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Two-stage unilateral versus one-stage bilateral single-port sympathectomy for palmar and axillary hyperhidrosis†

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Abstract

OBJECTIVES: Video-assisted thoracoscopic sympathectomy is currently the best treatment for palmar and axillary hyperhidrosis. It can be performed through either one or two stages of surgery. This study aimed to evaluate the operative and postoperative results of two-stage unilateral vs one-stage bilateral thoracoscopic sympathectomy.

METHODS: From November 1995 to February 2011, 270 patients with severe palmar and/or axillary hyperhidrosis were recruited for this study. One hundred and thirty patients received one-stage bilateral, single-port video-assisted thoracoscopic sympathectomy (one-stage group) and 140, two-stage unilateral, single-port video-assisted thoracoscopic sympathectomy, with a mean time interval of 4 months between the procedures (two-stage group).

RESULTS: The mean postoperative follow-up period was 12.5 (range: 1–24 months). After surgery, hands and axillae of all patients were dry and warm. Sixteen (12%) patients of the one-stage group and 15 (11%) of the two-stage group suffered from mild/moderate pain ($P = 0.8482$). The mean operative time was 38 ± 5 min in the one-stage group and 39 ± 8 min in the two-stage group ($P = 0.199$). Pneumothorax occurred in 8 (6%) patients of the one-stage group and in 11 (8%) of the two-stage group. Compensatory sweating occurred in 25 (19%) patients of the one-stage group and in 6 (4%) of the two-stage group ($P = 0.0001$). No patients developed Horner's syndrome.

CONCLUSIONS: Both two-stage unilateral and one-stage bilateral single-port video-assisted thoracoscopic sympathectomies are effective, safe and minimally invasive procedures. Two-stage unilateral sympathectomy can be performed with a lower occurrence of compensatory sweating, improving permanently the quality of life in patients with palmar and axillary hyperhidrosis.

Keywords: Palmar and axillary hyperhidrosis • Video-assisted thoracoscopic sympathectomy • Compensatory sweating

INTRODUCTION

Primary hyperhidrosis is a disorder characterized by excessive perspiration beyond thermoregulatory needs, particularly in response to temperature or emotional stimuli. Primary hyperhidrosis has an estimated prevalence of nearly 3–4% [1, 2]. Severe hyperhidrosis commonly affects hands, face, axillae and feet, causing significant medical and psychosocial consequences. Medical treatments, such as local antiperspirants, systemic anticholinergic agents, iontophoresis and botulinum toxin, alleviate symptoms only transiently. However, surgical therapy is the most effective approach and recognized as the treatment of choice for patients with primary hyperhidrosis.

To date, among all the different surgical approaches, video-assisted thoracoscopic sympathectomy has been shown as a safe and minimally invasive procedure for palmar and axillary hyperhidrosis [3]. In addition, it can be performed using single or multiple ports [4, 5].

The present retrospective study aims to show operative and postoperative results after two-stage unilateral vs one-stage bilateral thoracoscopic sympathectomy in 270 treated patients.

MATERIALS AND METHODS

Between November 1995 and February 2011 in the Department of Thoracic Surgery, University of Rome, Sapienza, 270 patients with severe palmar, or palmar and axillary, hyperhidrosis were recruited for this study. All patients had excessive sweating in the hands or hands and armpits, severely interfering with their work

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or social activities. One hundred and thirty patients received one-stage bilateral single-port video-assisted thoracoscopic sympathectomy (one-stage group) and 140, two-stage unilateral single-port video-assisted thoracoscopic sympathectomy (two-stage group). The clinical characteristics of both groups are listed in Table 1. Before surgery, all patients underwent a careful clinical history, preoperative routine blood examination, spirometry, cardiological consulting and chest X-ray to exclude pulmonary affections. Patients with secondary hyperhidrosis were excluded from this study. A written informed consent from all patients was obtained, and a study approval from the Ethics Committee was provided.

Operative and postoperative results such as operating time, hospital stay, residual pain, postoperative complications, compensatory sweating and recurrence of symptoms were analysed. Compensatory sweating and recurrence of symptoms were evaluated 1 year after surgery. Recurrence of symptoms was assessed by a quantitative sudomotor axon reflex. The mean postoperative follow-up period was 12.5 (range: 1–24 months).

Potential variables responsible for compensatory sweating and postoperative pneumothorax were evaluated in both groups.

Surgical technique

Surgery was performed under general anaesthesia. Double-lumen endotracheal intubation and selective one-lung ventilation were used. Patients were placed on the operating table in a semi-sitting position with arms abducted more than 90°. Only one incision of about 8 mm was performed in the third intercostal space on the anterior axillary line. In the one-stage group, the same body position was used to perform the procedure on the other side.

