



Anatomical clipping of sympathetic nerve to reduce compensatory sweating in primary hyperhidrosis: a novel technique

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Contributions: (I) Conception and design: All authors; (II) Administrative support: All authors; (III) Provision of study materials or patients: MC Angeli; (IV) Collection and assembly of data: F Raveglia; (V) Data analysis and interpretation: F Raveglia; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

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Background: Hyperhidrosis (HP) is a pathological condition presenting with extreme perspiration exceeding physiological range. At present, several treatments for HP are available, however, is common opinion that thoracoscopic sympathetic nerve trunk interruption is the most effective approach in terms of duration and outcomes. Its most feared side effect is excessive sweating emerging in a new body area that can be as embarrassing as the original form of HP that required surgery. It is generally thought that interruption of the nerve at a higher level including severing it at several level is more likely to determine dry skin whereas low resection tend to prevent compensatory hyperhidrosis (CH) occurrence. We reviewed our experience to determine the optimal nerve target level for sympathectomy in order to achieve patients' satisfaction.

Methods: We retrospectively collected data from patients who underwent surgical sympathetic nerve interruption for HP from 2001 to 2018 at our division. Since surgical strategy and technique have been modified over the years, patients were categorized in 4 groups depending on the period of surgery. Our primary outcome was sweating improvement. Secondary outcomes were CH onset, degree of satisfaction, complications and recurrences. Follow-up was up to 18 months.

Results: We consecutively operated on 2,725 patients (1,438 male and 1,287 female) with a mean age of 28 and a range between 15 and 72 years. From 2001 to 2003, 132 patients underwent non selective nerve dissection at the upper margin of 3rd rib. From 2003 to 2012, 643 patients underwent selective nerve clipping at the upper margins of predetermined ribs in accordance with specific skin area. From 2012 to 2018, 1,582 patients underwent selective nerve clipping at the lower pole of predetermined ganglia. Sweating management and degree of satisfaction progressively improved in the 4 groups, whereas disturbing CH shifted from 72% to 3%.

Conclusions: Selective ganglia interruption by titanium clips is a satisfactory option that guarantee successful management of excessive sweating and is associated with tolerable CH. Careful preoperative patient evaluation is mandatory to define correct surgical strategy that should be always decided in accordance with patient keeping into consideration the benefits on sweating reduction versus the risk of troubling CH.

Keywords: Hyperhidrosis (HP); compensatory hyperhidrosis (CH); target; video-assisted thoracoscopic surgery (VATS); sympathetic block

Received: 11 April 2019. Accepted: 25 April 2019; published: 04 June 2019.

doi: 10.21037/shc.2019.05.02

View this article at: <http://dx.doi.org/10.21037/shc.2019.05.02>

Introduction

Sweat is physiologically produced by eccrine glands present in the skin on the basis of emotional and thermic stimuli and mental activity, whereas hyperhidrosis (HP) is the pathological condition presenting with extreme perspiration exceeding physiological range. Primary or idiopathic hyperhidrosis (PH) is not an eccrine glands disease and usually affects palms, axillae, face and soles, singularly (focal HP) or together (diffuse HP). It determines severe functional and social disadvantages with a negative impact on quality of life. HP usually arises in young people, affecting equally man and women, and interests a percentage ranging from 0.6% to 5% of entire population (1).

At present, several surgical and non-surgical treatments for HP are available. Medical therapies are topical antiperspirants, iontophoresis and systemic medication (2), whereas surgical treatments are endoscopic thoracic sympathectomy (ETS) and excision of axillary tissue (3). Lastly, botulinum toxin injection it's a "bridge" option between medical and surgical approach (4,5).

These options differ by satisfaction rate, efficacy and collateral effects onset for each of the different body area treated. However, it is common opinion that ETS is the most effective approach in terms of duration and outcomes (6). ETS consists of sympathetic nerve trunk interruption at different level in accordance to the body area affected by HP.

Conversely, ETS is associated with some minor and unfrequent complications, whereas persistence of symptoms is not a true complication and should be ascribed to incorrect nerve interruption. Side effects are probably more relevant. Compensatory sweating is the most feared side effects of ETS. It consists of excessive sweating emerging after sympathectomy in another body areas. Compensatory hyperhidrosis (CH) is a physiological response to sympathetic chain interruption interesting the whole body area but usually mainly perceived at thorax, back or thighs, which is why its incidence varies from 3% to 98% in literature; it can be equally embarrassing and affects quality of life as much as the initial HP that required surgery (7).

Despite CH onset is unpredictable, cephalic nerve trunk interruption and numbers of interruptions are certainly determinant. As a general rule, the more the interruption level is high, the more CH risk is increased since that should preserve the negative afferent tone to hypothalamus itself.

