의학박사 학위논문

일차성 족부 다한증 치료를 위한 3번과 4번 요부 교감신경 클립술 시행 후 임상적 효과와 환자 만족도 차이에 대한 고찰

The comparison of surgical effect of L3 and L4 sympathetic clipping for the treatment of primary plantar hyperhidrosis

울산대학교 대학원

의학과

윤석원

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이 논문을 의학박사학위 논문으로 제출함

2022년 2월

울산대학교 대학원

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국문 요약

배경: 요부 교감신경 절제술은 일차성 족부 다한증의 효과적인 치료법으로 간주되어 왔으나, 가장 효율적인 요부 교감신경 차단 레벨을 제시하는 보고는 지금까지 거의 없었다. 따라서 본 연구는 단일 기관에서 시행된 족부 다한증을 위한 L3 또는 L4 요부 교감신경 클립술을 받은 환자들의 수술 후 임상적 효과와 만족도를 비교하는 것을 목적으로 하였다.

대상 및 방법: 2015년 12월부터 2018년 6월까지, 일차성 족부 다한증을 가진 500명의 환자들을 대상으로 3 mm 티나늄 클립을 이용한 요부 교감신경 클립술을 시행하였다. 이 중 436명은 초기 수술 후 결과 분석, 134명은 장기 추적 관찰 결과 분석의 대상이 되었으며, 64명은 양측의 클립 차단 레벨이 서로 같지 않아 통계적 편향을 피하기 위해 제외되었다. 표적 신경의 식별과 클립차단을 위해 손가락 터치 및 내시경적 보조 방법을 사용하였으며, 수술 직 후 시행한 엑스레이 검사를 이용하여 클립의 위치를 확인하였다. 환자의 만족도 척도와 다한증 관련 설문 (HidroQoL©) 은 수술 후 10일째, 그리고 3년 이상 경과한 후에 실시되었다.

결과: 436명의 환자들의 남녀 성비는 같았고, 평균 나이는 26.3 ± 7.2 (14~49) 세였다. 평균 수술 시간은 43.9 ± 8.7 분이었으며, L3와 L4 클립차단 레벨 비율은 4:1이었다. 134명의 장기 추척 관찰 기간은 50.7 ± 8.8 개월 (39.7~69.3 개월) 이었다. 요부 교감신경 절단술과 함께 동시에 내시경적 흉부 교감신경 절단술을 시행 받은 환자 수는 359명 (82.3%)이었다. 초기 수술 후 보상성 다한증은 40.1%에서 보고되었으며 0.5%의 환자들은 수술을 후회할 정도의 심한 보상성 다한증으로 분류되었다. 그러나 장기 추적 관찰 환자 군에서는 그 비율이 각각 88.1% 와 12.7%로 증가하였다. 마찬가지로 발 다한증 수술만을 받은 하위 그룹 분석에서도, 초기 결과에서는 심한 보상성 다한증 환자가 없었지만, 후기 결과에서는 3명 (12.5%)으로 나타났다. 하위 그룹 분석 대상 환자들의 초기 및 후기 만족도 척도는 각각 10점 만점에 9.7±0.6 점과 7.5±2.8 점이었으며, 이는 전체 환자 군에서도 유사하였다. 일시적 발한과 신경통은 각각 33.3% 와 2.3%의 환자에게서 발생하였다. 신경통 및 수술 시간을 제외하고, 클립 차단 레벨과 관련하여 대부분의 수술 전 후 결과와 장기 추척 관찰 결과에서 유의미한 차이가 없었다.

결론: 요부 교감신경 클립술은 일상생활의 불편함으로 고통받고 있는 족부 다한증 환자들이 선택할 수 있는 가치 있는 치료법이며, 낮은 합병증과 높은 만족도가 이를 뒷받침한다. 본 연구에서 L3 와 L4 교감신경 차단 그룹 간의 초기 및 후기 만족도는

유의미한 차이가 없었다.

중심단어 : 다한증, 요부 교감신경 클립술, 족부 다한증

차 례

표 차례

그림 차례

INTRODUCTION

Primary focal hyperhidrosis, which has a prevalence of 1.5%–2.5% in the general population [1], is idiopathic and characterized by excessive sweating for > 6 months (primarily on the bilateral palms, soles, and axillae), absent nocturnally, onset at < 25 years of age, positive family history, and impaired activities of daily living [2]. There are two major categories for treating primary hyperhidrosis: conservative and surgical treatment. Conservative treatment, including oral anticholinergic pills, aluminum chloride lotions, iontophoresis, and botulinum toxin injections, can improve the symptoms, but it does not provide a long-term resolution. Percutaneous chemical sympathectomy using alcohol and phenol may be applied; however, their long-term therapeutic effects are unclear [3-6].

Since the surgical approach for primary hyperhidrosis was first described in 1922 [7], various surgical modalities have been attempted and popularized. Lumbar sympathectomy was first introduced in Argentina and Austria by Diez J. [8] and Royle [9] in 1924, respectively, and was previously mainly performed for occlusive vascular diseases, such as Buerger disease, Raynaud's disease, and reflex sympathetic dystrophy. Endoscopic lumbar sympathectomy was not described until 1973 by Wittmoser [10], while endoscopic thoracic sympathectomy (ETS) was introduced in the 1940s. Since then, the usefulness of lumbar sympathectomy has decreased because of the development of arterial reconstruction techniques for vascular disease [1], in the late 2000s, endoscopic lumbar sympathectomy and sympathicotomy for plantar hyperhidrosis have become widespread standard surgical options with reproducible results. Loureiro [1] and Rieger [11-13] performed a sympathetic trunk resection of approximately 4 cm, including L2 and L3 or L3 and

L4 ganglia. Later, Reisfeld [14, 15] implemented lumbar sympathectomy using the clamping method at the level of L3 or L4 using multiple clips, and anhidrosis was achieved in 97.4% of patients. This showed that a single level of sympathetic block alone could achieve sufficient surgical effects. ETS has been performed at various levels from T2 to T4 in patient with palmar hyperhidrosis and reports according to the blocking level have been continuously published. However, in the case of plantar hyperhidrosis surgery, research on the surgical effects of a lumbar sympathetic truncal block besides multiple levels of nerve resection has been relatively rare, particularly in Asia including Korea. Additionally, worldwide, no study has compared the efficacy of L3 and L4 blocks. Therefore, standardization of surgical techniques is still needed to achieve consistent and effective treatment results.

This study aimed to evaluate the clinical effects and patient satisfaction with lumbar sympathetic clipping (LSC) on L3 or L4 for plantar hyperhidrosis and identify which lumbar level should be blocked for more effective results.

MATERIALS AND METHODS

Between December 2015 and June 2018, LSC was performed on 500 patients from a single center. Sixty-four patients who were blocked at different levels bilaterally were excluded to avoid a bias that could affect the reliability of the results; thus, a total of 436 patients were included in the early postoperative data analysis. Hyperhidrosis Disease Severity Scale (HDSS) [16] (Table 1) scores were 3 or 4, indicating barely tolerable or intolerable sweating and frequent or persistent interference of daily activity, whereas secondary hyperhidrosis was excluded. Preoperative examinations, such as chest radiography, electrocardiography, routine laboratory tests, and infrared thermography were performed. All patients were encouraged to complete the Hyperhidrosis Quality of Life Index (HidroQoL©) [17] (Figure 1) before the operation, and were required to sign an informed consent form concerning possible intraoperative and postoperative complications and permission for data collection.

