Lymphatic Interventions for Treatment of Chylothorax

Interventionen am Lymphsystem zur Behandlung des Chylothorax

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Abstract

Purpose: To determine effectiveness of lymphatic interventional procedures for treatment of chylothorax.

Material and methods: Analysis of interventions performed from 2001 to 2014.

Results: In 21 patients with therapy resistant chylothorax a lymphatic radiological intervention was attempted, which could be performed in 19 cases: 17 thoracic duct embolizations (15 transabdominal, one transzervical and one retrograde transvenous procedure), 2 percutaneous destructions of lymphatic vessels, one CT-guided injection of ethanol next to a duplicated thoracic duct. Fourteen of seventeen (82.3 %) of the technically successful embolizations lead to clinical cure. This encluded three patients with prior unsuccessful surgical thoracic duct ligation. Also the injection of ethanol was clinically effective. Complications were a bile peritonitis requiring operation, and one clinical deterioration of unknown cause.

Conclusion: Interventional lymphatic procedures allow for effective treatment in many cases of chylothorax, and should be considered early during treatment.

Key points:
- Thoracic duct embolization is an effective treatment method for chylothorax.
- If embolization is impossible, percutaneous lymphatic destruction or injection of sclerosants/tissue adhesive next to the thoracic duct may be tried

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Zusammenfassung

Ziel: Analyse der Ergebnisse radiologisch-interventioneller Eingriffe am Lymphsystem zur Chylothorax-Behandlung.

Material und Methoden: Auswertung der seit 2001 – 2014 durchgeführten Eingriffe hinsichtlich Durchführbarkeit, Effektivität und Komplikationen.

Ergebnisse: Bei 21 Patienten mit therapieresistentem Chylothorax wurde eine interventionell-radiologische Behandlung versucht, die in 19 Fällen durchgeführt werden konnte. Vorgenommen wurden 17 Ductus thoracicus-Embolisationen (15 transabdominell, eine transzervikal, eine retrograd transvenös), 2 Lymphbahndestruktionen sowie eine CT-gesteuerte Injektion von Äthanol bei einer Ductus thoracicus-Dopplung. Vierzehn der siebzehn (82,3 %) technisch erfolgreichen Embolisationen des Ductus thoracicus führten zur Ausheilung des Chylothorax; drei dieser Patienten waren erfolglos voroperiert. Ebenfalls sistierte der Chylothorax nach der Äthanolinjektion an einen gedoppelten Ductus thoracicus-Arm. Relevante Komplikationen waren eine operationspflichtige gallige Peritonitis, sowie eine Befundverschlechterung unklarer Ursache.

Schlussfolgerung: Interventionell-radiologische Eingriffe am Lymphsystem erlauben in vielen Fällen eine effektive Chylothorax-Behandlung und sollten differenzialtherapeutisch, wenn verfügbar, stets in Erwägung gezogen werden.

Introduction

In addition to conservative and operative therapy, interventional radiological methods have become established in recent years for the treatment of chylothorax [1 – 4]. Apart from the placement of a TIPS in cirrhosis-related chylothorax, these tend to be rarely performed, less widely available and less well-

known interventions. Therefore, we report our experience with interventional measures in the lymphatic system in the treatment of therapy-resistant chylothorax.

Materials and Methods

Patient collective

Since 2001, we have attempted interventional radiological chylothorax treatment in 21 patients (8 men, 13 women, age 38 to 75 years).

Chylothorax was traumatic/postoperative in 17 cases (esophageal/gastric resection [7], thyroid resection (1), mitral valve replacement (1), aortic replacement in Marfan syndrome (1), aortocoronary bypass (2), lobectomy (3) or pneumonectomy (2)); lymphangioleiomyomatosis was seen in one patient, one patient had AIDS with Kaposi's sarcomas, one patient had a lymphoma, and one patient had Schimmelpenning syndrome.

In 15 cases the chylothorax was on the right side, in 4 cases it was on the left side, and in 2 cases it was on both sides.

Conservative treatment was unsuccessful in all patients. This included placement of a chest tube, a medium-chain triglyceride diet and possibly parenteral nutrition, and also administration of somatostatin/octreotide in 7 patients. The subsequent surgical treatment (performed twice in one case) was unsuccessful in three cases.

The daily chyle/lymph output was between 800 ml and 3000 ml.

Technical procedure

The first 7 interventions were performed under local anesthesia and the rest were done under general anesthesia.

