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Direct lymphangiography as treatment option of lymphatic leakage: Indications, outcomes and role in patient's management

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ABSTRACT

Background: To evaluate the effectiveness of lymphography as a minimally invasive treatment option of lymphatic leakage in terms of local control and to investigate which parameters influence the success rate.
Method: This retrospective study protocol was approved by the ethic committee. Patient history, imaging data, therapeutic options and follow-up were recorded and retrospectively analyzed. Between June 1998 and February 2013, 71 patients (m:w = 42:29, mean age, 52.4; range 42–75 years) with lymphatic leakage in form of lymphatic fistulas (n = 37), lymphocele (n = 11), chylothorax (n = 13) and chylous ascites (n = 10) underwent lymphography. Sixty-four patients (90.1%) underwent successful lymphography while lymphography failed in 7 cases. Therapeutic success was evaluated and correlated to the volume of lymphatic leakage and to the volume of the applied iodized oil.
Result: Signs of leakage or contrast extravasation were directly detected in 64 patients. Of 64 patients, 45 patients (70.3%) were treated and cured after lymphography. Based on the lymphography findings, 19 patients (29.7%) underwent surgical intervention with a completely occlusion of lymphatic leakage. The lymphatic leak could be completely occluded in 96.8% of patients when the lymphatic drainage volume was less than 200 mL/day (n = 33). Even when lymphatic drainage was higher than 200 mL/day (n = 31), therapeutic lymphography was still successful in 58.1% of the patients.
Conclusion: Lymphography is an effective, minimally invasive method in the detection and treatment of lymphatic leakage. The volume of lymphatic drainage per day is a significant predictor of the therapeutic success rate.

1. Introduction

Directly lymphography can visualize and prove the lymphatic origin of a detected fluid collection as seen in chylaskos, lymphocele, chylothorax or lymphatic fistula in the postoperative or posttraumatic patient [1,2]. With the help of diagnostic lymphography, allocation of lymphatic fistula is possible because the lymphatic vessels are difficult to visualize intraoperatively due to the small size and the perioperative sobriety [3]. Initial therapy favors conservative measures including drainage, total parenteral nutrition and pressure dressings. Nevertheless, such measures may sometimes take several weeks to control lymphatic leakage and may therefore lead to prolonged hospitalization. Surgical options are recommended if conservative therapy fails. However, surgical reinterventions are associated with a significantly higher morbidity. Using iodized oil for lymphography as contrast agent, this substance has the potential to induce granulomatous reactions when extravasating [4,5] which may be further assisted by additive conservative measures [6–9].

To our knowledge, experience with lymphography as a treatment option for lymphatic leakage is rare. In addition, the number of patients investigated in the existing studies was relatively small.

The intention of our study was to demonstrate the therapeutic impact of lymphography on the postoperative patient with known

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lymphatic leakage refractory to conservative therapy in a large patient population ($n = 64$).

2. Methods

2.1. Patient population

Between June 1998 and February 2013, 71 patients (29 women, 42 men, mean age, 52.4 years; age range 42–75 years) with lymphatic leakage underwent direct lymphography (47 monopedal, 24 bipedal). Sixty-four patients (90.1%) underwent successful lymphography while lymphography failed in the other 7 cases. The lymphatic leakage presented in form of lymphatic fistulas ($n = 37$), lymphocele ($n = 11$), chylothorax ($n = 13$), or chylous ascites ($n = 10$). The reasons for lymphatic leakage were as follows: prior inguinal lymphadenectomy for cutaneous malignant melanoma (47.9%, $n = 34$) or for Merkel cell carcinoma (4.2%, $n = 3$), pelvic lymphadenectomy for ovarian cancer (2.8%, $n = 2$), renal transplantation (14.2%, $n = 10$), radical prostatectomy (9.8%, $n = 7$), cystectomy (2.8%, $n = 2$), splenectomy (1.4%, $n = 1$), oesophagectomy (9.8%, $n = 7$), and gastrectomy (7.1%, $n = 5$).

