Compensatory hyperhidrosis after different surgeries at the same sympathetic levels: a meta-analysis

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Background: Different techniques of video-assisted thoracoscopic sympathetic surgery have become the radical treatments for palmar and axillary hyperhidrosis (AH). However, there is no consensus over which technique can make a minimal incidence of compensatory hyperhidrosis (CH). This study was designed to compare the incidence of CH after different techniques at the same sympathetic levels in the treatment of upper limb and facial hyperhidrosis (FH).

Methods: The databases of PubMed, Web of Science, ScienceDirect, Ovid Medline, Embase, and Cochrane Library were searched to identify studies comparing different surgical techniques at the same sympathetic levels for upper limb and FH. The data was analyzed by Revman 5.3 software.

Results: A total of ten studies involving 896 patients were included, of whom 149 underwent sympathectomy, 435 underwent sympathicotomy, and 312 under endoscopic sympathetic clip (ESC). Meta-analysis showed that the difference of incidence of CH and patients' satisfaction was not significant between sympathectomy and sympathicotomy (P=0.05, 0.19, respectively). But, the incidence of CH is significant lower after ESC than after sympathicotomy (OR: 1.58, 95% CI: 1.04–2.38, P=0.03). However, the incidence of moderate/severe CH between these two groups is not significant different (OR: 1.49, 95% CI: 0.93–2.39, P=0.10).

Conclusions: If only CH and the same sympathetic levels concerned, sympathectomy and sympathicotomy is equal for upper limb hyperhidrosis and FH. And, ESC should be recommended for a lower incidence of CH, comparing with sympathicotomy.

Keywords: Compensatory hyperhidrosis (CH); sympathectomy; sympathicotomy; endoscopic sympathetic clip (ESC)

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Introduction

Hyperhidrosis is defined as a pathologic condition of excessive sweating in amounts greater than physiologically needed for thermoregulation. It may develop secondary to a variety of medical disorders or it may be primary or cryptogenic, with symptoms such as focal hyperhidrosis usually affecting the palms, axillae, or the feet (1). It has been verified that patients affected with hyperhidrosis suffer from social problems and impairments in daily activities, as well as emotional and physical strains (2,3). The treatment options for primary hyperhidrosis involve a range of topical or systemic medications, psychotherapy

and surgical or non-surgical invasive techniques (4). However, the radical and usually definite treatment of palmar hyperhidrosis (PH), axillary hyperhidrosis (AH) and facial hyperhidrosis (FH) is surgical ablation or blockade of the upper thoracic sympathetic chain. The open approaches used in the past are now replaced by the video-assisted thoracoscopic surgery (VATS) for its several disadvantages such as a higher rate of complications, esthetic discomfort and problems with lung function postoperatively (4). However, compensatory hyperhidrosis (CH) remains the common postoperative complications, and is a major source of dissatisfaction (5,6). To determine which surgical techniques make the lowest occurrence of CH at the same sympathetic levels after surgery, we performed this meta-analysis.

Methods

Criteria for considering studies for this review

Types of studies

Study design: attempts were made to identify all randomized clinical trials (RCTs) in which CH after different surgeries at the same sympathetic levels was compared to a control treatment in patients with facial, axillar or PH. Controlled clinical trials (CCTs) in which allocation to treatment or control group was not truly random (quasi-randomized), or in which treatment allocation was not concealed, were retrieved as well. Observational studies (cohorts and case-control studies) assessing effects of CH after different surgeries at the same sympathetic levels were also searched. Retrospective reviews of patient charts were included if an attempt was made to assess important prognostic factors that affected patients' outcomes, i.e., comparative studies. However, uncontrolled studies (case series, case reports, uncontrolled before and after studies) and controlled studies on CH after different surgeries at different sympathetic levels were not included in this review.

Language: the language was limited to English.

Time frame: with no limit.

Types of participants

Patients of any age, both gender and with any duration of facial, axillar or PH were included. But, who with pedal and secondary hyperhidrosis were excluded.

