Title page

(1) title of the article:

Comparison of leg volume ratio between inguinal lymphadenectomy and inguino-pelvic lymphadenectomy in patients with skin cancer of the lower extremity

(2) initials and name of each author:

Taku Maeda[1], MD, PhD, Kosuke Ishikawa[1], MD, PhD, Toshihiko Hayashi[2], MD, PhD, Hiroshi Furukawa[3], MD, PhD, Takahiro Miura[1], MD, PhD, Masahiro Hojo[1], MD, Emi Funayama[1], MD, PhD, Yuhei Yamamoto[1], MD, PhD

(3) name and address of the department or institution to which the work should be attributed:

1 Department of Plastic and Reconstructive Surgery, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Kita-15 Nishi-7, Kita-ku, Sapporo City, Hokkaido 060-8638, Japan

2 Department of Plastic and Reconstructive Surgery, Asahikawa Medical University, 2-1-1-1 Midorigaoka higashi, Asahikawa City, Hokkaido 078-8510, Japan

3 Department of Plastic and Reconstructive Surgery, School of Medicine, Aichi Medical University, 1-1 Yazakokarinata, Nagakute, Aichi 480-1195, Japan

(4) the name, address, telephone, fax and e-mail details of the author responsible for editorial correspondence

Yuhei Yamamoto

Department of Plastic and Reconstructive Surgery, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Kita-15 Nishi-7, Kita-ku, Sapporo City, Hokkaido 060-8638, Japan

TEL: +81-11-706-6978; FAX: +81-11-706-7827; E-mail: yu-h1@med.hokudai.ac.jp

(5) details of any meeting at which the work was presented, wholly or in part.

None

Abstract

Background. The timing of intervention to treat lymphedema differs among facilities. Understanding differences in the prevalence and severity of lymphedema following different surgical procedures for lymphadenectomy could promote early intervention to treat lymphedema. There is currently little evidence to support the notion that inguino-pelvic lymphadenectomy is associated with greater morbidity than inguinal lymphadenectomy, although it is believed that the difference in the extent of surgery results in a difference in severity of lymphedema. In this study, we compared volume percentage change between inguinal lymphadenectomy and inguino-pelvic lymphadenectomy in patients with skin cancer of the lower extremity.

Patients and Methods. Twenty-nine patients with skin cancer of a lower extremity who underwent lymphadenectomy were classified into an inguinal lymphadenectomy group and an inguino-pelvic lymphadenectomy group. The increase in the volume of the affected side compared with that of the unaffected side in the whole lower extremity, thigh, and lower leg was calculated on volume-rendered computed tomography images.

Results. The mean volume percentage increase in the inguinal lymphadenectomy group and inguino-pelvic lymphadenectomy group was respectively 6.72% and 11.18% in the whole lower extremity and 7.30% and 2.55% in the lower leg, showing no statistically significant differences. One the other hand, the mean volume percentage increase in the respective groups was 7.03% and 19.78% in the thigh, showing a statistically significant difference ($p=0.0275 < 0.05$).

Conclusions. The findings of this study indicate that the leg volume of the whole lower extremity may not have worse outcomes in inguino-pelvic lymphadenectomy compared with inguinal lymphadenectomy.

Key words: lymphedema, inguinal lymphadenectomy, inguino-pelvic lymphadenectomy, skin cancer, melanoma

Introduction

At present, observation of nodes by ultrasonography rather than complete lymph node dissection (LND) is preferred in patients with cutaneous melanoma and sentinel lymph node (SLN) metastasis based on the results of two randomized trials, namely, MSLT-II[1] and DECOG-SLT.[2] However, not all patients with SLN metastasis are suitable for observation by ultrasonography. Patients with extensive SLN metastasis in whom complete LND would provide regional control but who are unlikely to comply with an intensive surveillance protocol and those who are treated at centers where radiologists are not comfortable performing serial surveillance ultrasonography examinations are not good candidates for observation by ultrasonography.[3] For these patients, LND is still regarded as an important treatment option for melanoma with SLN metastasis. This surgical approach is also applicable for other skin cancers.

Lymphedema is a devastating condition in which impaired lymphatic transport manifests as chronic swelling and tissue fibrosis.[4] Deposition of adipose tissue starts along with the lymphedema and is the main contributor to the excess volume in lymphedema as a result of local inflammation.[5-7] This condition can be caused by radical resection of lymphatic tissue (i.e., LND) and then is known as cancer-related lymphedema. The mean incidence rate for cancer-related lymphedema is 11.8% after LND for melanoma in an upper extremity, 30.5% for melanoma in a lower extremity, 12.9% for genitourinary cancers, and 23.9% for gynecological malignancies.[8] The treatment options for patients with cancer-related lymphedema are broadly surgical and non-surgical. Worldwide, the first-line treatment for lymphedema is complete decongestive therapy.[9] Although careful patient selection after a course of conservative lymphedema therapy has been completed is essential, it is known that the fluid-predominant component of lymphedema can be improved by both transplantation of lymphatic tissue (vascularized lymph node transfer) and creation of direct connections between the lymphatic vessels and the veins (lymphaticovenous anastomoses).[10] However, the effectiveness of these surgeries in terms of restoring lymphatic drainage pathways is limited for progressive lymphedema because of subcutaneous tissue fibrosis. Understanding differences in the prevalence and severity of lymphedema following different surgical procedures for LND could promote early

intervention to treat lymphedema.

We have performed two types of LND for skin cancers arising in an extremity: inguinal lymphadenectomy for patients with stage III disease based on a positive SLN and inguinal plus pelvic (external iliac and obturator) lymphadenectomy for patients with clinically positive inguinofemoral nodes, 3 or more positive inguinofemoral nodes, or a positive Cloquet's node, as recommended by the National Comprehensive Cancer Network.[11] The difference in lymphedema between inguinal lymphadenectomy and inguino-pelvic lymphadenectomy has long been cited as a reason for limiting the extent of surgery to inguinal lymphadenectomy unless there is extensive disease. However, in some studies, this was not supported with data showing a significant difference in the lymphedema rate between these two operations.[12-14] In this study, we compared the volume percentage change between lymphadenectomy and inguino-pelvic lymphadenectomy in patients with skin cancer of the lower extremity.

