

# An objective assessment of the sudomotor response after thoracoscopic sympathectomy

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**Objective:** Thoracoscopic sympathectomy has become an accepted therapeutic option for palmar hyperhidrosis. Objective assessment of sweat output after sympathectomy, however, has not been reported to date. We report for the first time sweat output measurements after sympathectomy during a 3-year postoperative period.

**Methods:** Thoracoscopic sympathectomy was performed by division of T2 and T3 sympathetic ganglia in 17 healthy adult patients with no comorbidities. Preoperative and postoperative sweat measurements were done at 29°C (below sweat threshold, at baseline, after conversation, and after a mental arithmetic challenge) and at 40°C (baseline and after exercise) with the ventilated capsule technique in left palm, sole, and chest wall. Serial postoperative measurements were conducted at 1 and 6 months and 1, 2, and 3 years.

**Results:** Sweat output fell significantly after sympathectomy relative to preoperative levels under all experimental conditions ( $P < .001$ , analysis of variance) in the left palm. Differences in sweat outputs in the left palm were statistically significant between groups at baseline and postoperatively after mental arithmetic challenge and exercise at 40°C ( $P < .05$ , analysis of variance). Compensatory increases in the sweat outputs from the left sole and chest were observed after sympathectomy. No patients had recurrence of preoperative sweat output values at follow-up.

**Conclusion:** According to objective sweat output measurements, thoracoscopic sympathectomy results in long-term control of palmar hyperhidrosis. This evaluation method is valuable in investigating recurrence of symptoms or compensatory hyperhidrosis after sympathectomy, providing a robust and objective criterion for planning intervention.

**T**hermoregulatory mechanisms in human beings involve heat loss through sweat production by the eccrine gland, which is mediated through the sympathetic system. Primary palmar hyperhidrosis is excessive sweating, above that necessary for normal thermoregulatory mechanisms. Palmar hyperhidrosis, although of minimal medical significance, can be restrictive socially and in the workplace. Thoracoscopic sympathectomy has been proved to be of benefit, with immediate amelioration of symptoms; however, this benefit is frequently offset by troublesome compensatory hyperhidrosis from the trunk and lower extremities.

Several investigators have reported excellent long-term results, with improved subjective satisfaction reported by patients.<sup>1,2</sup> An objective assessment of sweat output after sympathectomy could assist in investigating the mechanisms of compensatory sweating as well as provide a research tool to determine the level of sympatholysis potentially needed to prevent complications associated with thoracoscopic sympathectomy. In this investigation, our aim was objective assessment of sweat outputs after sympathectomy.

## Materials and Methods

Institutional review board approval was granted for this study. Consecutive patients admitted for planned thoracoscopic sympathectomy with no comorbidities were counseled, and written

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### Abbreviations and Acronyms

MA = mental arithmetic

consent was obtained from those who elected to participate. Only patients with primary palmar hyperhidrosis were included in this study. We excluded any patients who had peripheral vascular disease, were older than 40 years, were undergoing reoperative sympathectomy, were unable to complete the study as a result of non-compliance, or had any surgical complications needing additional treatment.

### Thoracoscopic Sympathectomy

The preoperative, perioperative, and postoperative care regimens were identical for all patients. Patients were intubated with a double-lumen endotracheal tube. Thoracoscopic sympathectomy was performed through two 5-mm ports, and carbon dioxide insufflation was used to achieve partial lung collapse. Thoracic sympathetic ganglia over the second and third ribs were divided, with an extension laterally over the second rib to include division of accessory pathways by means of diathermy. The procedure was repeated on the other side after reinflation of the contralateral lung under visual guidance.

### Pretesting Preparation

All patients wore cotton surgical gowns in a heat chamber at 29°C (just below thermal sweating threshold). Patients rested for 30 minutes in a supine position for equilibration to environmental temperature. During this time, sweat capsules were attached to both palms, anterior chest wall, and left sole of the foot.

Sweat output was measured by a ventilated capsule technique<sup>3</sup> (Figure 1). The gas content that perfuses over the skin under the capsule is measured. This technique calculates sweat output in micrograms per square centimeter of skin per minute. The protocol was similar for preoperative and all postoperative visits. The total duration of each study was approximately 3 hours. Vascular measurements were estimated from finger blood flow measured at rest (finger at temperature of 32°C), responses to sympathetic vasoconstrictor stimuli, and finger systolic pressure before and after provocative cold testing for vasospasm. Vascular measurements were performed to rule out any vascular phenomena. Any patients who showed positive signs of vasospasm were excluded, and the protocol was terminated.