Table 1. Hyperhidrosis Disease Severity Scale (HDSS) (adapted from Solish, *et al.*)

HDSS 1	My sweating is never noticeable and never interferes with my daily activities.
HDSS 2	My sweating is tolerable but sometimes interferes with my daily activities.
HDSS 3	My sweating is barely tolerable and frequently interferes with my daily activities.
HDSS 4	My sweating is intolerable and always interferes with my daily activities.

Figure 1. The Hyperhidrosis Quality of Life Index (HidroQoL©).

The Hyperhidrosis Quality of Life Index

(HidroQOL©)

오늘을 포함해서 최근1주일 내에 과도한 땀으로 인해 얼마나 생활에 고통 받는지에 대한 설문입니다.
각 질문에 한 개의 답만 선택해 주십시오. 모든 질문에 빠짐없이 답해 주십시오.

PRE OP / POST OP

이름______________ (키 : cm / 몸무게 : kg)

Domain 1 일상생활에 영향	매우	조금	전혀그렇지않다
1. 입을 옷을 고르는 데에 신경 쓰인다.	☐	☐	☐
2. 신체활동(운동)에 영향을 받는다.	☐	☐	☐
3. 취미 생활 하는데에 영향을 받는다.	☐	☐	☐
4. 직업(학업)적으로 일(공부) 하는데에 영향을 받는다.	☐	☐	☐
5. 땀 관리하느라 다른 활동에 지장을 줄까 걱정이다.	☐	☐	☐
6. 휴일 계획을 세우는데 신경 쓰인다.	☐	☐	☐

Domain 2 정신사회적 영향	매우	조금	전혀그렇지않다
7. 나는 불안하고 예민하다.	☐	☐	☐
8. 나는 창피하다.	☐	☐	☐
9. 나는 짜증스럽다.	☐	☐	☐
10. 나는 신체적 표현에 불편하다.(예.껴안는 표현)	☐	☐	☐
11. 나는 땀에 대해 생각한다.	☐	☐	☐
12. 나의 미래의 건강에 대해 걱정이다.	☐	☐	☐
13. 나의 땀에 대한 사람들의 반응이 걱정이다.	☐	☐	☐
14. 나의 땀 자국이 어딘가에 남을까 걱정이다.	☐	☐	☐
15. 새로운 사람을 만나기를 꺼린다.	☐	☐	☐
16. 공공장소에서의 발표를 꺼린다.	☐	☐	☐
17. 나의 외모에 신경 쓰인다.	☐	☐	☐
18. 나의 성생활에 영향이 있다.	☐	☐	☐

Domain 1 Score:__Domain 2 Score:__Total Score:__(out of 36)

본인은 다한증 연구에 이 설문이
활용됨에 동의합니다.
signature { }

Operative technique

All patients underwent bilateral surgery under general anesthesia with single-lumen endotracheal intubation. Propofol-sevoflurane-nitrous oxide and rocuronium bromide were used as the anesthetic agent and muscle relaxant, respectively. The patients were placed in a supine position with slight hip flexion by a pillow underneath the knee joint. In cases of combined palmar hyperhidrosis, T4 ETS was performed in Semi-Fowler's position, using clips before the LSC. For the LSC, approximately 3 cm of horizontal skin was incised and extended from the navel to the lateral abdominal wall halfway between the upper margin of the iliac crest and the inferior rib cage margin of each side (Figure 2). The skin, subcutaneous fat layer, external oblique, internal oblique, and transversalis muscles were dissected using the splitting method to avoid muscle injury, thereby preventing muscular bleeding and postoperative muscular pain. The transversalis muscle was separated from the peritoneum using finger dissection with caution to avoid rupture of the peritoneum. Once the retroperitoneal space was opened, the operating view field was retained by the Deaver retractor until the anterior surface of the psoas major muscle fascia was identified by pushing all structures anteriorly.

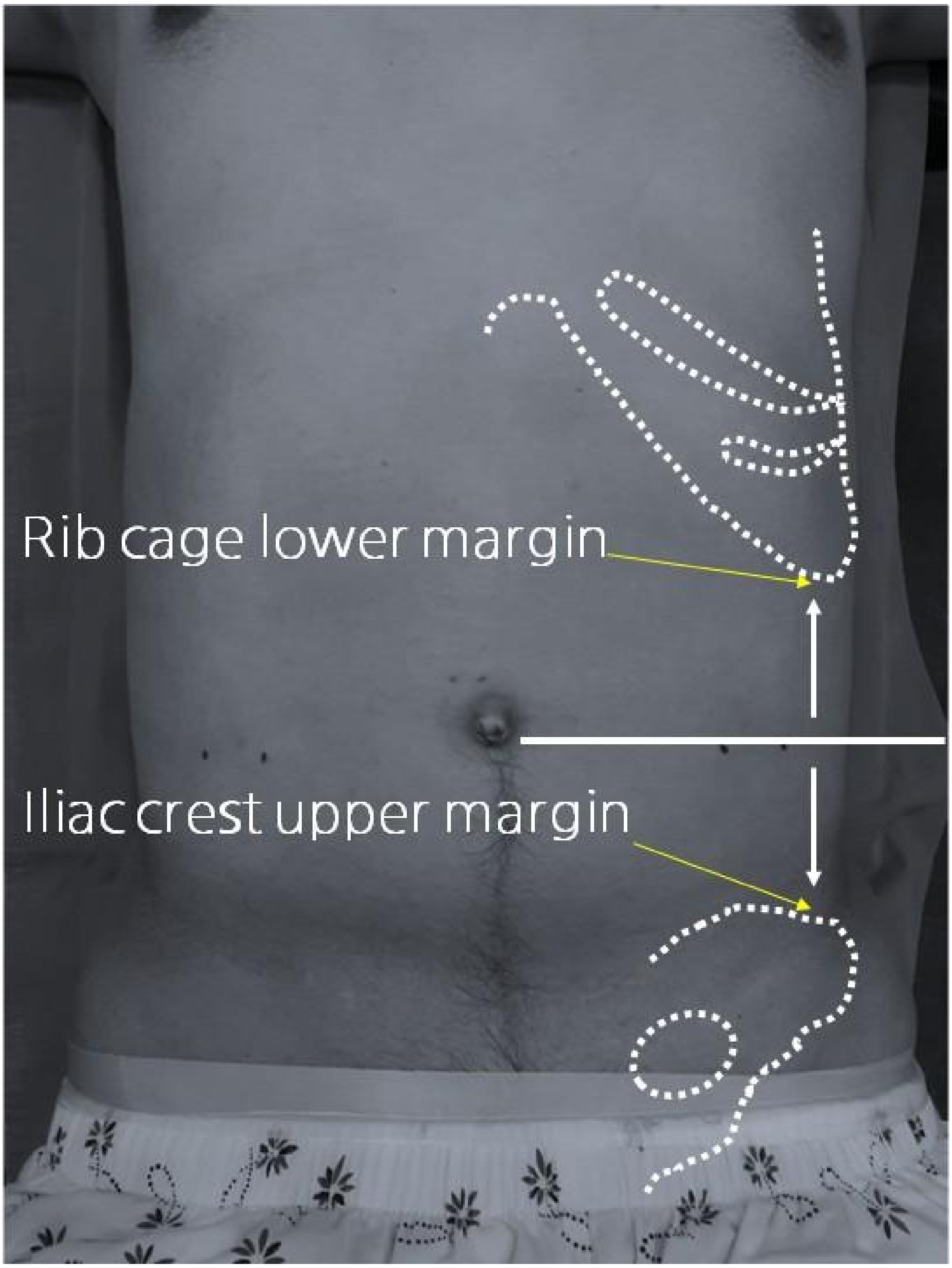
During this procedure, the structures that require attention are the genitofemoral nerve, lymphatics, inferior vena cava (IVC), lumbar veins, and their small branches, and the target of the sympathetic nerve is anatomically deep and superjacent on the vertebral body. To identify the sympathetic ganglion and chain, a finger touch technique that directly detects the ganglion using the surgeon’s finger was needed to avoid unnecessary damage to the surrounding tissue. After isolating the nerve and dividing all the rami communicants from the adjacent fat pad, at least two 3-mm titanium clips (Weck®, HORIZON™, Telefelx Medical, Morrisville, NC, USA), were applied to the sympathetic chain for full circumstance block.