Materials and Methods

The data analyzed in this study were obtained retrospectively by a chart review of all patients with melanoma or other tumors affecting an extremity who underwent inguinal or inguinal plus pelvic lymphadenectomy in the Department of Plastic and Reconstructive Surgery, Hokkaido University Hospital, between January 2009 and September 2020. All patients started complete decongestive therapy within 1 month of lymphadenectomy at a lymphedema outpatient clinic, where there were physical therapists and a gynecologist who were experienced with complete decongestive therapy. To avoid mistaking early-onset postoperative swelling for lymphedema, leg volume was assessed 3 to 6 months after lymphadenectomy by both a plastic surgeon (first author) and the gynecologist. For the objective evaluation, computed tomography (CT) scans were obtained. The patients received usual

care and were instructed to wear a compression garment. A round knitted custom-made compression garment (compression class 2, 23-32 mmHg) was first selected and was to be worn during the daytime. If a patient experienced discomfort, a flat-knitted garment was selected. In principle, the patients continued the conservative treatment throughout the follow-up after the resection of skin cancer.

Patients who underwent postoperative radiation therapy or preoperative chemotherapy were excluded. Patients with SLN metastasis received an explanation about the observation of nodes by ultrasonography instead of complete LND and those selecting the observation were excluded, considering the background of the introduction of targeted therapy and immune checkpoint inhibitors in Japan in 2014. A variety of terms have been used to describe various types of LND performed in patients with skin cancers arising from an extremity, including groin, inguinal, ilioinguinal and pelvic node dissection, which has resulted in confusion and reduced the effectiveness of literature searches. In this study, inguinal lymphadenectomy was defined as superficial and deep inguinal LND and inguino-pelvic lymphadenectomy was defined as inguinal lymphadenectomy plus external iliac and obturator LND.[15,16] Inguinal lymphadenectomy was performed in patients with a positive SLN (inguinal group), and inguino-pelvic lymphadenectomy was performed in those with clinically positive inguinofemoral nodes, 3 or more positive inguinofemoral nodes, or a positive Cloquet's node (inguino-pelvic group) (Fig. 1). Patient characteristics, including age, sex, disease, and number of excised LNs, were recorded.

To evaluate leg volume ratios, CT scans were obtained regularly during follow-up in all cases. We evaluated the CT images of the lower extremity obtained at least 6 months after surgery and compared the severity of lymphedema between the inguinal lymphadenectomy group and inguino-pelvic lymphadenectomy group. High-resolution images of the lower extremities were acquired using an 80-row multidetector CT. Three-dimensional (3D) CT images were reconstructed to evaluate the volume of the whole lower extremity, thigh, and lower leg using REVORAS image processing software (Ziosoft). The images were automatically extracted and drawn based on DICOM data for high-resolution CT using REVORAS, which accurately calculated volumes. A

whole-limb volume percentage change of ≥10% was diagnosed as lymphedema. The severity of lymphedema was categorized as minimal (5-20% increase in extremity volume), moderate (20%–40%), or severe (>40%) according to the severity of lymphedema designated by the International Society of Lymphology.[17]

The ratio of volume of the affected extremity to that of the unaffected extremity in the whole lower extremity, thigh, and lower leg was calculated on volume-rendered CT images. The increase in the volume of the affected side compared with that of the unaffected side was examined. For example, in the case presented in Fig. 2, the volume of both whole lower extremities was calculated as 17482.49 ml (Fig. 2a). Upper point was set at 20 cm above the upper edge of the patella. The volume of the affected whole extremity was calculated as 9815.28 ml, whereas that of the unaffected whole extremity was calculated as 7645.96 ml (Fig. 2b). This volume percentage increase was calculated using the following formula: (Affected volume - Unaffected volume)/Unaffected volume×100. The volume percentage increase of the whole lower extremity was 28.37%. The thigh was defined as the volume from 20 cm above the upper edge of the patella to the upper edge of the patella (Fig. 2c). Lower leg was defined as the lower edge of the patella to the toes (Fig. 2d). The volume percentage increase was similarly calculated as 26.77% in the thigh and 27.33% in the lower leg, respectively.

The study was approved by our institutional ethics committee (020-0504, C-T2021-0135). Written informed consent was obtained from all patients for use of their clinical data for research purposes.

Statistical Analysis

Patient characteristics and descriptive statistics were summarized and compared among the groups. Proportions were analyzed using Fisher's exact test. Continuous data were compared using the t-test assuming unequal variances. The Wilcoxon rank-sum test was used unless the assumption of normal distribution was required. A P-value < 0.05 was considered statistically significant. In the box-and-whisker plots, the boxes represent the medians with upper and lower quartiles and the whiskers

represent maximum and minimum values. The statistical analysis was performed using JMP 13.0 software (SAS Institute Inc., Cary, NC).

Results

The patients' demographic and clinical characteristics are summarized in Table 1. There were 16 men and 13 women, with median age of 68.2 (range 17–85) years. There were 21 cases of melanoma, 5 cases of squamous cell carcinoma, and 1 case each of invasive extramammary Paget's disease, porocarcinoma, and sebaceous carcinoma. Fourteen patients underwent inguinal lymphadenectomy, and 15 underwent inguino-pelvic lymphadenectomy. There was no significant difference in the number of excised inguinal LNs between the inguinal lymphadenectomy and inguino-pelvic lymphadenectomy groups. On the other hand, there was a statistical difference in the number of excised total LNs between the two groups, which was attributed to the additional excised pelvic LNs in the inguino-pelvic lymphadenectomy group.

A comparison of the volume percentage change according to extent of LND is shown in Fig. 3. The mean volume percentage increase in the inguinal lymphadenectomy group and inguino-pelvic lymphadenectomy group was respectively 6.72% and 11.18% in the whole lower extremity and 7.30% and 2.55% in lower leg, showing no statistically significant differences. One the other hand, the mean volume percentage increase in the respective groups was 7.03% and 19.78% in the thigh, showing statistically significant differences ($p=0.0275 < 0.05$).

The incidence of lymphedema (whole-limb volume percentage change $\geq 10\%$) was 1 of 14 patients (7.1%) in the inguinal lymphadenectomy group and 7 of 15 patients (46.7%) in the inguino-pelvic lymphadenectomy group, showing a statistically significant difference ($p=0.0225 < 0.05$). In the 14 patients who underwent inguinal lymphadenectomy, severity was classified as minimal in 5 patients and moderate in 1. In the 15 patients who underwent inguino-pelvic lymphadenectomy, severity was classified as minimal in 7 patients and moderate in 3 (Fig. 4), although the difference between two groups was not statistically significant.

Representative cases

Case 1 (inguinal lymphadenectomy)

The patient was a 75-year-old man who was diagnosed as having melanoma on the sole of the right foot (Fig. 5a). We performed wide local excision with a 2 cm margin and SLN biopsy. The SLN was metastatic. Subsequently, we performed inguinal lymphadenectomy (Fig. 5b-d). The CT images obtained 6 months after surgery showed that the volume percentage increase was 2.21% in the whole lower extremity, 1.63% in the thigh, and 7.61% in the lower leg (Fig. 5e).

