

Comparison between high and low levels thoracic sympathectomy for the treatment of palmar and axillary primary hyperhidrosis: systematic review and meta-analysis

Comparaç o da simpatectomia tor cica realizada em n veis altos e baixos para o tratamento da hiperidrose prim ria palmar e axilar: revis o sistem tica e metan lise

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ABSTRACT

Primary hyperhidrosis (PH) is a condition that has a great impact on affected individuals' quality of life, regardless of its location. Its surgical treatment is done through thoracic sympathectomy performed by videothoracoscopy. Standardization of the technique includes section of the sympathetic trunk at different levels, according to the site of symptoms. The aim of this review is to evaluate the efficacy of thoracic sympathectomy through a systematic literature review comparing sympathectomy at different levels of the sympathetic chain.

Keywords: Hyperhidrosis. Sympathectomy. Thoracic Surgery, Video-Assisted. Meta-Analysis.

INTRODUCTION

Hyperhidrosis is the excessive and uncontrollable sweating that goes beyond the thermoregulatory needs of the body. It occurs more often in the palm, axillary, plantar and face regions but can manifest in any region of the body. It is classified into primary, the most common, and secondary forms. The pathophysiology of primary hyperhidrosis (PH) is not yet well established, constituting an idiopathic, chronic, usually focal, bilateral and symmetric alteration. Secondary hyperhidrosis has several etiologies, among which we can highlight fever, antidepressant drug use, neurological disorders, hyperthyroidism, obesity, stress, among others^{1,2}.

PH affects men and women and manifests itself at various ages, being more common in adolescents and young adults. Approximately half of the patients have a positive family history^{3,4}. The literature shows a highly variable prevalence for PH and its incidence varies according to cultural, climatic, and even conceptual, differences⁴. Strutton *et al.*⁵ found a prevalence of 2.8% in the North American population. In Brazil, there

is little data on PH prevalence. A study conducted in the city of Botucatu-SP showed a prevalence of 0.93%, predominantly in female patients⁶.

Its pathophysiology is not well understood. Morphological studies in the sweat glands of PH patients did not show changes in their number and histology. A complex dysfunction of the sympathetic autonomic nervous system, responsible for its innervation, may be related to its etiology². In an PH family history analysis, Yamashita *et al.*⁷ found a pattern of non-dominant autosomal transmission.

Although PH is not a life-threatening condition, it has a major impact on quality of life, interfering in the social, professional, psychic and emotional domains⁸. This is the main factor that causes PH patients to seek medical help.

Treatment may be clinical or surgical. Conservative alternatives are topical agents, anticholinergic drugs and beta-blockers, iontophoresis and the use of botulinum toxin⁹. Surgical treatment can be done through resection of sweat glands, curettage of the subcutaneous tissue and liposuction. However, the most accepted and best-reported

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treatment is videothoroscopic sympathectomy, performed at different costal levels according to the location of symptoms⁴.

The purpose of this review was to compare the efficacy of videothoroscopic sympathectomy performed at different levels of the sympathetic chain in patients with PH.

METHODS

We performed a search for the interest studies in the following databases: Pubmed, Embase, Cochrane, Lilacs and Clinical trials. The descriptors used to construct the search strategy were: primary hyperhidrosis, assisted video thoracic sympathectomy or videothoracoscopy. In order to increase the search sensitivity, we adapted the strategy to each base and, in addition, we used meSH terms for Pubmed, Cochrane and Clinical Trials databases, Emtree terms for Embase, and DEC terms for Lilacs. Two reviewers independently selected the studies. The eligibility criteria used were: prospective, randomized or quasi-randomized studies; Patients with PH; Presence of two groups comparing different thoracic levels for the sympathectomy, the highest or broadest level being considered the standard procedure. The primary outcome was symptom remission, and the secondary, the incidence of compensatory sweating.

We analyzed the titles and abstracts of the works found to identify the articles that obeyed the

inclusion criteria. A third reviewer was available to resolve possible disagreements. We obtained the selected articles in their respective entireties and analyzed their bibliographic references in the search for other possibly eligible studies. Two reviewers independently extracted the data in a standard form. We evaluated the quality of the studies by verifying, for each one, the criteria of randomization, incomplete presence of outcome data, selective reporting of outcomes, presence of blindness for participants and investigators, and presence of other biases.

Since the primary goal of hyperhidrosis treatment is to improve patients' quality of life, for the primary outcome we included the data of patients who had complete remission of symptoms or who reported great satisfaction with surgery. We assessed compensatory sweating in a similar way, taking into account the data from all patients in whom the event significantly compromised quality of life.