The study protocol was approved by the local ethical committee. All lymphography procedures were performed with the written informed consent of the patient and in the absence of contraindications. The indication for lymphography was persisting lymphatic leakage, which was unlikely to be cured by conservative treatment only. Lymphography was performed if the lymphatic leakage has persisted for longer than 3 weeks. In cases of chylothorax or chylous ascites, lymphography was performed using a bipedal approach with evaluation of the thoracic duct. In cases of lymphatic fistula and lymphocele, monopedal lymphography was performed with identification of the pori of lymphatic vessels of the inguinal region or pelvis.

2.2. Lymphography procedure

After cutaneous disinfection of the feet (Kodan®, Schülke & Mayr GmbH, Norderstedt, Germany), we injected a mixture of 2 ml of mepivacainhydrochlorid (Scandicaine® 1%, Astra Zeneca GmbH, Wedel, Germany) and 2 ml of methylene blue dye (Patentblau V, Guerbet GmbH, Sulzbach, Germany) into the subcutaneous tissues of the first to the third interdigital spaces. After sufficient coloration of pedal lymphatic vessels, the patient was placed on

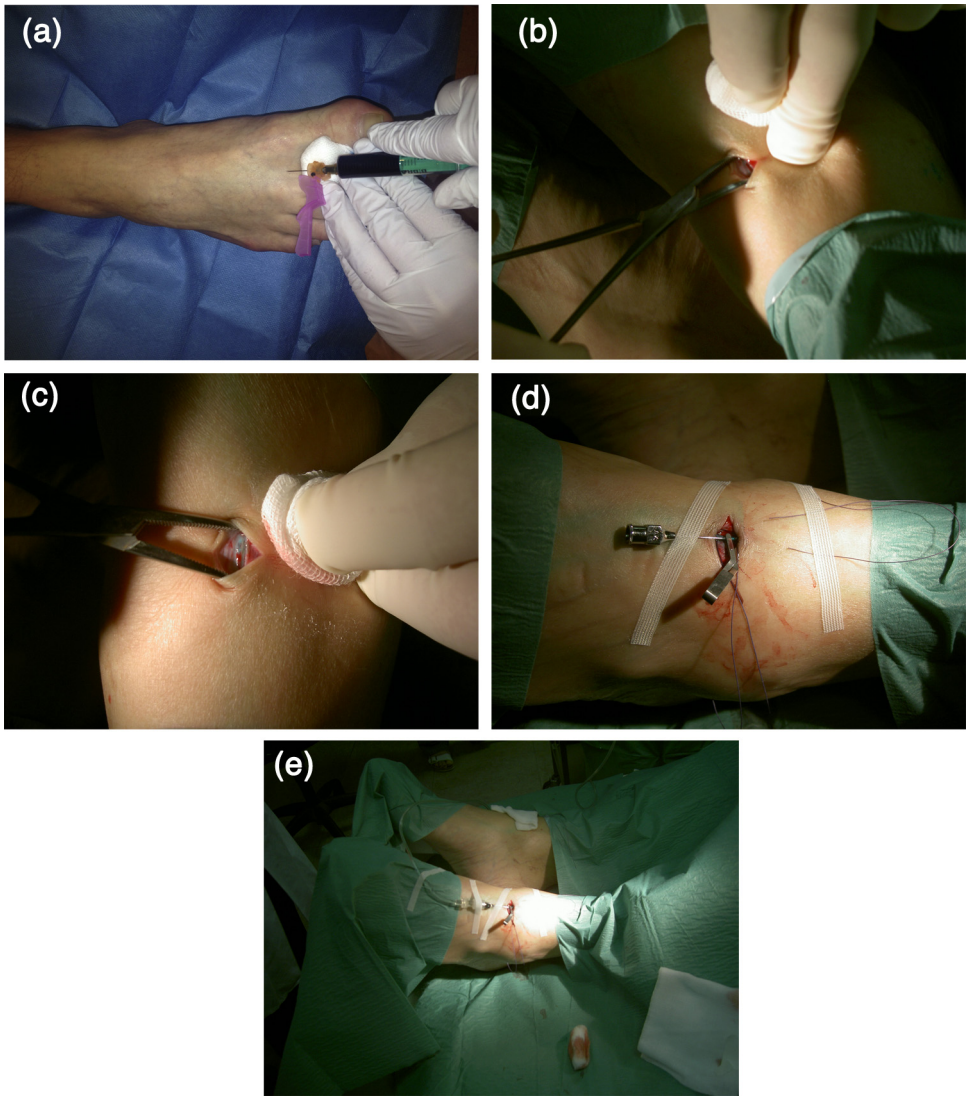

Fig. 1. Lymphography procedure. (a) After injection of a mixture of mepivacainhydrochlorid and methylene blue dye and sterile covering of the feet, a longitudinal cutaneous incision metatarsal near the ankle is exposed. (b) The best lymphathic vessel is found and prepared. (c) The lymphatic vessel is cannulated with the special needle (with spring and mandarin). The needle is then fixed with adhesive stripes. (d) The lmphatic vessel is ready for the injection of iodized oil. Needle and infusion line are connected and fixed with adhesive stripes.