Three millimetre, 30° thoracoscope (KARL STORZ, Tuttlingen, Germany) and 5-mm endoscopic dissector (B. BRAUN, Melsungen, Germany) were introduced into the thoracic cavity after lung exclusion on the operative side of surgery. The sympathetic chain was identified counting the ribs from the first rib. By opening the parietal pleura, the sympathetic chain was exposed, identifying the T2–T4 tract. Dissection was performed by electrocautery from the second to the fourth ganglia. Then, the thoracoscope and endoscopic instruments were removed. A temporary 10-Ch chest tube was inserted into the thoracic cavity through the surgical incision and connected to a water-seal system applying a mild suction. After reinflating the lungs, the chest tube was quickly removed and the incision was closed. A chest X-ray was performed during the first postoperative day before the discharge.

In the two-stage group, the surgical procedure was performed on one side and undertaken on the other side after a mean time interval of 4 (range: 1–12 months) from the controlateral procedure.

Statistical analysis

Data were described evaluating qualitative variables through the usual frequency tables, and quantitative variables through synthetic indices such as mean, standard deviation and range. The differences between the two groups were examined by significance through a χ^2 non-parametric test for qualitative variables and an unpaired Student's *t*-test for quantitative variables (operative time and age), subject to normal distribution. The evaluation of categorical outcomes as the presence/absence of compensatory sweating, or pneumothorax, was performed through univariate analysis using the methods described above. The multivariate analysis was performed using a logistic regression model to identify potential variables such as group (one- or two-stage procedure), gender, age (≤30/≥31 years), smoking status and hyperhidrosis localization (palmar, or palmar and axillary, localization). The odds ratio (OR) and corresponding 95% confidence intervals were reported for covariates, considering the 0.05 significance level to be clinically relevant.

RESULTS

All patients had an immediate result after surgery, with warm and dry hands, and showing full satisfaction. Histological analysis confirmed a normal nervous tissue.

Totally, 540 video-assisted thoracoscopic sympathectomies were performed in 270 patients. No operative mortality or conversion to open surgery was recorded. In Table 2, the main results of both groups are presented. The mean operative time was similar in both groups (38.05 ± 5.00 min in the one-stage group vs 39.09 ± 8.09 in the two-stage group, $P = 0.199$, considering the sum of the two-stage operative time). The mean hospital stay was 1.136 ± 0.6 and 2.42 ± 0.4 days in the one-stage and two-stage group, respectively, considering the two-stage

Table 1: Clinical characteristics of the patients

Variables	*n*		%	
	One-stage group	Two-stage group	One-stage group	Two-stage group
Sex (male/female)	49/81	56/84	37.7/62.3	40.0/60.0
Smoking status (yes/no)	55/75	59/81	42.3/57.7	42.1/57.9
Mean age/range/SD (years)	32.0/16–63/11.3	33.4/16–64/11.6		
Family history (yes/no)	23/107	21/119	17.7/82.3	15.0/85.0
Previous lung disease (yes/no)	0/130	0/140	0/100.0	0/100.0
Previous treatments (yes/no)	104/26	118/22	80.0/20.0	84.3/15.7
Palmar hyperhidrosis (yes/no)	130/0	140/0	100.0/0	100.0/0
Axillary hyperhidrosis (yes/no)	91/39	102/38	70.0/30.0	72.9/27.1

SD: standard deviation.

Table 2: Results

Variables	One-stage group	Two-stage group	*P*-value	95% Confidence interval of the difference
Age (mean ± SD)	32.04 ± 11.34	33.43 ± 11.66	0.32	−4.15–1.37
Mean operative time (min ± SD)	38.05 ± 5.00	39.09 ± 8.09[a]	0.19	−2.64–0.55
Mean hospital stay (*n*/%)[b]	8/6.2	140/100[c]		
Residual pain in 1 week (*n*/%)	16/12.3	15/10.7	0.84	
Pneumothorax (*n*/%)	8/6.2	11/7.9	0.75	
Axillary localization (*n*/%)	91/70.0	102/72.9	0.00	
Compensatory sweating (*n*/%)	25/19.2	6/4.3	0.00	
Horner's syndrome (*n*/%)	0/0	0/0		
Chilothorax (*n*/%)	0/0	0/0		
Recurrence (*n*/%)	0/0	0/0		

SD: standard deviation.
[a]Considering the sum of two-stage operative time.
[b]Considering a hospital stay ≥2 days.
[c]Considering the total two-stage hospitalization.

hospitalization. In the one-stage group, 8 (6.2%) patients had a hospital stay ≥2 days (according to the frequency distribution), while it was 140 (100%) patients in the two-stage group.