Summarizing criteria reported above, ETS strategy is based on the statement that high level and multiple nerve chain disruption more likely guarantee dry skin whereas low

resection decrease CH occurrence or severity.

This paper is aimed to review our experience in surgical management of HP comparing different techniques and strategies over the years and determine which is the optimal target nerve level to perform sympathectomy in order to obtain good patients satisfaction balancing skin dryness and CH onset.

Methods

This is a retrospective study reviewing our data, prospectively collected, concerning patients affected by HP who underwent video-assisted thoracoscopic surgery (VATS) sympathetic nerve interruption at our division of thoracic surgery.

From 2001 to 2018 we consecutively operated on 2,725 patients (1,438 male and 1,287 female) with a mean age of 28 and a range between 15 and 72 years.

All patients were enrolled at our clinic for increased sweating. Everyone had a medical interview which was thereafter complemented with a paper questionnaire to better quantify sweating severity.

The survey was organized into figures for each remarkable body area and patients were asked to add numeric value from 0 to 10 (numeric analogic scale) to quantify their maximal discomfort due to sweating (*Figure 1*).

Once we had measured HP severity and distribution, we focused our attention to predicted postoperative compensatory sweating severity by adding 2 points to initial score of each body area.

Surgical strategy was always set starting from survey results.

Serum catecholamine, thyroids hormones and urinary catecholamine were measured to distinguish between primary and secondary HP. Preoperative examinations always consisted of ECG and chest X-ray.

Exclusion criteria were: bleeding diathesis, local infection, justified pleural adhesion suspicion, plantar HP alone. In the last period pleural adhesion was no more an exclusion criteria. Surgery was always proposed after that advantages and disadvantages of non surgical approaches have been discussed.

Informed consent was obtained from all patients enrolled, after deep explanation of current different therapeutic options and related complications or side effects.

Follow-up was conducted at our clinic at 3 and 18 months by fulfilling of the same survey presented at first visit. No

divided using diathermy hook. This procedure is properly called sympathectomy. Then we shifted to a different technique and nerve interruption was obtained by clips application (8). This surgery is called sympathetic block. The block was obtained by a single branch 10 mm titanium clips until 2013; then double branch 5 or 10 mm clips were introduced. From 2006 both chest tubes were immediately removed at awakening. An X-ray was routinely performed after every procedure before to move out of recovery room.

Results

From 2001 to 2003

In this first period 132 patients (92 male and 40 female) underwent bilateral sympathetic nerve trunk division by diathermy hook in two different time. Nerve interruption was always performed at the same level in regardless of HP location; target level was the superior margin of the 3rd rib (3R), corresponding to 3rd ganglia. At preoperative examination all patients were affected by primary HP distributed as follows: palmar 22 cases, palmar and axillary 66 cases, axillary alone 22 cases, cephalic 14 cases and diffuse 8 cases. Diagnosis was obtained with a tailored interview without any survey support.

General anesthesia with double lumen was always adopted. Patients were always positioned in lateral decubitus. Surgical approach consisted of biportal thoracoscopy by two 10.5 mm ports. At the end of surgery, a 24 Fr chest tube was placed until air leak cessation.

All patients were satisfied at 3 and 18 months controls but unfortunately 72.15% of them reported severe CH (NAS >7/8), measured by paper survey. We recorded minor complications in 7% of cases and no relapse of disease.

From 2004 to 2005

In this second period we treated 183 patients (112 male and 71 female) for HP as follows: palmar 18 cases, palmar-axillary 117 cases, axillary alone 15 cases, cephalic 7 cases and diffuse 26 cases. Diagnostic criteria were and patients selection unchanged. However, based on previous results characterized by severe rate of CH, we decided to adopt a different technique. We changed both nerve target level and interruption technique. In fact, nerve interruption was always achieved by clipping, targeting the superior margin of a tailored rib. Rib selection was based on the skin area affected by HP according to the prevailing criteria at the

time. The assumption was that each rib matches with its ganglia.

In particular, we matched symptoms and target rib as follows: palmar HP corresponded to interruption at the 3th rib, axillary HP at the 4th rib, palmar and axillary at the 3th and 4th ribs, facial HP at the 2nd rib, and diffuse HP at the 3th, 4th and 5th ribs. Biportal VATS in lateral decubitus remained unchanged, whereas nerve interruption was obtained using single branch B-Braun titanium clips with the aim to avoid nerve dissection and guarantee any reversibility.

Few complications were recorded : 1 hemothorax, 1 Bernard-Horner syndrome, 2 pleuritic, 1 axillary hematoma, 3 chronic pain syndrome, 5 persistent air leaks. However, 117 patients were discharged in 1st post-operative day (POD), 1 in 2nd POD and 5 in a day ranging from 3th to 23th POD.