### Sweat Measurements

Three readings for each minute were noted. In addition, readings of sweat output were measured at peak stimulation during various experimental conditions. The peak values were subsequently analyzed.

### Stimuli and Measurements

**Baseline (29°C).** The baseline measurement was obtained after equilibrium, with a chamber temperature of 29°C. This was done after the subject had been left undisturbed for 5 minutes. Then sweat measurements were done for 5 minutes, with three recordings for each minute for 15 minutes. The mean value was chosen to represent the baseline sweat output.

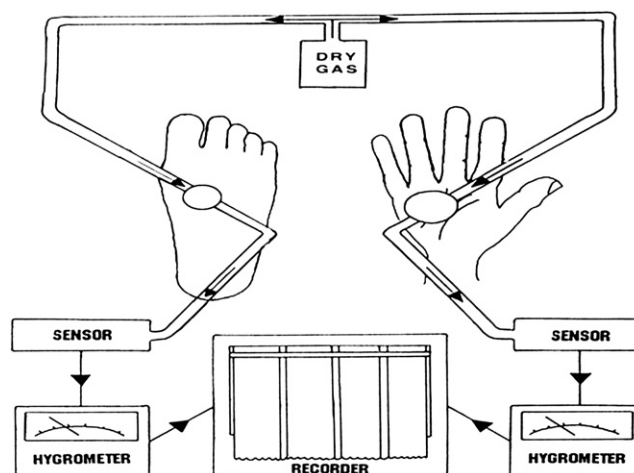


Figure 1. Ventilated capsule technique.

**Verbal stimulus (29°C).** A conversation was initiated about the subject's condition and continued for 2 minutes, with three measurements obtained during each minute. The mean value was chosen as the best response to verbal stimulus.

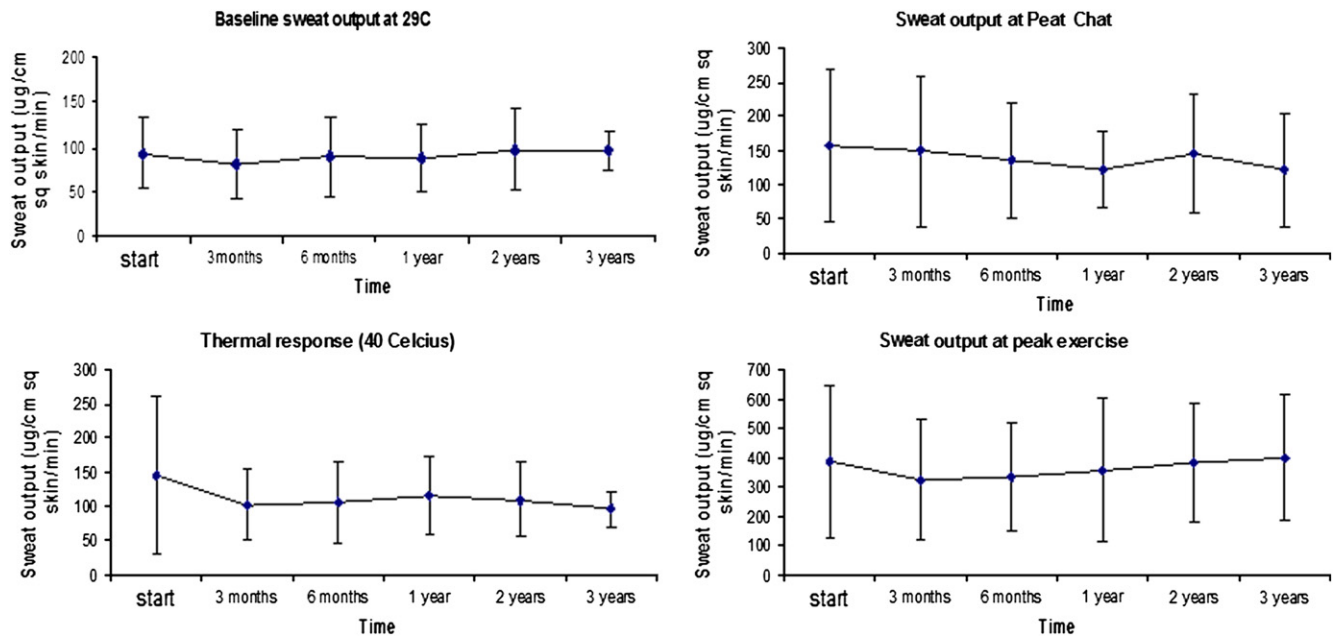
**Mental arithmetic challenge (29°C).** After verbal stimulus measurements, 5 minutes of resting recordings were made. Values for the last minute acted as controls for mental arithmetic (MA) mean. The subject was given simple arithmetic problems to solve; complexity of the problems was altered through time. Increasing pressure was put on the subject to obtain a solution within the specified, time with constant reminders of the time elapsed and a gentle but constant reprimand for the time taken to perform the calculations. Five minutes was given for the challenge, with three readings each minute; and means for fourth and fifth minutes and the overall peak were considered to represent the MA value. After this, 5 minutes was allowed for recovery. Although values during the recovery time were continuously recorded, they were not analyzed.

