**REVISION CONTENTS**

We thank the reviewers’ precious comments to our study. Our study was revised according to the reviewers’ suggestions, and the revised parts of the article was written in red font. In addition to these revisions we found an error in the statistical analysis and corrected the necessary values in the results section.

Reviewer 1:

1. Spelling mistakes were corrected in the manuscript.
2. The keywords were rearranged in alphabetical order.
3. The first “bilateral” was omitted in the sentence “In this prospective study involving bilateral patients who undergone
bilateral....”.

Reviewer 2:

1. Grammar of the article was revised.
2. We cannot add any images of the surgical technique because we did not obtain such information as per the informed consent form of our study.
3. The abbreviation PY was corrected to PC.
4. We added the limitations to ous study in the discussion section.
5. Conclusion part of the article was rearranged as a seperate part.
6. Fisher exact test values were added into the newly added tables according to the revision requested in the 7th row.
7. Two tables added to the results section about PC and CH.

**Research Article**

**The Results of Long Term Follow Up for Bilateral Single Port Sympathicotomy In Primary Hyperhidrosis: Should We Really Perform This Surgery?**

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**Abstract**

**Background:** Hyperhidrosis (HH), is the excessive sweating of the body in response to temperature or emotional stimuli rather than physiological stimuli. In this prospective study, we researched for long-term effects on complication development and patient satisfaction of this disease, which adversely affects the quality of life.

**Methods:** Thirty-one patients who underwent bilateral single-port endoscopic thoracic sympathicotomy (ETS) for HH between January 2010 and November 2014 were enrolled in this study. Patients were followed up until July 2017. Patient satisfaction was recorded with complications such as compensatory hyperhidrosis (CH) and primer complaints (PC) during short and long term follow up periods.

**Results:** The mean follow-up period was 60.6 ± 12.8 (min: 40, max: 89) months postoperatively. When both short and long term results were evaluated together, there was no effect of CH on patient satisfaction. Still, it was found that the continuation of PC in both short term (p = 0.020) and long term (p = 0.001) follow up periods to be significantly effective on satisfaction.

**Conclusion:** The most important factor affecting patient satisfaction in this study was the continuation of PC, which led to the conclusion that further studies should be performed to enlighten this complication even though it may remit with time. Whether or not the ETS is a permanent treatment that cannot successfully treat PC, possible complications and the ability to cope with them will seem to be open to debate as the most important issues that surgeons will have to face in the near future.

**Keywords:** complication; hyperhidrosis; surgery; sympathicotomy

**INTRODUCTION**

Hyperhidrosis (HH) can be described as excessive sweating of the body which is more than the physiological need[1]. Hyperhidrosis is studied in two groups, mainly as primary and secondary. Primary HH is present in the facial, palmar, axillary and plantar regions of the body, exhibiting regional and symmetrical involvement patterns due to overactivity of the sympathetic nervous system[1,2]. Secondary HH occurs due to factors such as malignancies, endocrine disorders such as thyrotoxicosis, and certain medications[3].

Hyperhidrosis treatment can be divided into two as medical and surgical. Endoscopic thoracic sympathicotomy (ETS) is the most commonly used method in surgical treatment today. ETS can be applied in a variety of ways, such as dissecting the sympathetic chain in the thoracic region, thermal damaging with the electrocautery, or clipping. ETS has complications such as hemo-pneumothorax, Horner's syndrome, bradycardia, but the complication that affects patient and physician satisfaction the most is compensatory hyperhidrosis (CH)[4,5].

In this prospective study involving patients who undergone bilateral ETS with single port, the rate of complications of the long-term postoperative period such as persistence of CH and primary complaints (PC) and their effects on patient satisfaction were investigated.

**METHODS**

Patients who underwent a single port ETS operation between January 2010 and November 2014 at Çanakkale Onsekiz Mart University Medical Faculty Thoracic Surgery Clinic were prospectively followed up until July 2017. Patients were questioned about their changes in CH and PC and their satisfaction about the operation during the postoperative period with the outpatient clinic examinations and telephone interviews.