The patient with Bernard-Horner syndrome underwent another surgery in 1st POD with clip removal and signs remitted in 3 months.

Follow-up was recorded at 3 and 18 months by paper questionnaire. Sweating improvement was obtained in overall study population.

Only 41% of cases reported severe (VAS >7/8) CH. However, 97.3% of them described CH as not severely influencing QoL. We also compared CH onset and clipping nerve level; data are reported in *Table 1*.

In this second period we observed that CH was more likely in male, isolated axillary HP and in case of preoperative highest score (NAS) >6.

From 2006 to 2012

Based on previous outcomes we changed our strategy once more with the aim to further reduce CH onset. Diagnosis had been completed by paper questionnaire to better quantify HP severity, define location and therefore identify optimal nerve target level. Moreover, since we supposed that CH is a diffuse and physiologic consequence of sympathetic interruption, we tried to quantify it by increasing of 2 points the score of each body area. Final scores gave us an estimate of postoperative CH onset, severity and location.

So, palmar, palmar and axillary, cephalic and diffuse HP were treated adopting a surgical strategy based on results of the survey. Instead, we decide not to treat pure axillary HP

In particular: in case of palmar or palmar-axillary HP, if any score was <7, nerve trunk was clipped at superior margin

Table 1 Nerve target level and related CH occurrence in patients operated from 2004 to 2005

Target level for nerve clipping	Patients without CH	Patients affected by CH
3R-4R-5R	0	5
2R	3	26
3R	16	106
4R	20	39

CH, compensatory hyperhidrosis.

of 3th and 4th rib. On the contrary, if any estimation was >7 , nerve trunk was clipped only at the upper margin of 4th rib. Cephalic HP was treated by one clip application at lower margin of 2nd rib if CH estimate was <7 . Lastly, diffuse HP was treated by clips application at the upper margin of 3th, 4th and 5th rib regardless of any CH estimate. This pattern was developed in order to reduce postoperative CH severity in high risk patients.

Moreover, we substantially changed many perioperative technical steps. We abandoned the use of double lumen intubation, introducing single lumen and apnea oxygenation. Patient were positioned in supine position with 25° anti-Trendelenburg inclination. Thoracic tubes were dismissed.

In this third period, we operated on 460 patients (310 males and 150 females). They were 320 cases of palmar HP, 100 cephalic HP and 40 diffuse HP. There were complications in 7% of cases (3 Bernard-Horner syndromes, 1 pleuritis, 24 PNx requiring chest tube, 1 hematoma, 2 chronic pain cases and 2 wing scapula). Concerning sweating improving, all patients were satisfied except one case of failure and 2 early relapses.

In our opinion, the most important finding was that severe CH (VAS >7) occurred in just 6.2% of cases. Two patients required clips removal due to excessive CH.

From 2013 to 2018

In this last period, we finally improved our approach. In particular, we decided to localize nerve target level looking directly for the ganglia rather than using rib margin as benchmark. We called it “anatomical clipping” since we ganglia were really identified. The rationale was that ganglia position and rib margin are not always consistent. Our assumption was that anatomical clipping should have guaranteed more precision in detecting correct level for interruption. In particular, nerve trunk was clipped at the lower polo of each selected ganglia. Patients selections proceeded with previous criteria. Uniportal VATS was

introduced using a 5 mm camera. Another innovation was the adoption of 5- and 10-mm double-branch clips, except for T2 interruption, since those were supposed to be safer in terms of local bleeding and more efficient in terms of correct nerve compression. Single branch clips were maintained for T2 interruption since supposed to avoid nerve stretching and related Horner syndrome.

We operated on 1,582 cases (924 male and 658 female). HP distribution was: 1,280 cases of palmar, 196 cephalic, 106 diffuse HP. Complications were 7% (2 Bernard-Horners syndromes, 1 pleuritis, 2 PNx requiring chest tube, 3 axillary hematoma and 2 chronic pain syndromes). There was only one case of failure and 2 relapses.

A remarkable achievement was that severe CH (VAS >7) occurred in just 3% of cases.

Discussion

Excessive sweating is a medical condition that can severely worsen patient's QoL. There are many treatments for HP, ranging from topical pharmacological products to thoracic surgery. Unfortunately, each therapy is characterized by advantages but also undesired effects. Moreover, outcomes are conditioned by PH severity and, over all, by sweating localization.

Usually, different non-invasive treatments are recommended at the start, based on body areas involved and patient's requirements as per NICE guidelines (9).

Surgery should be considered only in case of failure or unsatisfactory results. ETS is the most diffuse and effective surgical treatment. Nowadays it is common experience that sympathetic nerve trunk dissection guarantees dry skin in most of the cases, therefore ETS efficacy is not under discussion. Unfortunately sweat improvement at the target area may be associated to CH onset.

