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The relationship between the drainage function of inguinal lymph nodes and unilateral pelvic cancer-related lymphedema

A retrospective analysis

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Abstract

The aim of this study was to investigate the relationship between iliolumbar lymph nodes (LNs), inguinal LNs, and unilateral pelvic cancer-related lymphedema by retrospective analysis of lymphoscintigraphy data.

Ninety-six patients (3 men and 93 women; mean age, 53.3 ± 11.3 years) with pelvic cancer-related lymphedema were enrolled in this retrospective study. Lymphoscintigraphy was performed at 1 hour and 4 to 6 hours after injection. The visualization of inguinal LNs and iliolumbar LNs were recorded.

According to statistical analysis, the display of inguinal LNs in lymphoscintigraphy has a significant negative correlation with ipsilateral lower limb lymphedema ($P < .01$, $r = -0.561$). However, there is no correlation between the show of iliolumbar LNs and ipsilateral lower extremity lymphedema ($P = .056$, $r = -0.138$). When lymphoscintigraphy was performed at 1 hour after injection, there were 13 out of 96 patients without inguinal LNs revealed on imaging, but at 4 to 6 hours after injection, inguinal LNs were seen in lymphoscintigraphy.

The drainage function of inguinal LNs has a significant negative correlation with ipsilateral pelvic cancer-related lymphedema. Treatment dedicated to restoring the drainage function of LNs in the inguinal region may effectively relieve lymphedema. The image acquisition at 4 to 6 hours after injection is necessary for significant additional information.

Abbreviations: ASC = antimony sulfide colloid, LNs = lymph nodes, VLNT = vascularized lymph node transfer.

Keywords: inguinal, lymph nodes, lymphedema, lymphoscintigraphy

1. Introduction

Lymphedema is a chronic, progressive disease.[1] Severe lower limb lymphedema can significantly reduce the quality of life of patients, and even affect their mental health.[2,3] It has been reported that lymph nodes (LNs) have the function of "pump" for lymphatic drainage, and the better this function is, the less likely the incidence of lymphedema will be.[4] Therefore, the repair of lymph node drainage function has become an important direction of lymphedema, such as vascularized lymph node transfer (VLNT) surgery.[5,6] The treatment of pelvic malignant tumor is the main cause of secondary lymphedema of lower extremities.[7] Before the lymph is drained from the foot to the thoracic duct, it passes through the inguinal LNs and iliolumbar LNs. In the treatment of lymphedema of lower extremities, VLNT surgery can be performed in the inguinal LNs area. Therefore, correctly judging the drainage function of LNs can provide valuable information for clinic.

It has been reported that the function of drainage can be judged by the number and size of lymph nodes in CT.[8] However, the

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GH and YZ contributed equally to this work.

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number and size of lymph nodes only indirectly reflect the drainage function of lymph nodes. Lymphatic system imaging in nuclear medicine directly reflects the function of lymphatic drainage.[9–16] For many years, lymphoscintigraphy has been widely considered as the first-line imaging to confirm the diagnosis of lymphedema and to visualize the functional state of the lymphatic system.[15,17–23]

The purpose of this study was to investigate the relationship between iliolumbar LNs, inguinal LNs, and unilateral pelvic cancer-related lymphedema by retrospective analysis of ^{99m}Tc-antimony sulfide colloid (ASC) lymphoscintigraphy data.

2. Materials and methods

This retrospective study of existing patient data and images was approved by the institutional review board of Peking Union Medical College Hospital. The requirement for informed consent was waived. Ninety-six patients who were suspected to have lymphedema and underwent ^{99m}Tc-ASC lymphoscintigraphy from October 2014 to September 2020 were included in this retrospective study.

The inclusion criteria were patients (1) diagnosed with lymphedema of the unilateral lower limb based on ^{99m}Tc-ASC lymphoscintigraphy[24] and (2) treated by surgery including pelvic LNs dissection or surgery and pelvic radiotherapy due to pelvic malignant tumors. The exclusion criteria were patients with lymphedema of the unilateral lower extremity with unknown cause (Fig. 1).

