

# Diagnosis, impact and management of hyperhidrosis including endoscopic thoracic sympathectomy

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## ABSTRACT

**Introduction:** Hyperhidrosis is a disorder of excessive and uncontrollable sweating beyond the body's physiological needs. It can be categorised into primary or secondary hyperhidrosis based on its aetiology. Detailed history review including onset of symptoms, laterality of disease and family history are crucial which may suggest primary hyperhidrosis. Secondary causes such as neurological diseases, endocrine disorders, haematological malignancies, neuroendocrine tumours and drugs should be adequately examined and investigated prior to deciding on further management. The diagnosis of primary hyperhidrosis should only be made only after excluding secondary causes. Hyperhidrosis is a troublesome disorder that often results in social, professional, and psychological distress in sufferers. It remains, however, a treatment dilemma among some healthcare providers in this region.

**Methods:** The medical records and clinical outcomes of 35 patients who underwent endoscopic thoracic sympathectomy for primary hyperhidrosis from 2008 to 2018 in Department of Cardiothoracic Surgery were reviewed.

**Results:** The mean age of the patients was  $27 \pm 10.1$  years, with male and female distribution of 18 and 17, respectively. Fifty-one percent of patients complained of palmar hyperhidrosis, while 35% of them had concurrent palmar-axillary and 14% had palmar-plantar-axillary hyperhidrosis. Our data showed that 77% (n=27) of patients were not investigated for secondary causes of hyperhidrosis, and they were not counselled on the non-surgical therapies. All patients underwent single-staged bilateral endoscopic thoracic sympathectomy. There was resolution of symptoms in all 35 (100%) patients with palmar hyperhidrosis, 13(76%) patients with axillary hyperhidrosis and only 2 (50%) patients with plantar hyperhidrosis. Postoperatively 34.3% (n=12) of patients reported compensatory hyperhidrosis. There were no other complications such as pneumothorax, chylothorax, haemothorax and Horner's Syndrome.

**Conclusion:** Clinical evaluation of hyperhidrosis in local context has not been well described, which may inadvertently result in the delay of appropriate management, causing significant social and emotional embarrassment and impair the quality of life of the subjects. Detailed clinical assessment and appropriate timely treatment, be it surgical or non-surgical therapies, are crucial in managing this uncommon yet distressing disease.

## KEYWORDS:

*Primary Hyperhidrosis, Secondary Hyperhidrosis, Endoscopic Thoracic Sympathectomy (ETS), Compensatory Hyperhidrosis (CS), Outcomes of Endoscopic Thoracic Sympathectomy*

## INTRODUCTION

Hyperhidrosis is a disorder of excessive, unexpected and uncontrollable sweating in response to psychological stressors or emotional stimuli, beyond the body's physiological needs. It can be categorised into primary or secondary hyperhidrosis based on its aetiology. While primary hyperhidrosis is a condition by itself as a result of sympathetic hyperstimulation, secondary hyperhidrosis though is caused by a number of medical conditions, including neurological problems, endocrine disorder, chronic infection, haematological malignancies, neuroendocrine tumour and drugs. For many, this disorder has severe devastating emotional and social impact, causing embarrassment and decrease the quality of life. However, our experience throughout the years working in a tertiary referral centre showed that many of these patients were not adequately investigated for the causes of hyperhidrosis before they were referred for endoscopic thoracic sympathectomy (ETS). Often, patients were also not counselled on the non-surgical therapies which are readily available. The delay in diagnosis and treatment is not uncommon, often resulting in patients misunderstanding of their disease, fearing that there is no treatment, or that surgery is the only option.

This paper aims to describe the causes of primary and secondary hyperhidrosis, and the clinical evaluation of hyperhidrosis in local settings; and if primary hyperhidrosis is diagnosed, the options of non-surgical therapies available prior to ETS. We also present the clinical outcomes of ETS for primary hyperhidrosis in our centre.

## MATERIALS AND METHODS

### *Study Design and Setting*

This is a retrospective review conducted in the Department of Cardiothoracic Surgery, Hospital Pulau Pinang (CTS HPP), Malaysia between January 2008 and December 2018. The medical records of 35 patients with primary hyperhidrosis who underwent ETS were reviewed. Exclusion criteria included patients with secondary hyperhidrosis and generalised sweating, patients with menopausal symptoms as well as patients with multiple or severe comorbidities such

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as heart and lungs complications, neurological diseases, and uncontrolled chronic illnesses. The surgical outcomes (resolution of symptoms, complications including compensatory hyperhidrosis and lungs complications) were noted and recorded.