CH is excessive sweating in one or most different body area after ETS; it usually affects thorax, back or thighs. CH is a “physiological” side effect rather than a complication of

Table 2 Final pattern adopted from 2006 to identify optimal target level for sympathetic interruption in accordance with excessive sweating localization and postoperative CH estimate

HP localization	Suggested target level for nerve clipping
Axillary	Topical/systemic medical approach
Palmar and plamar/axillary (postoperative CH estimate <7)	3° and 4° ganglia
Palmar and plamar/axillary (postoperative CH estimate >7)	4° ganglia
Cephalic (postoperative CH estimate <7)	2° ganglia
Diffuse	3°, 4° and 5° ganglia

HP, hyperhidrosis; CH, compensatory hyperhidrosis.

ETS actually but sometimes greatly worsen patient's QoL. CH, if severe, can compromise QoL more than HP itself (10,11).

Despite CH severity is quite unpredictable, some factors seem to be predisposing. Among these, cephalic nerve trunk interruption and numbers of interruptions are the most important. Therefore, the real goal for thoracic surgeons treating HP is a balance between achieving dry skin and side effects (12).

In our study perceived severe CH (NAS >7) occurred in 72.15% of cases when we performed 3R interruption in every patient regardless of PH localization. This overall percentage improved significantly decreasing to 41%, 6.2% and 3% when we introduced respectively: (I) targeted nerve interruption for each location of PH, (II) careful preoperative HP mapping by the use of numeric questionnaire and (III) "anatomical clipping".

In accordance with literature (13-15), our data confirmed that selective sympathetic interruption is the best way to reduce CH occurrence and successfully treat HP. However, despite the adoption of different target level based on HP localization, we had to admit that CH onset was still disturbing in isolated cases and in case of pure axillary HP.

The introduction of nerve blockage by clipping did not negatively affected outcomes but allowed to recovery the nerve tone and reduce compensatory sweating in few cases presenting early excessive CH onset (16). We did not have experience with late clips removal, but many Authors showed that clipping is not reversible after few weeks from surgery (17).

Given this, the question about optimal criteria to perform selective interruption remains open. Based on our results we advance the following suggestions.

First, selective nerve interruption according to the pattern reported in *Table 2* is a satisfactory compromise

guaranteeing successful management of excessive sweating with low risk of severe CH onset. Anyway, surgical strategy should be based on an accurate preoperative evaluation possibly based on as much as possible objective information collected by paper survey.

Second, selected ganglia clipping at the lower pole is an effective technique that guarantees reversibility in case of early and severe CH onset.

Third, patients satisfaction is a combination of expected sweating improvement and tolerance of any CH. An accurate preoperative evaluation with the aim to correctly localize excessive sweating in each body area and its degree is mandatory. These preoperative informations are essential also to understand patient's requirement and expectations and to estimate postoperative CH pattern. Moreover, patient tolerance to possible CH onset is a meaningful topic that must be faced during clinic interview as well.

Conclusions

Sweating improvement and CH tolerance are subjective affairs just like patients expectation; therefore, therapy should be fashioned on personal requirements. In fact, despite many Authors have published rigorous recommendations for optimal nerve level targeting, we think that, dealing with this affliction, it doesn't make sense to strictly apply the same format for every patient. We prefer a customized approach from the beginning.

Preoperative interview is decisive and should be carried out in two important moments: (I) HP severity and localization measure (with the aid of the questionnaire) and postoperative CH pattern estimate; (II) patient expectancy and tolerance to CH comprehension.

Once patients have been informed that different nerve interruption levels correspond to different outcomes,

surgical strategy can be decided in accordance with their will weighting benefits and side effects.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the editorial office, *Shanghai Chest* for the series “Hyperhidrosis Management: from Diagnosis to Therapy”. The article has undergone external peer review.

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/shc.2019.05.02>). The series “Hyperhidrosis Management: from Diagnosis to Therapy” was commissioned by the editorial office without any funding or sponsorship. FR served as the unpaid Guest Editor of the series and serves as an unpaid editorial board member of *Shanghai Chest* from Jan 2019 to Dec 2020. MS served as the unpaid Guest Editor of the series and serves as an unpaid Associate Editor of *Shanghai Chest*. The authors have no other conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This is a retrospective study without the Ethics Committee and written informed consent was obtained from all patients.

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doi: 10.21037/shc.2019.05.02

Cite this article as: Raveglia F, Angeli MC, Scarci M. Anatomical clipping of sympathetic nerve to reduce compensatory sweating in primary hyperhidrosis: a novel technique. *Shanghai Chest* 2019;3:28.