



Endoscopic thoracic sympathectomy or sympathicotomy versus clipping in the surgical management of primary hyperhidrosis: a systematic review and meta-analysis

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Background: Primary hyperhidrosis is characterized by excessive sweating in distinct parts of the body. Surgery appears to be the best strategy considering the limited invasiveness of modern techniques. In this work, we compared the excision of main sympathetic trunk with ganglia (sympathectomy) or the interruption of sympathetic chain (sympathicotomy) with the positioning of metal clips.

Methods: A research via PubMed, including published articles between 2009 and 2019, was carried out. Meta-analysis was performed by combining the reported recurrence/failure and compensatory sweating outcomes of the individual studies using a random effect model.

Results: Of the one hundred and twenty-five articles identified, only 9 are considered valid for meta-analysis with overall information on 2,206 patients treated for primary hyperhidrosis. For the compensatory hyperhidrosis, despite a considerable data heterogeneity, we found a stronger correlation with the endoscopic sympathectomy/sympathetic procedure compared to clipping (odds ratio of 0.62). For the recurrence/failure of treatment, although the same heterogeneity of the data, we highlighted a strong correlation with the clipping procedure compared to endoscopic sympathectomy/sympathicotomy (odds ratio of 2.35).

Conclusions: Sympathectomy or sympathicotomy have instead proved to be a safe and effective technique, with a low rate of recurrences. Clipping showed a reduced percentage of compensatory sweating but the removal of device is never easy, exposing patients to higher risks of open approach.

Keywords: Hyperhidrosis; surgical treatment; outcomes; systematic review; meta-analysis

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Introduction

Primary hyperhidrosis affects males and females indifferently, mainly in adolescence, with an underestimated incidence due to the feeling of shame and guilt of patients. This pathology has important implications in the life of the subjects who are affected, sometimes causing problems in relationship and in social life. Over the years, numerous

conservative and surgical medical treatments have been proposed. However, surgery appears to be the best strategy considering the limited invasiveness of modern techniques. The excision of sympathetic chain and ganglia (conventional sympathectomy, CS) or the interruption of sympathetic trunk (sympathicotomy, ST) at various levels based on the sweaty areas and the positioning titanium clips along the

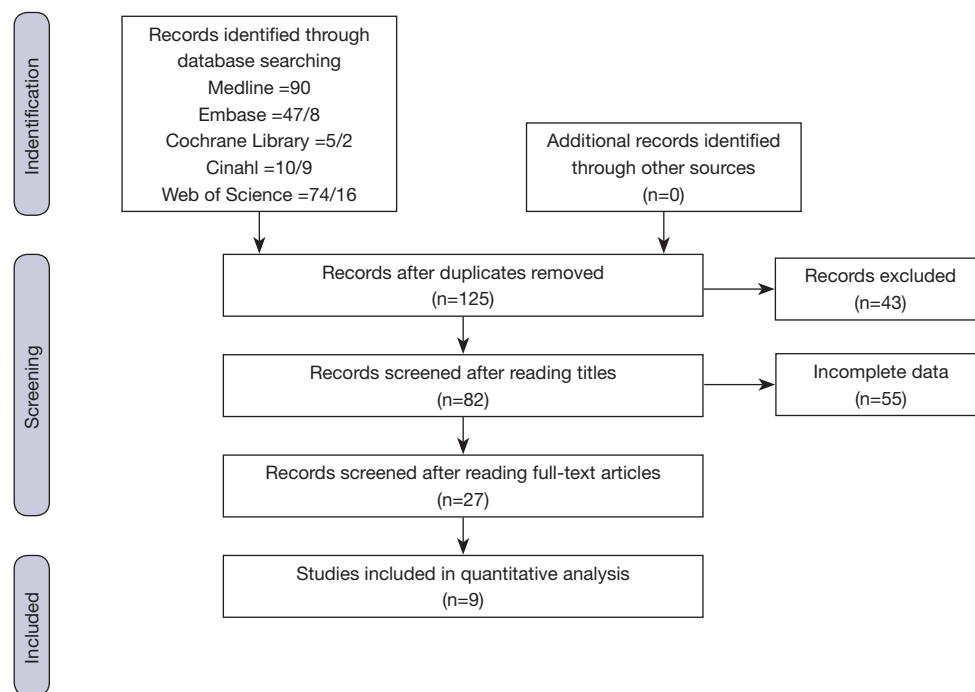


Figure 1 Flow chart according PRISMA statement.