**Thermal stimulus (40°C).** The temperature in the chamber was then raised to 40°C gradually during 10 minutes. Sweat measurements (three per minute for the last minute of every 5-minute interval) were undertaken for as long as 35 minutes at 40°C. Measurements were then made at a rate of three per minute for the remaining time to 40 minutes at 40°C, and an overall peak for the entire 40-minute period minutes was taken as the thermal stimulus mean value.

**Exercise (40°C).** Step exercise was explained to the subject. Briefly, the subject stood up with the sole and right palm disconnected and exercised for 2 minutes in time to a metronome. Three values and a mean for each minute plus the overall peak were recorded.

### Results

Reproducibility tests were conducted on 13 healthy subjects (controls). There were 7 female and 6 male control subjects (mean age  $27 \pm 8$  years, range 18–46 years). The control subjects had no history of hyperhidrosis, and their mean sweat outputs were plotted to show the variation with time for the stimulus conditions (Figure 2).



**Figure 2. Control subjects. Under similar experimental conditions, 13 healthy volunteers were subjected to various stimuli with mean sweat outputs from left palm measured at intervals under various conditions. *Baseline*, No extraneous stimuli at temperature of 29°C; *Peak Chat*, verbal stimulus at 29°C; *Thermal*, temperature increase to 40°C; *peak exercise*, exercise challenge at 40°C.**

Seventeen subjects underwent thoracoscopic sympathectomy in this study. All subjects completed the preoperative, 1-week, and 1-month postoperative measurements, with additional follow-up to 6 months (n = 13), 1 year (n = 10), 2 years (n = 9), and 3 years or more (n = 6). Subjects were all healthy adults between the ages of 20 and 30 years. None of the patients had any postoperative complications, and all were discharged on the day after the procedure. All reported subjective improvement after the procedure, with clinical examination confirming dry, warm hands.

The sweat outputs from both palmar surfaces were equal. For simplicity and clarity, the left palmar sweat output is presented here for all observations.

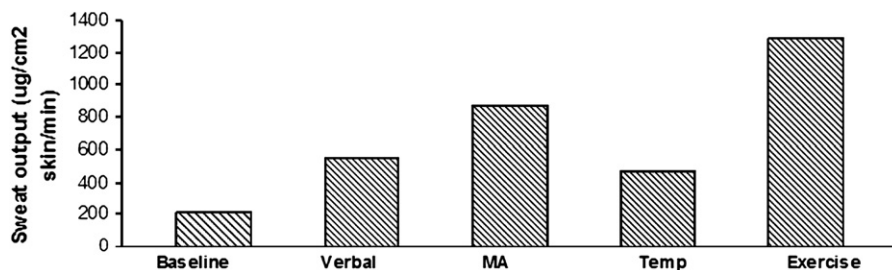
**Preoperative Sweat Output**

Preoperative sweat outputs from the left palmar surface were as follows: at baseline, 215  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$  (range 37–1070

