓↓	↔	↑
19*	F	26	25.9	123/74	57					↓↓↓	↔	↓↓	Abs.
20	F	21	20.5	109/63	63	2	20.4	109/59	76	↓↓↓	↔	↔	↑
21*	F	28	23.7	117/68	81					↓↓↓	↓↓	↓	↑
22	M	46	25.0	121/69	72	3	25.8	127/73	64	↓↓↓	↔	↓↓	↑

Table 2

Average physiological measurements at baseline and during mental stress

Variable	Pre-Operative			Post-Operative		
	Pre-stress BL	Mental Stress	Recovery	Pre-stress BL	Mental Stress	Recovery
Heart Rate (bpm)	72.1 ± 1.9	95.1 ± 1.7	71.6 ± 1.8	67.7 ± 1.9†	87.2 ± 2.6†	66.4 ± 1.8†
Systolic Blood Pressure (mmHg)	130.3 ± 3.4	139.1 ± 4.4	133.4 ± 4.3	131.3 ± 3.6	148.1 ± 3.3	131.3 ± 3.4
Diastolic Blood Pressure (mmHg)	67.5 ± 2.6	75.7 ± 3.1	70.3 ± 3.9	59.0 ± 2.9*	70.3 ± 2.4	60.6 ± 2.9*
Mean Arterial Pressure (mmHg)	85.7 ± 2.6	95.2 ± 2.9	88.8 ± 3.4	79.6 ± 3.2	92.9 ± 2.6	81.6 ± 3.3