an examination table of the X-ray radioscopic system (Siemens Axiom Artis MP, Siemens, Forchheim, Germany) in a supine position. After sterile covering of the feet (monopedal or bipedal) and subcutaneous injection of a local anesthetic (Scandicaine®), a longitudinal cutaneous incision metatarsal near the ankle was exposed. The adjacent tissues were stripped, thereby giving good access to the lymphatic vessel. The best lymphatic vessel visible was chosen and cannulated using a special needle with spring and mandarin. Needle and infusion line were fixed with adhesive stripes (Steri-Strip; 3M Health Care, St. Paul, MN). We injected lipiodol up to 1 ml/10 kg body weight per foot, not exceeding a total volume of 20 ml of iodized oil (48% iodinated glycerol ester, Lipiodol® Ultra-Fluid, Guerbet GmbH, Sulzbach, Germany), using an injector with an injection speed of 6–8 ml/h. An exploratory X-ray overview of the feet and legs was performed for documentation of the flow of the iodized oil in the lymph vessels and for exclusion of accidental venous injection. After the injection was completed, the injection materials were removed and the wound was cleansed and sutured. Sutures may be removed at post-interventional days 10–12. In cases of cutaneous lymphatic fistulas, the known cutaneous porus was identified using an X-ray absorbent marker prior to imaging. If the lymphatic leakage was not visible, about 24 h after the procedure unenhanced computed tomography was performed

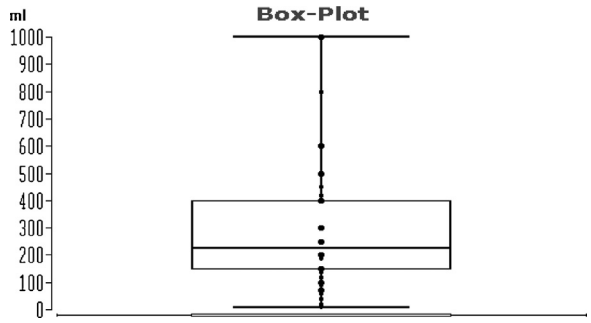

Fig. 2. The daily amount of drainage ranged between 10 ml and 1000 ml (mean, 300.4 ml).

