Observational Study

CT-guided Chemical Lumbar Sympathectomy in the Treatment of Cold Hypersensitivity in the Hands and Feet

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Background: Cold hypersensitivity in the hands and feet is a common clinical symptom in Asian women. Currently, treatment of cold hypersensitivity in the hands and feet is still limited to traditional Chinese medicine, mainly herbal medicine. However, many patients with cold hypersensitivity in the hands and feet in China are not satisfied with the therapeutic effect of herbal medicine, and took medication for a longer time. Chemical lumbar sympathectomy is widely used in the treatment of plantar hyperhidrosis, diabetic foot, recalcitrant erythromelalgia, and other diseases.

Objectives: This study was conducted to evaluate the short-term as well as long-term efficacy, complications, and patient satisfaction of chemical lumbar sympathectomy during treatment cold hypersensitivity in the hands and feet.

Study Design: A retrospective, observational study.

Setting: Department of Anesthesiology and Pain Medicine, Jiaxing, China.

Methods: A retrospective study of 72 patients with cold hypersensitivity in the hands and feet who received chemical lumbar sympathectomy treatment in our hospital from January 2015 to October 2018 was conducted. The heart rate, non-invasive blood pressure, oxygen saturation, visual analog scale, perfusion index, and plantar temperature were monitored and recorded in before treatment (T1) and after treatment (T2) groups. The patients were followed up on day 1, at week 1, 1 month, 3 months, 6 months, one year, and 2 years after operation for satisfaction, complications, and recurrence.

Results: There were no significant differences in heart rate, non-invasive blood pressure, and oxygen saturation between T1 and T2 groups ($P > 0.05$). Perfusion index and plantar temperature in T2 group were remarkably higher than T1 group, and the difference was statistically significant ($P < 0.01$). The visual analog scale score of the T2 group was significantly reduced ($P < 0.01$). Of all the patients who underwent chemical lumbar sympathectomy, the postoperative therapeutic effect was effective in 63 cases (87.5%) and ineffective in 9 cases (12.5%). Among the effective patients, the postoperative curative effect was shown to be excellent in 47 cases and improved in 16 cases. According to the follow-up results at day 1, 1 week, 1 month, 3 months, 6 months, 1 year, and 2 years after operation, the satisfaction rate was 87.5%, 87.5%, 81.9%, 61.1%, 52.7%, 41.6%, and 34.7%, respectively. There were no serious complications observed and 23 patients relapsed after two years. Multivariate logistic regression analysis results showed that the effect of visual analog scale (OR = 7.312, 95% CI: 1.598 – 33.646, $P = 0.011$) and plantar temperature (OR = 0.470, 95% CI: 0.288 – 0.766, $P = 0.002$) on therapeutic effect showed has statistical significance; the effect of gender (OR = 0.654, 95% CI: 0.134 – 3.181, $P = 0.599$), age (OR = 0.975, 95% CI: 0.916 – 1.039, $P = 0.441$), perfusion index (OR = 0.710, 95% CI: 0.367 – 1.375, $P = 0.310$), and disease course (OR = 1.019, 95% CI: 0.997 – 1.042, $P = 0.088$) on therapeutic effect showed no statistical significance. The effect of gender (OR = 0.451, 95% CI 0.131 – 1.554, $P = 0.207$), age (OR = 0.961, 95% CI 0.912 – 1.013, $P = 0.141$), and course of disease (OR = 1.006, 95% CI 0.997 – 1.015, $P = 0.203$) on postoperative recurrence showed no statistical significance.

Limitations: The nonrandomized, single-center, small sample size, retrospective design is a major limitation of this study.

Conclusions: Chemical lumbar sympathectomy is a valid treatment option for cold hypersensitivity in

hands and feet, and computed tomography-guided percutaneous puncture chemical lumbar sympathectomy has the advantages of high success rate, less invasion, less complications, and repeatablity.

Key words: Cold hypersensitivity in hands and feet, chemical lumbar sympathectomy, computed tomography-guided

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Cold hypersensitivity in the hands and feet (CHHF) commonly affects Asian people, especially women, and is defined as "a feeling of coldness on one's hands or feet when compared to people in temperatures that are not normally perceived as cold" (1). The incidence of CHHF is higher in women than in men, with an approximate ratio of 3:2 (2). The incidence rate was higher in lower limbs than in upper limbs (3). The patients with CHHF often feel coldness in their lower limbs at room temperatures that is aggravated in a low temperature environment. It has been reported that CHHF might be related to diabetes, chronic gastritis, gastroduodenal ulcer, and reflux esophagitis (4). Patients with CHHF have a high incidence of chronic functional dyspepsia (5). And women often have symptoms of menstrual pain (6).