When a nerve was undetectable because of its thickness, careful dissection in the upward and downward directions under direct or ancillary endoscopic vision was needed in most cases. Endoscopy was only used in limited situations, such as checking for anatomical structures and bleeding or ensuring accurate and complete nerve blocking. The choice of clip position was affected by the surrounding structures, such as the lumbar veins, small arteries, or lymphatic vessels. Once the right side was completed, the same procedure was performed contralaterally.

The skin temperature of both the soles of the feet was measured using a contactless infrared thermometer after 5 min of clipping the target nerve. Since the influence of anesthetics on temperature changes could not be ignored, the temperature was checked only to confirm the symmetricity. If the temperature difference between both feet was > 0.5° Celsius, whether the clip encompassed the whole trunk needed to be rechecked, and an additional clip application was performed if necessary.

The external and internal oblique muscle fascia were closed with absorbable sutures, and skin closure was performed. The level of sympathetic block by clips was confirmed on a radiograph of the lumbar spine before discharge. For young male patients, masturbation was advised on the first day, and groin sensory changes were checked for genitofemoral nerve injury in all patients. All patients were discharged on the day of surgery.

Figure 2. The relationship of the hip, rib cage, and umbilicus. The solid line is drawn half-way between the rib cage lower margin and the iliac crest upper margin.



Postoperative follow up

We examined the patients on postoperative day 10 using the 10-point satisfaction scale and HidroQoL© reassessment. Any side effects, including compensatory hyperhidrosis (CH), were also investigated. For the long-term results, the late satisfaction scale and HidroQoL© responses of 134 patients who we were able to contact 3–5 years postoperatively, were collected via Google Forms using text message correspondence (Figure 3). Additional information was obtained from medical chart reviews and telephone interviews.

CH severity was graded as "none" (not noticeable), "mild" (tolerable and barely or sometimes interferes with daily life), or "severe" (intolerable and always interferes with daily activities, resulting in regret for undergoing this surgery).

Statistical analysis

The data were statistically analyzed using the RStudio (version 4.0.3, R-Tools Technology Inc.). Descriptive statistics are presented as means with standard deviations for continuous variables and numbers with frequencies for categorical variables. The Mann–Whitney–Wilcoxon test and Kruskal–Wallis H test for ordinal variables or nonparametric data, and the chi-square test and Fisher's exact test for determining an association between two categorical variables, were used to evaluate clip location-based differences in perioperative outcomes. Changes in satisfaction scales and HidroQoL© scores were compared using the Wilcoxon signed-rank test (for nonparametric paired data comparison) and Tukey's post hoc test. Multiple linear and logistic regression analyses were performed to identify the influential factors associated with patient satisfaction, HidroQoL©, and CH. Statistical significance was set at $p < 0.05$.

Figure 3. Postoperative questionnaire (Google Forms).

https://docs.google.com/forms/d/1CCjcGC_nnAU2OG29b_Uz3Nul7xGDkLJpFQ_9L5GZT7E/edit

발 다한증 수술 후 평가

현재 환자분의 발에 대한 땀의 상태에 대해 답하여 제출해 주세요.

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○ 없거나 잘 모르겠다.

○ 있지만 수술을 후회할 정도는 아니다.

○ 매우 심하여 수술을 후회한다.

현재 발 다한증 수술 후 만족도 *

	1	2	3	4	5	6	7	8	9	10	
매우 불만족	○	○	○	○	○	○	○	○	○	○	매우 만족

일상생활에 영향 *

	매우 그렇다	조금 그렇다	전혀 그렇지 않다.
입을 옷을 고르는 데에 신경이 쓰인다.	○	○	○
신체활동(운동)에 영향을 받는다.	○	○	○
취미활동에 영향을 받는다.	○	○	○
직업(학업)적으로 일(공부) 하는데에 영향을 받는다.	○	○	○
땀 관리하느라 다른 활동에 지장을 줄까 걱정이다.	○	○	○
휴일 계획을 세우는데 신경 쓰인다.	○	○	○

정신사회적 영향 *

	매우 그렇다.	조금 그렇다.	전혀 그렇지 않다.
땀 때문에 불안하고 예민하다.	○	○	○
땀 때문에 창피하다.	○	○	○
땀 때문에 짜증스럽다.	○	○	○
땀 때문에 신체적 표현에 불편하다. (껴안는 표현)	○	○	○
땀에 대해 생각한다.	○	○	○
땀으로 인한 미래의 건강에 대해 걱정이다.	○	○	○
땀에 대한 사람들의 반응이 걱정이다.	○	○	○
나의 땀 자국이 어딘가에 남을까 걱정이다.	○	○	○
땀 때문에 새로운 사람을 만나기 꺼려진다.	○	○	○
땀 때문에 공공장소에서의 발표를 꺼린다.	○	○	○
땀으로 인해 외모에 신경이 쓰인다.	○	○	○
땀으로 인해 나의 성생활에 영향이 있다.	○	○	○

특별히 전하고 싶은 내용이 있으면 적어주세요

내 답변

제출

양식 지우기

RESULTS

The characteristics of the 436 patients are presented in Table 2. The L3:L4 ratio was 351:85. The mean age was 26.3 years (range, 14–49 years), and > 70% of the patients were teenagers and young adults. Overall, there was no difference in each variable by clip location, but L3 was higher in males, and L4 was higher in females. The most commonly associated hyperhidrosis site was palmar (67.9%), and the proportion of patients with plantar hyperhidrosis alone at the time of surgery was 16.5%. A total of 359 patients (82.3%) underwent simultaneous operation with ETS, and five out of 77 patients who underwent LSC only wanted to treat plantar hyperhidrosis, rather than other areas.

The perioperative outcomes and complications of LSC are shown in Table 3. In the total patient group analysis (N = 436), the skin-to-skin operation time was 43.9 ± 8.7 min. There were no significant differences in most of the investigated variables between L3 and L4 clipping, except for the rate of neuralgia and operation time, which were higher and longer, respectively, in the L4 group than in the L3 group. However, the LSC-only subgroup analysis showed that temporary hidrosis was higher in the L3 group. The descriptive statistics of the early and late postoperative results by clip location is shown in Table 4; no significant difference in both total and subgroup analyses was noted in any of the variables.

Meanwhile, statistically significant improvements in the HidroQoL© scores were noted between the preoperative and early survey results on postoperative day 10, but the HidroQoL© scores slightly rebounded and the satisfaction scores decreased in the long-term results (Figures 4–5). All these changes were statistically significant (Tukey's post-hoc test, $p < 0.017$).

The early and late postoperative results according to the combined ETS are shown in Table 5. The early postoperative HidroQoL© scores and their difference from the baseline of the ETS-combined group were lower and larger than those of the LSC-only group, whereas the other variables were not significantly different between the groups.

Multiple linear regression analysis for factors associated with patient satisfaction scales showed that early and late CH were the key predictors of postoperative outcomes (Table 6). Logistic regression analysis of CH for early outcomes identified only the presence of comorbid hyperhidrosis in other areas as an influencing factor. The odds ratios (95% confidence intervals) for plantar-palmar-axillar and plantar-palmar-other sites were 2.61 (1.27–5.37) and 7.96 (1.25–50.63), respectively (Figure 6). However, there were no influencing factors in the analysis of late CH.