The procedure has already been described multiple times in detail [1, 5 – 7]. In principle, the abdominal and thoracic lymphatic vessels are initially visualized by lymphographic injection of Lipiodol Ultra Fluid (Guerbet) (amount of contrast agent applied up to approx. 40 ml, usually 25 – 30 ml), with contrast injection on one side being sufficient in 16 cases. Injection was performed manually in our patients and the flow rate was approx. 8 ml/h.

The ascending contrast agent is followed by intermittent fluoroscopy. If a large lymphatic vessel that is suitable for puncture is identified in the upper abdomen (ideally a cisterna chyli), transabdominal puncture is performed with a fine needle (0.7 mm diameter, length of 22 cm, e. g. manufactured by Cook). A guide wire (e. g. Transend-18, Boston Scientific) is then inserted so that a microcatheter (e. g. Renegade Hi-Flo, Fa. Boston Scientific) can be introduced (**Fig. 1 – 4**). The local conditions are then visualized by injecting a water-soluble non-ionic contrast agent (Iopromid, Ultravist 300, Bayer) via the catheter.

Starting from a verified or suspected leakage site, microspirals (e. g.: VortX-18, Complex Helical 18, Boston Scientific) are placed in the thoracic duct in a distal direction. These serve as a scaffold for the subsequently injected tissue adhesive (N-butyl cyanoacrylate, Histoacryl, Braun). The tissue adhesive is injected after the catheter is rinsed with a 40 % glucose solution during careful continuous retraction of the catheter so that the catheter does not become accidentally fixed and the duct is sealed over a long stretch ideally including the entry point into the lymphatic vessel used for access.

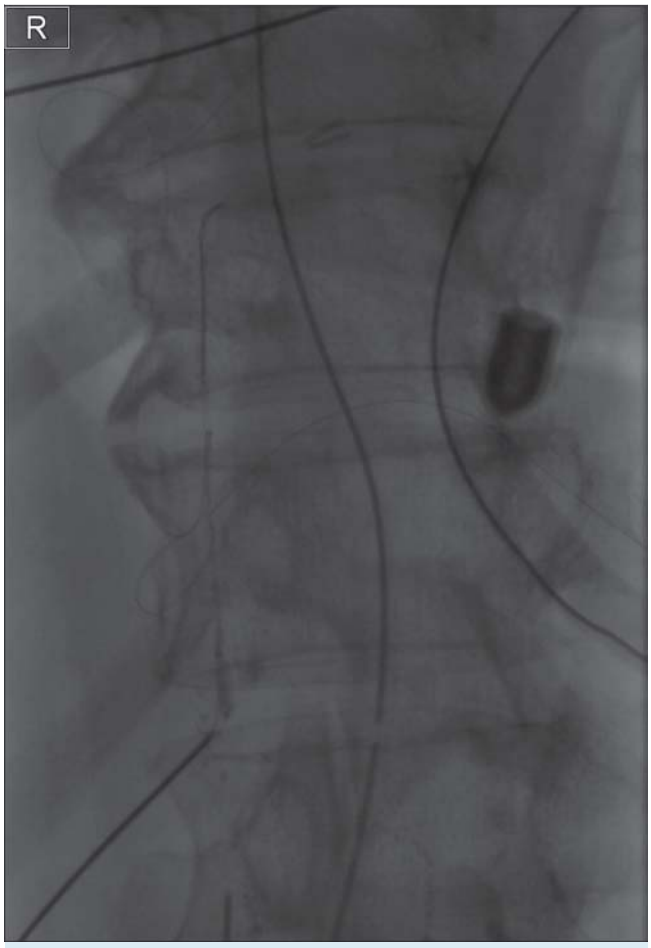

Fig. 1 Puncture of a thoracic duct and coaxial insertion of a microwire.

Undiluted tissue adhesive can be injected. However, an initial mixture with Lipiodol in a ratio of 1:1 is recommended. Injection volume is titrated according to the (very varied) volume capacity of the thoracic duct and was between almost two and five milliliters.

After removal of the catheter, patients remained in bed until the following day. CT of the thorax and upper abdomen (Philips MX 8000 IDT, Philips Brilliance 64) was then performed to document the local conditions to serve as a baseline finding for any further follow-ups. CT was performed immediately if complications were suspected in the peri- or postinterventional follow-up.

Routine peri-interventional antibiotic prophylaxis was not performed.