Case 2 (inguino-pelvic lymphadenectomy)

The case was a 69-year-old woman who had presented to a local clinic 4 months earlier with an area of black pigmentation on the sole of the right foot. The pathological diagnosis was malignant melanoma. Three SLN biopsies confirmed lymph node metastasis. We therefore performed inguino-pelvic lymphadenectomy (Fig. 6a-6d). A CT image obtained 14 months after lymphadenectomy confirmed lymphedema in the right lower extremity. The volume percentage increase was 15.27% in the whole lower extremity, 26.12% in the thigh, and 0.65% in the lower leg (Fig. 6e).

Discussion

The findings of this study highlight the following important two clinical issues. First, based on a strict definition of the resected lymphatic area, worse severity of the leg volume in the whole lower extremity after lymphadenectomy was not observed in inguino-pelvic lymphadenectomy compared with inguinal lymphadenectomy, excluding postoperative radiation therapy and previous chemotherapy. Second, the difference in volume percentage change was observed in the thigh but not the lower leg.

The lymphatic system is composed of both the circulatory system, which includes the lymphatic vessels, and the immune system, which includes the lymphoid organs. Abnormal vessel development or obstruction or obliteration of the lymphatic vessels reduces lymphatic transport capacity, causing pooling of proteins and water in the interstitium and resulting in lymphedema.[18] Understanding of

this physiological process has led to the hypothesis that the extent of lymphatic tissue impairment due to LND may be proportional to the severity of lymphedema. The findings of this study did not provide enough support for this hypothesis. Although the incidence of lymphedema based on one definition was higher in the inguino-pelvic lymphadenectomy group than in the inguinal lymphadenectomy group, the difference in severity between the two groups was ultimately not significant.

Radiotherapy or previous chemotherapy infusion in the affected limb, obesity, and postoperative seroma increase the risk of lymphedema.[19] Early-stage abnormalities in the lymphography pattern (stardust, diffuse, and no flow) may be helpful for predicting lymphedema.[20] However, there have been few studies of the relationship between the severity of lymphedema and treatment outcome according to the extent of LND. Kim et al. reported that lymphedema was less severe in patients with axillary node uptake on lymphoscintigraphy, regardless of the extent of LND, hypothesizing that the bypass pathway had a crucial role in lymphedema following extensive axillary LND. In this study, we focused on the relationship between volume percentage change and the extent of LND in patients with skin cancers of a lower extremity based on a strict definition of the resected lymphatic area. Although a difference in volume percentage change was demonstrated between inguinal lymphadenectomy and inguino-pelvic lymphadenectomy in the thigh, the difference was not significant in the whole lower extremity or the lower leg. It is reported that dermal backflow first becomes apparent in the thigh, not in the lower leg, when lymphedema gradually worsens without proper treatment.[21] The results of this study were similar to those of that previous report in that the difference between the two groups first appeared at the thigh during the early stage. Considering the high incidence and severity of lymphedema after both inguinal lymphadenectomy and inguino-pelvic lymphadenectomy, early surgical intervention to restore lymphatic drainage pathways may reduce the deterioration of lymphedema in these cases.

Differences in lymphedema between inguinal lymphadenectomy and inguino-pelvic lymphadenectomy have long been cited as a reason for limiting the extent of surgery to inguinal lymphadenectomy unless there is extensive disease. Spillane et al. demonstrated that the rate of

lymphedema was not significantly different between inguinal lymphadenectomy and inguino-pelvic lymphadenectomy. [12] This was also supported by others.[13] Hughes and Thomas reviewed the literature on this topic and also concluded that there was no difference in lymphedema rates between inguinal lymphadenectomy and inguino-pelvic lymphadenectomy.[14] Therefore, it is apparent from this previous review that there is little evidence to support the notion that inguino-pelvic lymphadenectomy is associated with greater morbidity than inguinal lymphadenectomy. However, in those studies, there was non-negligible selection bias, such as the inclusion of postoperative radiation cases and differences in postoperative compression therapy. In the present study, postoperative radiation cases were excluded, and all patients received compression therapy under the same protocol. In addition, there were no significant differences in age and male to female ratio between the two groups.

Lymphatic vessels in the lower extremities can be divided into superficial and deep vessels. Most lymphatic vessels drain to first-tier superficial inguinal lymph nodes in the groin area. In contrast, one or two lymph collecting vessels coming from the lateral side of the Achilles tendon drain through the popliteal and femoral lymph nodes and finally to the deep inguinal, external iliac, obturator, or inferior gluteal lymph node groups.[22] In LND for a skin cancer in a lower extremity, in principle both the superficial and deep inguinal lymph nodes, as well as the external iliac and obturator lymph nodes if necessary, are resected along with the anatomical structure of the lymphatic vessels described above.

The National Comprehensive Cancer Network recommends that patients with stage III melanoma and a positive SLN should be offered complete LND of the involved nodal basin. Inguinal lymphadenectomy is essential for melanoma arising in a lower extremity. In the setting of inguinal lymphadenectomy, pelvic dissection is recommended if a positron emission tomography/CT or pelvic CT scan demonstrates iliac and/or obturator lymph node involvement or if a positive Cloquet's lymph node is detected intraoperatively. Pelvic dissection is also recommended for clinically positive inguinal/femoral nodes or if 3 or more inguino-femoral nodes are involved. Following this treatment strategy, we clearly separated the patients with melanoma in a lower

extremity and lymph node involvement into the inguinal group and the inguino-pelvic group. This approach has also been applied for other advanced skin cancers. The obturator nerve, artery, and veins ascend posterior to the psoas major muscle,[23] enter the pelvis via the obturator canal formed in the obturator foramen, and then travel posterior to the common iliac artery. Viamonte et al. reported that deep lymphatic vessels accompanied the obturator artery.[24] This route is different from the route receiving flow from the superficial and deep inguinal lymph nodes; the latter route is resected and the former route is preserved in inguinal lymphadenectomy. However, both routes are resected simultaneously in inguino-pelvic lymphadenectomy. Thus, the greater the amount of lymphatic tissue resected, the more the route for lymphatic flow is involved. This anatomic difference might account for the difference in the mean volume percentage increase in the thigh between the two groups.

The circumference of a limb is often used to evaluate its volume because of its consistency and ease of measurement for both clinicians and patients. Alternative methods have also been developed, including the water displacement method, perometry, bioimpedance spectroscopy, three-dimensional photography, and radiography, CT, ultrasonography, and magnetic resonance imaging.[25-28] Although water displacement and circumference measurement are reported to be reliable techniques for assessment of lymphedema in clinical practice,[29] volume-rendered CT imaging is reported to be superior for estimating the amount of excess adipose tissue in lymphedema.[30] In this study, we used volume-rendered CT images to analyze lower extremity volume.