Types of interventions

Only surgical interventions were included. Surgical interventions in this review are defined as sympathectomy, sympathicotomy, ramicotomy, and endoscopic sympathetic clip (ESC) of the thoracic sympathetic chain by means of open or endoscopic procedures. Studies about dealing with lumbar sympathetic chain and local injection therapy, such as botulinum or alcohol solution, were excluded.

Types of outcome measures

Primary outcomes

The primary outcome measure for this systematic review was the occurrence of CH complained by patients or evaluated by the surgeons.

Secondary outcomes

Secondary outcomes included: (I) resolution, (II) satisfaction, (III) occurrence of moderate-sever CH, (IV) occurrence of over dry hands, (V) occurrence of gustatory sweating, (VI) recurrence.

Search strategy

The study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses criteria (PRISMA) as shown in S1 File. Two investigators performed the literature search independently and in duplicate. To maximize the potential studies, the PubMed, Web of Science, ScienceDirect, Ovid Medline, Embase, Cochrane Library were searched up to December 3, 2017 by using following strategies (*Table 1*).

The following inclusion criteria were applied: (I) articles/abstracts published in English; (II) studies focused on CH after surgery; (III) the study compared different surgical techniques, including sympathectomy, sympathicotomy, ramicotomy, and ESC at the same sympathetic levels; (IV) 10 or more patients were included in each group; and (V) for data reported in multiple articles, the most recent or most detailed article was chosen. We excluded systematic reviews, meta-analyses, case reports, animal experiments, editorials, letters, and articles not about sympathetic surgery for palmar, AH and FH. The studies comparing the same two techniques less than three articles were also excluded (*Figure 1*).

Data collection

Two investigators independently extracted data from all studies eligible for inclusion in this meta-analysis. The following data were extracted: name of first author, year of publication, study design, number of patients in each study arm, surgical techniques, follow-up duration, symptom

Table 1 Searching strategies and results

Databases	Searching strategies	Results
PubMed		
#1	compensatory[Title/Abstract]	41,665
#2	reflex[Title/Abstract]	70,377
#3	hyperhidrosis[MeSH Terms]	3,438
#4	sweat*[Title/Abstract]	21,250
#5	sympath*[Title/Abstract]	99,622
#6	clip*[Title/Abstract]	24,911
#7	bolck*[Title/Abstract]	8
#8	"humans"[MeSH Terms]	
#9	"humans"[MeSH Terms]	
#10	(#1 OR #2) AND (#3 OR #4) AND (#5 OR #6 OR #7) AND #8 AND #9	513
Web of Science		
#1	TS=compensatory	43,688
#2	TS=reflex	83,889
#3	TS=hyperhidrosis	3,095
#4	TS=sweat*	20,407
#5	TS=sympath*	100,552
#6	TS=clip*	38,526
#7	TS=block*	1,044,339
#8	#2 OR #1	126,567
#9	#4 OR #3	22,562
#10	#7 OR #6 OR #5	1,167,520
Science Direct	(TITLE-ABSTR-KEY(compensatory) or TITLE-ABSTR-KEY(reflex)) and (TITLE-ABSTR-KEY(hyperhidrosis) or TITLE-ABSTR-KEY(sweat*)) and (TITLE-ABSTR-KEY(sympath*) or TITLE-ABSTR-KEY(clip*) or TITLE-ABSTR-KEY(block*)) AND LIMIT-TO(contenttype, "JL,BS", "Journal")	215
Embase		
#1	'compensatory':ab,ti	52,496
#2	'reflex':ab,ti	80,362
#3	'hyperhidrosis'/exp/mj	2,813
#4	'sweat*':ab,ti	29,522
#5	'sympath*':ab,ti	117,516
#6	'clip*':ab,ti	34,708
#7	'block*':ab,ti	861,464
#8	#1 OR #2	131,870
#9	#3 OR #4	31,128
#10	#5 OR #6 OR #7	991,461
#11	#8 AND #9 AND #10	805
#12	#11 AND ('clinical article'/de OR 'clinical trial'/de OR 'cohort analysis'/de OR 'comparative study'/de OR 'controlled clinical trial'/de OR 'controlled study'/de OR 'human'/de OR 'human experiment'/de OR 'human tissue'/de OR 'intermethod comparison'/de OR 'interview'/de OR 'major clinical study'/de OR 'medical record review'/de OR 'methodology'/de OR 'normal human'/de OR 'observational study'/de OR 'prospective study'/de OR 'questionnaire'/de OR 'randomized controlled trial'/de OR 'retrospective study'/de OR 'systematic review'/de)	769
Cochrane Library		
#1	compensatory:ti,ab,kw	1,428
#2	reflex:ti,ab,kw	5,360
#3	hyperhidrosis:ti,ab,kw	659
#4	sweat*:ti,ab,kw	2,598
#5	sympath*:ti,ab,kw	6,655
#6	clip*:ti,ab,kw	1,479
#7	block*:ti,ab,kw	52,222
#8	(#1 or #2) and (#3 or #4) and (#5 or #6 or #7)	66