For the meta-analysis, we considered the outcomes as dichotomous variables and the measure of effect was the relative risk, with fixed effect and confidence interval (CI) of 95%. We assessed the inconsistencies between studies through the heterogeneity test (I²), considering values above 70% as important. We summarized the results in the forest plot, with the combined estimate of the effect marked as a diamond at the bottom of the chart. Subgroup analyzes and sensitivity analyzes were planned to explain the possible causes of high

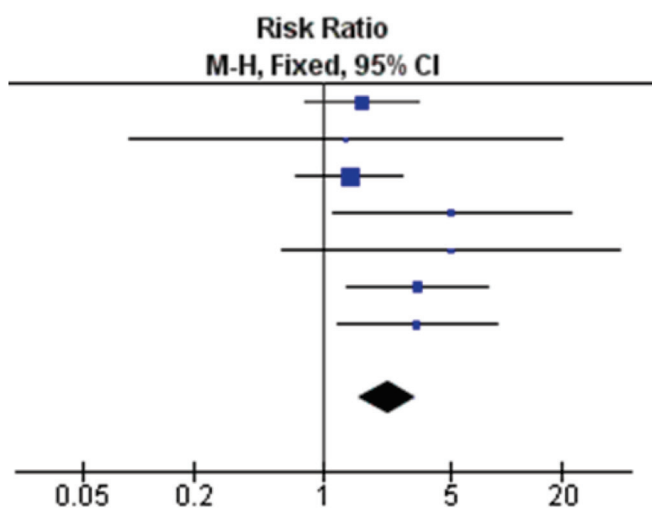


Table 1. Studies included in the review.

Author/Year	High levels	Low levels	Levels compared	Location of symptoms
Baumgartner, 2007	61	60	T2/T3	Palmar
Ishy, 2010	20	20	T3/T4	Palmar
Li, 2008	115	117	T2-4/T3	Palmar
Liu, 2009	68	73	T3/T4	Palmar
Munia, 2007	32	30	T3-4/T4	Axillary
Munia, 2008	31	33	T3-4/T4	Axillary
Vicidomi, 2011	50	50	T2-4/T3	Palmar
Yang, 2009	78	85	T3/T4	Palmar
Yasbek, 2009	30	30	T2/T3	Palmar
Yuncu, 2013	17	43	T3-4/T4	Axillary

heterogeneity. We performed statistical analysis with the software Review Manager from Cochrane Collaboration, version 5.3.5, available free of charge for download.

RESULTS

The search conducted in April 2015 returned 1086 articles in Pubmed, 60 articles in Lilacs, 92 articles in Embase, two articles in Cochrane Central Station and five articles in Clinical Trials. After the removal of duplicate sources and analysis of titles and abstracts, we selected 33 articles for integral evaluation. From this amount, ten articles brought the inclusion criteria for this review. We performed a new search in August 2015, and included no more study in the review. The works analyzed data from 857 patients with palmar hyperhidrosis and 186 patients with axillary hyperhidrosis, totaling 1,043 individuals. There was a slight predominance of female patients and the mean age ranged from 21.2 to 29.7 years. Table 1 summarizes the main characteristics of each study.

As for the levels of surgery, for palmar hyperhidrosis, Yazbek *et al.*¹⁰ and Baumgartner *et al.*¹¹ compared levels T2 and T3. Vicidomini *et al.*¹² and Li *et al.*¹³ compared levels T2-4 and T3, and Liu *et al.*¹⁴, Yang *et al.*¹⁵ and Ishy *et al.*¹⁶ compared levels T3 and T4. To perform the meta-analysis of the primary outcome, we

considered the larger resections taking into account the first sectioned level. For palmar PH, was carried out the meta-analysis without two articles that were not included because they brought the results as averages.

The analysis performed with the four remaining articles included data from 413 patients. The relative risk (RR) found was 0.86 (95% CI 0.79-0.94) favoring the group submitted to the lowest resection. However, the heterogeneity (I²) found was 83% (p=0.0007). In order to explain this high heterogeneity, we performed a sensitivity analysis with the withdrawal of one study. Thus, we found an I² of 0% (p=0.91) and RR of 0.95 (95% CI 0.88-1.03) without significant difference between the two types of resection (Table 2, Figure 1). For the secondary outcome (Table 2, Figure 2), compensatory sweating, the meta-analysis showed a greater risk of this event for the group submitted to the higher or larger resections, with RR of 2.26 (95% CI 1.57-3.25), and I² of 0% (p=0.46).