2.1. ^{99m}Tc-ASC lymphoscintigraphy

Lymphoscintigraphy was performed at 1 hour and 4 to 6 hours after ^{99m}Tc-ASC was subcutaneously injected into the first and second interdigital spaces of both feet (0.5 mL, 37 MBq/foot). Images were acquired with a SPECT (Discovery NM 630; GE Healthcare) including double-head gamma camera and a low-energy high-resolution parallel whole collimator in whole-body scanning mode with a 256×1024 matrix at a scan speed of 15 cm/min and then analyzed with a workstation (Xeleris; GE).

2.2. Image analysis

The images were analyzed by two nuclear medicine physicians with more than 20 years of experience, who visually evaluated the lymphatic system. The visualization of inguinal LNs and iliolumbar LNs were recorded. The visual condition of lymph node imaging was evaluated by assign points method. If the lymph node can be shown by lymphoscintigraphy at 1 hour or 4 to 6 hours after injection, it is defined as a score of 1, and if it is not shown, it is defined as a score of 0.

According to the principle of assign points and the presence of lymphedema, 192 lower extremities images were divided into 6 categories as follows: "type I" (the score of inguinal LNs is 0, the score of iliolumbar LNs is 0, with lymphedema; Fig. 2); "type II" (the score of inguinal LNs is 0, the score of iliolumbar LNs is 1, with lymphedema; Fig. 3); "type III" (the score of inguinal LNs is 1, the score of iliolumbar LNs is 0, without lymphedema; Figs. 2 and 4); "type IV" (the score of inguinal LNs is 1, the score of iliolumbar LNs is 1, without lymphedema; Fig. 3); "type V" (the score of inguinal LNs is 1, the score of iliolumbar LNs is 1, with lymphedema; Fig. 5); "type VI" (the score of inguinal LNs is 1, the score of iliolumbar LNs is 0, with lymphedema; Fig. 4).

2.3. Statistical analysis

Statistical analyses were done with the SPSS Statistics software (version 22.0, IBM SPSS Inc.). Kendall's correlation coefficients were conducted. A P value $< .05$ was considered statistically significant. Continuous variables were expressed as mean ± SD, while categorical variables were described in numbers and percentages.

3. Results

Ninety-six patients (3 men and 93 women; mean age, 53.3 ± 11.3 [28–76] years) with lymphedema were enrolled in this retrospective study. About 91/96 female patients were diagnosed lymphedema after the treatment of gynecological oncology (including endometrial carcinoma, cervical cancer, ovarian cancer); 1/96 female and 2/96 male patients were diagnosed lymphedema after the treatment of bladder cancer; 1/96 male patients were diagnosed lymphedema after the treatment of carcinoma of penis. The number of lymphedema in the left lower limb was significantly more than that in the right (59 vs 37, $P < .05$) (Table 1).

The details of assign points of LNs and lymphedema were shown in Table 2. One hundred ninety-two lymphoscintigraphy images of lower extremities in 96 patients were calculated. The number of 6 categories are listed as follows: 33 for "type I", 13 for "type II", 51 for "type III", 45 for "type IV", 19 for "type V", and 31 for "type VI".

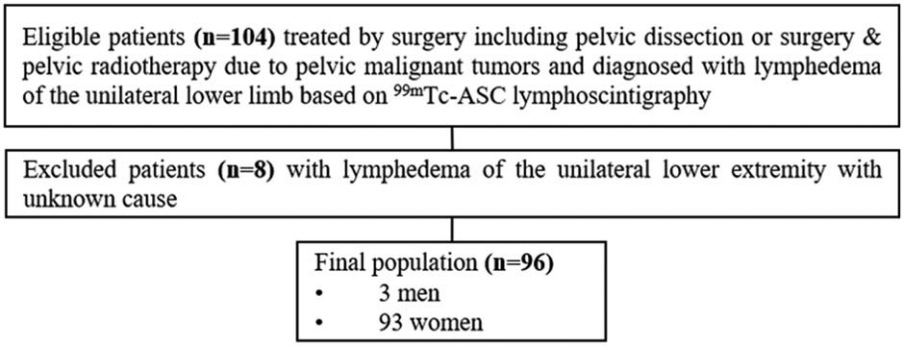

Figure 1. Flowchart to shows patients including process of the study.