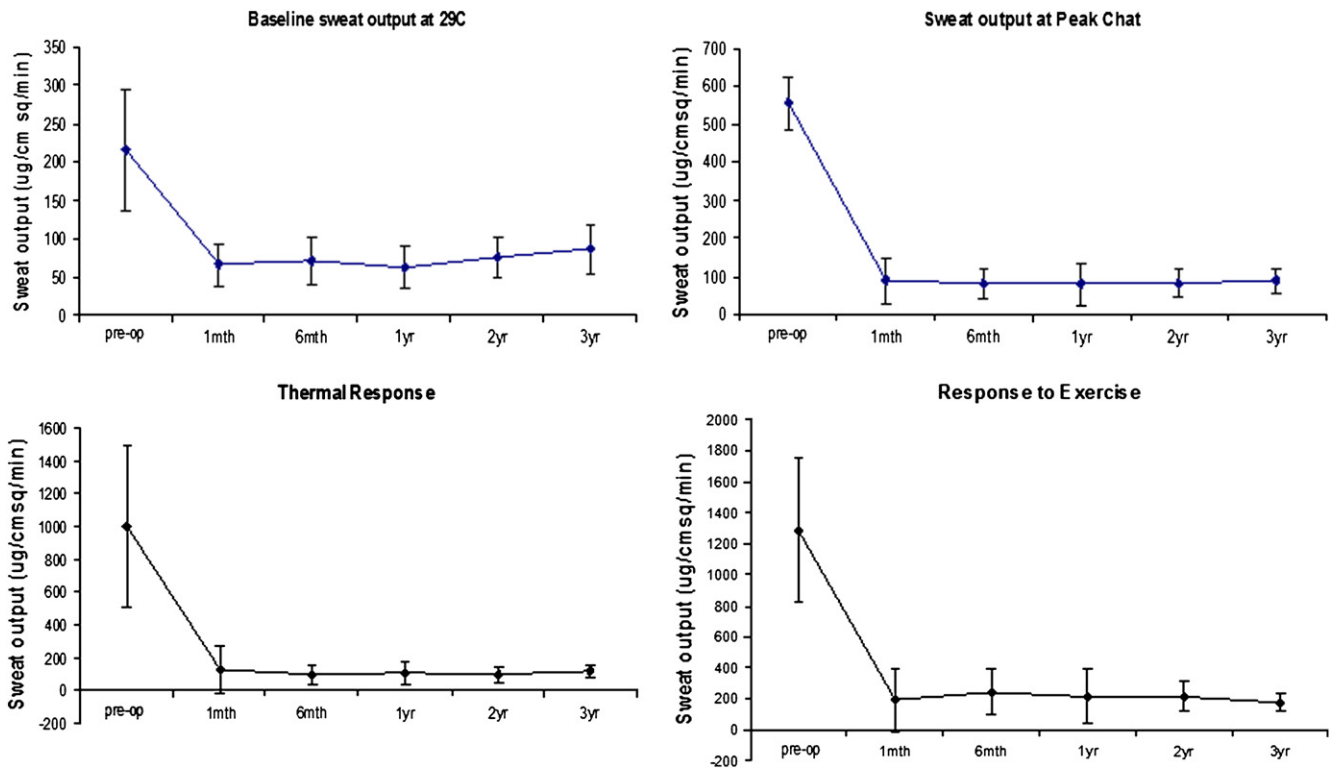
$\mu\text{g}/(\text{cm}^2 \cdot \text{min})$ ); under verbal stimulus, 555.7  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$  (range 59–1708  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$ ); after MA, 877  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$  (range 207–1899  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$ ); after thermal stimulus, 1017  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$  (range 390–1870  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$ ); and after exercise, 1289  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$  (range 425–2098  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$ ); **Figure 3**.

**Postoperative Sweat Output**

Sweat outputs from the palmar surfaces fell sharply relative to preoperative levels (analysis of variance,  $P < .01$ ) under all experimental conditions. The baseline values were as follows: 1 month,  $66.2 \pm 27.8 \mu\text{g}/(\text{cm}^2 \cdot \text{min})$ ; 6 months,  $71.3 \pm 31 \mu\text{g}/(\text{cm}^2 \cdot \text{min})$ ; 1 year,  $62.9 \pm 27.1 \mu\text{g}/(\text{cm}^2 \cdot \text{min})$ ; 2 years,  $76.3 \pm 26.2 \mu\text{g}/(\text{cm}^2 \cdot \text{min})$ ; and 3 years,  $86.1 \pm 26.2 \mu\text{g}/(\text{cm}^2 \cdot \text{min})$ . The postoperative response to stimuli was characterized by sweat production less than 200  $\mu\text{g}/(\text{cm}^2 \cdot \text{min})$  under all experimental conditions,