Table 1 (*continued*)

Databases	Searching strategies	Results
Ovid		
#1	compensatory.ab.	54,234
#2	reflex.ab.	74,596
#3	hyperhidrosis.ab.	3,344
#4	sweat*.ab.	24,062
#5	sympath*.ab.	112,756
#6	clip*.ab.	33,048
#7	block*.ab.	864,289
#8	#1 or #2	127,704
#9	#3 or #4	25,993
#10	#5 or #6 or #7	985,817
#11	#8 and #9 and #10	958
#12	limit 11 to English language [Limit not valid in Books@Ovid,Journals@Ovid,Your Journals@Ovid; records were retained]	888
#13	12 to humans [Limit not valid in Books@Ovid,Journals@Ovid, Your Journals@Ovid; records were retained]	835
Scopus	(TITLE-ABS-KEY (compensatory) OR TITLE-ABS-KEY (reflex)) AND (TITLE-ABS-KEY (hyperhidrosis) OR TITLE-ABS-KEY (sweat*)) AND (TITLE-ABS-KEY (sympath*) OR TITLE-ABS-KEY (clip*) OR TITLE-ABS-KEY (block*)) AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re") OR LIMIT-TO (DOCTYPE, "cp") OR LIMIT-TO (DOCTYPE, "le") OR LIMIT-TO (DOCTYPE, "no") OR LIMIT-TO (DOCTYPE, "sh") OR LIMIT-TO (DOCTYPE, "ed") OR LIMIT-TO (DOCTYPE, "ip") OR LIMIT-TO (DOCTYPE, "er")) AND (LIMIT-TO (LANGUAGE, "English")) AND (LIMIT-TO (SRCTYPE, "j") OR LIMIT-TO (SRCTYPE, "p"))	1,065

Date: up to December 3, 2017.

resolution, patient satisfaction, postoperative complications (recurrence, dry hands, and gustatory sweating), and postoperative CH (incidence).

Assessments of risk of bias

We used the 'risk of bias' tool in the Review Manager software to assess and summary the risk of bias for each included study. Each domain in the tool includes six specific entries in a 'Risk of bias' table, which consist of two selection biases, one performance bias, one detection bias, one attrition bias, one reporting bias and one other bias. Within each entry, the first part of the tool describes what was reported to have happened in the study, in sufficient detail to support a judgement about the risk of bias. The second part of the tool assigns a judgement relating to the risk of bias for that entry. This is achieved by assigning a judgement of 'Low risk' of bias, 'High risk' of bias, or 'Unclear risk' of bias. The forest plots ordered by judgements on each 'Risk of bias' entry give a visual impression both of the relative contributions of the studies at low, unclear and high risk of bias, and also of the extent of differences in intervention effect estimates between studies at low, unclear and high risk of bias. It is usually sensible to restrict such plots to key bias domains (7).

Statistical analysis

Meta-analysis was conducted using Review Manager 5.3 software (Offline, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). In the case of dichotomous variables, we calculated the odds ratio between the two groups along with 95% confidence intervals (CIs). We used the Cochrane Chi^2 and I^2 statistics to analyze between-study heterogeneity. A fixed-effects model was used. A two-tailed P value <0.05 was considered statistically significant.