As for the axillary symptoms, Munia *et al.*^{17,18} compared levels T3-4 and T4 alone, and Yunku *et al.*¹⁹ compared levels T3-4 with T3 alone. We made the meta-analysis for the primary outcome without including one study that reported the results as means. The results showed a RR of 0.83 (95% CI 0.70-0.99) and I² 41% (p=0.19), favoring the group submitted to the lower section (Table 2,

Figure 3). The chance of presenting compensatory sweating was higher in the group submitted to the higher section, with RR of 2.03 (95% CI 1.49-2.76), but with I² of 94% (p<0.0001). We then performed a sensitivity analysis by excluding one study in which all patients in the higher resection group had compensatory sweating. Thus, the meta-analysis showed a RR of 7.25 (95% CI 2.30-22.84) and I² of

0% (p=0.51), favoring the group submitted to the lowest resection (Table 2, Figure 4).

DISCUSSION

PH is a condition that, despite benignity, severely compromises the quality of life of affected individuals. Symptoms may begin in childhood and

Table 2. Palma HP.

Study or Subgroup	Higher level		Lower level		Weight	Risk Ratio
	Events	Total	Events	Total		M-H, Fixed 95% CI
* Symptom control for palmar PH.						
Baumgartner, 2001	37	41	38	40	21.4%	0.95 [0.84, 1.07]
Li, 2008	89	115	96	117	53.0%	0.94 [0.83, 1.07]
Liu, 2009	15	62	40	69	0.0%	0.42 [0.26, 0.68]
Vicidomini, 2011	45	50	46	50	25.6%	0.98 [0.86, 1.11]
Total (95% CI)		206		207	100.0%	0.95 [0.88, 1.03]
Total events	171		180			
** Compensatory Sweating for palmar PH.						
Baumgartner, 2001	16	50	9	46	26.2%	1.64 [0.80, 3.33]
Ishi, 2010	1	15	1	20	2.4%	1.33 [0.09, 19.64]
Li, 2008	18	115	13	117	36.0%	1.41 [0.72, 2.74]
Liu, 2009	9	62	2	69	5.3%	5.01 [1.12, 22.29]
Vicidomini, 2011	5	50	1	50	2.8%	5.00 [0.61, 41.28]
Yang, 2009	18	78	6	85	16.1%	3.27 [1.37, 7.81]
Yasbek, 2009	13	30	4	30	11.2%	3.25 [1.20, 8.83]
Total (95% CI)		400			100.0%	2.26 [1.57, 3.25]
Total events	80		36	417		
*** Symptom Control for axillary PH.						
Munia, 2007	28	32	29	30	58.2%	0.91 [0.78, 1.05]
Yuncu, 2013	11	17	38	43	41.8%	0.73 [0.51, 1.06]
Total (95% CI)		49		73	100.0%	0.83 [0.70, 0.99]
Total events	39		67			
**** Compensatory sweating for axillary PH.						
Munia, 2007	11	32	2	30	68.1%	5.16 [1.24, 21.37]
Munia, 2008	11	31	1	33	31.9%	11.71 [1.60, 85.45]
Yuncu, 2013	17	17	34	43	0.0%	1.24 [1.04, 1.48]
Total (95% CI)		63		63	100.0%	7.25 [2.30, 22.84]
Total events	22		3			

* Heterogeneity: $Chi^2=0.20$, $df=2$ ($P=0.91$); $I^2=0\%$ - Test for overall effect: $Z=1.16$ ($P=0.25$)

** Heterogeneity: $Chi^2=5.71$, $df=6$ ($P=0.46$); $I^2=0\%$ - Test for overall effect: $Z=4.42$ ($P<0.0001$).

*** Heterogeneity: $Chi^2=1.71$, $df=1$ ($P=0.19$); $I^2=41\%$ - Test for overall effect: $Z=2.12$ ($P=0.03$).

**** Heterogeneity: $Chi^2=0.44$, $df=1$ ($P=0.51$); $I^2=0\%$ - Test for overall effect: $Z=3.38$ ($P=0.0007$).

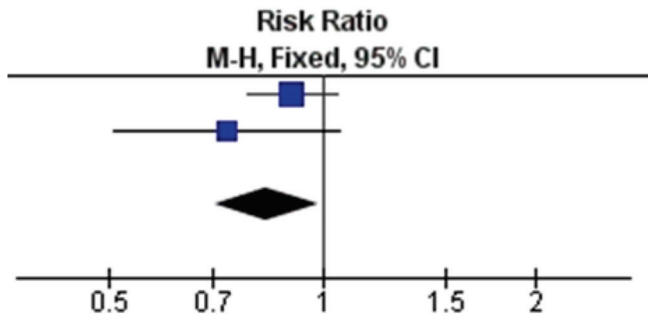


Figure 3. Symptom Control for axillary PH.

tend to worsen during adolescence⁴. Responses with clinical treatments vary widely, but generally do not show satisfactory results. In this context, videothoroscopic sympathectomy presents as an effective alternative, with low complications rates and satisfactory results^{4,8}.