All patients were medically treated for at least six months during the preoperative period, but none of them had any improvements for their PC. Informed consent of all patients was obtained. In cases with multiple HH defining cases, only the region with the major complaints was treated. ETS was performed using a 10 mm 0 degree thoracoscope (Karl Storz 26034 AA) with a 6 mm working channel under general anesthesia via a double-lumen endotracheal tube. After the patients were positioned to the lateral decubitus position, a single thoracoport of 10.5 mm width was inserted into the thorax through a single incision of 11 mm at the intersection of fourth intercostal space (ICS) and the mid-axillary line. The sympathetic chain was cauterized with endoscopic electrocautery from T2 for fascial hyperhidrosis, T3 for palmar hyperhidrosis, T4 for axillary hyperhidrosis and T5 for plantar hyperhidrosis. In addition, during the sympathicotomy operations of T2-T3, the presence of the nerve of Kuntz was verified and such nervous tissue was cauterized. The rib bed was cauterized laterally for an additional 2 cm to allow the dissection of possible by-passing nerve fibers. After the hemorrhage control, the air in the pleural cavity was evacuated via a small catheter. The incision line was closed by subcutaneous suturing, and the same procedure was repeated for the other side.

The patients were evaluated on the postoperative first day by physical examination, posterior-anterior (PA) chest X-ray, hemogram and blood biochemistry tests. Patients whose physical examination and examination results revealed no abnormalities were discharged from the hospital on the first postoperative day. The patients were referred to the outpatient clinic on the seventh postoperative day and reevaluated with physical examination and PA chest X-ray. All cases were interviewed by telephone in the third postoperative month, and the third postoperative year. They were questioned about their hyperhidrosis status, compensatory hyperhidrosis status, and satisfaction with operation. Patients were asked to rate their hyperhidrosis at the site of primer complaints from 0 to 10, where 0 represented no sweating, and 10 represented the most severe sweating.

Follow-up times ranged from the operation date to the last follow-up date (July 2017) expressed in months. Subsequently, the cutoff values for 48, 60, and 72 months were coded as a dichotomous variable for those below and above the follow-up period. CH, PC, patient satisfaction, and the decision that if the patient would have undergone the surgery at the day of the interview were coded as dichotomous variables. The CH and PC intensities were coded as continuous variables ranging from 1-10. After the data were transferred to the digital medium, the normal distribution matching of the continuous variables were examined for the frequency and distribution of variables. Relations between continuous variables were analyzed by appropriate correlation tests, relationships between dichotomous variables were analyzed by Chi-square and, if necessary, Fisher's exact test. The general significance limit of these statistical analysis tests was accepted as p-value <0.05, and the absolute p values were given for the analysis results.

**RESULTS**

Thirty-one patients who underwent bilateral single port ETS operation at Çanakkale Onsekiz Mart University Medical Faculty Chest Surgery Clinic between January 2010 and November 2014 were included in the study. Sixteen (51.6%) of the patients were male, and 15 (48.4%) were female. The mean age of the cases was 24.13 ± 4.64 (min: 13, max: 34). The complaint rates of the patients were 6.5% (n = 2) at craniofacial, 12.9% (n = 4) at palmar-facial and 67.7% (n = 21) at palmar, 9.7% (n = 3) at axillary and 3.2% (n = 1) at palmoplantar region. Postoperative complications were pneumothorax in 1 patient and hemopneumothorax in 1 patient. Tube thoracostomy was performed to the patient who developed hemopneumothorax and air evacuation via thoracentesis was performed to the other patient. All other patients were discharged on the first postoperative day. Thus, the average duration of hospital stay of the cases was 1.13 ± 0.56 (min: 1, max: 4) days. The mean follow-up period was 60.6 ± 12.8 (min: 40, max: 89) months postoperatively.

When the patients were questioned about their PC status, 10 (32.3%) of the 31 patients responded that their PC did not heal. The remaining 21 cases responded that their PC was on remission. The most frequent site for the persistent PC was palmar HH (Table 1).

When the patients were asked about their CH status at postoperative third-month, 15 (48.4%) of 31 patients reported that they had developed CH. When the severity of CH was asked, responses were obtained ranging from 3-10 (Table 2).

When the localizations of the diseased CH were questioned, cases responded that the most frequent site of CH was the dorsal region (Table 3).