Table 2. Descriptive statistics of patient characteristics by clip location of LSC.

	Mean ± SD or Number of patients (%)			
	Overall (N=436)	L3 (N=351)	L4 (N=85)	*p*-value
Age (years)	26.3 ± 7.2	26.2 ± 7.2	26.8 ± 7.6	0.476
Sex				0.001
-Male	218(50.0)	190(54.1)	28(32.9)	
-Female	218(50.0)	161(45.9)	57(67.1)	
BMI* (kg/m^2)	21.6 ± 2.6	21.7 ± 2.5	21.4 ± 3.0	0.336
-Normal (≤19.9)	272(62.4)	219(62.4)	53(62.4)	
-Obesity (20~24.9)	41(9.4)	33(9.4)	8(9.4)	
-Overweight (25~29.9)	82(18.8)	68(19.4)	14(16.5)	
-Underweight (30≤)	41(9.4)	31(8.8)	10(11.8)	
Hyperhidrosis site				0.103
-Plantar-Palmar	296(67.9)	247(70.4)	49(57.6)	
-Plantar only	72(16.5)	52(14.8)	20(23.5)	
-Plantar-Palmar-Axillar	60(13.8)	45(12.8)	15(17.6)	
-Plantar-Palmar-others	8(1.8)	7(2.0)	1(1.2)	
Simultaneous ETS**				0.040
-LSC and ETS**	359(82.3)	296(84.3)	63(74.1)	
-LSC*** only	77(17.7)	55(15.7)	22(25.9)	
-LSC without pETS****	38(8.7)	29(8.3)	9(10.6)	
Major Symptoms				

-Slippery sandals	426(97.7)	342(97.4)	84(98.8)	0.717
-Damp socks and shoes	369(84.6)	296(84.3)	73(85.9)	0.851
-Bromhidrosis	340(78.0)	273(77.8)	67(78.8)	0.950
-Cold feet	291(66.7)	235(67.0)	56(65.9)	0.953
-Skin lesions	233(53.4)	191(54.4)	42(49.4)	0.479

Values are presented as mean ± standard deviation; *BMI, body mass index; **ETS, endoscopic thoracic sympathectomy; *** LSC, lumbar sympathetic clipping; pETS****, previous ETS history.

Table 3. Perioperative outcomes and complications by clip location.

Total patient group (N=436)

	Mean ± SD or Number of patients (%)			*p*-value
	Overall (N=436)	L3 (N=351)	L4 (N=85)	
LSC* operation time (minute)	43.9 ± 8.7	43.4 ± 8.6	45.9 ± 9.0	0.019
Temporary hidrosis	145(33.3)	124(35.3)	21(24.7)	0.082
Complications				
-Asymmetry effect	16(3.7)	12(3.4)	4(4.7)	0.807
-Neuralgia	10(2.3)	5(1.4)	5(5.9)	0.039
-Peritoneal tear	3(0.7)	1(0.3)	2(2.4)	0.181
-Hematoma	2(0.5)	2(0.6)	0	1.000
-Chyle leak	2(0.5)	2(0.6)	0	1.000
-Wound infection	1(0.2)	1(0.3)	0	1.000

*LSC, lumbar sympathetic clipping.

LSC-only subgroup (N=77)

	Mean ± SD or Number of patients (%)			*p*-value
	Overall (N=77)	L3 (N=55)	L4 (N=22)	
LSC* operation time (minute)	48.3 ± 9.9	47.9 ± 10.0	49.2 ± 10.0	0.620
Temporary hidrosis	29(37.7)	26(47.3)	3(13.6)	0.013
Complications				
-Asymmetry effect	3(3.9)	3(5.5)	0	0.642
-Neuralgia	6(7.8)	3(5.5)	3(13.6)	0.460
-Peritoneal tear	0	0	0	
-Hematoma	1(1.3)	1(1.8)	0	1.000
-Chyle leak	0	0	0	
-Wound infection	1(1.3)	1(1.8)	0	1.000

*LSC, lumbar sympathetic clipping.

Table 4. Early and late postoperative results by clip location.

Total patient group (N=436)

	Mean ± SD or Number of patients (%)					
	Early results (N=436)			Late results (N=134)		
	L3(N=351)	L4(N=85)	*p*-value	L3(N=106)	L4(N=28)	*p*-value
CH*			0.456			0.943
-None	208(59.3))	53(62.4)		13(12.3)	3(10.7)	
-Mild	142(40.5)	31(36.5)		80(75.5)	21(75.0)	
-Severe	1(0.3)	1(1.2)		13(12.3)	4(14.3)	
HidroQoL© score						
-Preoperative	22.1±6.0	23.2±6.2	0.161	21.9±5.6	23.4±7.0	0.234
-Postoperative	3.5±4.0	3.9±3.9	0.343	10.8±9.6	11.5±11.2	0.748
-Difference	18.7±6.6	19.2±6.4	0.475	11.1±10.4	11.9±12.4	0.723
Satisfaction scale	9.7±0.7	9.8±0.6	0.321	7.4±2.6	7.3±2.5	0.851

*CH, compensatory hyperhidrosis.

LSC-only subgroup (N=77)

	Mean ± SD or Number of patients (%)					
	Early results (N=77)			Late results (N=24)		
	L3(N=55)	L4(N=22)	*p*-value	L3(N=15)	L4(N=9)	*p*-value
CH*			1.000			0.504
-None	35(63.6)	14(63.6)		3(20.0)	2(22.2)	
-Mild	20(36.4)	8(36.4)		11(73.3)	5(55.6)	
-Severe	0	0		1(6.7)	2(22.2)	
HidroQoL© score						
-Preoperative	22.3±6.1	21.7±7.4	0.748	21.3±5.7	21.0±8.3	0.908
-Postoperative	5.0±4.9	3.9±3.7	0.333	10.5±10.5	9.6±10.9	0.847
-Difference	17.2±7.1	17.8±7.0	0.738	10.9±11.4	11.4±15.0	0.916
Satisfaction scale	9.7±0.7	9.7±0.6	0.821	7.9±2.5	6.7±3.2	0.284

*CH, compensatory hyperhidrosis.

Figure 4. The changes in preoperative, early, and late results of HidroQoL© scores.