Within 7 days after operation, in the one-stage group, 16 (12%) patients suffered from mild/moderate pain, requiring more analgesics (morphinics or local analgesia with naropin infiltration) than the standard doses (90 mg of ketorolac) vs 15 (11%) in the two-stage group ($P = 0.8482$). After 7 days following surgery, no cases of residual pain were recorded in both groups. Unilateral pneumothorax occurred in 8 (6%) patients after surgery in the one-stage group, while it occurred in 11 (8%) in the two-stage group ($P = 0.758$). One patient of the one-stage group and two of the two-stage group (1.1%) required positioning of chest drainage; the other patients who experienced this complication were treated by rest and respiratory physiotherapy. Patients with pneumothorax were discharged after a mean time of 4 (range: 1–6 days). Compensatory sweating occurred in 25 (19%) cases in the one-stage group and in 6 (4%) in the two-stage group ($P = 0.0001$). No patients experienced Horner's syndrome. No recurrence was observed during the follow-up period, with a complete resolution in 100% of patients of both groups. According to the logistic regression analysis (Table 3), group and hyperhidrosis localization variables seem to affect the compensatory sweating occurrence. Thus, undergoing to a two-stage surgical approach was identified as a protective factor for compensatory sweating occurrence (OR = 0.292, $P = 0.015$). Otherwise, a double hyperhidrosis localization (palmar and axillary hyperhidrosis) was identified as a risk factor for compensatory sweating occurrence (OR = 3.386, $P = 0.015$). Logistic regression analysis of postoperative pneumothorax did not show any significant association between the independent variables and this early complication.

Table 3: Logistic regression analysis of compensatory sweating

Variables	OR	*P*-value	95% Confidence interval
Group	0.29	0.01	0.10–0.78
Age	0.71	0.41	0.31–1.60
Smoking status	1.31	0.49	0.59–2.89
Gender	0.74	0.45	0.33–1.63
Axillary localization	3.38	0.01	1.26–9.08

OR: odds ratio.

DISCUSSION

Before the introduction of video-assisted thoracoscopic surgery (VATS) and the advances in video-endoscopic technology, thoracotomy was the standard surgical approach for hyperhidrosis [6]. VATS had replaced open surgery for performing sympathectomy, determining a shorter hospital stay, reduced morbidity rates, less pain and better cosmetic results for a non-life risk disease [7]. Primary hyperhidrosis seems to affect negatively the following areas of life: work (88%), friendships (73%), relations with partners (46%) and family (21%). Indeed, this negative repercussion motivates patients to undergo surgery to solve their problems [8].

In 1995, we started to perform surgery with a two-stage approach in our institution. Only in the first years of 2000 did we convert our approach to the worldwide one-stage surgery to obtain low hospitalization costs, decreased risk of complications and one single quick admission. However, we recently considered investigating the outcomes of both groups. In this report, we have shown that both one-stage bilateral and two-stage unilateral video-assisted thoracoscopic sympathectomies for palmar and axillary hyperhidrosis carried out through a single port can be successful and riskless procedures with minimal invasiveness and slight postoperative pain.

The mean operative time was quite short in both groups (38 and 39 min), considering the sum of two-stage operative time for the two-stage group. We did not need to reposition the patient to operate on the other side. However, in the two-stage group, the hospitalization costs obviously increased since the mean hospital stay was 2.42 ± 0.4 vs 1.13 ± 0.6 days of the one-stage group.

To date, the results achieved in treating palmar and axillary hyperhidrosis are conditioned by the surgical technique used (level of sympathetic chain interruption, cauterizing, cutting or clipping the sympathetic chain) and, therefore, they still remain