Results

Literature search and study quality

The literature search identified 1,510 potentially eligible articles. After comprehensively screening there were 10 eligible articles included in the final analysis, of which 5 were retrospective studies, 4 were RCTs, and 1 was prospective studies (*Figure 1*). Seven articles compared sympathicotomy with ESC, and three compare sympathectomy with sympathicotomy. All of the 10 articles referred to PH, 2 also to AH, and 1 also to FH. The included 10 articles involved 896 patients, of whom 149 underwent sympathectomy, 435 underwent sympathicotomy, and

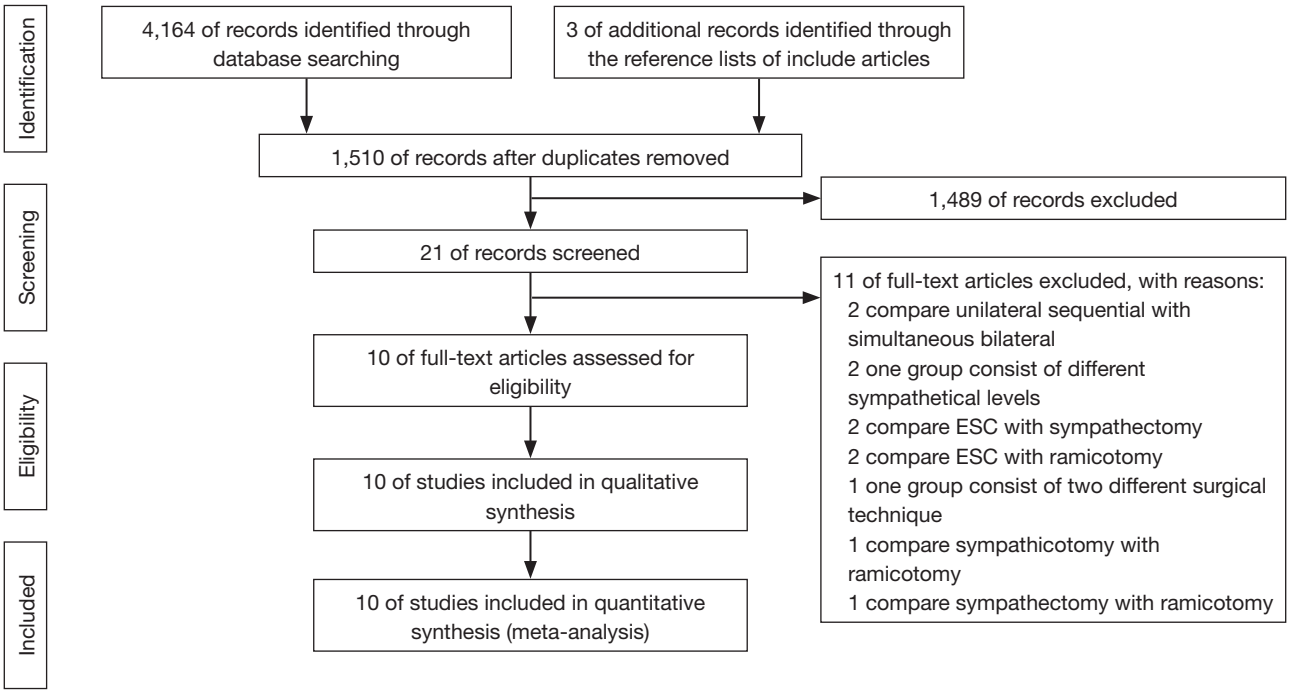

Figure 1 Flow diagram of screened and included articles. CH, compensatory hyperhidrosis; ESC, endoscopic sympathetic clip.

312 under ESC. The baseline characteristics of the included studies and the main evaluation indexes are shown in *Table 2*.