**Figure 3. Preoperative sweat outputs from left palm in response to various stimuli. *Baseline*, No extraneous stimuli at temperature of 29°C; *Verbal*, verbal stimulus at 29°C; *MA*, mental arithmetic challenge at 29°C; *Temp*, temperature increase to 40°C; *Exercise*, exercise challenge at 40°C.**



**Figure 4.** Sweat outputs from left palm in response to different stimuli. Reduction in sweat outputs after sympathectomy in response to different stimuli. *Baseline*, No extraneous stimuli at temperature of 29°C; *Peak Chat*, verbal stimulus at 29°C; *Thermal*, temperature increase to 40°C; *peak exercise*, exercise challenge at 40°C.

irrespective of the nature of stimuli. The effect of the thoracoscopic sympathectomy was evident even at 3 years when serially measured (Figure 4).

**Compensatory Sweat Output from Chest and Feet**

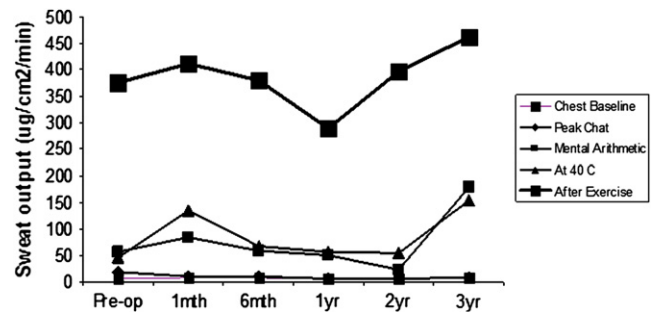
There were compensatory rises in sweat outputs from the anterior chest noted with MA, with temperature rise, and after exercise (Figure 5). There was no difference noted between preoperative and postoperative values under baseline conditions and after verbal stimulus. The compensatory sweat outputs returned to preoperative levels by 6 months for MA and temperature rise and stayed such for 2 years. After 2 years, there were significant rises in compensatory sweating under these experimental conditions relative to preoperative values. Compensatory sweat output from the anterior chest wall after exercise was considerably higher and took a year to reach the baseline; after reaching the preoperative level, however, it also showed a rise from 2 years after the procedure and was significantly higher than the preoperative level.

There was no compensatory sweat output from the feet except under thermal stimulation in the early postoperative period (Figure 6). Sweat production showed a decreasing trend in the 2-year postoperative period, during which the actual values under experimental conditions fell below the

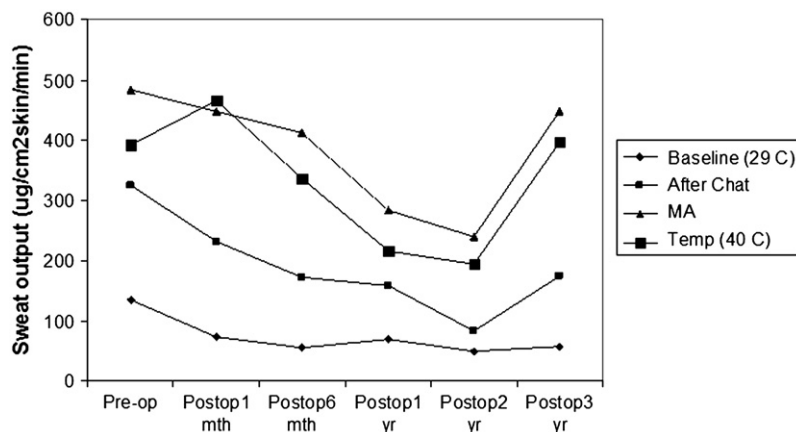
preoperative levels. After 2 years, however, this sympathetic effect was lost, with increasing sweat outputs noted under all the experimental conditions.