Our study has some limitations, the main one being the small number of patients. The study has many of the limitations inherent to retrospective studies and was performed at a single facility. Multicenter prospective studies with standardized protocols are needed in the future. With respect to the conservative treatment after lymphadenectomy in this study, the prophylactic decongestive therapy may have varied in terms of compliance and other factors even though all patients started complete decongestive therapy within 1 month of lymphadenectomy based on the constant protocol. In addition, to assess the degree of lymphedema, only volume-rendered CT was used, without additional evaluation by lymphoscintigraphy or indocyanine green lymphography.

In conclusion, the findings of this study indicate that the leg volume of the whole lower extremity may not have worse outcomes in inguino-pelvic lymphadenectomy compared with inguinal lymphadenectomy.

Conflict of interest

No author has any conflict of interest to declare.

Ethics

This retrospective study was approved by our institutional ethics committee (020-0504, C-T2021-0135).

Funding

None.

Acknowledgement

The authors thank Aogu Yamaguchi for providing technical support for REVORAS (Ziosoft).

References

1. Faries MB, Thompson JF, Cochran AJ, et al. Completion Dissection or Observation for Sentinel-Node Metastasis in Melanoma. *N Engl J Med* 2017;376(23):2211-22.

2. Leiter U, Stadler R, Mauch C, et al. Complete lymph node dissection versus no dissection in patients with sentinel lymph node biopsy positive melanoma (DeCOG-SLT): a multicentre, randomised, phase 3 trial. *Lancet Oncol* 2016;17(6):757-67.

3. Wright FC, Souter LH, Kellett S, et al. Primary excision margins, sentinel lymph node biopsy, and completion lymph node dissection in cutaneous melanoma: a clinical practice guideline. *Curr Oncol* 2019;26(4):e541-e50.

4. Szuba A, Rockson SG. Lymphedema: classification, diagnosis and therapy. *Vasc Med* 1998;3(2):145-56.

5. Hoffner M, Peterson P, Mansson S, et al. Lymphedema leads to fat deposition in muscle and decreased muscle/water volume after liposuction: A magnetic resonance imaging study. *Lymphat Res Biol* 2018;16(2):174-81.

6. Karlsson T, Karlsson M, Ohlin K, et al. Liposuction of breast cancer-related arm lymphedema reduces fat and muscle hypertrophy. *Lymphat Res Biol* 2022;20(1):53-63

7. Westcott GP, Rosen ED. Crosstalk between adipose and lymphatics in health and disease. Endocrinology 2022;163(1):bqab224. doi: 10.1210/endocr/bqab224

8. Cormier JN, Askew RL, Mungovan KS, et al. Lymphedema beyond breast cancer: a systematic review and meta-analysis of cancer-related secondary lymphedema. *Cancer* 2010;116(22):5138-49.

9. Executive Committee of the International Society of Lymphology. The diagnosis and

treatment of peripheral lymphedema: 2020 Consensus Document of the International Society of Lymphology. *Lymphology* 2020; 53(1):3-19.

10. Granzow JW. Lymphedema surgery: the current state of the art. *Clin Exp Metastasis* 2018; 35(5-6):553-8.

11. National Comprehensive Cancer Network. Melanoma Cutaneous (Version 2.2021). https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed October 23, 2021.

12. Spillane AJ, Saw RP, Tucker M, Byth K, Thompson JF. Defining lower limb lymphedema after inguinal or ilio-inguinal dissection in patients with melanoma using classification and regression tree analysis. *Ann Surg* 2008;248(2):286-93.

13. Karakousis CP, Driscoll DL, Rose B, Walsh DL. Groin dissection in malignant melanoma. *Ann Surg Oncol* 1994;1(4):271-7.

14. Hughes TM, Thomas JM. Combined inguinal and pelvic lymph node dissection for stage III melanoma. *Br J Surg* 1999;86(12):1493-8.

15. Smith OJ, Lee-Rodgers L, Ross GL. The nomenclature of groin dissection for melanoma - Time to simplify. *J Plast Reconstr Aesthet Surg* 2015;68(11):1588-91.

16. Maeda T, Yamamoto Y, Hayashi T, et al. Restoration of lymph flow by flap transfer can prevent severe lower extremity lymphedema after inguino-pelvic lymphadenectomy. *Surg Today* 2023;53(5):588-595.

17. Executive Committee of the International Society of L. The diagnosis and treatment of peripheral lymphedema: 2020 Consensus Document of the International Society of Lymphology. *Lymphology* 2020; 53:3-19.

18. Tammela T, Alitalo K. Lymphangiogenesis: Molecular mechanisms and future promise. *Cell* 2010;140(4):460-76.

19. Ribeiro Pereira ACP, Koifman RJ, et al. Incidence and risk factors of lymphedema after breast cancer treatment: 10 years of follow-up. *Breast* 2017;36:67-73.

20. Akita S, Nakamura R, Yamamoto N, et al. Early Detection of Lymphatic Disorder and Treatment for Lymphedema following Breast Cancer. *Plast Reconstr Surg* 2016;138(2):192e-202e.

21. Akita S, Nitsukawa N, Kazama T, et al. Comparison of lymphoscintigraphy and indocyanine green lymphography for the diagnosis of extremity lymphoedema. *J Plast Reconstr Aesthet Surg* 2013;66(6):792-8.

22. Pan WR, le Roux CM, Levy SM. Alternative lymphatic drainage routes from the lateral heel to the inguinal lymph nodes: anatomic study and clinical implications. *ANZ J Surg* 2011;81(6):431-5.

23. Iwanaga J, Warner T, Scullen TA, et al. Relationship of the Obturator Nerve and Psoas Major: Anatomic Study with Application to Avoiding Iatrogenic Injuries. *World Neurosurg* 2020;136:e365-e70.

24. Viamonte MJ, Ruttimann A. Atlas of lymphography. New York: Thieme-Stuttgart, 1980.

25. Stanton AW, Northfield JW, Holroyd B, et al. Validation of an optoelectronic limb volumeter (Perometer). *Lymphology* 1997;30(2):77-97.

26. Taylor R, Jayasinghe UW, Koelmeyer L, et al. Reliability and validity of arm volume measurements for assessment of lymphedema. *Phys Ther* 2006;86(2):205-14.

27. Tierney S, Aslam M, Rennie K, et al. Infrared optoelectronic volumetry, the ideal way to measure limb volume. *Eur J Vasc Endovasc Surg* 1996;12(4):412-7.

28. Ward LC. Bioelectrical impedance analysis: proven utility in lymphedema risk assessment and therapeutic monitoring. *Lymphat Res Biol* 2006;4(1):51-6.

29. Chen YW, Tsai HJ, Hung HC, et al. Reliability study of measurements for lymphedema in breast cancer patients. *Am J Phys Med Rehabil* 2008;87(1):33-8.