The first sympathectomy reported was made in 1889. Kux, in 1940, performed the first thoracoscopic sympathectomy²⁰. Since then, sympathectomy has gained strength in the treatment of PH and has become the standard procedure for these cases. Several techniques for the interruption of the sympathetic chain have been described and the literature does not yet indicate the superiority of any of them⁴. Despite the large number of published studies, a point of great interest and still a source of divergence is the costal level of sympathetic trunk section. In the literature there are retrospective series that did not show significant differences between the high and low surgical approaches⁴. This systematic review of prospective and randomized studies evaluated symptom control in 413 patients with palmar PH and the incidence of compensatory sweating in 817. For axillary PH, the number of patients was lower, 122 for the primary outcome and 126 for the secondary. Despite this, there was no significant heterogeneity in the analyzes.

The studies recorded no deaths and, although the rates of complications were poorly reported, they were low. This is due to the standardization of the surgical technique and the profile of the operated patients, who are usually young and without comorbidities.

For palmar hyperhidrosis, the meta-analysis did not show significant differences between the

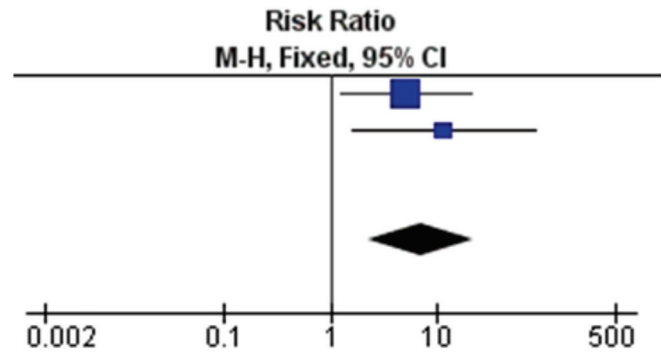


Figure 4. Compensatory Sweating for axillary PH.

groups for the primary outcome. In the upper sections, 83% of the patients had remission of symptoms or significant improvement. For the intervention group, 86% of the patients presented the same results. For compensatory sweating, the difference between the groups was very clear, with a risk 2.07 times higher of the event occurring in the higher or broader resections. In the last consensus based on the literature organized by The Society of Thoracic Surgeons (STS)⁴, the indication lower levels section for axillary hyperhidrosis showed low rates of compensatory sweating, but also lower rates of symptoms remission. This difference in outcome probably occurred because the STS review included prospective, randomized, non-randomized, and even retrospective studies.

For axillary, axillary-palmar, or axillary-palmar-plantar PH cases, the STS revision showed better results with surgery performed at lower costal levels. This review found similar results, and with statistical significance. For the primary outcome, rates in the high and low section groups were, respectively, 79% and 91%. The risk of developing compensatory sweating was 7.25 times higher in the control group. Data from the literature show important rates of compensatory sweating, varying from 14 to 90%. Obviously, there are many associated factors that must be considered, since a good part of these data derive from retrospective series with different indications and surgical techniques. In this review, in the control group, approximately 34% of the patients reported compensatory sweating, whereas this number was 5% for lower sections.

Despite the small number of studies available, the meta-analysis has shown that for palmar PH, lower

sections are as effective as high ones for symptoms control or remission, but display lower rates of compensatory sweating. As for axillary PH, procedures done at lower levels are more effective and have lower rates of compensatory sweating. Thus, low resections, based on data from the current literature, are the

best options for the treatment of axillary and palmar PH, with good satisfaction rates and improvement of patients' quality of life. Further prospective and randomized studies are needed to elucidate which groups of patients benefit most from surgical treatment and which techniques may be most effective.

R E S U M O

A hiperidrose primária (HP) é uma condição que, independentemente de sua localização, apresenta grande impacto na qualidade de vida dos indivíduos acometidos. Seu tratamento cirúrgico é feito através da simpatectomia torácica realizada por videotoracoscopia. A padronização da técnica inclui a secção do tronco simpático em diferentes níveis, de acordo com o local dos sintomas. O objetivo desta revisão é avaliar a eficácia da simpatectomia torácica por meio de uma revisão sistemática da literatura, comparando a simpatectomia em diferentes níveis da cadeia simpática.

Descritores: Hiperidrose. Simpatectomia. Cirurgia Torácica Videoassistida. Metanálise.

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