**Discussion**

This study shows that the efficacy of thoracoscopic sympathectomy for primary palmar hyperhidrosis can be assessed



**Figure 5.** Compensatory outputs from chest. Changes in sweat outputs from chest (as indicator of axillary sweating) with time after sympathectomy. *Baseline*, No extraneous stimuli at temperature of 29°C; *Peak Chat*, verbal stimulus at 29°C; *MA*, mental arithmetic challenge at 29°C; *40°C*, temperature increase to 40°C; *Exercise*, exercise challenge at 40°C.



**Figure 6. Compensatory output from left sole. Changes in sweat outputs from left sole with time after sympathectomy. Baseline, No extraneous stimuli at temperature of 29°C; Chat, verbal stimulus at 29°C; MA, mental arithmetic challenge at 29°C; Temp, temperature increase to 40°C.**

objectively. We have also demonstrated objective measurements of compensatory hyperhidrosis and how this varies with mental stress (MA), temperature, and exercise. Another aspect, one that is seldom mentioned by patients or reported in literature, is the reduced sweating from the feet after thoracoscopic sympathectomy for palmar hyperhidrosis that was noted in this study.

Several recent reports and a detailed review have claimed excellent results after thoracoscopic sympathectomy.<sup>1,2,4</sup> Only one report, however, has examined actual sweat output measurements at 3-month intervals to study the effect of thoracoscopic sympathectomy.<sup>5</sup> One consistently reported drawback of this procedure is compensatory hyperhidrosis.<sup>4,6</sup>

Published reports have tended to use patient satisfaction surveys or quality of life indicators to assess the postoperative outcome after sympathectomy for various indications. On the basis of these reports, several attempts have been made to modify the extent of resection of the sympathetic ganglia to abolish or diminish compensatory hyperhidrosis.<sup>7</sup> Patient satisfaction can be based on various factors, however—including the duration of symptoms, severity of symptoms, extent and distribution of sweating patterns, previous interventions, and postoperative outcome—and may be variable vary from patient to patient. Compensatory hyperhidrosis also depends on geography, climate, seasonal variations, occupational factors, psychologic state of the patient, and the specific stimuli that may lead to symptoms.

This study showed significant reductions after thoracic sympathectomy in sweat production on the palmar surface under all experimental conditions. The experimental conditions were designed to simulate stressful situations and encourage excess sweating. Postprocedure, baseline, and verbal stimulation measurements did not show alteration in the severity of compensatory hyperhidrosis. There was, however, increasing compensatory hyperhidrosis noted with mental stress (MA), with thermal stimulation, and after exercise; this may be due to the body's initial attempt to maintain adequate thermoregulatory balance in the absence

of the reduced or abolished palmar hidrosis by surgery. The initial compensatory hyperhidrosis pattern returned to baseline 6 months after the procedure, as was reported in many earlier studies.<sup>1</sup> This effect eventually disappeared, however, and there was increasing compensatory hyperhidrosis observed after 2 years. This effect may be unrelated to the original division of the ganglia and may reflect either regrowth or activation of other compensatory sympathetic pathways that affect the thermoregulatory mechanisms in the upper part of the body. Such increases were not noticed when the actual sweat productions from the palms were measured during this period.

Sweat production from the lower limbs was noted to be significantly lower than preoperative values, and this decrease continued for 2 years. Interestingly, observed values eventually returned to preoperative levels under all experimental conditions. Although the lower limbs are supplied by T10 to L2 sympathetic ganglia, there appear to be preganglionic fibers in the T2 and T3 (divided sympathetic ganglia) that may contribute to the synapses in the lower (T10–L2) sympathetic ganglia, although this study is unable to prove this assumption conclusively.

In conclusion, these findings demonstrate that thoracoscopic sympathectomy results in long-term control of primary palmar hyperhidrosis. The actual measurement of sweat output is valuable in quantifying preoperative severity and in investigating recurrence of symptoms or onset of compensatory hyperhidrosis following sympathectomy. Such evaluation provides robust and objective criteria for planning intervention and postoperative lifestyle modifications that may reduce the severity of compensatory hyperhidrosis.

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## Discussion

**Dr Mark J. Krasna** (*Baltimore, Md*). This study purports to measure sweat output after thoracoscopic sympathectomy with a technique not previously described. Dr Bonde, I congratulate you on making it here through your visa issues, and I did get a chance to look quickly at the manuscript before the meeting.