#### *Diagnosing Criteria for Primary and Secondary Hyperhidrosis*

The diagnosis of primary hyperhidrosis was confirmed by excluding all the possible secondary causes of hyperhidrosis. Secondary hyperhidrosis is excessive sweating that is not idiopathic and secondary to another underlying condition or side effect of medications, including spinal cord diseases, diseases involving central nervous system, autoimmune diseases, thyroid diseases, chronic infections such as tuberculosis, HIV-related diseases, haematological malignancies, and neuroendocrine tumours. Details regarding baseline demographic features, clinical presentations, treatment received prior to referring to CTS HPP were recorded. All of the patients underwent laboratory investigations including full blood count, renal profile, serum albumin, C-reactive protein (CRP), thyroid function test, biohazards, tumour markers, tuberculosis workup, blood glucose level, urine catecholamine, as well as chest X-ray to exclude secondary hyperhidrosis prior to ETS.

#### *Hyperhidrosis Disease Severity Scale*

In CTS HPP, hyperhidrosis disease Severity Scale (HDSS) is used for objective measurement of severity of primary hyperhidrosis. It assesses the severity of hyperhidrosis based on the extent of excessive sweating-related impairment of daily activities. Patients rate the severity as: 1="my underarm sweating is never noticeable and never interferes with my daily activities"; 2="my underarm sweating is tolerable but sometimes interferes with my daily activities"; 3 ="my underarm sweating is barely tolerable and frequently interferes with my daily activities"; or 4="my underarm sweating is intolerable and always interferes with my daily activities". The severity of the symptoms was scored during each clinic visit and consultation.

#### *Treatment Prior to ETS*

All patients who were referred to us for ETS were counselled on the available non-surgical treatments. Referrals are made to experts in Dermatological unit to discuss regarding the medical therapies which include topical antiperspirants, iontophoresis, and topical anticholinergics in all patients prior to ETS.

#### *Endoscopic Thoracic Sympathectomy (ETS)*

Surgery was performed under general anaesthesia with double lumen intubation. We performed single-staged bilateral ETS with two-ports video-assisted thoracoscopic surgery (VATS) while on single lung ventilation in lateral decubitus position. A thoracoscopic port is incised at the 6th intercostal space on mid-axillary line, and another instrument port is incised at the 3rd intercostal space on anterior axillary line. Sympathetic chains are transected at the level of 3rd and 4th ribs with electrocautery and extend to 5th rib if axillary hyperhidrosis was present. Care was taken to avoid injury to intercostal neurovascular bundles at the lower border of the ribs. The exact location of the trunk was identified by using surrounding landmarks such as azygous vein and arch of aorta. Another important landmark is the

1st rib, which appears as a closed C-shaped ring where pulsating subclavian artery can be found above it. We do not advise excessive unnecessary 'palpation' of the sympathetic chain with instruments to prevent hyperaemia or bleeding which might obscure the endoscopic view. To ensure complete transection of potential bypass or collateral nerve fibres (Kuntz nerve) which is not easily visualized, extension of lateral transection along the ribs by approximately 2cm was done on each rib. We routinely performed the right ETS first, then proceed to left ETS. After right sided sympathectomy, a chest tube is inserted into right pleural cavity through the thoracoscopic port. The lungs were then inflated under vision to ensure full expansion before closing the instrument port. Then, the right chest tube was removed and the thoracoscopic port is immediately closed while on continuous positive pressure. However, after left sided sympathectomy, a chest tube was routinely left inserted in the left hemithorax to prevent pneumothorax and was usually removed if chest X-ray postoperatively showed no pneumothorax.

## RESULTS

#### *Demographic and Clinical Presentation*

The mean age of our patients was 27±10.1years, with the youngest being 18 years old and the oldest being 60 years old, with nearly equal gender distribution. 51% of patients complained of only excessive sweating at the palm alone, while 35% and 14% of them had concurrent palmar-axillary and palmar-plantar-axillary hyperhidrosis, respectively. Out of the 35 patients, 20 were referred from government and private clinics, eight were referred from our Dermatology Department (DD), and seven were referred inpatients from other departments when they were admitted for other reasons but noted hyperhidrosis as an incidental finding. Table I shows the preoperative characteristics of our patients in this series.