Figure 2. A 60-year-old woman with swelling of her right lower limb for 1 month underwent radical hysterectomy for cervical cancer 6 years ago. Four hours after injection, lymphoscintigraphy (anterior and posterior) showed that there was dermal backflow in the right lower limb, no tracer uptake in the right inguinal lymph nodes and bilateral iliolumbar lymph nodes scored "0 score", and tracer uptake in the left groin scored "1 score".

Figure 3. A 74-year-old woman suffered from swelling of her left lower limb for one and a half years after radical resection of ovarian cancer. Four hours after injection, lymphoscintigraphy (anterior and posterior) revealed that there was dermal backflow in the left lower limb, no tracer uptake in the left groin scored "0 score" and tracer uptake in the right inguinal lymph nodes and bilateral iliolumbar lymph nodes scored "1 score".

According to statistical analysis, the display of inguinal LNs in lymphoscintigraphy has a significant negative correlation with ipsilateral lower limb lymphedema ($P < .01, r = -0.561$). However, there is no correlation between the show of iliolumbar LNs and ipsilateral lower extremity lymphedema ($P = .056, r = -0.138$).

When lymphoscintigraphy was performed at 1 hour after injection, there were 13 out of 96 patients without inguinal LNs revealed on imaging, but at 4 to 6 hours after injection, inguinal LNs were seen in lymphoscintigraphy (Fig. 6).

4. Discussion

Our analysis of lymphoscintigraphy characteristics finds that the drainage function of inguinal LNs has a significant negative correlation with ipsilateral pelvic cancer-related lymphedema. The result shows that if the inguinal LNs have the function of drainage, then the ipsilateral lower extremities are less likely to develop lymphedema. In a study based on CT, Onoda et al[8] found that secondary lymphedema was less severe in patients with more and larger inguinal LNs. However, the size and number of LNs cannot fully reflect the function of lymphatic drainage, because metastatic LNs may also occur. Lymphoscintigraphy can directly reflect the drainage function of LNs. Therefore, in order to prevent lower limb lymphedema after surgical treatment and/or radiotherapy of pelvic malignant tumor, the drainage function of inguinal LNs should be paid more attention. Promoting the regeneration of inguinal LNs drainage[25] or VLNT surgery[5] may relieve the lymphedema of the lower extremities. Whether VLNT surgery is performed proximally or distally is controversial.[5] Because of the importance of inguinal LNs drainage function for lower limb lymphedema found in this study, VLNT surgery and the local use of cytokines in the inguinal LNs area may be a good choice for the treatment of lymphedema. Meanwhile, we do not recommend harvesting LNs from the groin for VLNT surgical treatment of upper limb lymphedema. Vignes et al[26] found that after collecting inguinal LNs for VLNT, about 38% of patients developed iatrogenic ipsilateral limb lymphedema.

However, there was no similar correlation between the drainage function of iliolumbar LNs and lymphedema. This

Figure 4. A 42-year-old woman suffered from swelling of her left lower limb for several years after radical resection of ovarian cancer and postoperative radiotherapy. Four hours after injection, lymphoscintigraphy (anterior and posterior) demonstrated that there was dermal backflow in the left lower limb, no tracer uptake in the bilateral iliolumbar lymph nodes scored "0 score" and tracer uptake in the bilateral inguinal lymph nodes scored "1 score".