According to the traditional medical point of view, it is believed that the pathogenesis of CHHF is similar to that of Raynaud's syndrome (RS) (7). So, CHHF treatment mainly involves lifestyle changes and the use of vasodilators such as calcium channel blockers. In addition, varieties of herbal medicines are also widely used for the treatment of CHHF (8-10). Until now, no treatment strategy has achieved successful results in patients with CHHF disease. Thus, it is necessary to explore the treatment options that help to improve the prognosis of CHHF patients. Sympathectomy has been an effective treatment approach for improving the peripheral blood flow of patients. Chemical lumbar sympathectomy (CLS), which is considered as a safe and effective technique, is widely used in the treatment of plantar hyperhidrosis (11), diabetic foot (12), recalcitrant erythromelalgia (13), and idiopathic livedo reticularis (14). Therefore, the short-term as well as long-term efficacy, patient satisfaction, complications, and recurrence of CLS when treating CHHF were evaluated.

Methods

Patients

Retrospective analysis of 72 patients with CHHF who underwent CLS in our hospital from January 2015 to October 2018 was performed. The inclusion criteria were as follows: patients (1) aged over 18 years; (2) with involvement of the lower extremities; (3) with visual analog scale (VAS) of ≥ 4; and (4) with poor therapeutic effects after other treatments, such as lifestyle changes and herbal and acupuncture treatments. The exclusion criteria are as follows: patients (1) who rejected CLS treatment; (2) diagnosed with other diseases such as Raynaud's syndrome, diabetic peripheral neuropathy, hypothyroidism, anemia, anorexia, disorder of the hypothalamus, vascular occlusive angiitis, and arteriosclerosis obliterans of lower extremities; (3) with pregnancy or lactation; (4) with severe depression or mental illness; (5) with severe heart, lung, brain, liver, or kidney diseases; (6) with abnormal blood coagulation function due to the use of thrombolysis and anticoagulants; and (7) with puncture site or systemic infection. CLS was performed in 72 patients with CHHF, 7 patients with CHHF were treated with chemical thoracic sympathectomy (CTS) based on CLS. This study was approved by the Ethics Committee of the Affiliated Hospital of Jiaxing University. All patients underwent CLS in the same institution by the same treatment team. After strict controlling of indications and contraindications, all patients were informed of the risks associated with treatment and signed the written informed consent form.

Procedures

The patients were placed in a prone position on the table for undergoing computed tomography (CT) treatment and used a thin pillow under the abdomen. The temperature monitoring probe was bundled on the soles of the patients' feet. Patients' heart rate (HR), non-invasive blood pressure (NIBP), oxygen saturation (SpO_2), perfusion index (PI) (Masimo Corp., Irvine, CA, USA), and temperature of the plantar (T) (PhysitempNTE-2A; Physitemp Instruments, Clifton, NJ, USA) were monitored and recorded. First, the L3 vertebral body was marked and positioned. An optimal puncture path was designed under the guidance of CT, the puncture target was the anterolateral of the L3 vertebral body and the medial anterior border of the psoas major. The distance and angle from the puncture point to the puncture target were measured, the dis-

tance from the puncture point to the posterior midline was also surveyed (Fig. 1). 1.0% lidocaine hydrochloride was used for local anesthesia at the selected puncture point, a 10 cm 22-gauge needle was advanced from the skin puncture point to the target position under the guidance of CT. After negative aspiration for cerebral spinal fluid (CSF), heme, urine, or gas, 2.7 mL of 1% lidocaine was mixed with 0.3 mL of 30% iohexol and injected to the target position at an approximate speed of 1 mL/s. Scanned again by CT, the results showed no entry of the injected local anesthetics into the spinal canal but was distributed in the anterolateral side of L3 vertebral body and the medial anterior border of the psoas major (Fig. 2). If the patients' plantar changed from coldness to warm and the temperature was increased by more than 2 °C, then 5 mL anhydrous alcohol containing iohexol was injected into the target position. CT scan was performed again and the distribution of anhydrous alcohol was reconstructed in 3 dimensions, so that the liquid can cover the anterolateral of L3 vertebrae body (Fig. 3). The patient's HR, NIBP, SpO_2, PI, T, and VAS scores were recorded before treatment (T1) and after treatment of 10 minutes (T2).