#### *Non-Surgical treatments before ETS*

Out of the 35 patients who underwent ETS, only the eight patients who were referred from DD were diagnosed with primary hyperhidrosis by proper investigations to exclude secondary causes. These eight patients underwent medical treatments including iontophoresis and topical antiperspirants for 8 months to 2 years but requested for ETS after complained of persistent symptoms despite optimal medical therapies. Meanwhile, the other 27 patients had had history of multiple clinic visits for hyperhidrosis but were not referred for medical treatment before referrals were made to us for ETS. The eight patients who were referred from DD had early ETS done but the other 27 patients required an average period of three months from the time of referral before surgery was performed. The delay was mainly due to arranging investigations to exclude secondary causes of hyperhidrosis prior to ETS. These 27 patients were referred to DD for non-surgical therapies while waiting for surgery.

#### *Outcomes of ETS*

Immediate improvements were observed in all of the patients following ETS. There was resolution of palmar hyperhidrosis in all of the cases, and improvement of 13 (76%) out of 17 patients with axillary hyperhidrosis and only two (50%) out of four patients with plantar hyperhidrosis. All patients were

Table I: Preoperative patients' characteristics

Clinical Profile	n=35 (%)
<b>Age</b>	
<20 years old	3 (8.6)
21-30 years old	20 (57.1)
31-40 years old	9 (25.7)
≥40 years old	3 (8.6)
<b>Gender</b>	
Male	18 (51.4)
Female	17 (48.6)
<b>Site of involvement</b>	
Palmar hyperhidrosis	18 (51)
Palmar + axillary hyperhidrosis	12 (35)
Palmar + axillary + plantar hyperhidrosis	5 (14)
<b>Referral</b>	
Clinic (government and private)	20 (57.1)
Dermatology Unit	8 (22.9)
Palmar hyperhidrosis	2 (5.7)
Palmar + axillary hyperhidrosis	2 (5.7)
Palmar + axillary + plantar hyperhidrosis	4 (11.4)
Other disciplines in hospital	7 (20)
<b>Hyperhidrosis Disease Severity Scale (HDSS)</b>	
1	0 (0)
2	1 (2.9)
3	14 (40.0)
4	20 (57.1)

Table II: Postoperative complications

Complications	n=35 (%)
Compensatory hyperhidrosis	
Palmar hyperhidrosis	2 (5.7)
Palmar + axillary hyperhidrosis	5 (14.3)
Palmar + axillary + plantar hyperhidrosis	5 (14.3)
Horner's syndrome	0 (0)
Symptoms recurrence	0 (0)
Other complications, i.e., Pneumothorax, haemothorax, chylothorax	0 (0)

discharged 1 day after surgery. The follow up period ranged from 2 to 4 years. All the patients were satisfied with the marked improvement in functional limitations, work performance and quality of life. 34.3% (n=12) of patients reported compensatory hyperhidrosis (postoperative increase of sweating in regions of the body where it had not been previously observed), in which the most common area affected were the back. There were no other complications such as pneumothorax, chylothorax, haemothorax and Horner's Syndrome. Table II shows the postoperative complications of our patients.

## DISCUSSION

### *Primary Hyperhidrosis vs Secondary Hyperhidrosis*

Hyperhidrosis is a skin disorder characterised by sweating excessive of what is required to maintain regulation of normal skin temperature.<sup>1</sup> It is classified into either primary or secondary in nature. Primary hyperhidrosis is idiopathic, due to hyper-activation of sympathetic nerves and it usually affect a focal area of body, most often the palms, axillas, soles, or craniofacial region.<sup>2</sup> Secondary hyperhidrosis usually results from underlying medical conditions or complications of diseases such as spinal cord diseases, diseases involving central nervous system, autoimmune