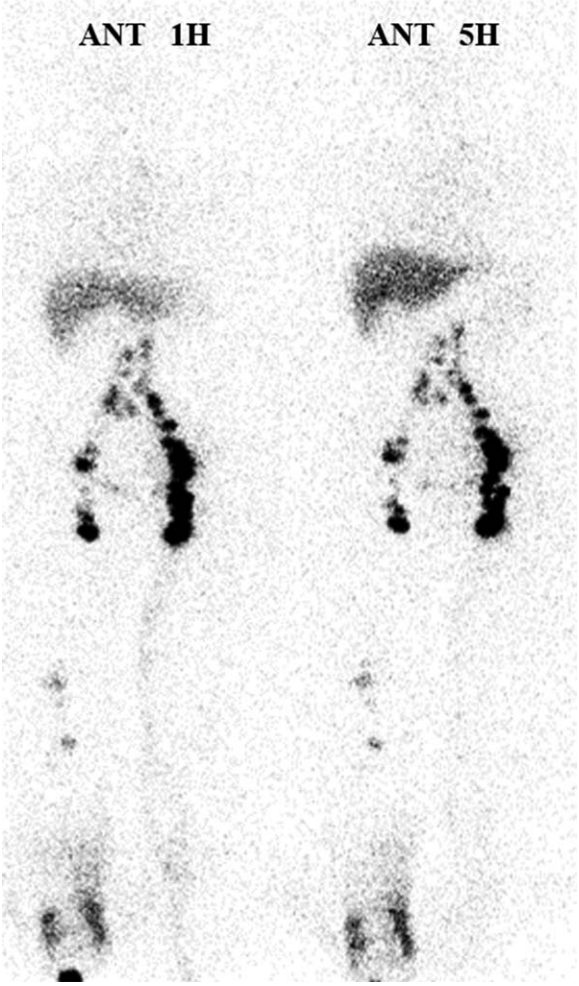

Figure 5. A 37-year-old woman suffered from swelling of her left lower limb for 6 months after radical resection of ovarian cancer. One and five hours after injection, lymphoscintigraphy (anterior) showed that there was dermal backflow in the right lower limb, tracer uptake in the bilateral inguinal and iliolumbar lymph nodes scored "1 score".

result suggests that the drainage function of iliolumbar LNs is not critical for lower limb lymphedema. At the same time, it should be noted that the statistically significant correlation is absent, there is still a certain trend of correlation ($P = .056$). Even if there is such a trend, it is not worth protecting iliolumbar LNs for the treatment of lymphedema. On the one hand, the iliolumbar LNs are dissected in most cases during the surgical treatment of pelvic malignant tumors; on the other hand, the iliolumbar LNs are located in the deep part of the pelvis, which is not feasible for VLNT surgery and the local use of cytokines.

Maclellan et al[27] reported that the acquisition of lymphoscintigraphy does not need to exceed 2 hours after injection for the diagnosis of lymphedema and the 4 hours image does not provide any significant additional information. This conclusion may cause a certain degree of misleading and lead to the failure of image acquisition at more than 2 hours after injection. In our study, we found that 10/96 patients without inguinal LNs revealed by lymphoscintigraphy at 1 hour after injection, but at 4 to 6 hours, inguinal LNs were seen in lymphoscintigraphy. We believe that image acquisition at 4 to 6 hours after injection is necessary because

Table 1

Clinical characteristics of patients with lymphedema.

Characteristics	Value
Number of patients	96
__Female	93
__Male	3
Age, median (range) years	53.3 ± 11.3 (28–76)
Cancer type	
__Gynecological pelvic tumor	92
__Bladder tumor	3
__Carcinoma of penis	1
The number of lymphedema in the lower extremities	96
__Left	59
__Right	37
The duration of lymphedema	
__Within 1 month	9
__1–3 months	15
__3–6 months	11
__6–12 months	19
Over 12 months	42

Table 2

The details of assign points of LNs and lymphedema.

Scoring type	Inguinal LNs	Iliolumbar LNs	Lymphedema	Number
I	0	0	Yes	33
II	0	1	Yes	13
III	1	0	No	51
IV	1	1	No	45
V	1	1	Yes	19
VI	1	0	Yes	31

1: lymph node can be shown by lymphoscintigraphy; 0: lymph node is not shown by lymphoscintigraphy.
LNs, lymph nodes.

it can help to find some inguinal LNs that still have drainage function. The discovery of these inguinal LNs may provide some reference information for the treatment of lymphedema.