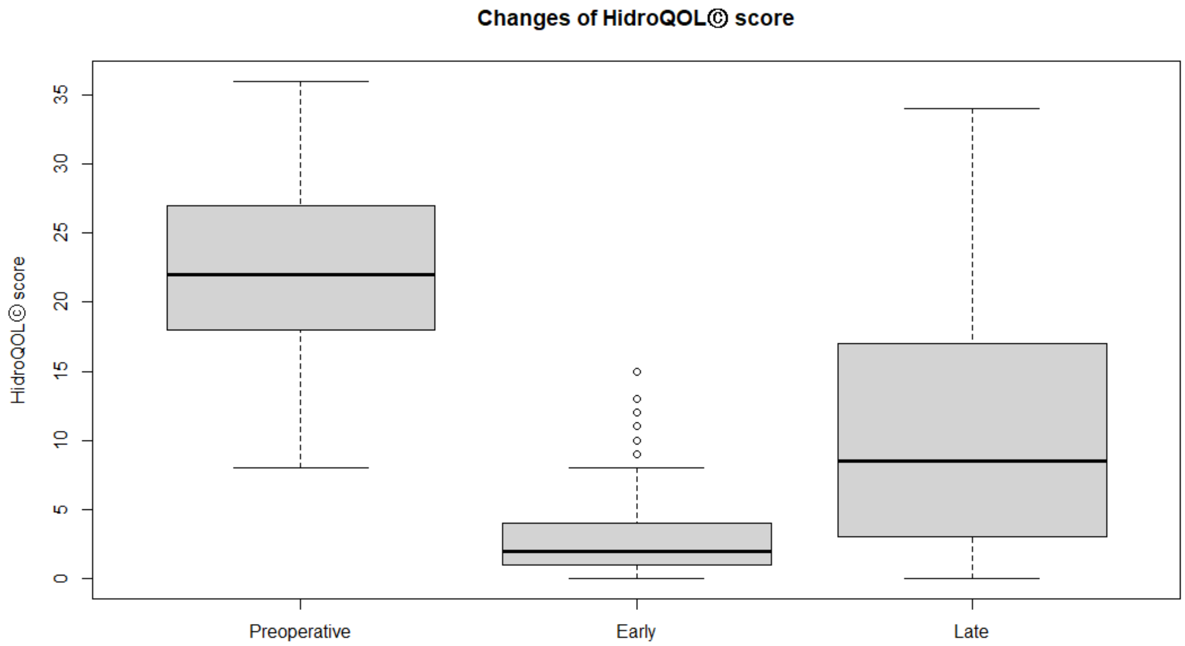


Figure 5. The changes of Satisfaction scale between early postoperative and late results.

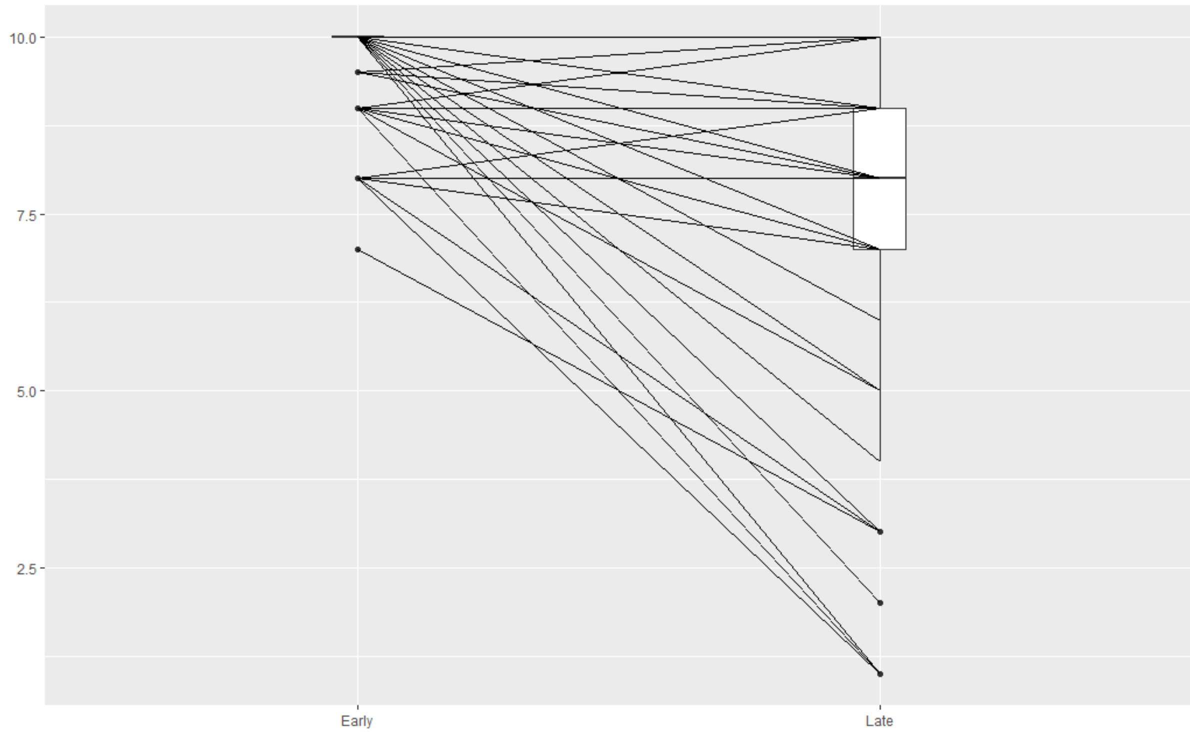


Table 5. Early and late postoperative results by operation type.

	Mean ± SD or Number of patients (%)					
	Early results (N=436)			Late results (N=134)		
	ETS&LSC (N=359)	LSC only (N=77)	*p*-value	ETS&LSC (N=110)	LSC only (N=24)	*p*-value
CH*			0.634			0.328
-None	212(59.1)	49(63.6)		11(10.0)	5(20.8)	
-Mild	145(40.4)	28(36.4)		85(77.3)	16(66.7)	
-Severe	2(0.6)	0(0.0)		14(12.7)	3(12.5)	
HidroQoL© score						
-Preoperative	22.4±6.0	22.1±6.4	0.707	22.4±5.7	21.2±6.6	0.361
-Postoperative	3.3±3.8	4.7±4.6	0.013	11.1±9.8	10.1±10.4	0.649
-Difference	19.1±6.4	17.4±7.0	0.038	11.3±10.4	11.1±12.6	0.935
Satisfaction scale	9.7±0.6	9.7±0.6	0.983	7.4±2.5	7.5±2.8	0.907

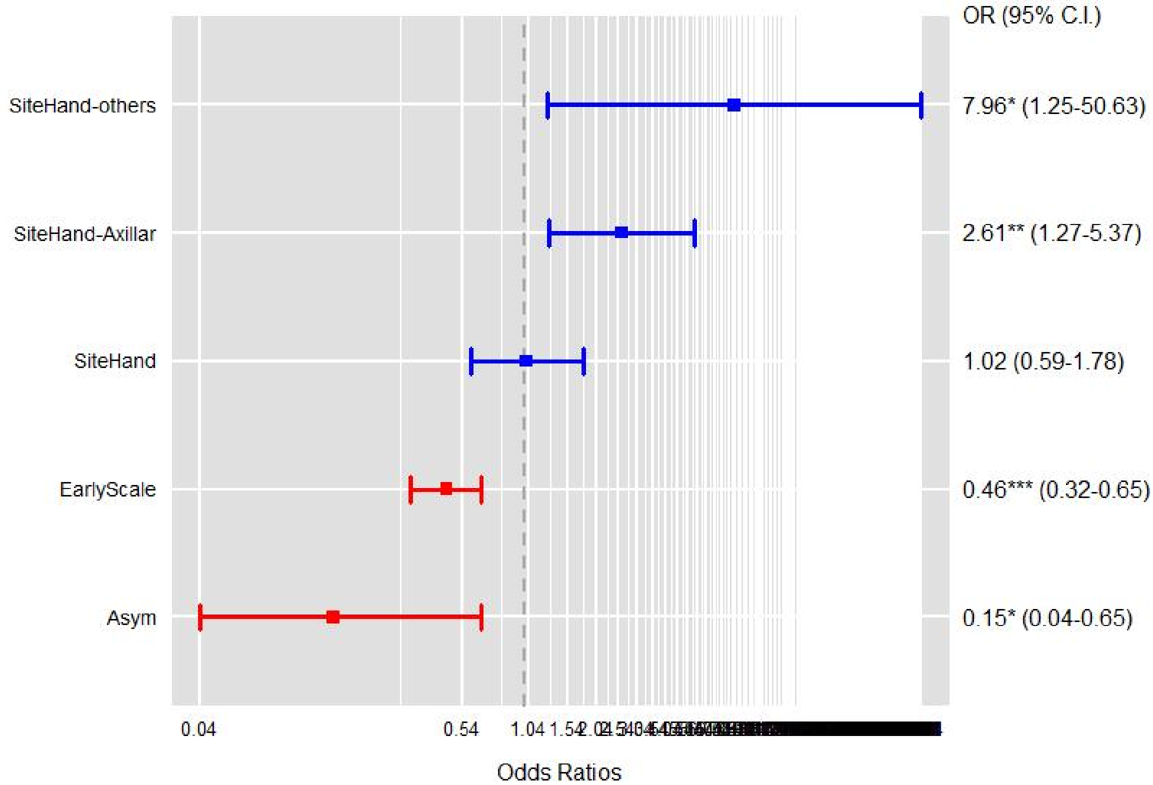
*CH, compensatory hyperhidrosis.

