Retrospective Study

Lumbar Sympathetic Ganglion Block for Cancer-Associated Secondary Lower Limb Lymphedema: A Retrospective Study

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Background: Although lower limb lymphedema (LLL) is more or equally as frequent and harmful as upper limb lymphedema after cancer treatment, there are only a few studies on this topic. Cancer-related secondary LLL not only has physical implications, but also affects quality of life among patients who underwent gynecological cancer treatment. Despite numerous studies of various therapies, the optimal treatment for cancer-related LLL is still unknown.

Objectives: We aimed to investigate the efficacy of lumbar sympathetic ganglion block (LSGB) in patients with secondary LLL in the present study.

Study Design: This study is a retrospective study.

Setting: A single academic hospital, outpatient setting.

Methods: A total of 30 patients with secondary unilateral LLL and failed complex decongestive treatment, from January 2017 through May 2021, were reviewed for inclusion in this study. The patients underwent fluoroscopy-guided LSGB 2 times with the help of digital subtraction angiography at 3-day intervals. Leg circumference was measured, and the volume of the leg was calculated before surgery, on the first day after the first surgery, on the first day after the second surgery, and on the seventh day after the second surgery. The World Health Organization Quality of Life Instrument Questionnaire scores were monitored before and after LSGB.

Results: The leg circumference and volume decreased significantly from baseline after the treatment ($P < 0.001$). One week after 2 rounds of LSGB, the physical health score, psychological score, and social relationships score were higher than those before treatment (all $P < 0.05$). There was no difference in the environmental health score ($P = 0.2731$).

Limitations: This study was limited by its sample size and retrospective observational design.

Conclusions: LSGB can be a safe and effective treatment option for patients with secondary LLL after gynecological cancer treatment.

Key words: Lymphedema, lumbar sympathetic ganglion block, LSGB, gynecological cancer, WHOQoL-BREF, secondary lymphedema, LLL, sympathetic ganglion block

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Lymphedema is a chronic pathologic condition of interstitial fluid retention and subcutaneous tissue swelling resulting from the lymphatic obstruction or a compromised lymphatic system (1). Secondary lymphedema is mainly related to trauma, filariasis infection, malignant tumors, lymph node dissection, radiotherapy,

etc. There are approximately 120 million patients with lymphedema worldwide and 20 million people with lower limb lymphedema (LLL) (2). In developed countries, the incidence of LLL is mainly related to cancer treatment, and one out of every 6 patients undergoing solid tumor surgery experience lymphedema (3). Approximately 18% to 25% of patients with gynecological cancer suffer from LLL (3). Cancer-related secondary LLL not only causes physical abnormalities and functional impairment, but may also lead to depression or social isolation in affected patients (4).

Currently, complex decongestive physical therapy (CDT) is accepted as the international standard treatment for lymphedema. Surgeries, such as lymphaticovenular anastomosis and vascularized lymph node transfer (VLNT), are mainstay treatments for severe extremity lymphedema (5). However, the current conservative physical strategies and surgical interventions provide only incomplete relief. Therefore, there is an urgent need to develop novel therapies for the management of secondary lymphedema improvement.

Lumbar sympathetic ganglion block (LSGB) is a treatment method involving the injection of a drug mixture around the sympathetic trunk. In recent years, LSGB has been widely used to manage various medical conditions, including sympathetically maintained pain, neuropathies, diabetic polyneuropathy, and ischemic pain due to vascular insufficiency in the lower leg (6,7). Moreover, previous studies (6,7) used sympathetic ganglion block for the improvement of lymphedema and reported good results. However, there is little evidence supporting the use of LSGB as an alternative treatment for LLL. Therefore, we aimed to assess the clinical effect of LSGB for patients with LLL after gynecological cancer treatment and to explore the impact of the treatment on quality of life.

Methods

Study Design and Patients

A total of 30 secondary unilateral LLL patients whose lymphatic obstruction was confirmed via lymphoscintigraphy at the time of diagnosis and who underwent gynecological cancer treatment and 2 rounds of LSGB at Fujian Cancer Hospital, between January 2017 and May 2021, were included. Patients with unsuccessful LSGB, an interval not 3 days, ischaemic vascular disease, or cellulitis or lymphedema in other parts of the body were excluded (Fig. 1). Electronic medical records were reviewed in detail, and the data collected for each patient included age, body mass index (BMI), date and results of LSGB, leg circumference, leg volume, and scores on the World Health Organization Quality of Life Instrument Questionnaire (WHOQoL-BREF).