The technique described is actually elegant, and the trial of that small a number is to be commended as a good prospective evaluation. The procedure in clinical terms is generally more than 95%, even 98%, successful, so it is not 100% clear to me how this information can be used in clinical practice.

I have a couple of questions. As we know, most reports on thoracoscopic sympathectomy have demonstrated such a high success rate that the only limitation is in fact compensatory sweating. Compensatory sweating in different institutional reports has ranged from as low as 30% to a more typical 60% and even 80%. It seems that in your series even those patients who had compensatory sweating did not have a significant amount of sweat output, which is remarkable. So my first question is, how do you account for such a low incidence and low volume of compensatory sweating?

I think another question needs clarification is the surgical technique involved. In a recent review of thoracoscopic sympathectomy techniques throughout the world, there is a great disparity between what people call a T2 and a T3 sympathectomy. Can you clarify for us exactly where the cuts were made along the sympathetic chain? It is my impression now that I've seen the manuscript that you actually cut over the second rib and over the third rib, which some people would call simply a T2 sympathectomy and not a T2-T3. If you can, please clarify that. Otherwise, I enjoyed your presentation. I think the technique is elegant. I would like to hear, though, how you think you would use this in the future, either in clinical practice or in research.

**Dr Bonde.** Thank you, Dr Krasna. Regarding your first question as to the low volume amount of compensatory hyperhidrosis in these patients, it's actually not the case. All the patients showed a presence of compensatory hyperhidrosis, as objectively shown in measurement of sweat outputs from the anterior chest wall, particularly in response to three specific stimuli: thermal stimulation, exercise, and stress (MA) stimulation. There was a significant rise, which was statistically significant, by about 6 months; by 1 year or so, this effect had passed off, but after 2 years, there was again a rise in compensatory hyperhidrosis. We looked at all 17 patients closely, and actually most of them did have this trend, so it wasn't as though there were a pooling of data on one side. So all these patients did show compensatory hyperhidrosis, although they did not show increased sweating from the lower extremities. They mostly showed

increased sweating from the anterior chest wall. We do have limitations in terms of using the technique, because there are only so many capsules that you can attach to the body and make the subject move about and do all the different things that you want. The total experiment, for each measurement, takes about 3 hours to complete.

Regarding your second question about the exact technique that we used, we used an inert gas, such as xenon. The gas basically gets perfused over the surface of the skin, and as it gets perfused over the surface of the skin, the water over the skin is absorbed by the gas, and we measure the water content. The probe is roughly the size of a quarter. So it can fit nicely onto the palm or the anterior chest wall. We did apply it to the sole; as you can imagine, however, when the patient exercises, and in this case we used step exercise, the capsule tends to fall off. That's why I didn't present our results of exercise-induced sweating from the feet. This is one of the techniques. There are three techniques that can be used to assess the effect of the autonomic nervous system: spectroscopic measurement, thermographic measurement, and the technique that I just described, the ventilated capsule. Naturally, all these techniques are used by autonomic physiologists, and two of our coauthors are actually physiologists. There is agreement among the physiologists that the ventilated capsule method yields the most accurate measurement of sweat output, although it does not determine the vasomotor aspect that the autonomic sympathetic system gives you.

Regarding your third question, I understand and I agree with you that we basically did the T2, and at the most, the upper part of the T3. We basically used a technique of thoracoscopic sympathectomy in which we used 5-mm ports and two probes, with a double-lumen endotracheal tube and carbon dioxide insufflation to drop the ipsilateral lung for the interposition. We divided the sympathetic ganglia over the neck of the second rib and extended the incision 2 cm laterally to divide all the accessory pathways, and we went down to the third rib, right from the neck, and divided the ganglia there. In this particular series, I am only presenting the patients with palmar hyperhidrosis, and that's exactly what we did for these patients. Naturally, we repeated the procedure on the other side, after evacuating the carbon dioxide, re-clamping the tube, and making sure that the contralateral lung was fully up. The patients were all extubated the same way.

**Dr Hyo Chae Paik** (*Seoul, South Korea*). Dr Bonde, I enjoyed your presentation. I have a few comments and questions. Personally, I no longer perform sympathetic surgery in patients with hyperhidrosis, because I cannot predict my surgical results. That is, I cannot predict in whom the compensatory hyperhidrosis will occur and how severe it might be, because some patients have such a severe compensatory hyperhidrosis that they regret the surgery. As Dr Krasna mentioned, you saw little compensatory hyperhidrosis, and it doesn't seem to have bothered your patients. Although your series is small, I was wondering whether you had any complaints at all regarding that problem.