controversial. Although an expert consensus exists and provides standardized suggested treatment strategies [8], in our experience surgical ablation of the T2–T4 ganglia is fully effective, perhaps due to the subsequent removal of the chain and the collateral branches. The target resolution of the disorder was achieved in 100% of the patients. No recurrence was observed. These results are in line with those reported by other authors [9, 10]. No mortality was reported in our experience. Previous studies showed that the overall intraoperative morbidity (i.e. chylothorax, lung or vessels damage) is nearly 0.2% [10], reporting complications during surgery and conversion to thoracotomy [11, 12]. However none of these issues was observed in our study. In our reports, pneumothorax was the most common early complication (6–8% of patients), although only 1.1% of cases required pleural drainage. However, an exertion of continuous positive pressure for a few seconds in coordination with the anaesthesiologist during the suture of the skin and the application of a mild suction to the temporary chest tube are essential to prevent residual air and possible incomplete re-expansion of the lung [13, 14]. Postoperative pain lasting <1 week was observed in 11–12% of our cases: only a few patients required morphinics or local analgesia with naropin infiltration in addition to the standard doses of analgesics. There was no significant relevance for constant residual pain after 7 days following operation. We confirmed that the use of unilateral or bilateral uniportal VATS to perform sympathectomy allows the achievement of lower morbidity rates and satisfying postoperative outcomes [15, 16]. Compensatory hyperhidrosis (postoperative increase of sweating in regions of the body where it had not been previously observed) is the most common late complication, with different incidences reported in previous studies, ranging from 33 to 85% [17–19], regardless of the number of ganglia removed [20], showing a gradually decreasing intensity over the follow-up period. However, the mechanism of compensatory hyperhidrosis is still unclear. An alternative to reducing compensatory sweating consists in applying metal clips to interrupt the sympathetic chain by compression [21]. In our study, single-port thoracoscopic sympathectomy was associated with a low rate of compensatory hyperhidrosis. However, we showed that compensatory sweating is more frequent in the one-stage group (19 vs 4%, $P = 0.0001$). We can speculate that undergoing a controlateral sympathectomy, after at least 1 month from the previous single-side surgery, could provide a definitive thermoregulatory balance, determining a complete shock to the *rami communicanti* or accessory Kuntz's fibres potentially regenerated [22]. Specifically, we provided, for the first time, a possible strategy to avoid compensatory sweating occurrence, the main side effect after this surgical procedure. We recently investigated whether variables such as age, weather factors, gender, hyperhidrosis localization and smoking habits could impact on compensatory sweating incidence (Ibrahim and Menna, manuscript in preparation). In this report, we affirmed that the above-mentioned variables did not affect compensatory sweating occurrences, but group and hyperhidrosis localization. When sympathectomy is performed with a time interval between the two procedures (at least 1 month) and when primary hyperhidrosis does not affect the axillae (only palmar localization), patients have a lower risk of presenting compensatory sweating.

Our retrospective study could be useful to address the compensatory sweating issue, the most common late complication after thoracoscopic sympathectomy, giving a starting point for future, more detailed studies.

In conclusion, our results suggest that one-stage mini-uniportal bilateral video-assisted thoracoscopic sympathectomy is a valid and secure treatment for palmar and axillary hyperhidrosis. However, two-stage unilateral video-assisted thoracoscopic sympathectomy allows the achievement of better results in terms of side effects.

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APPENDIX. CONFERENCE DISCUSSION

Dr A. Sihoe *(Hong Kong, China)*: Now, hyperhidrosis, in contrast to most of the other diseases we have seen here in this room today, is a condition that does not threaten life. It doesn't cause any physical harm to the patient. So when we do hyperhidrosis surgery, in terms of outcome measures, we are actually trying to improve the patient's quality of life and at the same time we are trying to reduce harm, and in terms of harm from this kind of surgery, I think compensatory hyperhidrosis obviously tops the list.

My first question to you concerns this compensatory hyperhidrosis. I think you have chosen a very good outcome measure to highlight here, but when you talk about compensatory hyperhidrosis, you open a can of worms. There are a few issues involved. First of all, of course, is the definition of compensatory hyperhidrosis. I am sure you are well aware that in publications on hyperhidrosis surgery over the years, every author uses a slightly different definition, ranging from just a little bit of sweating, if you ask the patient about it, all the way to needing to change clothes every day. So it really depends on how you define it.

After you define it, you also are begging the question, when you produce a result like this, of how do you explain why the two-stage procedure reduces the compensatory sweating? Now, I have had the luck of reading your paper, first of all, and I know that in your full paper you suggest that it is the time in between the first and the second operation, allowing for the Kuntz fibres and *rami communicantes* to regenerate, that might explain the reduced compensatory hyperhidrosis. But if this speculation is correct, then really the more time you give it, the less compensatory hyperhidrosis you should see, and perhaps even in the one-stage patients you might see a reduction over time in compensatory hyperhidrosis. Did you observe that? More importantly, in the two-stage group, I noticed that there was quite a wide range in the interval between surgeries. Did the patients with shorter intervals and the patients with longer intervals have different rates of compensatory hyperhidrosis?

Dr Menna: We did not analyse our results in relation to the different time intervals between surgeries. I cannot answer your question because we did not investigate that. Regarding the explanation for the reduced compensatory sweating occurrence, I can say that we cannot demonstrate it; we can just hypothesize. A cadaveric study could allow us to demonstrate our results. We can hypothesize that a two-hit strategy for the autonomic system could allow us to achieve better results in terms of thermo-regulatory balance, but it is just a hypothesis.