Intervention

LSGB

The surgical procedure was carried out with the help of a digital subtraction angiography (DSA) machine. The patient lay prone with hands crossed on the forehead and a thin pillow placed under their abdomen. Noninvasive blood pressure, blood oxygen saturation, and heart rate were continuously recorded. The robotic arm of the DSA machine is perpendicular to the patient and tilted 20° to 30° until the L3 transverse process covers the anterolateral edge of the vertebra. The patient's skin was locally anesthetized with 1% lidocaine, and a 22-G 15-cm needle was punctured to the anterior margin of the L3 vertebra using a coaxial technique puncture method. Positioned the needle tip during the puncture using the DSA machine until the needle tip lightly contacts the bone surface. Injected a small amount of iodinated contrast agent (0.5 mL). Images were taken anteroposterior and lateral to confirm the correct needle tip position (Fig. 2). Before injecting the medicine, we ensured that no blood or cerebrospinal fluid was pumped back. Then, 20 mL of 0.25% ropivacaine (AstraZeneca Pty Ltd., New South Wales, Australia) was injected. The hallmark of the successful block was venous dilatation of the lower extremities and a 2°C increase in skin temperature. Each patient underwent 2 LSGB sessions separated by 3 days. If LSGB was deemed unsuccessful, patient data were excluded from the statistical analysis.

Outcome Assessment

Leg Circumference and Leg Volume

A positioning line was made at admission with a marker pen, and a waterproofing transparent sterile patch was applied on it. The measurement points include:

1. Foot: perimeter of the highest point of the dorsum of the foot,
2. Ankle: maximum circumference around the ankle,
3. Calf: the circumference of 10 cm below the patella,
4. Thigh1: the circumference of 10 cm above the patella,

5. Thigh2: the circumference of 15 cm above the patella.

The circumference of the affected lower limbs was recorded before LSGB, on the first day after the first LSGB, on the first day after the second LSGB, and on the seventh day after the second LSGB. In addition, measurements were taken every 4 cm, starting just above the level of the ankle, and the volume of the affected leg was calculated according to the Kuhnke formula (Vlimb = $\Sigma X^2/\pi$) (9) (Fig. 3).

WHOQoL-BREF

The WHOQoL-BREF (10,11) (Table 1) is used to assess symptoms one week before and after treatment, including physical health, psychological health, level of independence, social relationships, and environment health. This questionnaire has 26 questions. The response anchors for the subscales vary across items, but the response options for each item range from 1 to 5. The statistical results are classified into 4 domains:

Physical health (PH; 9 items)
Psychological well-being (PS; 6 items)
Social relationships (SR; 4 items)
Environmental health (EH; 7 items)

Statistical Analysis

Statistical analyses were performed using SPSS Version 16.0 (SPSS Inc., Chicago, IL) software. Normally distributed quantitative data are presented as the mean and standard deviation (x ± s). Repeated-measures analysis of variance was used to compare perimeter changes before and after treatment, and a P value < 0.05 was considered statistically significant.