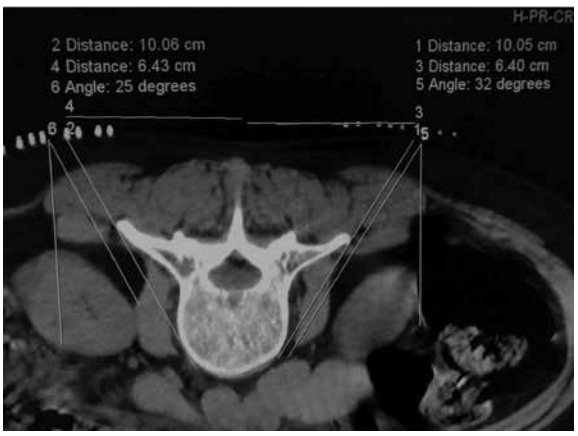

Fig. 1. *CT scan of the puncture path in chemical lumbar sympathectomy.*

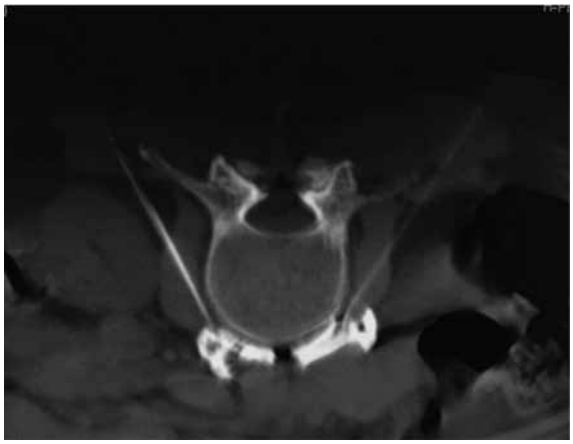

Fig. 2. *Distribution of local anesthetics injected.*

Efficacy Assessment and Follow-Up

VAS scores ranging from 0 (no coldness) to 10 (most severe coldness) were used to evaluate the severity of CHHF symptoms (8,9). The higher the score, the more severe the CHHF. The therapeutic effect on the patients was graded as 1 (excellent; VAS score points of ≤ 2); 2 (improved; VAS score was 2 to 4 points); or 3 (ineffective; VAS score points of ≥ 4). The patients were

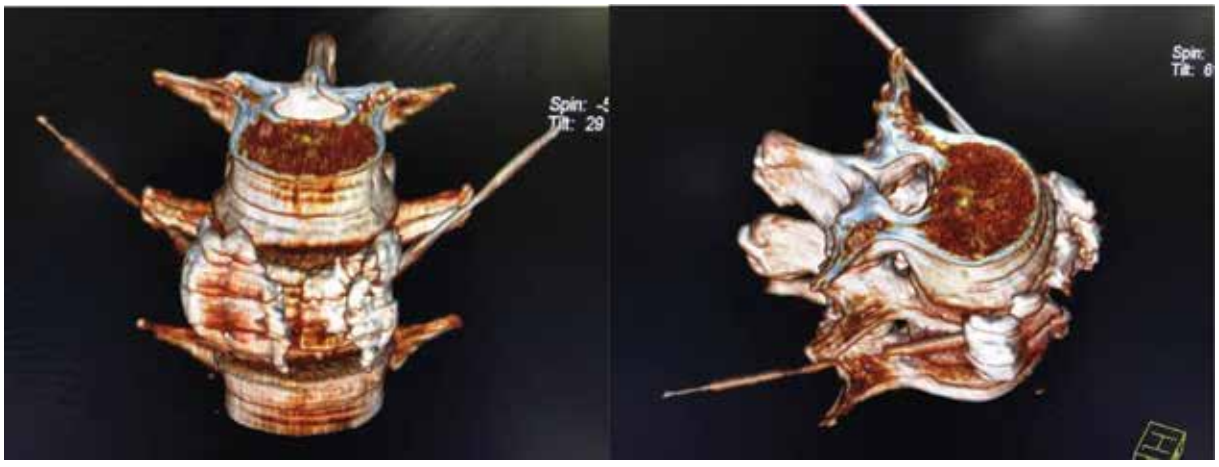

Fig. 3. *Three-dimensional reconstruction of anhydrous ethanol injection.*

followed up at 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, and 2 years after CLS treatment. The 2-part scale (very satisfied, partially satisfied, and dissatisfied) was used to evaluate the overall outcome satisfaction of patients. The postoperative complications, adverse reactions, and recurrence were also recorded.