Dr Sihoe: And how did you define compensatory hyperhidrosis? You have very excellent results.

Dr Menna: We defined compensatory hyperhidrosis as a postoperative increase of sweating in regions of the body where it had not been previously described.

Dr Sihoe: My other question to you relates to patient allocation to the two study arms. Reading from the abstract which you have published here in the abstract book, you do mention the word 'randomize,' but I notice in your presentation and also in your full paper that that word was not used. There was no mention of randomization.

Dr Menna: We did not randomize patients because it is a retrospective study.

Dr Sihoe: A typing error, I assume. But that begs the question, how did the patients end up being allocated to the two study arms? Did you use certain selection criteria which may have introduced bias, for example? Most importantly, did the patients have a choice about whether they went for a one-stage or a two-stage operation? I ask that because, as I said, this is an elective procedure for non-life-saving surgery. Now, if I were a patient with hyperhidrosis and I was asked if I just want one operation or undergo two operations, it is pretty obvious what I would choose. Do the patients have a choice? Did you ask about patient satisfaction in the two groups after surgery? Would they have chosen one-stage if they were given the opportunity to do so?

Dr Menna: In 1995 when we started with this kind of treatment, we began with a two-stage unilateral approach. When the one-stage strategy became widespread, we converted our approach to the one-stage bilateral strategy. So we just retrospectively analysed the data and now we do it in the same way as the rest of the world, with the one-stage bilateral approach. I know that if patients could have the possibility of choosing, maybe they would choose the one single, quick admission with a short hospitalization and less risk of complications, but you have to also take into account the occurrence of compensatory sweating.

Dr Sihoe: Thank you for a very honest answer. So what you are saying to me is that despite the fact that you can reduce compensatory hyperhidrosis with a two-stage approach, you are actually using the one-stage approach now for all patients?

Dr Menna: Sorry, can you repeat the question?

Dr Sihoe: I am just saying that your study here showed that the two-stage approach has an advantage in reducing compensatory sweating, and yet now you are using the one-stage approach for your patients.

Dr Menna: I think we are going to start giving patients the possibility of choosing.

Dr J.R. De Campos *(São Paulo, Brazil)*: My comments here are constructive. We are really interested in these results. We started like you, with the two-stage and then we changed to the one-stage. My question and my concern is that you have an interval between the first and the second stage between one month and one year.

Dr Menna: Yes.

Dr De Campos: The perception of the patient has changed a lot. We all know that the compensatory sweating is like a physiological thermo-regulation. So one thing, I operate on you today and the next day you are completely different in your thermo-regulatory sense, your perception. So for me, the comments about your conclusion, if you operate at two times, two different times, maybe the perception of the compensatory sweating is a little bit different. Do you understand my question? You have the perception. You operate one stage; one year after, another stage. And then the most important thing, the follow-up, you have one month and 24 months. It is a completely different situation, completely different season of the year. Your paper is very important, but you have to consider the time and then follow these same patients with the time, and you can show us the quality of life questionnaire that you are using in all of these patients and then maybe we will have a very good answer. What I mean is that you have a lot of things to analyse. Maybe if you put everything together and follow some rules, you will have a very nice result for us. That is why I'm trying to say it is a constructive analysis of your paper and very nice presentation.

Dr E. Rendina *(Rome, Italy)*: I take your comments as they are; they are constructive comments. I just want to jump in. We are in a very particular environment. We are in a university environment and most of our cases are very big cancer cases or tracheal cases or severe emphysema cases. As you were saying, non-life-threatening cases, such as palmar or axillary hyperhidrosis, they are done in the 'holes' that we have in the operating schedules. Of course, we are very concerned with our patients, and it is surprising how many of these patients, when informed carefully about the possibilities, the pros and the cons of a one-stage versus a two-stage operation, select the two-stage operation. They prefer the two-stage operation. We see them and we talk to them during the period which separates the first operation and the second operation and they are happy during this period. They are happy because their social life is very strongly impacted. As you who do this surgery all know, by the work of their right hand, they can caress people, they can shake hands with the right hand, and even if the left hand still sweats, it is not a big deal, and they are happy with that. They can wait for a long time and they do not care. As you were rightly saying, these patients have to be followed very carefully, but many of them do not bother so much with waiting time. The work with these patients, in our centre at least, is strongly impacted, as I was saying, by the environment. So we have limited resources for them, although we care for them very much, as you must, of course, believe.