Table 6. Factors associated with early and late satisfaction scale.

Variables	Early Satisfaction Scale			
	β	SE*	t	*p*-value
Age	0.009640	0.003866	2.493	0.013
CH**	-0.232283	0.007087	-5.054	0.000
Postoperative HidroQOL©	-0.035819	0.424848	0.611	0.542
Temporary hidrosis	-0.188462	0.059720	-3.156	0.002
Asymmetric effect	-0.988687	0.149773	-6.601	0.000
	F = 22.14, p-value < 0.000, Adjusted R^2 = 0.1958			
	Late Satisfaction Scale			
CH**	-2.0430	0.4107	-4.975	0.008
	F = 24.75, p-value < 0.000, Adjusted R^2 = 0.1515			

*SE, standard error; **CH, compensatory hyperhidrosis

Figure 6. Odds-ratio plot of compensatory hyperhidrosis in early outcomes.



DISCUSSION

Preoperative patient selection and surgical technique

Primary hyperhidrosis causes serious challenges in daily life, despite being a non-life-threatening and non-painful disease [12]. In most cases, symptoms begin in adolescence and lead to serious deterioration of the patient's quality of life. Usually, patients initially seek non-surgical therapy, such as oral and topical agents, iontophoresis, or botulinum toxin. However, patients who are classified as HDSS 3–4 with severe sweating (Figure 7) often find that non-surgical methods only have a temporary effect and therefore seek surgery, a permanent treatment method. The diagnostic criteria for hyperhidrosis depend on the individual's occupation, personality, sex, and age. The same amount of sweating may be considered hyperhidrosis by one individual, but not by others. Therefore, sufficient history taking examining the interference with quality of life using questionnaires such as HidroQoL© is needed to correctly determine patients who need surgery. The HidroQoL© (Figure 1) consists of six items in domain 1 (daily life activities) and 12 items in domain 2 (psychosocial life), each of which is scored on a 3-point scale: no, not at all = 0; a little = 1; and very much = 2 [17].

An epidemiological study in Korea [18] found that approximately 54.6% of hyperhidrosis patients complained of simultaneous hyperhidrosis in their hands and feet, whereas < 5% complained of hyperhidrosis in their hands or feet independently. In our study, 359 (82.3%) patients underwent ETS and LSC simultaneously, and 77 (17.7%) underwent LSC alone. Of these 77 patients, 39 had already undergone a previous ETS. In total, 8.7% (38 out of 436) of the patients in this study had plantar hyperhidrosis alone.

If ETS and LSC had to be performed simultaneously, the ETS was first implemented under general anesthesia with single-lumen endotracheal intubation in the Semi-Fowler's position and then replaced in the supine position for LSC, and T4 clipping was applied to all ETSs. ETS alone could improve plantar hyperhidrosis, but the long-term results remain unclear due to the small number of cases and relatively short-term follow-up period [19-22]. Furthermore, most patients prefer ETS-LSC because of the burden of repeated general anesthesia, and 82.3 % of patients in this study also received both procedures simultaneously.

Right-side LSC has always been challenging because of the anatomical complexity of the IVC, lumbar veins, retroperitoneal fat fad, and lymphatic network around the sympathetic chain. Therefore, detection should be very delicate and undertaken with care. The nerve chain is usually located deep between the IVC and the psoas muscle, and rough manipulation can tear off the IVC or lumbar veins, which not only interferes with the surgical view but also results in a retroperitoneal hematom. In addition, the genitofemoral nerve, which is usually anterior to the psoas muscle, may be confused with the sympathetic chain when it skews too medially. Therefore, the symptoms of genitofemoral nerve injury after surgery, such as groin pain, paresthesia, and a burning sensation spreading from the lower abdomen to the medial aspect of the thigh [23] should be carefully checked. In this study, there was no case of genitofemoral nerve injury.

Another major issue before clipping is discriminating between L3 and L4. Just as ETS has been historically performed in a variety of ways, such as resection or ablation of the ganglion, transection of the chain, severing the rami, and finally sympathetic block using the clipping method on a specific level to solve compensatory hyperhidrosis [24], over the past decade, plantar hyperhidrosis surgery has been adapted by several surgeons (Table 7) [25]. All these changes have been made to minimize complications and maximize surgical effects. Loureiro *et al*. performed a sympathectomy from the L2 to L3 ganglion, after anatomical confirmation of the kidney's lower pole using preoperative ultrasonography, leaving the L4 ganglion, to delimit the sympathetic denervation to the territory below the knee line, and reported sexual alterations [1]. Jani *et al*. recommended sectioning the lumbar sympathetic chain from the upper border of L3 to the lower border of L4 [26]; otherwise, it could result in failure to achieve anhidrosis [11, 26]. Reiger *et al*. resected a segment of the sympathetic trunk situated between the L3 and L4 ganglia after clipping of both ends, but reported post-sympathetic neuralgia in 42% of patients [11]. In addition, ETS surgical results of clipping have been similar to those with resection of the sympathetic chain [27-30]. Accordingly, Reisfeld *et al*. reduced complications and obtained similar surgical effects by performing a sympathetic truncal clamping using clips on the L3 or L4 after confirming its location with fluoroscopy, which is no longer nerve resection [14, 15]. In our previous study, satisfaction scores in the L3 group were significantly higher than those in the L4/5 group in the late postoperative period [31]. Thus, it is still important to identify and block L3 and L4, and the lumbar vein could be a good landmark. Once the lumbar vein is identified, the L3 ganglion, which is usually located just above it, can be easily blocked without confusion. However, identification of these anatomical structures is not always feasible, depending on the patient's condition. Particularly in the case of patients with scoliosis, high body mass index (BMI), or a history of chemical sympathectomy, dissection can be highly time-consuming and lead to unexpected bleeding, making the space more indistinct. To resolve this issue, we blocked the sympathetic trunk that could be easily found via endoscopy or the finger touch technique along with skin temperature measurement after clipping, without any further efforts to find L3. In the present study, this technique was applied to most of the patients who underwent clipping at the L4 level, and this explains the analysis results that the operation time was longer, and neuralgia was more common in the L4 group (Table 3), although further evaluation is still needed.

Performing left-side LSC is easier than right-side LSC. After identifying the genitofemoral nerve and ureter, clipping can be performed at the same level as much as possible; however, occasionally, it may not be the target level due to anatomical variants. In this case, an appropriate clipping level may be selected by continuous skin temperature measurements.

There are two main causes of surgical failures. The first is the mechanical failure of a complete nerve block, which is prevented by multiple blocks using at least two clips to encompass the whole trunk, with sufficient dissection and nerve isolation. The other cause is anatomical variations, such as relatively thin chains or asymmetrically tapered out [32]. In addition, a less experienced surgeon due to the learning period, could be another cause. There was only one case in this study that showed no significant temperature changes on the legs and no effect of anhidrosis, indicating that the block was incomplete. A relocation of clips on L3 on the day of surgery was performed and a satisfactory result was observed. Meanwhile, there were three patients who complained of recurrence in the long-term follow-up survey, but this was not sufficient to require reoperation.