disease, thyroid disease, chronic infections such as tuberculosis, HIV-related diseases, haematological malignancies, and neuroendocrine tumours. The use of prescription medications can sometimes cause excessive sweating as adverse effects. Unlike primary hyperhidrosis, secondary hyperhidrosis usually causes generalised sweating. In patients with excessive sweating, several clinical features are identified to favour the diagnosis of primary hyperhidrosis. In 2004, a multispecialty working group has defined the criteria to diagnose primary hyperhidrosis, which must involve focal, visible, excessive sweating of at least 6 month duration with no apparent causes which includes at least two of the following: bilateral or symmetrical disease, impairs daily activities, frequency of at least 1 episode per week, age of onset less than 25 years, positive family history, and cessation of focal sweating during sleep.<sup>7</sup> These criteria are often used in CTS HPP as a guide to aid the diagnosis of primary hyperhidrosis.

In contrast, if the excessive sweating is generalized, secondary causes must be considered, investigated and treated accordingly. Other indications suggesting of secondary hyperhidrosis include presence of constitutional symptoms (malignancies, chronic infection such as tuberculosis), time-specific sweating (night time sweating in

blood malignancies and tuberculosis), generalised symptoms (such as palpitation in hyperthyroidism, polyuria and polydipsia in uncontrolled diabetes mellitus), neurological deficit (for central or peripheral nervous disease), history of illicit drugs use, or general feeling of unwell. Although primary hyperhidrosis is usually diagnosed clinically, it is crucial to exclude possible secondary causes prior to determining the subsequent management, and laboratory blood tests and imaging modalities ought to be carried out as mentioned above.

#### *Impact of Hyperhidrosis*

Hyperhidrosis has significant impact on the lives of patients, causing them substantial physical discomfort, social embarrassment and negatively impacting self-image, resulting in functional limitation and reduced quality of life. It has negative effects in virtually all aspects of life, from occupational tasks, occupational choices and activity of daily living including gripping tools, playing musical instruments, using electronic devices, doing house-chores, carrying babies, handling papers and many more such activities. Indeed, numerous studies have shown that the impact of life in patients of hyperhidrosis is equal to or greater than that of psoriasis, severe acne, vitiligo and chronic pruritus.<sup>3</sup> In a national survey conducted in United State of America, it is reported to be as high as 75% of those with hyperhidrosis complained of negative impact of the disease on their social life, sense of well-being, and emotional and mental health.<sup>2</sup> Another study even noted 5% of hyperhidrosis patients consume antidepressant or anti-anxiety medications due to their sweating.<sup>4</sup> A more recent study showed 69% of patients experiencing emotional ramification, 75% of them admitted that they have difficulty to be in public view and 40% of them reported some level of physical discomfort.<sup>5</sup> In our cases, most of the patients reported constant worry and uneasy of the noticeable sweating, underperformance in their workplace, embarrassment in a party or social events, and as a result, they avoid touching, holding, shaking hands, sitting close to others, standing in a line, group presentation, and even using public transport. Furthermore, they usually perform extra 'chores', which includes taking a shower several times a day, changes shoes often, using strong antiperspirants, and bringing extra clothes to change. Anger, frustration and sadness and helplessness are common in these patients.

In addition, patients with hyperhidrosis were found to have a 300% greater risk of skin infection.<sup>6</sup> The constant moist environment promotes fungal and bacteria overgrowth, leading to various skin infection such as intertrigo, bromhidrosis, and cellulitis. Safety is also a major concern in certain individuals with hyperhidrosis, especially those working in healthcare industry, electric cable works, construction workers, sales and marketing as well as machine handlers. In fact, two of our patients were medical students, two medical assistants, three teachers and another eight factory workers. All of them were frequently absent from work due to these issues.

The Hyperhidrosis Disease Severity Scale (HDSS) is a reliable and easily understood diagnostic tool that provides a qualitative measure of the severity and tolerability the

conditions of patients based on the interference with daily activities.<sup>2</sup> Almost all of our patients scored 3 and 4 with this scale. This scale is also important to consider the urgency of the surgery, and if surgery could not be done promptly, referral should be made for topical or medical therapies while waiting for surgery.