30. Brorson H, Ohlin K, Olsson G, et al. Adipose Tissue Dominates Chronic Arm Lymphedema Following Breast Cancer: An Analysis Using Volume Rendered CT Images. *Lymphat Res Biol* 2006;4(4):199-210.

Figure legends

Figure 1. Schematic representations and intraoperative photographs of inguinal lymphadenectomy and inguino-pelvic lymphadenectomy. Inguinal lymphadenectomy is defined as dissection of the superficial and deep inguinal lymph nodes. Inguino-pelvic lymphadenectomy is defined as inguinal lymphadenectomy plus dissection of the external iliac and obturator lymph node.

Figure 2. The evaluation of volume using REVORAS image processing software (Ziosoft). The thigh was defined as the volume from 20 cm above the upper edge of the patella to the upper edge of the patella. The lower leg was defined as the lower edge of the patella to the toes. (a) Both whole lower extremities. (b) The affected whole extremity and the unaffected one. (c) The thigh. (d) The lower leg.

Figure 3. Volume percentage change of the patients with lymphedema using volume-rendered CT images in (a) the whole lower extremity, (b) the thigh, and (c) the lower leg according to surgical group.

Figure 4. Distribution of severity of lymphedema according to surgical group.

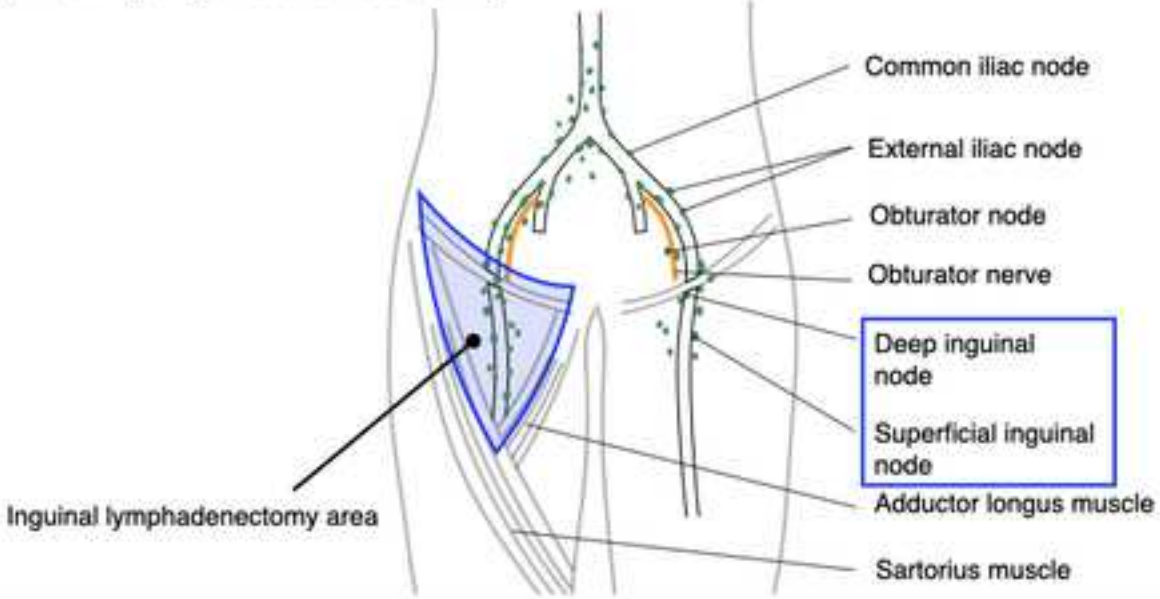
Figure 5. Images for a 75-year-old man with melanoma on the sole of the right foot who was treated by inguinal lymphadenectomy. (a) Presentation of melanoma on the sole of the right foot. (b) Inguinal lymphadenectomy in the right groin area. (c) Lymphatic tissue was resected under the inguinal ligament, including Cloquet's lymph node. (d) Immediately after the procedure. (e) Volume-rendered CT images of the lower extremities.

Figure 6. Images for a 69-year-old woman with melanoma on the sole of the right foot that was treated by inguino-pelvic lymphadenectomy. (a) Incisional line for inguino-pelvic lymphadenectomy. (b) Inguino-pelvic lymphadenectomy was performed. Presentation after dissection of the external iliac region (c). Presentation after dissection of the obturator region with

securing of the obturator nerve with yellow vessel tape (d) and overall presentation after the procedure. (e) Volume-rendered CT images of lower extremities.