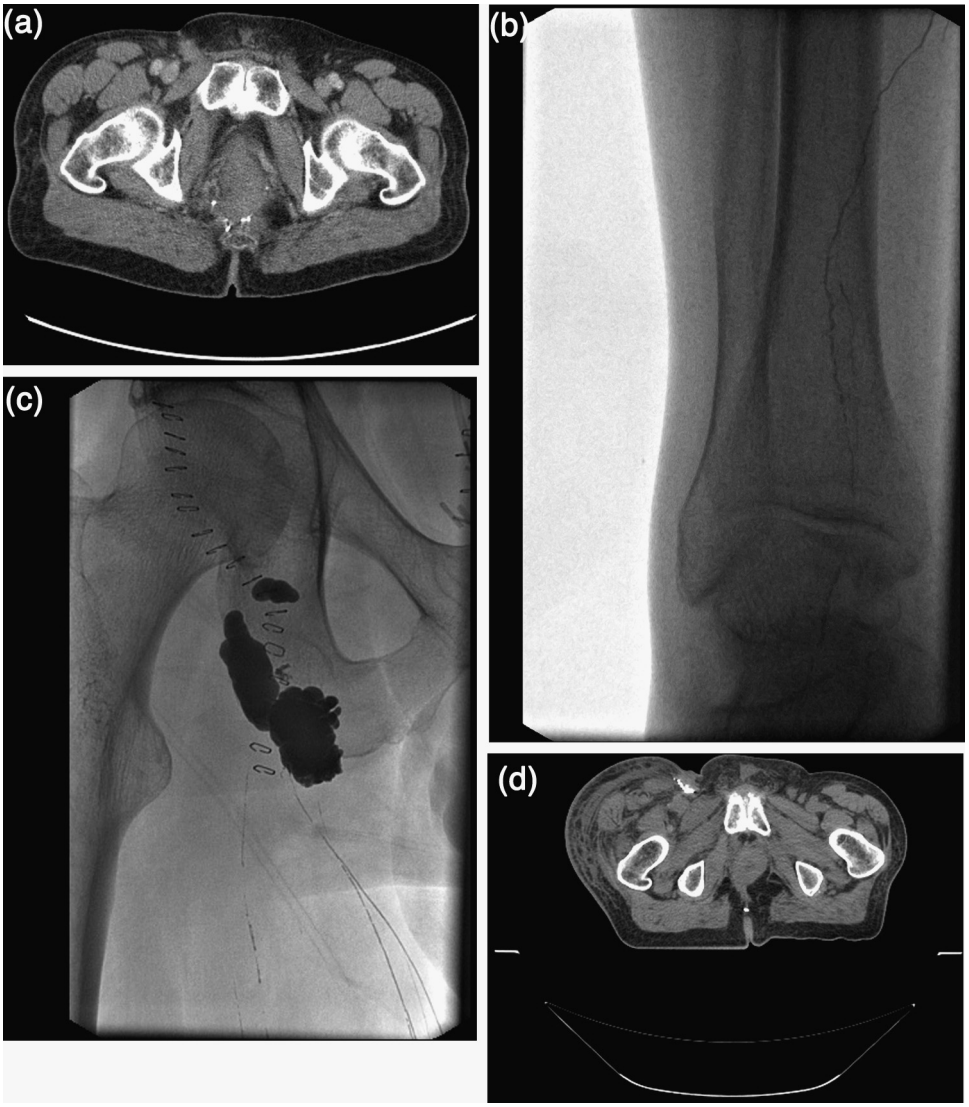

Fig. 3. A 54-year-old patient with lymphatic fistula after inguinal lymphadenectomy due to metastasis in lymph nodes from cutaneous malignant melanoma. The daily amount of drained lymph was 150 ml. Ten days after lymphography the lymphatic fistula was occluded. (a) CT of pelvis before lymphography. Documentation of the lymphatic fistula in the right inguinal region. (b) X-ray image documenting contrasted lymph vessels of the right feet after injection of iodized oil. (c) X-ray image documenting lymph leakage in the right inguinal region. (d) CT of the pelvis one day after lymphography. Documentation of lymphatic leakage.

for documentation of aggregation of iodized oil in the region of the leakage. Fig. 1 demonstrates the setup of a typical lymphography procedure.

2.3. Quantitative and statistical evaluation

Clinical and radiological data of all patients were retrospectively evaluated. Statistical assessment was performed as follows: the frequency of detecting the leakage site on post-lymphographic abdominal or chest radiograph and post-lymphographic CT images, the period of time between the day of lymphography and the day when lymphatic leakage disappeared, and whether surgical ligation was performed after lymphography. Therapeutic success was evaluated and correlated to the volume of lymphatic leakage and volume of injected iodized oil. All imaging and evaluations were performed by two radiologists (with more than 5 [T.G.] and 30 [V. J.] years of experience in lymphography) in consensus. Data were entered as events occurred. Statistical analysis was performed using statistical software (BiAs 8.3.6, Epsilon Verlag, Frankfurt, Germany).

3. Results

Between June 1998 and February 2013, 71 patients (m:w = 42:29, mean age, 52.4; range 42–75 years) underwent lymphography. Sixty-four patients (90.1%) underwent successful lymphography while lymphography failed in 7 cases. In these 7 cases, 3 patients had fragile lymphatic vessels and 4 patients suffered from lymphedema. Signs of leakage or contrast extravasation were directly detected in 64 patients. The mean duration of the lymphography procedure was 5.5 h (range: 2–8 h). The average amount of iodized oil used was 11.7 ml (range: 4–20 ml). After

Fig. 4. A 32-year-old patient with lymphatic leakage after lymphadenectomy. The daily amount of drained lymph was 800 ml. Documentation of the accumulation of iodized oil in the region of the lymphatic fistula and flow into the drainage.

lymphography, two patients had lipiodol in the pulmonary arteries (asymptomatic pulmonary embolism). A probable cause might be the proximity of the lymphatic leakage to the venous angle. Both patients suffered from chylothorax. No major complications were noted.