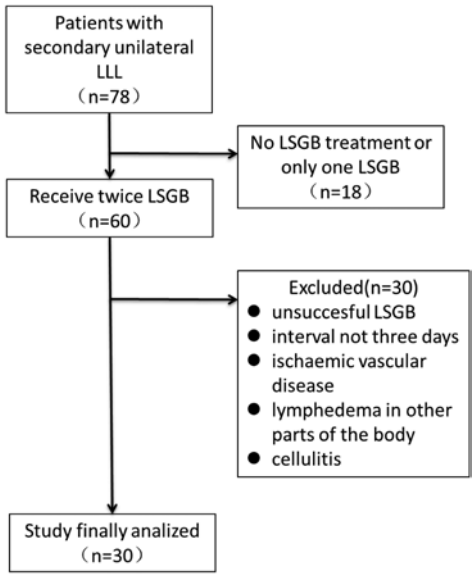

Fig. 1. *Patient selection flow chart.*

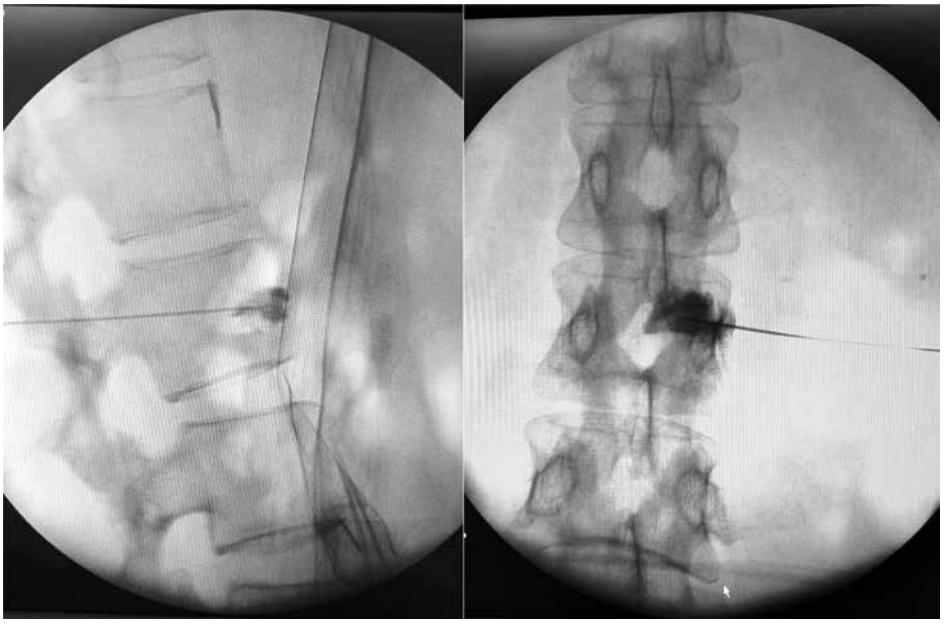

Fig. 2. *Fluoroscopic images during LSGB. The anteroposterior (right) and lateral (left) images show the linear spread of the contrast agent in the longitudinal axis without any lateral or posterior extension. LSGB, lumbar sympathetic ganglion block.*

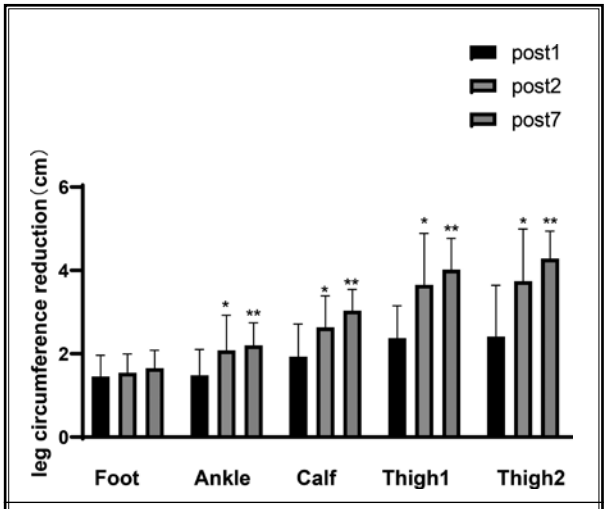

Fig. 3. *Comparison of leg circumference reduction of the swollen limb before and after LSGB (n = 30). *P < 0.05, compare post1 with post2: foot, P = 0.734; ankle, P < 0.05; calf, P < 0.05; thigh1, P < 0.05; and thigh2, P < 0.05. **P < 0.05, compare post1 with post7: foot, P = 0.224; ankle, P < 0.05; calf, P < 0.05; thigh1, P < 0.05; and thigh2, P < 0.05. LSGB, lumbar sympathetic ganglion block, post1: the first day after the first LSGB, post2: the first day after the second LSGB, post7: the seventh day after the second LSGB.*

Results

Demographic Characteristics

In this study, 30 patients were included, and their demographic characteristics are listed in Table 2. The mean patient age was 54.2 ± 5.5 years (range 38-68 years), and the mean BMI was 22.36 ± 4.27. These patients included 15 (50.0%) with cervical cancer, 10 (33.3%) with endometrial cancer, and 5 (16.7%) with ovarian cancer. According to the International Society of Lymphology (Tables 2 and 3) (9), there were 17 (56.7%) patients in stage 1, 10 (33.3%) patients in stage 2, and 3 (10.0%) patients in stage 3. The mean baseline volume of the swollen lower limb was 2842 ± 486 mL.