CH and patients' satisfaction

There is no significant difference of CH between sympathectomy and sympathicotomy (OR: 0.56, 95% CI: 0.31–1.01, P=0.05) (*Figure 2*). Moreover, the difference of patients' satisfaction between sympathectomy and sympathicotomy is not significant either (OR: 0.68, 95% CI: 0.38–1.22, P=0.19) (*Figure 2*). On the other hand, the incidence of CH is lower in ESC than in sympathicotomy (OR: 1.58, 95% CI: 1.04–2.38, P=0.03) (*Figure 3*). However, the difference of moderate/severe CH between these two techniques is not significant (OR: 1.49, 95% CI: 0.93–2.39, P=0.10) (*Figure 3*).

Discussion

Comments

The treatment options for primary upper limb hyperhidrosis and FH involve a range of topical or systemic medications, psychotherapy and surgical or non-surgical invasive techniques (4). However, the radical and usually definite treatment of upper limb hyperhidrosis is surgical ablation of the upper thoracic sympathetic chain. In 1990, Endoscopic thoracic sympathectomy was performed using VATS (18). Currently, this procedure is accepted as a standard treatment technique for upper limb hyperhidrosis and FH for its remarkable benefits over open approaches. These benefits include reducing postoperative pain, shorter hospitalization, earlier recovery and return to work, and fewer complications. Furthermore, both sides can be treated in the same sitting, thus avoiding readmission for a second procedure in bilateral cases (19). But, CH remains the common postoperative complications, and is a major source of dissatisfaction (5,6). The etiology of CH is not known. Some authors deemed that it was associated with extensive sympathetic blockage (20-22). While others believed that the extent of resection had no effect on the occurrence of CH (23,24). Although plenty of studies have paid attention to the sympathetic levels (25-28), the optimal sympathetic levels are still controversial. To determine which sympathetic surgical technique makes the lowest incidence of CH after surgery, we performed this meta-analysis.

This is the first meta-analysis comparing different sympathetic surgical techniques at the same levels. The results demonstrate that there is more CH after sympathicotomy than after sympathectomy (76% *vs.* 67%),

Table 2 The primary characteristics of the eligible studies

Years	Study	Design	Location	Techniques	No. of patients (n)	Resolution (%)	Satisfied cases (%)	CH (%)	Moderate-sever CH (%)	Over dry hands (%)	Gustatory sweating (%)	Recurrence (%)	Follow up (mo)
2016	Joo (8)	Retrospective	PH	T4 sympathicotomy	16	NR	15 (93.85)	9 (56.3)	0	NR	NR	2 (12.5)	10
				ESC4	20	NR	20 (100.0)	13 (65.0)	5 (25.0)	NR	NR	7 (35.0)	30
2015	Hida (9)	Retrospective	PH	T3 Sympathicotomy	54	NR	NR	52 (96.2)	48 (88.9)	NR	23 (42.5)	0	95.1
				ESC3	38	NR	NR	32 (84.2)	26 (68.4)	NR	18 (47.3)	5 (13.1)	73.9
2015	Aydemir (10)	Retrospective	PH	T3 sympathectomy	45	45 (100.0)	41 (91.1)	40 (88.9)	36 (80.0)	NR	NR	NR	6
				T3 sympathicotomy	47	47 (100.0)	44 (93.6)	40 (85.1)	37 (78.7)	NR	NR	NR	6
2015	Kocher (11)	Retrospective	PH, AH	T2-3 sympathectomy	18	NR	NR	NR	3 (16.7)	NR	NR	NR	57.8
			FH	ESC2-3 sympathicotomy	16	NR	NR	NR	5 (31.0)	NR	NR	NR	57.8
2014	Findikcioglu (12)	Retrospective	PH	T3 sympathicotomy	28	26 (93.0)	NR	20 (71.4)	13 (46.4)	NR	NR	11 (39.3)	33
				ESC3	32	32 (100.0)	NR	23 (71.8)	18 (56.3)	NR	NR	4 (12.5)	33
2014	Panhofer (13)	Prospective	PH	ESC4	114	113 (99.2)	NR	9 (7.9)	1 (0.9)	NR	16 (14.0)	0	12
				T4 sympathicotomy	91	89 (97.8)	NR	10 (11.0)	9 (9.9)	NR	3 (3.3)	5 (5.5)	13
2014	Coelho (14)	RCT	PH	ESC3	35	31 (86.0)	NR	22 (62.85)	NR	NR	NR	NR	24
				T3 sympathicotomy	35	33 (99.2)	NR	19 (54.28)	3 (8.6)	NR	NR	NR	24
2011	Wang (15)	RCT	PH	T4 sympathicotomy	60	60 (100.0)	39 (70.9)	29/55	13/55	NR	NR	NR	2
				ESC4	60	60 (100.0)	43 (75.4)	13/57	8/57	NR	NR	NR	2
2008	Inan (16)	RCT	PH, AH	T2-4 sympathectomy	20	19 (95.0)	19 (95.0)	3 (15.0)	NR	NR	NR	0	36
				T2-4 sympathicotomy	20	20 (100.0)	20 (100.0)	5 (25.0)	NR	NR	NR	0	36
1999	Lin (17)	Retrospective	PH	T2-3 sympathectomy	84	NR	46 (56.7)	57 (67.8)	NR	5 (6.0)	NR	5 (6.0)	143.2
				T2-3 sympathicotomy	71	NR	45 (63.3)	60 (84.8)	NR	4 (5.6)	NR	2 (2.8)	42.8