#### *Non-Surgical Treatments for Primary Hyperhidrosis*

We strongly emphasize prompt referral to DD for non-surgical intervention if the diagnosis of primary hyperhidrosis is established. These therapies are simple yet effective, and often able to provide satisfactory symptomatic relief. Aluminium salt solution such as aluminium chloride is the most common antiperspirant used presently, and a study showed up to 87% of patients reported dryness and satisfaction.<sup>9</sup> It works by damaging the epithelial cells along the lumen of sweat ducts, forming a plug thereby obstructing the distal sweat ducts. However, renewal of sweat gland function returns with epithelial renewal, necessitating retreatment once or twice a week. This therapy is most effective in axillary hyperhidrosis, but less so in palmar hyperhidrosis which often requires higher concentration to be effective, with risks producing side effects such as pruritus and skin irritation.<sup>9,11,12</sup>

Topical anticholinergics such as oxybutynin and scopolamine has proved to be effective in the reduction of primary hyperhidrosis, which itself is a disorder of sympathetic over-activity.<sup>9</sup> These topical application has shown to reduce symptoms severity in 70% of patients for up to four weeks.<sup>10</sup> These medications can be delivered via contact sensitization, aerosol and iontophoresis. It is thought that use of topical anticholinergics can reduce the systemic side effects. However, while the medication is absorbed through the skin to affect the cholinergic nerve ending, most of the times a higher concentration of drugs is required to achieve satisfactory symptomatic relief, thus risking systemic absorption and side effects. Fortunately, these adverse effects are often mild and reversible. Recently, FDA has approved topical glycopyrronium as a topical treatment of axillary hyperhidrosis, which improves the symptoms severity by up to 30%, with 50% reduction in sweat volume after four weeks of usage.<sup>9</sup>

Another novel treatment for palmar and plantar hyperhidrosis is iontophoresis. In fact, tap water iontophoresis has been considered as the first line therapy for palmoplantar hyperhidrosis.<sup>13,14</sup> The exact mechanism is still unknown, although it is understood that activation of charged molecules generate electromagnetism causing a functional impairment of sweat glands, either by its denervation of sympathetic nerves, or alteration of cellular secretory threshold and physiology.<sup>14,15</sup> A 2002 study showed successful reduction of 81.2% of sweating from baseline after 8 treatments, with return of symptoms after 35 days.<sup>16</sup> This method is relatively safe, and a trial studied the source of electricity reported that usage of alternating current (AC) with direct current (DC) has a better safety profile compared to DC alone, with comparable clinical improvement.<sup>17</sup> Nonetheless, patients must be counselled that while these medical and topical therapies are beneficial, they may require multiple trials and applications to achieve and

maintain remission, and it does not provide immediate symptoms relief. Maintenance therapy is required in most cases. Even with these options, patients may not achieve complete nor permanent euhydrosis as evident in this case study.

#### *Surgical Treatment of Hyperhidrosis*

ETS has been considered as the definite curative treatment modality for primary hyperhidrosis, or those who failed to respond to the non-surgical intervention.<sup>18</sup> The global recurrence rate of hyperhidrosis after ETS is 8.8%, but Herbst et al., reported only 1.5% of recurrence.<sup>20,25</sup> The short term and long term outcomes of ETS are excellent with significant improvement in quality of life, which are also observed in patients who underwent ETS in our centres.<sup>19,20</sup> Complications of ETS include pneumothorax, haemothorax, compensatory hyperhidrosis (CS), gustatory sweating, Horner's syndrome and recurrence of symptoms. Compensatory hyperhidrosis is often the main cause of dissatisfaction after ETS. Both Gossot et al., and Horslen et al., described the incidence of compensatory hyperhidrosis to be as high as 86.4% and 86% respectively.<sup>19,20</sup> In contrary, we reported no incidence of haemothorax, pneumothorax, gustatory sweating and Horner's syndrome. However, our series of cases showed as many as 34% (n=12) of patients complained of compensatory hyperhidrosis following ETS, although majority of them reported this complication as only a minor problem and mainly affecting the back, and the symptoms are not particularly disturbing causing significant distress. All our patients have palmar hyperhidrosis and their main concern were often unable to carry out their duties satisfactorily, thus they were willing to accept the risk of compensatory hyperhidrosis as they wanted their hands to be completely dry and functional. Furthermore, during the follow up, these patients remained satisfied with the improvement in social and work performance, as well as the overall quality of life. From our experience, risk of compensatory hyperhidrosis is higher when more trunk levels are transacted. Transection of 2nd rib is avoided to reduce the risk of compensatory hyperhidrosis. However, we routinely performed nerve transection of at least two levels to ensure complete dryness postoperatively, although single-level nerve disruption may reduce the risk of compensatory hyperhidrosis but risk incomplete resolution of symptoms.<sup>26</sup> Depending on the site of symptoms, we perform sympathetic chain transection for isolated palmar hyperhidrosis only at level of 3rd rib and 4th rib, and extend the level of nerve transection to 5th rib in patient with palmar-axillary hyperhidrosis, an approach similar to that of Vannucci et al.<sup>26</sup> Here, we emphasize the importance of proper and detailed explanation and counselling of the possible risks and complications of ETS to our patients according to local hospital guidelines. Ibrahim et al suggested a two-staged ETS rather than one-staged ETS in reducing the incidence of compensatory hyperhidrosis, which is supported by study done by Youssef et al.<sup>23,24</sup> However, this approach is not adopted in our centre, not only due to the reduction of hospitalisation costs with single short admission, but also to decrease other risks associated with general anaesthesia and the surgery itself.