Statistical Analysis

SPSS 25.0 (SPSS Inc., Chicago, IL) was used to analyze the data. Measurement data are expressed as means ± standard deviation (x ± s), and counting data are expressed as quantity or percentage. If the measurement data are in accordance with normal distribution, then a paired t-test was used for comparison between groups, and a rank sum test was used if it does not meet normal distribution. A logistic regression model was used to analyze the related factors that affect the therapeutic effect and recurrence. α = 0.05 was regarded as the level of inspection, and $P < 0.05$ was considered to be statistically significant.

Results

This study included 72 CHHF patients, including 54 women and 18 men, with an average age of (56.21 ± 11.05). The course of the disease ranged from 6 to 360 months, with an average duration of (76.75 ± 68.29). There were 65 patients with lower limb coldness (63 cases with both lower limbs and 2 cases with left lower limb). The general clinical characteristics of the patients are shown in Table 1.

There were no significant differences in HR, NIBP, and SpO_2 between T1 and T2 groups ($P > 0.05$). The T group was significantly higher in T2 group than in T1 group ($P < 0.01$). However, VAS was notably lower in T2 group than in T1 group ($P < 0.01$, Table 2).

Table 1. *Characteristics of patients with CHHF.*

Characteristic	Index
Age	56.21 ± 11.05
Course of CHHF	76.75 ± 68.29
Gender	
Women	54 (75%)
Men	18 (25%)
Site of CHHF	
Lower limbs	
Left and right	63 (87.5)
Left	2 (2.8%)
Limbs	7 (9.7%)
VAS score	5.60 ± 0.78

Data are presented as numbers (%) or means ± SD.
CHHF: cold hypersensitivity in the hands and feet; VAS: visual analog scale; SD: standard deviation.

Among the 72 patients with CHHF, 47 achieved excellent therapeutic effects, 16 achieved improvement, and 9 had ineffective results. The clinical effective number of lumbar sympathectomy was achieved in 63 cases (87.5%). Postoperative pain at the injection site was found in 4 patients, which lasted for about a week. Two patients had transient groin and thigh pain. One patient complained of dryness and had no sweating in the right lower limb, which improved after one month. No death was recorded and no other complications were reported. Follow-up results revealed recurrence in 23 patients, and time of recurrence was 1 – 24 months (with a mean of 12 months). Recurrence in patients still showed a certain effect after undergoing the same treatment. Satisfaction was evaluated at 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, and 2 years after operation, which were 87.5%, 87.5%, 81.9%, 61.1%, 52.7%, 41.6%, and 34.7%, respectively.

The relationship between the therapeutic effect and gender, age, VAS, T, PI, and the course of disease was analyzed by multivariate logistic regression model. The results showed that the effect of VAS (OR = 7.312, 95% CI: 1.598 – 33.646, $P = 0.011$) and T (OR = 0.470, 95% CI: 0.288 – 0.766, $P = 0.002$) on therapeutic effect showed statistical significance. However, the effect of gender on therapeutic effect showed no statistical significance (OR = 0.654, 95% CI: 0.134 – 3.181, $P = 0.599$). Similarly, the effect of age (OR = 0.975, 95% CI: 0.916 – 1.039, $P = 0.441$), the effect of PI (OR = 0.710, 95% CI: 0.367 – 1.375, $P = 0.310$), and the effect of disease course on therapeutic effect showed no statistical significance (OR = 1.019, 95% CI: 0.997 – 1.042, $P = 0.088$), as shown in Table 3.

Multivariate logistic regression model was performed to analyze the relationship between postoperative recurrence and gender, age, and course of disease. The results showed that the effect of gender (OR = 0.451, 95% CI 0.131 – 1.554, $P = 0.207$), the effect of age (OR = 0.961, 95% CI 0.912 – 1.013, $P = 0.141$), and the effect of disease course on recurrence showed no statistical significance (OR = 1.006, 95% CI 0.997 – 1.015, $P = 0.203$), as shown in Table 4.

Discussion

CHHF is reported to be associated with hypertensive vasoconstriction (15,16), stress, lack of exercise, and physical constitution (cold pattern of Sasang constitution) (1,17), and it is a highly heritable phenotype (2).