Figure(s) 1

Inguinal lymphadenectomy



Inguino-pelvic lymphadenectomy

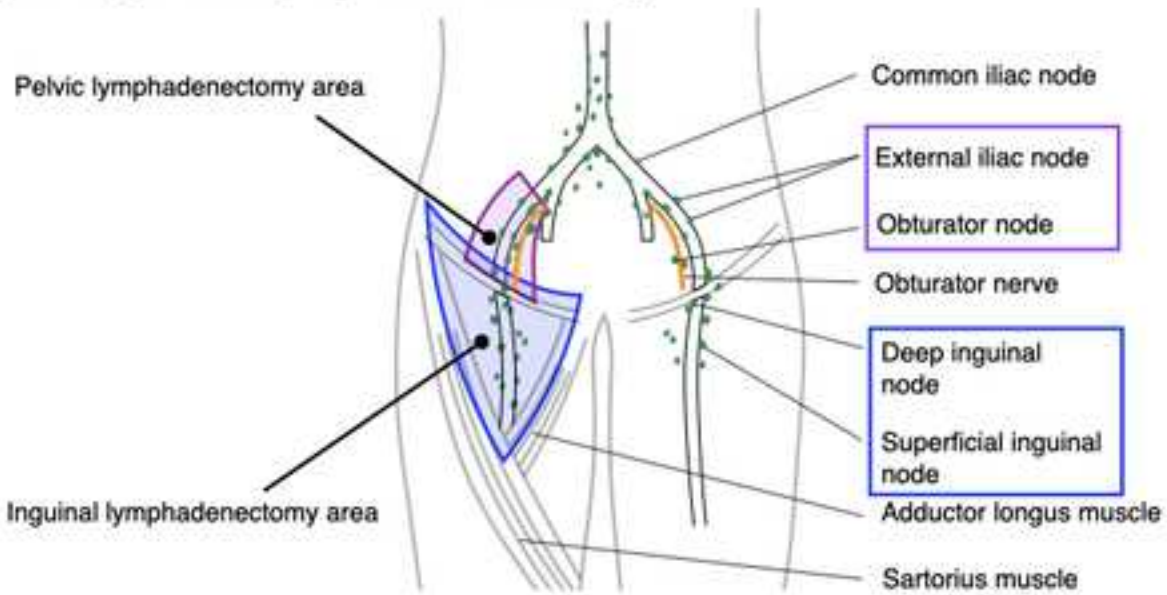


Fig. 1

Figure(s) 2

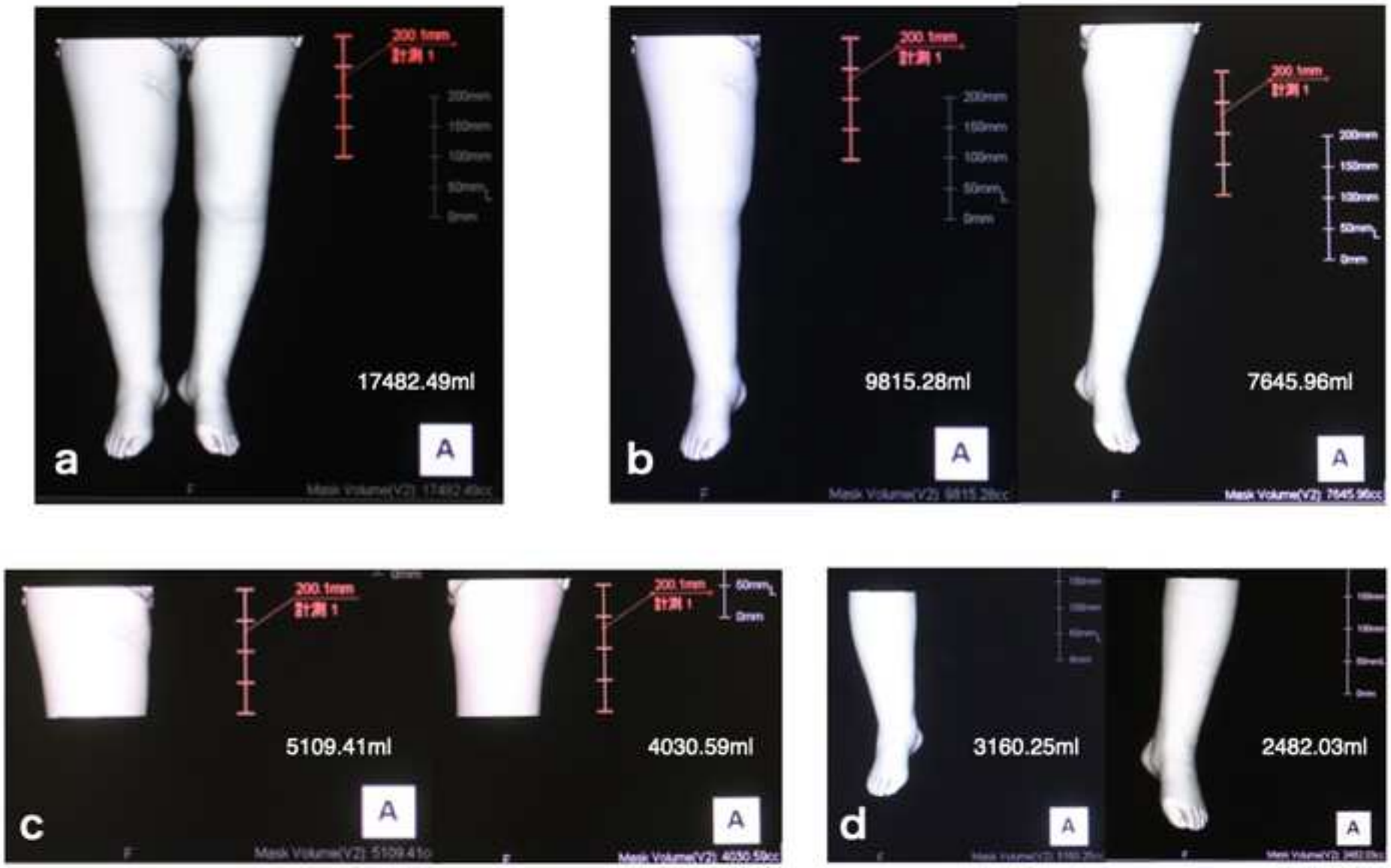


Fig. 2

Figure(s) 3

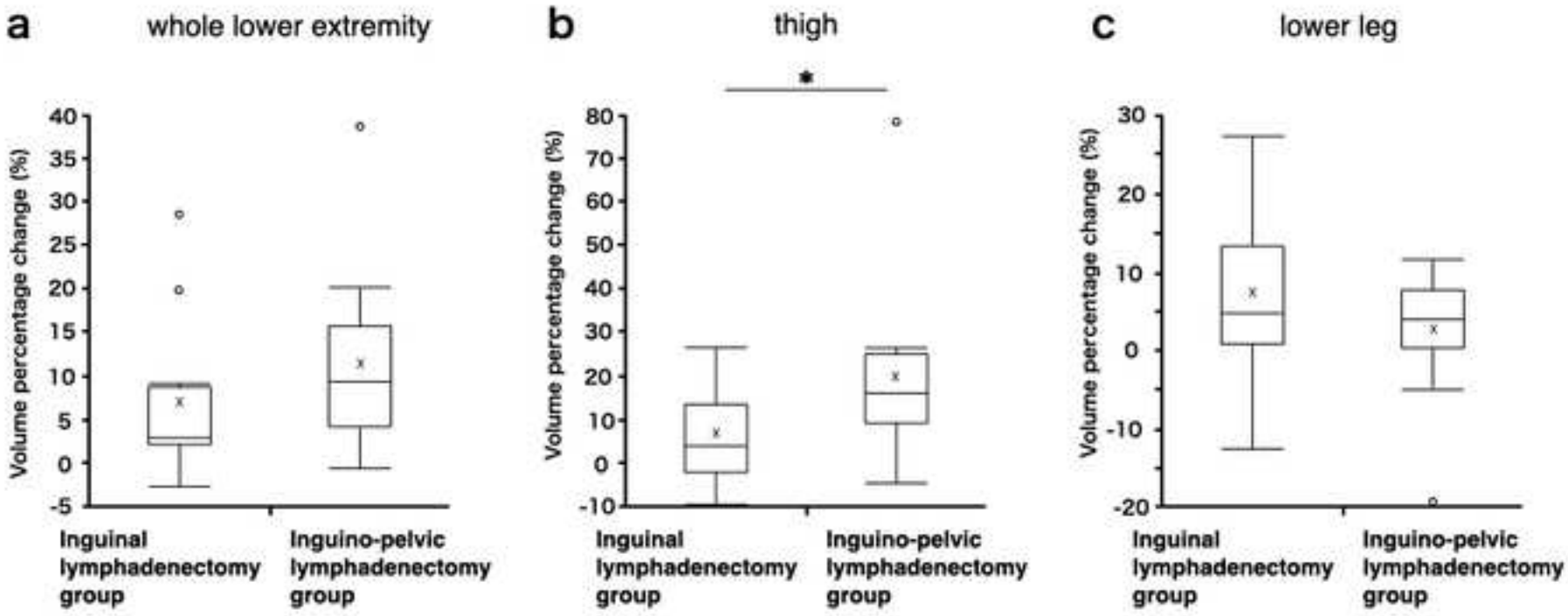


Fig. 3

Figure(s) 4

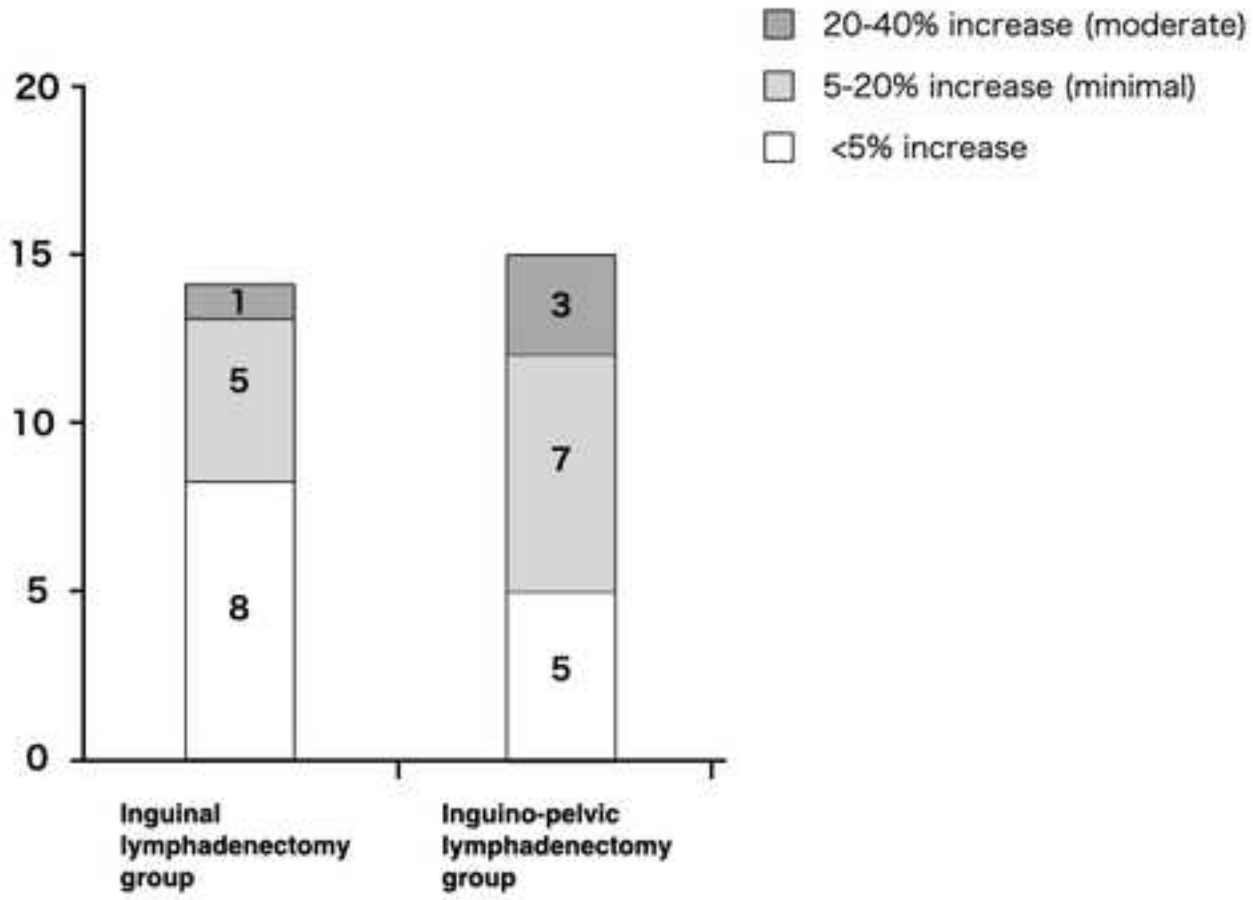


Fig. 4

Figure(s) 5

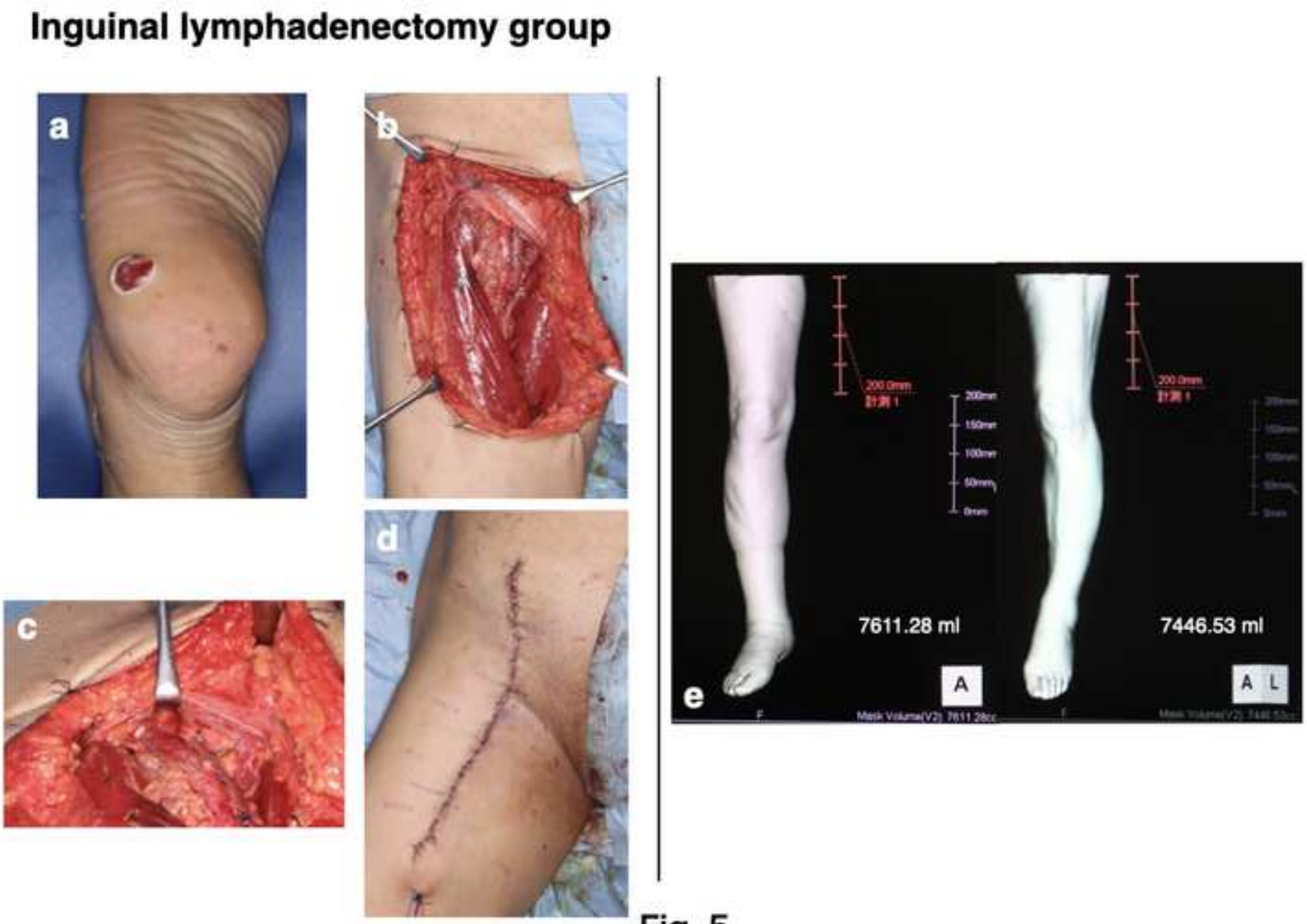


Fig. 5

Figure(s) 6

Inguino-pelvic lymphadenectomy group

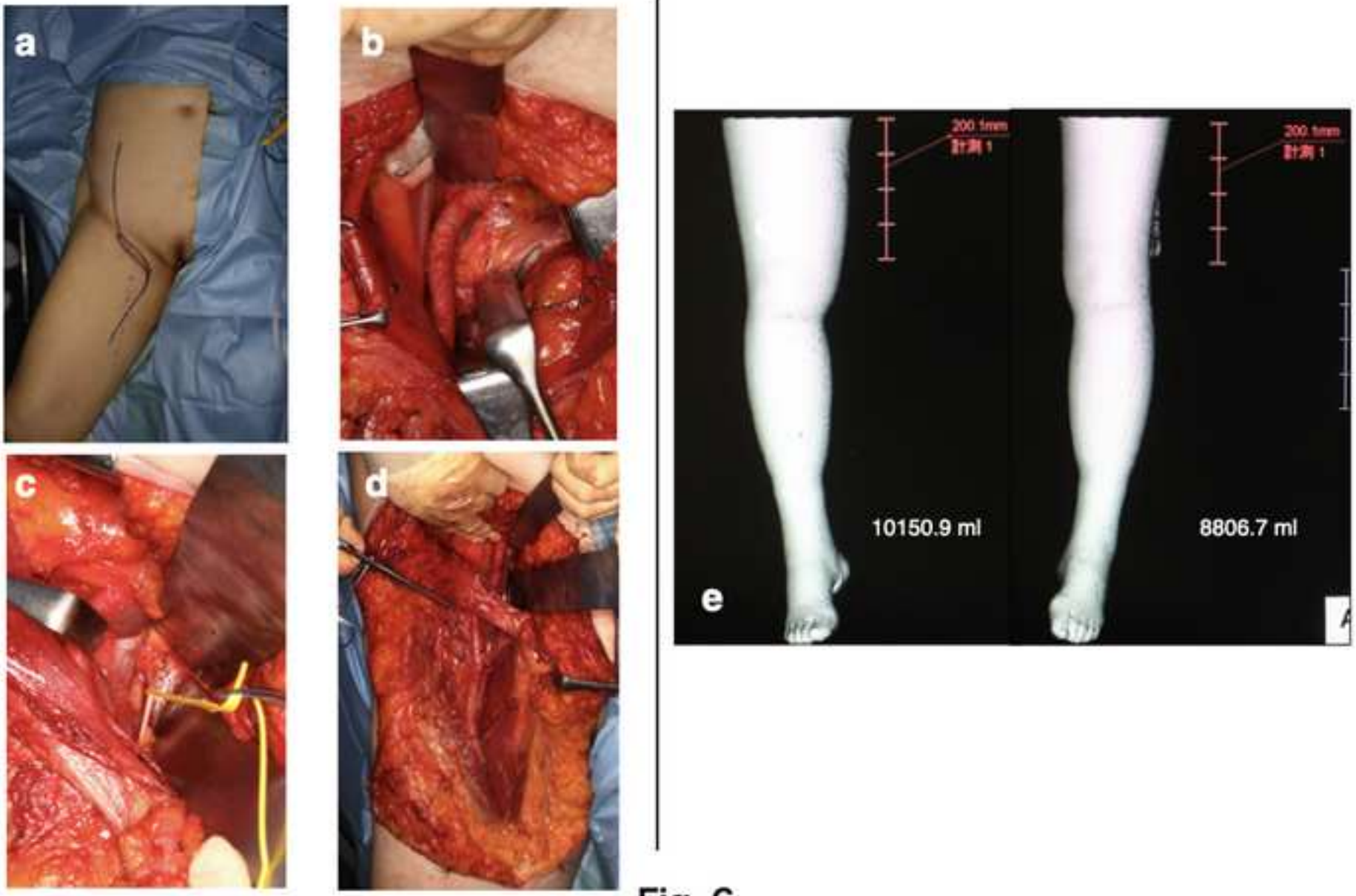


Fig. 6

Table(s)

Table 1. Patient characteristics

	Inguinal lymphadenectomy group	Inguino-pelvic lymphadenectomy group	p value
No. of patients	14	15	
Age, yr (Median (Range))	71 (56-84)	67 (17-85)	>0.05[a]
Male-to-female	9:5 (64%:36%)	7:8 (47%:53%)	>0.05[b]
Disease			
Melanoma	11	10	
SCC	1	4	
Invasive EMPD	1	0	
Porocarcinoma	1	0	
Sebaceous carcinoma	0	1	
No. of excised LNs			
Inguinal LNs (Median (Range))	13 (9-21)	14 (8-29)	>0.05[a]
Pelvic LNs (Median (Range))	–	12 (3-19)	
Total LNs (Median (Range))	13 (9-21)	24 (11-43)	<0.0001[a]

[a] Continuous data were compared using the t-test assuming unequal variances.

[b] Proportion was analyzed using Fisher's exact test.

SCC, squamous cell carcinoma; EMPD, extramammary Paget's disease; LN, lymph node

Lay summary

In patients with skin cancer of the lower extremity, worse severity of the leg volume in the whole lower extremity after lymphadenectomy was not observed in inguino-pelvic lymphadenectomy compared with inguinal lymphadenectomy, excluding postoperative radiation therapy and previous chemotherapy.