PH, palmar hyperhidrosis; AH, axillary hyperhidrosis; FH, facial hyperhidrosis; ESC, endoscopic sympathetic clip; NR, not report.

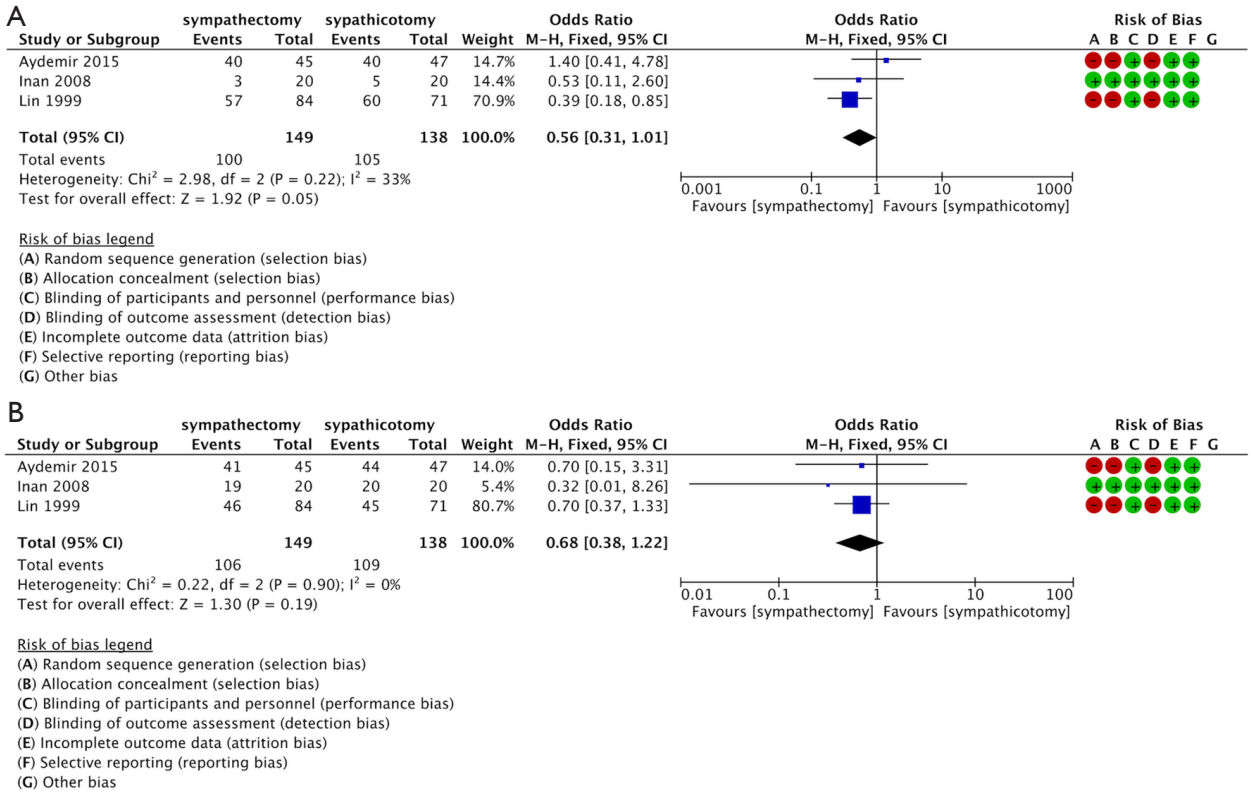

Figure 2 Odds ration compared sympathectomy with sympathicotomy. (A) Odds ratio for compensatory hyperhidrosis; (B) odds ratio for satisfaction.

but, the difference is not significant (P=0.05). It is consistent with other studies comparing these two techniques regardless of sympathetic levels. Mohebbi (29) made such a prospectively study, which included 30 patients in each group. And they found that the difference of CH for PH and AH at any severity levels (nor, mild, mod, severe) were all not significant (P=0.94 for PH, 0.504 for AH, respectively) between sympathectomy and sympathicotomy. Moreover, the difference of satisfaction between these two groups were not significant either (P=0.461 for PH, 0.09 for AH respectively). Furthermore, Cheng (30) made a relevant retrospective medical chart review. In this review, 108 patients underwent sympathicotomies and 83 underwent sympathectomies, and the operative level(s) interrupted were not standardized and ranged from R1 to R8 (185 of 210 patients were PH). After 5.5 years follow-up, 78 (72.2%) patients in the sympathicotomy group and 64 (77.1%) in the sympathectomy group experienced CH (P<0.05). These results imply that when if only CH concerned, either surgical technique is equal for upper limb hyperhidrosis and FH. And sympathicotomy should be preferred for technical easier and less invasive (29).

Furthermore, our results also show that although the difference of moderate/severe CH between sympathicotomy and ESC is not significant (OR: 1.49, 95% CI: 0.93–2.39, P=0.10), ESC can achieve a significant lower incidence of CH (OR: 1.58, 95% CI: 1.04–2.38, P=0.03). This may be attribute to that sympathicotomy caused more damage to the afferent sympathetic tone to hypothalamus though thermal conduction than ESC did, which as a result led to more amplified efferent sympathetic tone to sweat glands and finally more occurrence of CH. That coincides with the hypothesis that compensatory sweating was a reflex phenomenon regulated by a cycle of negative and/or positive feedback mechanism between body thermoreceptors, hypothalamus and sweat glands (31). Joo (8) reported that the operative time of ESC was the same as sympathicotomy. What's more, the another overwhelming superiority ESC hold over sympathectomy and sympathicotomy is that it offers the potential of reversal operation (unclipping) when severe CH would occur (32-34). Sugimura (34) reported that fifteen patients (48%) experienced a substantial