chain (sympathetic block, SB) are the most used methods. Many authors debate the validity of one or other technique. In this work, we have tried to identify which of the sympathectomy/sympathicotomy versus SB offers the best results.

Methods

A search strategy using a combination of free-text words, relevant MeSH terms and appropriate filters was designed; the searching strategy was developed in MEDLINE (via PubMed) from 2009 until 2019, without imposing any language restrictions. Records identified through our search strategy were imported into reference management software. Two authors worked independently to assess each identified study based on the eligibility criteria. The two independent reviewers when in disagreements assessed the risk of bias by discussion and consensus. The following items were extracted from each study if available: first author's surname, publication year, surgical strategy, recurrence/failure and compensatory sweating. The meta-analysis was performed by combining the reported recurrence/failure and compensatory sweating results of the individual studies using a random effect model. The Preferred Reporting Items for Systematic Reviews and

Meta-Analyses (PRISMA) Statement was used to improve the report of this systematic review.

Results

The selection of the articles was carried out by interrogating five databases: Medline, Scopus, Cinahl, Web of Science, Cochrane. The following search string was used: "hyperhidrosis AND (thoracic simpatic * OR clip *)". Two hundred twenty-six results were obtained and, after the duplicates were removed, 125 articles were identified. Of these, only 82 were relevant after reading the title and the abstract. Afterwards only 49 were retained relevant after reading the full text. This step was performed independently by two researchers. In case of doubt, a third independent researcher was consulted. For the statistical analysis, 9 articles (1-9) were identified and taken into consideration (*Figure 1*). These provided overall information on 2,206 patients treated for primary hyperhidrosis. Of these, 670 patients were treated with a sympathetic chain clipping procedure and 1,536 were treated with endoscopic sympathectomy/sympathicotomy. Patients were divided into two distinct groups based on the parameters considered in this study. The first category included patients who developed compensatory hyperhidrosis, while the second

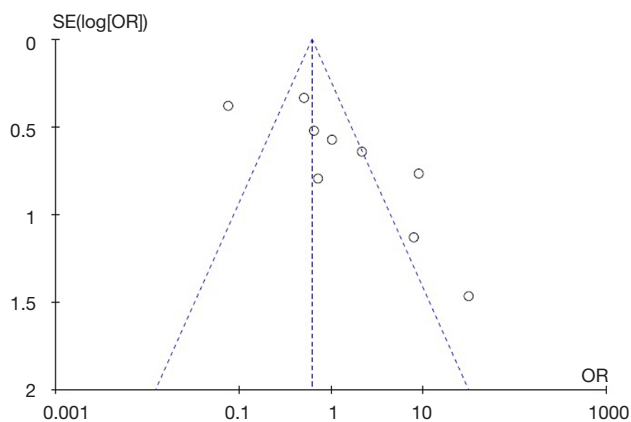


Figure 2 Funnel plot of compensatory hyperhidrosis.

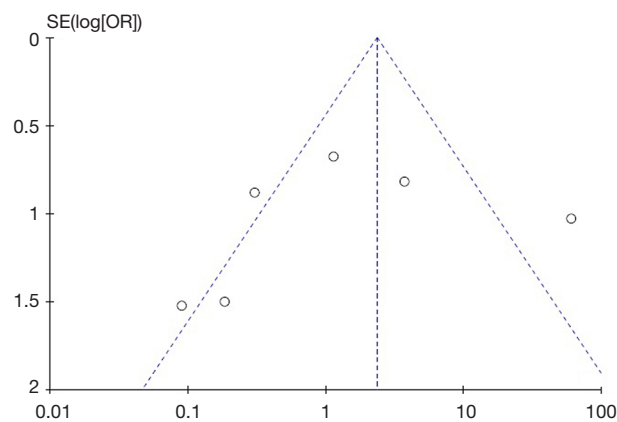


Figure 3 Funnel plot of recurrence/failure.