Leg Circumference Reduction

The needle insertion positions were on the diseased side anterolateral edge of the L3 vertebral bodies, where the lumbar sympathetic nerve was located (Fig. 2). All patients had a successful puncturing process. Only one patient had transient lower limb weakness after the operation; no other adverse reactions were observed. The lower limb circumferences were dramatically reduced (Figs. 3 and 4). After the first and the second LSGB, the leg circumference of the detected site was reduced, and the degree of reduction was obvious between the 2 times ($P < 0.05$), except for the foot. However, the degree of leg circumference reduction one week after the second LSGB showed no difference compared with one day after the second LSGB ($P > 0.05$).

Leg Volume

The patient's leg volume decreased as the number of treatment increased, with the smallest leg volume at one week after the LSGB treatment (Fig. 5). Compared with baseline, there was a vast difference between pre and post7 ($P < 0.05$), and between post1 and post7 ($P < 0.05$).

WHOQoL-BREF

Table 4 shows that the mean scores of PH, PS, SR, and EH were higher at posttreatment than at pretreatment. Of these, the mean scores of PH, PS, and SR showed obvious difference before and after LSGB (all $P < 0.05$). Regarding the environment, there was no difference in the EH score ($P = 0.2731$).

Discussion

Currently, lymphedema treatment includes conservative therapies (10-12), such as manual drainage, massage, compression garments, intermittent pneumatic compression, and dietary modifications, but some patients are ineffective and incurable. For surgeries (12,13), operations, such as lymphovenous shunt, lymphatic-lymphatic shunt, VLNT, and liposuction, are invasive and expensive. Some patients may be reluctant to undergo operations and eager for less invasive and useful methods to cure LLL. In the present study, we evaluated the efficacy of LSGB in 30 patients with secondary LLL after gynecological cancer treatment. Overall, these results suggest that LSGB reduces leg circumference and volume in swollen legs compared to baseline. Even 7 days after the second LSGB, the leg circumference and volume remained in a small range compared to baseline. Our results suggested that LSGB may be a safe and effective procedure for the treatment of secondary LLL (Fig. 3).

To date, the majority of research on the prevention of secondary lymphedema has been on the upper limbs after breast cancer surgery. Little is known about lower extremity lymphedema in patients after gynecological cancer treatment. There have been several reports (14-18) of stellate ganglion block (SGB) for the treatment of upper limb lymphedema with positive clinical

Table 2. *The WHOQOL-BREF.*

		Very Poor	**Poor**	**Neither Poor nor Good**	**Good**	**Very Good**
1	How would you rate your quality of life?	1	2	3	4	5
		Very Dissatisfied	**Dissatisfied**	**Neither Satisfied nor Dissatisfied**	**Satisfied**	**Very Satisfied**
2	How satisfied are you with your health?	1	2	3	4	5
		Not at all	**A Little**	**A Moderate Amount**	**Very Much**	**An Extreme Amount**
3	To what extent do you feel that (physical) pain prevents you from doing what you need to do?	1	2	3	4	5
4	How much do you need any medical treatment to function in your daily life?	1	2	3	4	5
5	How much do you enjoy life?	1	2	3	4	5
6	To what extent do you feel your life to be meaningful?	1	2	3	4	5
		Not at all	**A Little**	**A Moderate Amount**	**Very Much**	**An Extreme Amount**
7	How well are you able to concentrate?	1	2	3	4	5
8	How safe do you feel in your daily life?	1	2	3	4	5
9	How healthy is your physical environment?	1	2	3	4	5
		Not at all	**A Little**	**A Moderate Amount**	**Very Much**	**An Extreme Amount**
10	Do you have enough energy for everyday life?	1	2	3	4	5
11	Are you able to accept your bodily appearance?	1	2	3	4	5
12	Have you enough money to meet your needs?	1	2	3	4	5
13	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5
		Very Poor	**Poor**	**Neither Poor nor Good**	**Good**	**Very Good**
15	How well are you able to get around?	1	2	3	4	5
		Very Dissatisfied	**Dissatisfied**	**Neither Satisfied nor Dissatisfied**	**Satisfied**	**Very Satisfied**
16	How satisfied are you with your sleep?	1	2	3	4	5
17	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
18	How satisfied are you with your capacity for work?	1	2	3	4	5
19	How satisfied are you with yourself?	1	2	3	4	5
20	How satisfied are you with your personal relationships?	1	2	3	4	5
21	How satisfied are you with your sex life?	1	2	3	4	5
22	How satisfied are you with the support you get from your friends?	1	2	3	4	5