As per our previous study that analyzed 82 patients [31], the target nerve of LSC was L3 as same as this study. However, its operation time was reduced from 76.4 min in the previous study to 43.9 min in the present study, and as mentioned above, it was longer with significant differences in the L4 group than in the L3 group. This result might be due to the learning period effect but could also signify that the surgeon spent more time differentiating L3 from L4. This time-consuming process can lead to unnecessary complications, such as retroperitoneal hematoma and lymphatic damage, which can reduce patient satisfaction. Since sensory innervation is rich around vertebral bodies, the greater the dissection and mobilization of the sympathetic chain cause the greater postoperative neuralgia and pain [15]. In addition, the longer operation time is related to the longer recovery time, which may delay the patient's return to daily life. Therefore, efforts to reduce the operation time are critical, and it is necessary to decrease efforts to distinguish between L3 and L4. In this study, we compared the L3 sympathetic block groups with the "unintended" L4 group in the early and late postoperative results. As shown in Table 4, there was no significant difference in the postoperative quality of life and satisfaction scores between the two groups, and this was replicated in the subgroup analysis, indicating that clipping level is not a crucial factor for determining the surgical outcomes. The target area is a very narrow surgical field that is packed with various anatomic structures; therefore, it is advisable to avoid spending time searching for the exact level of L3 for the effects of the surgery, since L3 or L4 can be reached by going along the preoperative incision marking unless there is an anatomical variation. In addition, unnecessary radiation exposure caused by fluoroscopy, which has been used in many previous studies [12-15, 33], can be avoided. If the procedure for identifying the exact level of L3 and L4 can be abbreviated, postoperative patient satisfaction may increase.

Figure 7. A typical plantar hyperhidrosis patient.

Table 7. Summary of the previous studies for lumbar sympathectomy (adapted from Lima, *et al.*).

Study	Intervention site	Patients	Resolution (%)	Compensatory hyperhidrosis (%)	Transient neuralgia	Transient Sexual dysfunction
Loureiro *et al.* [1]	L2/L3 resection with ganglionectomy	15	93	53	4	2
Rieger *et al.* [10]	L2/L3/L4 resection with ganglionectomy	90	97	44	38	3
Reisfeld *et al.* [13]	L3 or L4 clipping	63	89	90	11	0
Rieger *et al.* [11]	L3 or L4 resection with ganglionectomy	52	94	63	-	-
Yun *et al.* [30]	L3, L4, or L5 clipping	82	83	39	3	0
Lima *et al.* [41]	L2/L3 or L3/L4 resection with ganglionectomy	49	98	53	3	0

Compensatory hyperhidrosis

The common areas of CH were the anterior and posterior chest, back, abdomen, and thighs. The early occurrence rate for CH was 40.1%, but it increased significantly to 88.1% in the long-term follow-up of > 3 years. Specifically, the proportion of patients with severe CH in which clip removal could be considered was only 0.5% (2 of 436 patients) in the early stage; however, it increased to 12.7% (17 of 134) with an increase in the HidroQoL© score in the late survey. This rate change of CH is similar to that in previous studies examining the long-term follow-up results of ETS [34-36]. Both severe CH patients in the early results were those who underwent ETS simultaneously, and one of them complained of sweating heavily on the back. Eventually, CH was alleviated by removing the clip of the thoracic sympathetic chain on postoperative day 4. The other patient complained of severe CH throughout the body but did not want to remove the clip, and sweating was controlled with oral anticholinergic pills. In the late results of 134 patients (Table 4), three out of 17 patients with severe CH underwent LSC-only with ETS history, and the remaining 14 patients underwent ETS simultaneously. The CH areas they complained of were the back, chest, and abdomen, which did not differ widely from the CH areas caused by ETS. On the other hand, none of the 38 patients who underwent LSC-only without a previous ETS history complained of severe CH in the early and late follow-up periods. In this group, all patients with mild CH identified their hands as sweaty areas, and Reisfeld *et al.* explained that this could be the result of a surge in signals reaching the brain through the spinal cord; however, this remains unclear [15].

Based on these results, the CH that occurred in this study is presumed to be the effect of the accompanying ETS, rather than LSC per se. These findings support the preexisting reports that severe CH is rare after LSC alone [11], and even if it occurs, it is mild and primarily limited to the lower leg area. Moreover, there were little changes in the levels of CH in patients with prior ETS

[14] [37]. In addition, Reisfeld *et al.* explained that ETS plays a greater role in the interruption of the sympathetic chain than LSC, and found no severe CH in a small cohort of patients who underwent only LSC [15].

Meanwhile, in both early and late follow-up, the CH incidence rate according to the clip location and operation type showed no statistically significant difference (Tables 4 and 5). The same result was observed even in the LSC-only subgroup analysis. Additionally, no statistically significant difference was found in the comparative analysis of BMI, which is known to be associated with CH [38].

Table 8. Factors associated with early and late HidroQoL© differences from preoperative score.

Variables	Early score difference			
	β	SE*	t	*p*-value
Accompanied hidrosis				
-Palmar-Axillar	2.9972	0.9125	3.285	0.0011
-Palmar-Other site	2.5161	2.3358	1.077	0.2820
-Plantar only	-1.3143	0.8466	-1.553	0.1213
Asymmetric effect	-2.6524	1.6621	-1.596	0.1113
	F = 4.795, p-value = 0.001, Adjusted R^2 = 0.03372			
	Late score difference			
Sex - Male	-3.08736	1.62412	-1.901	0.0595
Operation Time	-0.15314	0.09316	-1.644	0.1026
CH**	-10.36205	1.62896	-6.361	0.0000
	F = 16.13, p-value < 0.000, Adjusted R^2 = 0.2544			

*SE, standard error; **CH, compensatory hyperhidrosis

Satisfaction

As mentioned earlier, to diagnose hyperhidrosis, we must consider the subjective aspects of the patient. While the same amount of sweat might resemble hyperhidrosis for someone, it could be normal for others depending on their job, personality, age, and sex. Postoperative satisfaction also depends on these variables. In this study, to evaluate the effectiveness of surgery more objectively, the HiroQoL© and satisfaction scale were used, and there was no statistically significant correlation between clip location and ETS-combined or not. As shown in Table 4, the LSC-only subgroup analysis showed the same results. Although the pattern of the changes in postoperative satisfaction and HidroQoL© showed slightly different results in the LSC-only group without ETS history, the number of subjects was too small to achieve statistical significance, which is a limitation of this study. Epidemiologically, the number of patients with pure plantar hyperhidrosis is < 5% of the total hyperhidrosis patient group, and more cases and a longer study period are required for meaningful long-term follow-up results of these patients. In the multiple linear regression analysis of the early HidroQoL© score difference (Table 8), interestingly, there were greater score changes in patients who had plantar-palmar-axillary hyperhidrosis. The most reasonable explanation is that the effect of LSC may be masked when palmar or axillary hyperhidrosis is resolved at the same time.

Complications

Sexual dysfunction (retrograde ejaculation) is one of the most serious complications that surgeons are concerned with [39]; however, it is not often encountered, because retrograde ejaculation occurs when the level of L2 or higher is blocked [14, 40, 41], and it is difficult to approach the level of L2 without dissecting intentionally and excessively. To avoid this complication, Lima *et al.*

resected L3 and L4 in males and L2, L3, and L4 ganglia in female patients [42]. In the current study, no patients presented with retrograde ejaculation. However, young men are advised to masturbate on the first day after surgery to check for this issue.