| Study or Subgroup | SB | | CS/ST | | Weight | Odds Ratio M-H, Fixed, 95% CI | Odds Ratio M-H, Fixed, 95% CI |
|---|--------|------------|--------|-------------|---------------|----------------------------------|----------------------------------|
| | Events | Total | Events | Total | | | |
| Cheng 2015 | 13 | 19 | 147 | 191 | 7.0% | 0.65 [0.23, 1.81] | |
| Findikcioglu 2014 | 23 | 32 | 20 | 28 | 5.0% | 1.02 [0.33, 3.15] | |
| Inan 2008 | 5 | 20 | 8 | 60 | 2.5% | 2.17 [0.62, 7.61] | |
| Joo 2016 | 21 | 43 | 0 | 16 | 0.3% | 31.53 [1.78, 558.89] | |
| Kim 2004 | 21 | 22 | 16 | 22 | 0.6% | 7.88 [0.86, 72.12] | |
| Lee 2003 | 38 | 40 | 46 | 68 | 1.4% | 9.09 [2.01, 41.13] | |
| Neumayer 2003 | 9 | 103 | 98 | 176 | 55.2% | 0.08 [0.04, 0.16] | |
| Reisfeld 2002 | 11 | 354 | 57 | 958 | 24.9% | 0.51 [0.26, 0.98] | |
| Whitson 2007 | 5 | 37 | 3 | 17 | 3.0% | 0.73 [0.15, 3.48] | |
| Total (95% CI) | | 670 | | 1536 | 100.0% | 0.62 [0.46, 0.82] | |
| Total events | 146 | | 395 | | | | |
| Heterogeneity: Chi ² = 59.67, df = 8 (P < 0.00001); I ² = 87% | | | | | | | |
| Test for overall effect: Z = 3.27 (P = 0.001) | | | | | | | |

Figure 4 Forrest plot of compensatory hyperhidrosis.

category included patients with relapse/strategy failure. As far as compensatory hyperhidrosis is concerned, an asymmetry of the funnel graph to the right is evident. This suggests the presence of publication bias (Figure 2). Similarly, as regards the data relating to recurrences, an asymmetry of the funnel graph is evident, this time to the left. This suggests the presence of publication bias (Figure 3). As for the compensatory hyperhidrosis, the study of the graphs shows the presence of a considerable heterogeneity of the data. The latter is demonstrated by the value of I² even by 87%. It must therefore be considered that the currently available studies do not reach a high level of statistical significance. However, the data in our possession indicate a stronger correlation between compensatory hyperhidrosis and the endoscopic sympathectomy/sympathetic procedure compared to clipping. This is confirmed by an odds ratio of 0.62 (Figure 4). Therefore, it is less frequently

found in patients subjected to clipping. As for the rate of recurrence/failure of treatment, the graphs show once again a considerable heterogeneity, demonstrated by the value of I² even by 79%. Therefore, even in this case, the currently available studies do not reach a high statistical significance. Nevertheless, the data in possession indicate a strong correlation between recurrence/failure rate and the clipping procedure compared to that of endoscopic sympathectomy/sympathicotomy. This is confirmed by an odds ratio of 2.35 (Figure 5). The clear benefit of CS/ST against relapses is therefore evident compared to the SB technique.