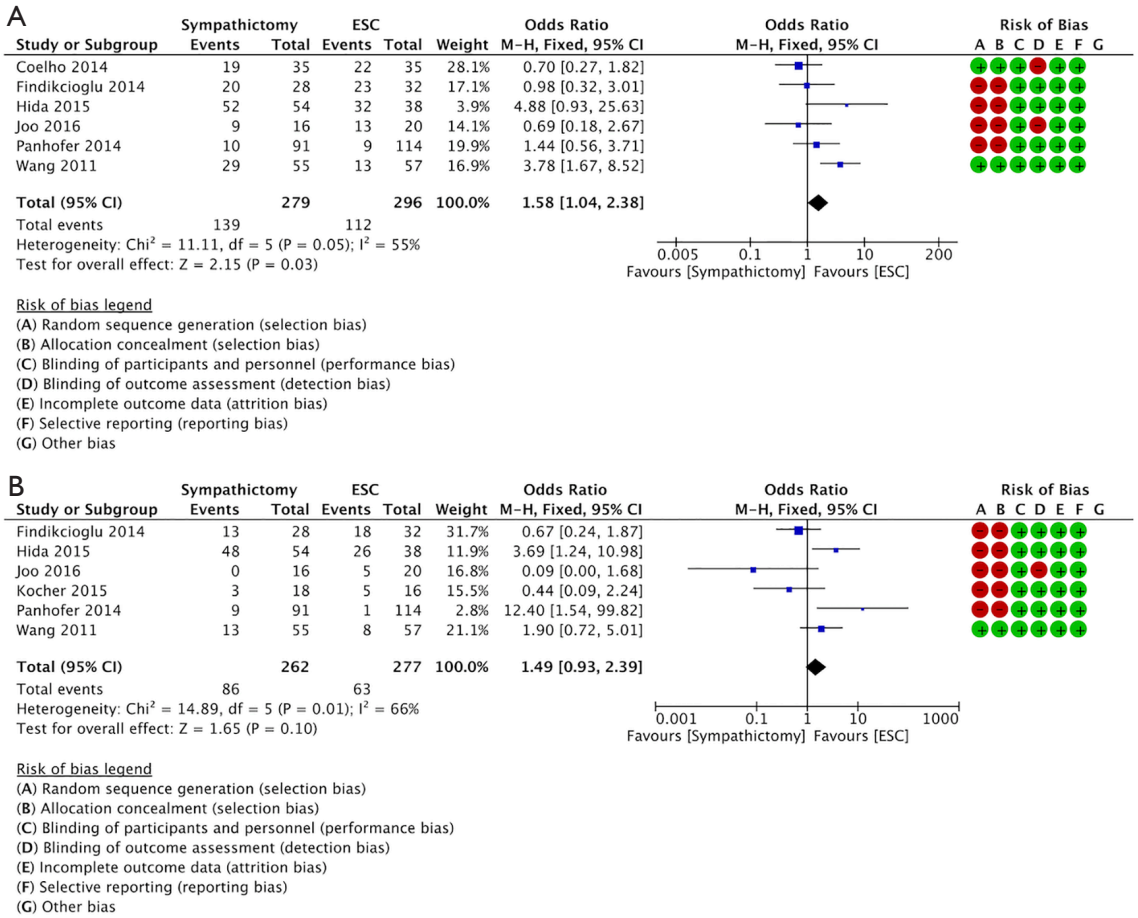

Figure 3 Odds ratio compared sympathicotomy with ESC. (A) Odds ratio for compensatory hyperhidrosis; (B) odds ratio for moderate/severe compensatory hyperhidrosis. ESC, endoscopic sympathetic clip.

decrease in their compensatory sweating after reversal. Therefore, the ESC should be recommended to treat upper limb hyperhidrosis and FH.

Study limitations

Our study has several limitations. First, there are too few studies which compared other different surgical techniques at the same sympathetic levels to be eligible for present meta-analysis (*Figure 1*, 11 of articles excluded). Consequently, we cannot make a real comprehensive meta-analysis on this topic. For instance, more control studies are needed to make comparison between ESC with sympathectomy, ESC with ramicotomy, sympathicotomy with ramicotomy, sympathectomy with ramicotomy. Second, due to inter-study heterogeneity and the inherent limitations of our meta-analysis, this conclusion requires further validation through more high-quality and large-scale RCTs. Third, the included studies did not clearly introduce the methods they used to measure CH. As is well-known, there are a variety of methods to evaluate it (35-37). So, it is necessary to recommend a consolidated appraising method, which can be easily and internationally used. Fourth, the follow-up period in included studies ranged from 2 to 143.2 mon. And many studies have confirmed that the incidence and severity of CH could change with time (38-41). Therefore, the follow-up should be as Yazbek suggested which was patients should have follow-up appointments or surveyed at 1 month, 6 months, 1 year, and yearly thereafter for at least 5 years if possible (42).

Conclusions

If only CH and the same sympathetic levels concerned, sympathectomy and sympathicotomy is equal for upper

limb hyperhidrosis and FH, and sympathicotomy should be preferred for technical easier and less invasive. Furthermore, when comparing with sympathicotomy, ESC has the significant advantages of a lower incidence of CH and the potential of reversal operation when severe CH would occur.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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