Table 2. *Changes of monitoring indicators before and after CLS treatment in patients with CHHF.*

	HR (bpm)	NIBP (mmHg)		SpO_2 (%)	VAS	T (°C)		PI (%)	
		SBP	DBP			Left	Right	Left	Right
T1	78.41 ± 9.25	126.58 ± 15.24	74.67 ± 5.73	97.68 ± 1.26	5.60 ± 0.78	29.69 ± 1.97	29.84 ± 1.98	1.21 ± 0.89	1.36 ± 1.17
T2	76.37 ± 8.42	122.76 ± 12.83	72.58 ± 7.06	98.56 ± 0.97	1.89 ± 1.15	34.63 ± 1.01	34.47 ± 1.23	6.83 ± 2.78	7.02 ± 3.19
t	0.381	0.152	0.643	0.275	21.730	18.563	14.898	17.774	16.400
P	0.736	0.827	0.218	0.794	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01

CHHF: cold hypersensitivity in the hands and feet; CLS: chemical lumbar sympathectomy; T1: before treatment; T2: 10 minutes after treatment; HR = heart rate; NIBP = non-invasive blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; SpO2 = arterial oxygen saturation; bpm = beats per minute; PI = perfusion index; T = plantar temperature

Up to now, the etiology and pathogenesis of CHHF were unclear. In this study, there were 54 women and 18 men, and the number of women was 3 times that of men. This was consistent with the results of the previous studies (2).

In Japan, the concept of "HIE" (cold sensation) or "HIESHO" (cold disorder) is similar to that of CHHF, and is often accompanied by neck and shoulder stiffness, fatigue, eyestrain, depression, constipation, upper back stiffness, dry skin, flatulence, and other symptoms (6). Raynaud's syndrome (RS) involves terminal coldness, but CHHF does not have the typical skin color change of RS, such as fingers becoming white, turning into blue-purple, and then into red. Some studies believe that CHHF cannot be completely distinguished from RS, and can be diagnosed when the skin color changes on the hands or feet in a cold environment. This view suggests CHHF as latent RS (18), and a large number of samples are needed to further study and observe whether the 2 are related. Flammer syndrome (FS) is characterized by primary vascular dysregulation and cold extremities, but it is associated with some clinical symptoms that CHHF patients do not have. FS patients have hypotension, prolonged sleep onset time, tinnitus, muscle cramps, and increased general sensitivity, including pain sensitivity (19). FS mainly damages the eyes, and is associated with increased risk of normal-tension glaucoma, optic nerve compartment syndrome, and retinal arteriovenous occlusion (20). In addition, complex regional pain syndrome (CRPS) also has manifestations of cold limbs, but CRPS is typically characterized by pain, allodynia, and hyperalgesia, and it often occurs in patients with limb fractures or limb surgeries (21,22).

The results of this study indicate CLS as a safe and effective method for treating CHHF. Lumbar sympathetic block was effective in 63 (87.5%) patients. Lumbar sympathectomy is widely used for treating lower limb ischemic disease, pain, and hyperhidrosis. Although endoscopic lumbar sympathectomy (ELS) has greatly reduced surgical trauma when compared with traditional open surgery, ELS is still associated with postoperative complications such as bleeding, muscle hematoma, postoperative pulmonary infection, accidental peritoneal laceration, pneumoperitoneum, retroperitoneal hematoma, and incision infection. In addition, ELS should be performed under general anesthesia, and the right and left side lumbar sympathectomies should be performed separately, with an interval of 2 to 3 days (11,23-25). CT-guided percutaneous lumbar sympathectomy can be completed under only local anesthesia, and patients recover quickly,

Table 3. *Multivariate logistic regression analysis affecting the therapeutic effect of CLS.*

	B	S.E.	Wald	Exp (B)	95% CI		*P*
					Lower limit	Upper limit	
Gender	-0.425	0.807	0.277	0.654	0.134	3.181	0.599
Age	-0.025	0.032	0.593	0.975	0.916	1.039	0.441
Course	0.019	0.011	2.913	1.019	0.997	1.042	0.088
VAS	1.990	0.779	6.526	7.312	1.589	33.646	0.011
T	-0.756	0.250	9.175	0.470	0.288	0.766	0.002
PI	-0.343	0.337	1.033	0.710	0.367	1.375	0.310

CLS: chemical lumbar sympathectomy; VAS: visual analog scale; T: plantar temperature; PI: perfusion index.