Discussion

In primary hyperhidrosis, surgery is now considered the treatment of choice. Alternatives to surgery have limited or temporary efficacy (10). Modern video-assisted

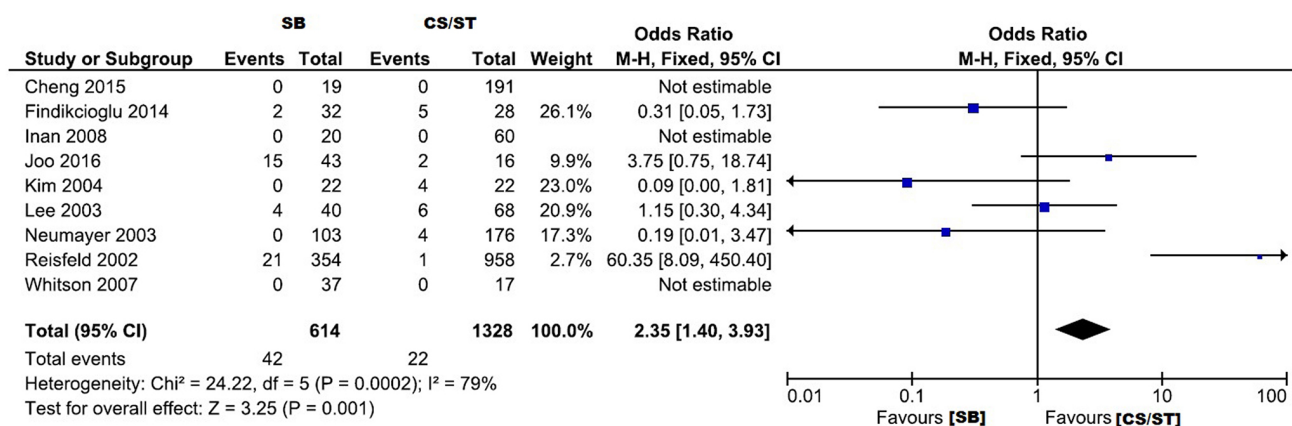


Figure 5 Forrest plot of recurrence/failure.

thoracoscopic surgery (VATS) techniques allow the interruption or section of the sympathetic chain at different levels (11,12). The advantages are considerable in terms of effectiveness, recurrence rate and complications. However, it is necessary to consider the risk of complications both intraoperative such as hemorrhage, irreversible ganglia injury (such as the lesion of the stellate ganglion resulting in Horner's syndrome) and postoperative such as pneumothorax, compensatory hyperhidrosis, strategy relapse/failure (13-16). The choice of the best technique is a debated topic. According to many authors, CS/ST would be preferred but there are also some variations with respect to the standard method as the Wittmoser technique where the communicating branches are interrupted to avoid the failure of the surgical strategy. Other authors instead consider the irreversible interruption of the sympathetic chain to be unsafe and prefer the block through the positioning of metal clips along the course of the chain itself, with the possibility of removing the latter in case of adverse events. Reversibility is the major advantage of this method as opposed to the CS/ST which is a very effective but irreversible procedure (17-19). According to the data emerging from our analysis, "clipping" is characterized by a slightly lower or almost overlapping compensatory hyperhidrosis rate compared to CS/ST although some authors believe that compensatory hyperhidrosis is independent of the method used (20). Furthermore, the strategy relapse/failure rate is significantly higher. Considering these data and according to the experience of many authors, the irreversible excision/interruption of the sympathetic chain should be preferred for several reasons. In fact, the interventions are similar in

terms of invasiveness, present the same risks and require an equal hospitalization period (21,22). Moreover, a limitation of the SB is represented by the impossibility to selectively interrupt the communicating branches given the small size of the latter. This is often the cause of relapse/strategy failure. In regard to the possibility of removing the clips, it should be emphasized that the fibrotic phenomena, which often occurs a few days after the operation, makes this procedure sometimes difficult or even impossible to complete. Also, the removal is characterized by a high risk of complications, involves a greater discomfort for patients who have to undergo a double operation and often does not may restore the nerve to the original functionality (23,24). In conclusion, considering the results emerged from the analysis of the data present in the literature we believe that sympathectomy/sympathicotomy is the preferred techniques in terms of efficacy and complication rate.

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None.

Footnote

Conflicts of Interest: The authors have no 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.

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