Table 2 cont. *The WHOQOL-BREF.*

23	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24	How satisfied are you with your access to health services?	1	2	3	4	5
25	How satisfied are you with your transport?	1	2	3	4	5
		Never	**Seldom**	**Quite Often**	**Very Often**	**Always**
26	How often do you have negative feelings, such as blue mood, despair, anxiety, or depression?	1	2	3	4	5

Abbreviation: WHOQoL-BREF, The World Health Organization Quality of Life Instrument Questionnaire.

Table 3. *Demographic characteristics.*

Variable	Stage 1 (n = 17)	Stage 2 (n = 10)	Stage 3 (n = 3)	Total (n = 30)
Age	52.4 ± 5.4	53.6 ± 5.8	58.7 ± 5.3	54.2 ± 5.5
BMI	21.93 ± 4.40	23.26 ± 3.52	27.93 ± 4.66	22.36 ± 4.27
Cancers				
Cervical Cancer	10 (58.8)	4 (40.0)	1 (33.3)	15 (50.0)
Endometrial Cancer	5 (29.4)	4 (40.0)	1 (33.3)	10 (33.3)
Ovarian Cancer	2 (11.8)	2 (20.0)	1 (33.3)	5 (16.7)
Lymphedema Duration				
< 1 year	12 (70.6)	5 (50.0)	-	17 (56.7)
1-10 years	5 (29.4)	5 (50.0)	2 (66.7)	12 (40.0)
> 10 years	-	-	1 (33.3)	1 (3.3)
Baseline Volume (mL)	2835 ± 212	2667 ± 671	3465 ± 554	2842 ± 486

The data were presented as x±s or number and percentage (%).
Abbreviations: BMI, body mass index; x±s, mean and standard deviation.

Table 1. *The stage of the lymphedema by 2020 consensus document of the International Society of Lymphology (8).*

Stage	Description
Stage 0	Swelling is not evident despite impaired lymph transport.
Stage I	An early accumulation of fluid relatively high in protein content which subsides with limb elevation.
Stage II	Limb elevation alone rarely reduces tissue swelling and pitting is manifest. Late in Stage II, the limb may or may not pit as excess fat and fibrosis supervenes.
Stage III	Lymphostatic elephantiasis where pitting can be absent and trophic skin changes, such as acanthosis, further deposition of fat and fibrosis, and warty overgrowths, have developed.

Fig. 4. *Pictures about the outcome of LSGB. The left picture was before LSGB treatment, the right picture was after twice LSGB. LSGB, lumbar sympathetic ganglion block.*

outcomes. Swedborg et al (19) were the first to report sympathetic blocks as a treatment for a patient with breast cancer-related lymphedema in 1983. Choi et al (18) conducted a retrospective study and confirmed that SGB was effective in decreasing the affected arm circumference of breast cancer-related lymphedema (BCRL) patients. They concluded that SGB could be an alternative option in BCRL patients who do not respond to conservative therapy. Seo et al (14) compared SGB with CDT in upper limb lymphedema patients with specific lymphoscintigraphy and found that SGB had a better therapeutic effect than CDT.

For LSGB, Asai et al (20) reported a single case in which LSGB might be very effective in treating lymphedema after cervical cancer surgery and radiation therapy in 2001. In line with our study, Woo et al (7) conducted a prospective study to demonstrate that LSGB has a therapeutic effect on patients who did not respond to conservative treatment. Howarth et al (21) observed that lymphatic flow in the lower extremities increased in 3 patients with complex regional pain syndrome type 1 after ipsilateral lumbar sympathectomy. Mignini et al (22) demonstrated that lymphatic vessels have sympathetic and parasympathetic supplies with the help of immunohistochemistry. Therefore, some scholars hold the view that sympathetic nervous system directly regulate lymphatic flow and may be a new way to treat lymphoedema (18).