Also, is it necessary to cut at two levels for patients with palmar hyperhidrosis? Just cutting at either the top of T3 or T4 rib is probably just as effective and takes a shorter time than cutting at two locations. Finally, I don't know whether you have tried the technique of ramicotomy, cutting the rami communicantes near the level of T2 or T3. What do you think of this?

**Dr Bonde.** Thank you for your question. I'll answer the last two questions first, because they are easy to answer. With regard to the

cuts, we particularly did not vary that part, because we thought that we would use the same technique in all cases and that the message of article should be objective assessment of the amount of sweat produced when a specific structure is surgically divided. The third question was about the technique of ramicotomy. We are not familiar with the technique, and we do not use it routinely in our center.

Coming back to the question of compensatory hyperhidrosis, I would again stress that all the patients in this series had compensatory hyperhidrosis. Naturally, most of the series presented so far have addressed the issue in a subjective manner, which is sometimes a drawback because compensatory hyperhidrosis is quite patient specific. A patient who has had hyperhidrosis for a long period and gets immediate relief from symptoms after the procedure is unlikely to be bothered by compensatory hyperhidrosis. Another patient, however, who has not been bothered so much by the initial condition and hasn't had so many treatments may well perceive the compensatory hyperhidrosis as much more severe. There are several factors in addition to the subjective on which compensatory hyperhidrosis depends: the geography, whether you are doing the procedure in North America, in Europe, in Asia; the climate, with the seasonal variations; the occupation of the patient. There are various factors, and that's why we selected and we chose a completely controlled environment in which we could measure the actual sweat output and to quantify compensatory hyperhidrosis.

Another point that I would make is that because there is so much variation among the studies in terms of the division being made, where the ganglia have been removed, how much compensatory hyperhidrosis took place, and what questions were asked, you cannot really compare the results. We have proposed this technique as a more objective means of comparison between groups. I hope that answers your question.

**Dr Paik.** Would you suggest operating selectively on patients who have had a long period of hyperhidrosis, to avoid complaints of compensatory hyperhidrosis?

**Dr Bonde.** No. I was just giving an example as to how the patients might respond. If the preoperative assessment is done,

and if the patient is willing to undergo that procedure, I don't think that not doing the procedure would be in the patient's interest. It is all subjective. The purpose of this study was plain and simple, to see whether when the patient reports compensatory hyperhidrosis or says that there has been a response to the treatment that this is actually the fact, and that's what our results show. I would refrain from giving any more suggestions or guidelines as to how the patient has to be dealt with, because this investigation is still underway. We have just 3 years of data, and at 3 years we have been seeing a rise in the compensatory hyperhidrosis. There may be explanations for this. For example, the early compensatory hyperhidrosis may be the thermal regulatory mechanisms coming into play, and the later rise in the compensatory hyperhidrosis may be because of regrowth of the ganglia, all the nerve fibers, as well as other accessory mechanisms coming into play. So all these things need to be taken into account when you consider surgically which ganglia are going to be divided.

**Dr Anthony P. Yim (Hong Kong, China).** Dr Bonde, I enjoyed your presentation. In none of your graphs did you put in SDs. I think that information is particularly pertinent to the interpretation of data from this kind of a study. Would you please comment?

**Dr Bonde.** We are in the process of looking at 25 different subjects who do not have palmar hyperhidrosis, and some of the data that I did not present but will be in the article is that there is variation in sweat output among healthy subjects. Also, as I pointed out, geography, climate, seasonal variations, occupation, and other factors may affect this. So when you talk about the SD, for that particular patient it is better to compare preoperative levels to postoperative levels, and that's why we did not much go into the SD. If you look at the healthy subject population SD, the variation can be quite wide and is based on different factors. So to bring it down to a particular stage and particular level is difficult. As I pointed out, the experiment is not easy to do, in the sense that you can only do 1 subject per day and it requires a willingness to be in that chamber for 4 hours. That is one of the big limitations of not having a large number of patients in this study.

**Dr Yim.** But that's exactly the point of my question.