Based on the lymphography findings, 19 patients (19/64; 29.7%) underwent surgical intervention with a completely occlusion of lymphatic leakage. 45 of 64 patients (45/64; 70.3%) were cured after lymphography.

The daily amount of drainage ranged between 10 ml and 1000 ml (mean, 300.4 ml) (Fig. 2). The lymphatic leakage was completely occluded in 96.8% of the patients with a lymphatic drainage volume of less than 200 mL/day ($n = 33$) (Fig. 3). Even when the lymphatic drainage was higher than 200 mL/day ($n = 31$), therapeutic lymphography was successful in 58.1% of the patients. The lymphatic leakage persisted for between 10 days and 4 weeks after lymphography was performed. There was not any recurrence of lymphatic leakage after occlusion by lymphography during follow-up (range, 1–24 months) (Fig. 4).

Therapeutic success was correlated to the volume of lymphatic leakage and to the volume of the administered iodized oil. Analysis using the Wilcoxon–Mann–Whitney test demonstrated that the therapeutic effect of lymphographywas not directly correlated with the volume of applied iodized oil ($p = 0.488$). However, the volume of lymphatic drainage per day was a significant predictor of the therapeutic success rate ($p = 0.002$).

4. Discussion

The application of lymphography for the detection of lymphatic leakage is well established. Lymphography is helpful to visualize the anatomy of lymphatic vessels of the treatment-relevant region and the leakage site for preoperative planning of fistula occlusion [10,11]. Furthermore, lymphography itself is an effective, minimally invasive method not only for the detection but also for treatment of lymphatic leakage [10,12]. Recent studies show that magnetic resonance (MR) lymphography is a promising approach to identify specific features of lymphatic vessel leakage, but MR lymphography as a treatment option of lymphatic leakage cannot be possible [13–15].

In our present study, we investigated the effectiveness of lymphography as a treatment option for lymphatic leakage refractory to conservative therapy in a larger patient population ($n = 71$). Our results show that 70.3% of patients in our study were cured after lymphography. Only 29.7% of the patients underwent surgical intervention with a completely occlusion of lymphatic leakage. However, our results indicate that the volume of lymphatic drainage per day is a significant predictor of the therapeutic success rate ($p = 0.002$). The lymphatic leakage could be completely occluded in 96.8% of patients if the lymphatic drainage volume was less than 200 mL/day ($n = 33$). Even in case lymphatic drainage was higher than 200 mL/day ($n = 31$), therapeutic lymphography was still successful in 58.1% of the patients.

In a study by Kos et al. [12], 22 patients underwent lymphography. 73.3% of the reported patients had an occlusion of the postoperatively damaged lymphatic vessel and did not undergo surgery after lymphography. The results of Kos et al. almost coincide with our study results, in which 70.3% of patients were cured after lymphography.

In a similar study of Matsumoto et al. [10], 9 patients with various lymphatic leakages underwent lymphography. In 8 of the 9 patients (89%), lymphatic leakage was stopped after lymphography, and surgical re-intervention was avoided. No cases showed a recurrence of lymphatic leakage during follow-up (range, 1–54 months). In comparison, 70.3% of the patients in our study showed an occlusion of lymphatic leakage after lymphography. In the study of Matsumoto et al., the occlusion rate was higher than in our study, but in our study, more lymphography procedures were performed ($n = 71$). However, the results of several prior studies have shown that lymphography is effective not only for diagnosis but also as treatment for various lymphatic leakages [10–12]. Early lymphography is therefore recommended for patients with lymphatic leakage who are unlikely to be cured by conservative treatment only [10]. In therapy refractory lymphatic leakage, direct lymphography is a relevant treatment option.

Limitation of the current study is its retrospective design. However, we considered the current work as a base for further prospective studies.

5. Conclusion

In summary, our results indicate that lymphography is an effective, minimally invasive method for the detection and treatment of lymphatic leakage. The volume of lymphatic drainage per day is a significant predictor of the therapeutic success rate.

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