The mechanism of LSGB in LLL was unclear, but the following speculation may explain the phenomenon. First, venous dilation after LSGB may contribute to reduced postcapillary resistance, thereby releasing the accumulated interstitial fluid into the venous system. Second, LSGB can raise the skin temperature, resulting in a reduction in swelling, and the process is similar to that of regional heat therapy (16). This leads to the near resolution of perivascular cellular infiltration, the disappearance of the lymph lakes, and the dilatation of capillaries. In addition, LSGB may affect the immune system of the lower limb and decrease the inflammatory response (7).

For the first time, we adopted the method of performing LSGB at an interval of 3 days. At present, many pieces of literature (7,17,18) support LSGB every 2 weeks for the treatment of LLL. We found that an interval of 2 weeks was too long, and sometimes the patient's leg volume was restored to the original state or even worse. This phenomenon may be related to the metabolism of local anesthetics over time. As a result, neurological function recovery from the anesthetic state and the power of LSGBs disappear. More research may be needed to discover the most appropriate treatment interval in the future.

Lymphedema is a chronic condition that can bring multiple problems, making normal daily activities difficult. Lymphedema causes pain, muscular weakness, loss of sensation, and less elasticity (23). When lymphedema is chronic, articulation movement is damaged, and the skin thickens, making it stiffer and more vulnerable to infections (24). This negatively affects the daily life

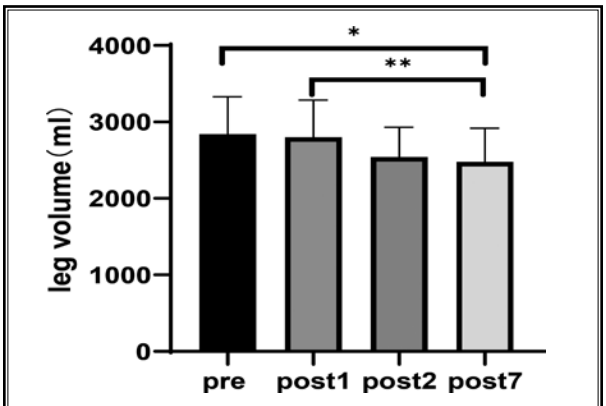

Fig. 5. *Comparison of leg volume of the swollen limb before and after treatment (n = 30). LSGB, lumbar sympathetic ganglion block, pre: before LSGB, post1: the first day after the first LSGB, post2: the first day after the second LSGB, post7: the seventh day after the second LSGB, *P < 0.05, compare pre with post7. **P < 0.05, compare post1 with post7.*

Table 4. *Comparison between the mean scores of the 4 domains of the WHOQoL-BREF.*

Variables	PH	PS	SR	EH	Total
Before LSGB	12.29 ± 1.95	14.19 ± 2.29	8.32 ± 3.37	28.15 ± 4.19	63.66 ± 5.42
After LSGB	16.51 ± 3.68	18.53 ± 2.69	12.47 ± 4.54	29.35 ± 4.21	77.32 ± 3.87
P value	< 0.001	< 0.001	< 0.001	0.2731	< 0.001
t test	5.550	6.729	4.020	1.107	11.23

Abbreviations: WHOQoL-BREF, The World Health Organization Quality of Life Instrument Questionnaire; PH, physical health; PS, psychological health; SR, social relationships; EH, environmental health; LSGB, lumbar sympathetic ganglion block.

of individuals, as they are not able to complete daily life activities alone, and they may suffer from psychological and social problems (23,25,26). We selected the WHOQoL-BREF Instrument to assess the influence of lymphedema on their lives. Table 4 shows that 1 week after 2 rounds of LSGB, the mean scores of PH, PS, and SR were superior to those before treatment ($P < 0.05$). There was no difference in the EH score ($P = 0.2731$). We could conclude that after LSGB, the quality of life improved in patients with LLL.

There are some potential limitations of the study. First, this study was a retrospective study, and the level of evidence was not as high as that of prospective studies. Second, the data of 30 patients may not be enough to verify the critical findings due to its small sample size. However, this is the first study to investigate the power of twice LSGB with an interval of 3 days in LLL, and it will serve as a foundation for further research. These deficiencies should be eliminated in our next in-depth study.

Conclusions

This study showed that LSGB could reduce the leg circumstance and leg volume of LLL patients and improve their quality of life. Our findings indicate that LSGB could be one of the options for patients suffering from LLL after gynecological cancer treatment.

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