At the final interview on July 2017, the patients were inquired about their surgical satisfaction. Six patients (19%) were not satisfied with the operation. Thus, the satisfaction of the operation was found to be 81%. Five out of six (83%) patients who were not satisfied with the operation were found to have developed CH, and 5 out of 6 (83%) cases had ongoing PC (Table 4,5). In total, seven patients indicated that they would not have undergone this surgery today but the interesting finding is that only 2 of them had developed CH, and the remaining 5 had ongoing PC. One of these patients who was satisfied with the surgery, but reported that he would not have undergone this surgery today, mentioned that he had a certain degree of remission of his PC but the remission was not complete.

When the long-term follow-up of the cases were examined, it was found that PC terminated in 2 patients, and CH was developed in 3 patients. As a result, 8 (25%) cases of PC persistence and 18 (58%) cases of CH persistence was found. It was found that the continuation of PC was effective on patient satisfaction in both short (p = 0.007) and long (p = 0.001) term. Contrary to this finding, CH had no effect on patient satisfaction in short (p = 0.083) and long (p = 0.359) term.

**DISCUSSION**

Although the precise pathophysiological mechanism is not known in primary hyperhidrosis, it is thought that the excessive stimulation of thermoregulatory and emotional sweating control centers or secretion of excessive amounts of acetylcholine by the sympathetic nervous system as an overreaction to the stimuli of these centers[3]. Primary hyperhidrosis, which usually begins in childhood or adolescence, causes admittance to physicians because of the psychosocial problems that were caused by HH[6].

The medical therapy options of HH include, topical or systemic antiperspirants, iontophoresis, botulinum toxin injection, microwave and laser therapy (6). Antiperspirant agents are the topical form of the 20% solution of aluminum hydrochloride and the topical or systemic forms of anticholinergics such as glycopyrrolate or oxybutynin[7]. Iontophoresis is preferred in the treatment of palmoplantar hyperhidrosis. It is based on the principle that the palmoplantar zone is kept in tap-water in which low voltage electrical current is applied for about 30 minutes[8,9]. Botulinum toxin A injection is a treatment method that can be applied in palmoplantar and axillary hyperhidrosis. It provides a longer remission time than any other medical method. After injection of botulinum toxin A, HH goes into remission for about 6 months[10]. Neodynium yttrium aluminum garnet (Nd: YAG) laser therapy can also be used for hyperhidrosis treatment[11]. Microwave therapy involves the thermolysis of eccrine sweat glands, and the main difference of this method is that it is irreversible[12]. The major disadvantage of medical treatments in HH compared to the surgical treatment is that they offer a temporary solution to an ongoing problem and should be repeated. However, their most important advantage over surgical treatment is the absence of CH. For this reason, it is recommended that all patients scheduled for surgical treatment should have tried a medical treatment method for at least 6 months and did not experience satisfactory results as such were the cases that were included in our study.

CH can be described as excessive sweating that can be observed in various parts of the body after ETS. The development mechanism of CH is not known precisely. Although some authors have argued that this condition develops because negative feedback stimuli of this sympathetic chain cannot reach the hypothalamus, there is no scientific evidence to support this hypothesis[13,14]. Approximately 3-98% of patients are observed to develop CH after ETS, and it is most commonly observed in the trunk area. It is not possible to predict who may develop CH and how severely it will become[4,5,13]. Although some studies on this subject have shown that sympathicotomy made at the T2 level, sympathectomy applied at multiple levels and increased age enhances the risk of developing CH, there are also studies that contradict these findings[13,15-17]. In our study, the rate of CH determined as 48% in the short term, and 58% in the long term developed most commonly at the trunk region similarly to the scientific literature about this subject.

It has been reported that the development of CH and the continuation of PC are the two most important factors affecting patient satisfaction after ETS operations. PC continuation reported in the literature at rates ranging from 0 to 21.4% is comparable with the results of our study that was 32% for short-term follow up and 25% in long-term follow up[13,16,18]. However, the interesting result of the long-term follow-up is that the continuation of PC is the most important factor affecting patient satisfaction.