ETS may be the best modalities in treating palmar hyperhidrosis, but it is less effective in reducing axillary and

plantar hyperhidrosis. Our study reported immediate relief of palmar hyperhidrosis in all our patients, but only 80% of axillary hyperhidrosis and 50% of plantar hyperhidrosis has symptomatic relief. In one series of cases, 95% of the patients with palmar hyperhidrosis was dry postoperatively but only 83% of patients with axillary hyperhidrosis has symptomatic relief.<sup>8</sup> Nonetheless, the selection of appropriate surgical candidate is crucial, and we agreed on the consensus that ETS in patients with axillary and plantar hyperhidrosis alone is often less successful and associated with higher incidence of complications such as compensatory hyperhidrosis.<sup>18,19</sup> This is also a crucial factor to consider in patients who were referred to us for axillary, plantar and craniofacial hyperhidrosis without significant palmar hyperhidrosis, and such cases will be discussed with our dermatology colleagues for non-surgical therapies which may provide effective symptomatic treatment.

There are different methods of sympathetic nerve interruption, but no clear differences have been demonstrated.<sup>18</sup> Methods such as transection, resection, ablation with cautery and clipping have been described. Regardless of the method adopted, the main concept is to achieve adequate separation between the end of the sympathetic chains so that regrowth is not possible, although it also depends on the preferences of the surgeons' and the local practises. Nerve ablation alone may result in recurrence of symptoms and surgical reversal of clipping may have the advantage for reversibility of adverse effects such as compensatory hyperhidrosis.<sup>18,27</sup>

Despite numerous reports available and studies on the guidelines of management of hyperhidrosis, the management approach of patients complaining of hyperhidrosis remains a dilemma in some healthcare personnel in our local settings. In our experience over the years as a tertiary referral centre, most of the patients referred for ETS were inadequately investigated for secondary causes of hyperhidrosis. Often they were not counselled and offered the non-surgical therapies which are available in most of the healthcare facilities. On average, the delay for surgery was more than three months from time of referral. This delay was due to investigations for secondary causes of hyperhidrosis, arrangement of imaging modalities and discussion with respective specialities in suspected secondary hyperhidrosis, referral to dermatology units for symptomatic relief, and numerous counselling if patients undecided for surgery. As a result, frustration and disappointment are commonly observed among these patients. Therefore, we recommend proper counselling and investigations in patients complaining of excessive sweating, and if primary hyperhidrosis is attended to early, and given prompt referrals for non-surgical therapies and to Cardiothoracic Surgery Department for ETS if symptoms persist.

#### **CONCLUSION**

Hyperhidrosis is a troublesome disorder that often results in social, professional, and psychological distress in sufferers. Their quality of life is impaired with severe disruption in daily lives. Further studies need to be done to determine the prevalence of hyperhidrosis in local context, but we believe

there are still many unreported cases where patients do not seek medical treatment. Early detection and prompt management are able to provide rapid symptomatic relief and significant improvement in the quality of life of the patients. Our patients also showed that ETS is an effective curative treatment for primary palmar or palmar-axillary hyperhidrosis, with excellent outcomes and no recurrence of symptoms.

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