Table 4. *Multivariate logistic regression analysis affecting postoperative recurrence.*

	B	S.E.	Wald	Exp (B)	95% CI		*P*
					Lower limit	Upper limit	
Gender	-0.796	0.631	1.592	0.451	0.131	1.554	0.207
Age	-0.039	0.027	2.166	0.961	0.912	1.013	0.141
Course	0.006	0.004	1.623	1.006	0.997	1.015	0.203

and can be discharged from the hospital the next day. This avoids general anesthesia and its related adverse reactions, reduces hospitalization time and treatment costs of patients, and saves a lot of medical resources. CLS has the procedural advantage of being minimally invasive with a high safety profile compared to open sympathectomy. Before CLS nerve destruction, an appropriate amount of local anesthetic was injected at the puncture site to conduct the diagnostic block. The changes of PI and T indicated the success of CT-guided sympathetic block. PI is considered as a more significant and sensitive index than T (26). In this study, the curative effect of 9 patients after CLS was ineffective, and the common characteristics of T and PI showed no significant increase after the operation when compared to before the operation.

In this study, the PI and T were increased significantly and VAS score was decreased obviously 10 minutes after treatment. There were 2 cases with genitofemoral neuralgia, one case with right lower limb dryness and without sweat, and no other complications after the operation were observed. Genitofemoral neuralgia has been reported to be the most common complication after lumbar sympathectomy (13,14,27). It originates from L1-L2, moves downward along the psoas major muscle, and emits from the anterior fascia of the psoas major muscle at about L3 level. The CLS in L3 is prone to affect the genitofemoral nerve due to the flow of the fluid, presenting at the groin, thigh, or back, and the symptoms are mild and usually self-relieved without any special treatment. The postoperative dry and anhidrotic symptoms of the right lower limb might be due to the inhibitory function of sweat glands after sympathetic nerve block, and were returned to normal by the regression of drug action and nerve repair. No sexual dysfunction or ureteral injury was observed during the follow-up period. Sexual dysfunction is a serious and rare side effect of lumbar sympathectomy. T12 and L1 ganglia plays a key role in ejaculation, and so the destruction of lumbar sympathetic nerve below L2 can avoid the occurrence of sexual dysfunction (27,28). During treatment, if a drug inadvertently spreads to the adjacent tissues and not found in time, it can lead to the injury of the renal pelvis and ureter.

The results of this study showed that gender, age, and disease course showed no significant differences for CLS treatment ($P > 0.05$), indicating no preferences in gender, age, and course of disease between CLS reactive and non-reactive patients. This is consistent with the results of the previous studies (13). The therapeutic effect of preoperative VAS and T on CLS showed statistically significant differences ($P < 0.05$), indicating that the levels of VAS and T before treatment would affect the postoperative efficacy of patients. The effects of gender, age, and course of disease on postoperative recurrence showed no significant difference ($P > 0.05$), suggesting that gender, age, and course of disease as not influential factors of postoperative recurrence in patients with CHHF.

The postoperative recurrence rate of patients with clinically effective results was 36.5%, and the high recurrence rate was the main reason for the declination of patient satisfaction. CLS involves the use of nerve destruction agents (such as phenol, anhydrous ethanol) for lumbar sympathetic nerve injury and their release achieves the purpose of lumbar sympathetic nerve resection. The duration of neurolysis continues to be short, and the symptoms often recur after a few months, which might be related to nerve regeneration and repair (12,29). It has been reported that radiofrequency thermocoagulation (RFT) of lumbar sympathectomy is associated with fewer complications such as neuralgia and a longer duration of postoperative efficacy when compared with CLS (12,30). RFT of the sympathetic chain might be regarded as a more effective treatment for patients with CHHF. In the following work, we will take a randomized, double blind, controlled and large sample size study to compare RFT with CLS.

Limitations

There are some limitations in our study. Firstly, this is a nonrandomized study, there is no control arm, and the study size is small. In addition, the single-center, facility nature and retrospective nature of the review produces moderate selection bias. Future multicenter, randomized, and controlled studies could be improved by prospectively evaluating a larger number of patients, which could lower the bias.

Conclusions

In conclusion, CLS is a valid treatment option for CHHF, and CT-guided percutaneous puncture chemical lumbar sympathectomy has the advantages of a high success rate, less invasion, less complications, and repeatability.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Author Contributions

Jiachun Tao collected the data and drafted the manuscript. Jiachun Tao, Bing Huang and Ming Yao had the original idea for the manuscript. Tingting Wang and Qiuli He analyzed the data. Huadong Ni and Keyue Xie revised the manuscript. Jianjun Zhu, Ge Luo, and Longsheng Xu assisted in drafting the manuscript, revision of the text, and approved the final manuscript. All authors read and approved the final manuscript.

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