Rieger *et al*. reported that postoperative neuralgia, which is described as a spasmodic and piercing pain, localized to the back, buttock, or thigh, could occur in 42% of patients after sympathectomy [11]. However, this result seems to be due to the surgical technique of sympathetic truncal resection, including ganglia. Post-sympathectomy neuralgia can be avoided by using the clip method without electrocautery during the procedure, instead of nerve resection. Nevertheless, mild neuralgia, characterized by numbness, a tingling sensation, and paresthesia, might last for > 6 weeks, and it is believed to be caused by damage to the abdominal muscle nerve branch. In the present study, nine out of 10 patients with postoperative neuralgia complained of these mild symptoms, but the remaining patient experienced severe right back pain of unknown origin immediately after surgery, which was clearly distinguished from musculoskeletal pain at the surgical site. We determined that the cause of this pain was damage to the sensory nerve network around the vertebral body. Ultimately, the symptoms disappeared soon after clip repositioning from L3 to L4 on the same day. Therefore, if severe pain is experienced on only one side after surgery, clip replacement may be considered as a treatment option.

Temporary hidrosis usually appears 3 to 4 days after surgery, lasts a day or two, and is also known to occur with ETS [13]. The amount of sweating varies from patient to patient, and some individuals only feel an “aura” of sweating, not actual sweating; however, in some cases, sweating occurs as much as before surgery. Therefore, without a sufficient explanation, patients may become disconcerted and misunderstand this phenomenon as a recurrence. As a physiological explanation, Reisfeld *et al*. suggested that temporary hidrosis is due to the neurotransmitter-mediated sweating process that might have already commenced before the LSC [15]. In this study, temporary hidrosis occurred in 33.3% of patients and was one of the factors associated with early satisfaction scale, along with CH and asymmetry. However, this variable did not affect the late results of satisfaction and HidroQoL© scores because of its temporary duration. Following analysis of a possible association between the occurrence of temporary hidrosis and clip location, no significant differences were found in the total patient group. However, the LSC-only subgroup analysis revealed that temporary hidrosis occurred more frequently in the L3 group than in the L4.

Hematoma is another complication of LSC, typically originating from the retroperitoneal fat fad and muscles. After surgery, if there is ecchymosis and focal tenderness in the flank area, a hematoma workup should be considered. In particular, left-sided retroperitoneal hematoma may cause fecal impaction and constipation due to the mass effect on the sigmoid colon; therefore, meticulous bleeding control should be encouraged before wound closure. In this study, there were 2 cases of left-sided retroperitoneal hematoma, which were removed after ultrasound confirmation on the second day post-surgery. On the right side, particular attention is warranted because there are many vulnerable vascular structures, such as lumbar veins or unexpected small vessels between the psoas muscle and IVC, which may cause heavy bleeding. Subcutaneous hematoma of the wound site can also lead to severe tenderness in patients who have low tolerance for pain; therefore, a differential diagnosis is required.

In the present study, there were two cases of lymphatic damage and one case of wound infection. Chyle leakage due to lymphatic injury was resolved without further action, and there were no late-onset complications. Wound infection was controlled with oral antibiotics. Peritoneal tears can be avoided with a careful layer-by-layer approach. Even if peritoneal damage occurs, it does not prevent the surgery from proceeding, but without immediate repair, surgery becomes difficult. In this study, three patients (0.5%) had peritoneal tears. Asymmetry of the surgical effect was observed in 16 patients (3.7%), and most of these patients had anatomical variations in the lumbar sympathetic trunk. Postoperative surgical site pain that presents in most patients is regarded as a fascial origin of the abdominal muscles (myofascial pain), which can be controlled with an appropriate intravenous or oral painkiller. In general, these symptoms are relieved on postoperative day 3, but they sometimes last about a week. In the current study, no patients were hospitalized or required aggressive pain control. Vasodilatation, postural hypotension, and temporary mild lower leg edema may also occur. For these patients, wearing compression stockings may be helpful.

Limitations of this study

First, this study was retrospective and there was a difference in the number of patients in L3 group and "unintended" L4, which could lead to a bias. Second, mid-term follow-up was not performed; thus, accurate analysis for the occurrence of compensatory hyperhidrosis was not possible. Finally, the number of subjects with pure plantar hyperhidrosis was small; therefore, a longer study period was needed to ensure statistical significance. To obtain the standardization of surgical techniques, a prospective randomized controlled trial targeting these patient groups will be needed in the future.

CONCLUSIONS

The lumbar sympathetic clipping of L3 or L4 may be a valid surgical option for primary plantar hyperhidrosis and showed positive surgical outcomes and negligible postoperative complications. There were no significant differences in postoperative satisfaction and compensatory hyperhidrosis between the L3 and L4 groups.

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ABSTRACT

Background: Lumbar sympathectomy is considered effective for treating primary plantar hyperhidrosis. However, only a few reports have reported on the most efficient target level in lumbar sympathectomy. Therefore, this study aimed to compare patient satisfaction after L3 or L4 lumbar sympathetic clipping for plantar hyperhidrosis in a large series of consecutive patients at a single center.

Materials and Methods: Between December 2015 and June 2018, we performed lumbar sympathetic clipping using 3-mm titanium clips on 500 patients with primary plantar hyperhidrosis. Among these, 436 patients were analyzed for immediate postoperative outcomes, and 134 patients who were followed up were included in the long-term analysis. Sixty-four patients were excluded because of bilaterally mismatched clipping levels to avoid a bias. Target nerve identification and clipping were performed using finger touch and video-assisted endoscopic methods. The clip location was immediately evaluated postoperatively using radiography. Patients' satisfaction scale and hyperhidrosis-specific questionnaires (HidroQoL©) were administered on the 10th day and > 3 years postoperatively.

Results: Of the 436 patients, the sex ratio was the same, and their mean age was 26.3 ± 7.2 years (range, 14 to 49 years). The mean operation time was 43.9 ± 8.7 min, and the L3:L4 clipping level ratio was 4:1. The mean follow-up period was 50.7 ± 8.8 months (range, 39.7 to 69.3 months). The number of patients who underwent simultaneous endoscopic thoracic sympathicotomy was 359 (82.3%). Seventy-seven (17.7%) patients underwent lumbar sympathicotomy alone, of which 39 (8.9%) had previously undergone thoracic sympathicotomy. Early postoperative compensatory hidrosis was reported in 40.1% of patients, with 0.5% rated as severe with a regret of undergoing surgery. However, the proportions increased to 88.1% and 12.7%, respectively, in the long-term results group. Similarly, in the subgroup analysis of patients who underwent only lumbar sympathetic clipping, no severe compensatory hyperhidrosis was noted in the early results; however, severe compensatory hyperhidrosis was noted in three patients (12.5%) in the late results. The early and late satisfaction scales of subgroup patients were 9.7 ± 0.6 and 7.5 ± 2.8 out of 10, respectively, and they were similar in the total patients group. The incidences of temporary hidrosis and self-limited neuralgia were 33.3% and 2.3%, respectively. There was no significant difference in most perioperative outcomes and long-term results with respect to the clipping level, except for neuralgia and operation time.

Conclusion: Lumbar sympathetic clipping is a valuable choice of treatment for patients with plantar hyperhidrosis. This is supported by the low complication rate and the high post-operative satisfaction scores. There was no significant difference in early and late satisfaction between the L3 and L4 levels of sympathetic clipping.

Keywords: Hyperhidrosis, Lumbar sympathetic clipping, Plantar hyperhidrosis