When the studies conducted about HH, in general, are examined, it is seen that the postoperative follow-up period of the cases is less than 1 year and mostly is approximately 6 months. We have limited knowledge of these patients’ conditions over the long term. In our cases who were followed up for a long time (mean 60 months), the increase in the number of CH did not increase patient satisfaction, but on the contrary, while a decrease in PC was observed, there was also a decrease in the patient satisfaction. And thus, the most important factor affecting satisfaction was the continuation of PC in contrast to our current knowledge. The results of the intermittent unilateral ETS for reducing CH, which is affecting short-term satisfaction are promising, although the duration of follow-up in that study is 1 year[19]. However, factors affecting hospital costs, such as two surgeries, two anesthesia and two hospitalizations, seem to be the disadvantages of this technique. But we believe that the primary goal of surgery should be to end the PC. Self-remission of the PC with age should also be seen as a disadvantage for the ETS[20]. So, the possibility that the PC may regress in time while the PC rather than CH affecting the satisfaction of the patients brings about doubts about whether this operation should be performed or not.

The limitations of our study are; the number of cases is 31 that may be considered as low in contrast to other studies about ETS, this study does not compare the ETS to the medical treatment methods in terms of patient satisfaction.

**CONCLUSION**

As a result, it is known that ETS is the only definitive treatment that has proven to be successful with the long-term results of HH. Nevertheless, the two most important factors affecting patient satisfaction in ETS are the continuation of PC and the CH. Intermittent unilateral ETS may be considered as an alternative for the surgeon in terms of CH, but it should be conveyed that the likelihood of CH may increase in the long term and as the patient gets older the PC of HH may regress as well. This treatment should be described as temporary (at least until the end of the adolescence period) rather than permanent. The decision whether or not to perform this surgery is the surgeon's choice, but the decision whether or not to be treated with surgery for HH definitely should be patient’s after all these data have been conveyed.

**DECLARATIONS**

**Authors’ contributions**

Made substantial contributions to conception and design of the study and performed data analysis and interpretation: Alar T, Gedik İ E.

Performed data acquisition, as well as provided administrative, technical, and material support: Alar T, Gedik İ E.

**Availability of Data and Materials**

Not applicable.

**Financial support and sponsorship**

None.

**Conflicts of interest**

All authors declared that there are no conflicts of interest.

**Ethical approval and consent to participate**

Not applicable.

**Consent for publication**

Not applicable.

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**Figure Legend**

**Table 1. Regional Distribution of Ongoing Hyperhidroses**

|  |  |  |
| --- | --- | --- |
| **Region** | ***n*** | ***%*** |
| Craniofacial | 1 | 10 |
| Palmar | 5 | 50 |
| Axillary | 3 | 30 |
| Plantar | 1 | 10 |
| **Total** | **10** | **100** |

**Table 2. The Distribution of the Severity of Compensatory Hyperhidrosis.**

|  |  |  |
| --- | --- | --- |
| **Severity** | ***n*** | ***%*** |
| 3 | 1 | 6.8 |
| 4 | 2 | 13.3 |
| 5 | 2 | 13.3 |
| 6 | 2 | 13.3 |
| 7 | 3 | 20 |
| 8 | 3 | 20 |
| 10 | 2 | 13.3 |
| **Total** | **15** | **100** |

**Table 3. The Regional Distribution of Compensatory Hyperhidrosis.**

|  |  |  |
| --- | --- | --- |
| **Location** | ***n*** | ***%*** |
| Dorsal | 9 | 60 |
| Abdomen | 3 | 20 |
| Chest | 3 | 20 |
| **Total** | **15** | **100** |

**Table 4. Primary Complaint (PC) vs. Satisfaction Crosstable**

|  |  |  |
| --- | --- | --- |
|  | **Primary Complaint** |  |
|  | **-** | **+** | **Total** |
| **Satisfaction** |  |  |  |
| No | 1 | 5 | 6 |
| Yes | 20 | 5 | 25 |
| **Total** | **21** | **10** | **31** |

\* p>0.05 Fisher’s exact test value 0.007

**Table 5. Compensatory Hyperhidrosis (CH) vs. Satisfaction Crosstable**

|  |  |  |
| --- | --- | --- |
|  | **Compensatory Hyperhidrosis** |  |
|  | **-** | **+** | **Total** |
| **Satisfaction** |  |  |  |
| No | 1 | 5 | 6 |
| Yes | 15 | 10 | 25 |
| **Total** | **16** | **15** | **31** |

\* p<0.05 Fisher’s exact test value 0.083