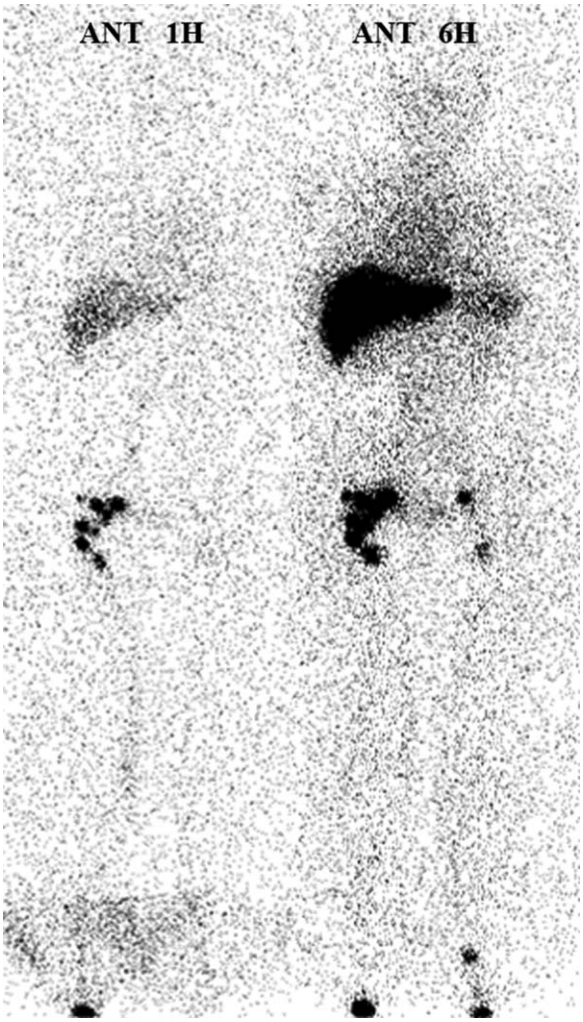

Figure 6. A 70-year-old woman with lymphedema of the left lower limb after radical resection of endometrial carcinoma for 2 years. One hour after injection, lymphoscintigraphy (anterior) revealed that the lymphatic vessels of the right lower extremities were visible, and there was tracer uptake in the right inguinal lymph nodes scored "1 score", no tracer uptake in the bilateral iliolumbar lymph nodes scored "0 score" and no tracer uptake in the left inguinal lymph nodes. However, six hours after injection, lymphoscintigraphy (anterior) revealed that there was tracer uptake in the left inguinal lymph nodes scored "1 score".

The present study shows that the number of lymphedema in the left lower limb was significantly more than that in the right ($P < 0.05$). The reason for this difference is unclear. Since postoperative radiotherapy and the number of lymph nodes removed are independent risk factors for lymphedema,[28] we speculate that it may be caused by the large number of lymph nodes removed on the right and the high dose of radiation therapy on the right.

The limitations of this study should be pointed out that as a retrospective study using existing data, the study could be subject to selection bias. Secondly, most of the subjects included in this study are women, which may cause some data deviation. According to the retrieval of HIS system, 96 patients were eligible for inclusion in the study among all the patients who underwent lymphography from October 2014 to September 2020. The number of participants was so limited that we did not set a control group, which may affect the diagnostic efficiency.

5. Conclusion

The drainage function of inguinal LNs revealed by lymphoscintigraphy has a significant negative correlation with ipsilateral pelvic cancer-related lymphedema. VLNT surgery and the local use of cytokines performed in the inguinal LNs area may achieve good therapeutic results. The image acquisition at 4 to 6 hours after injection is necessary for significant additional information.

Author contributions

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Writing – original draft: Guozhu Hou, Yuwei Zhang.

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