If transabdominal lymphatic vessel intubation was not possible, alternative interventions were performed:

- Destruction of the prevertebral lymphatic vessels by puncturing them multiple times with a fine needle (diameter 0.7 mm, length 22 cm, manufactured by Cook) and, if feasible, also scratching them slightly. This may seal the lymph leak via the resulting local hematoma and scarring.
- CT-guided injection of 6 ml of 70 % alcohol as a sclerosing agent at the left-sided portion of a duplicated thoracic duct (the right main branch was transabdominally occlu-

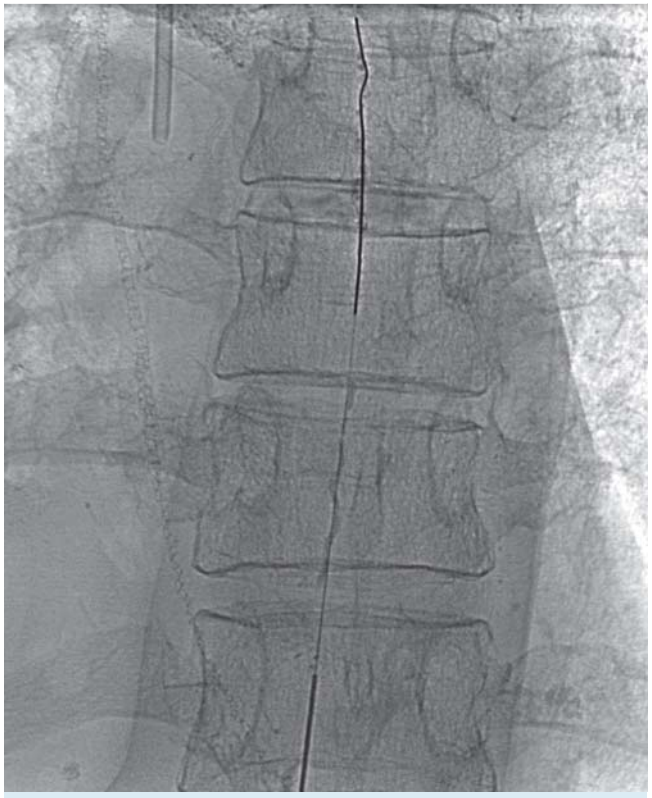

Fig. 2 An embolization spiral is pushed into the upper thoracic duct via a microcatheter.

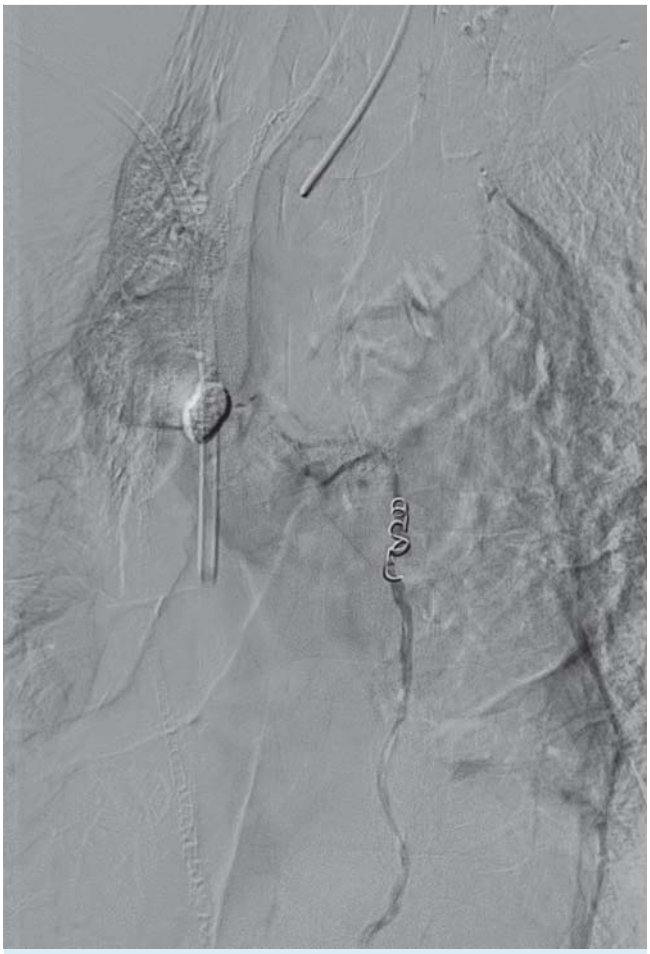

Fig. 3 Patient with lymph leak after pneumonectomy. A microspiral was already placed below the leak site.

ded which was not clinically successful even though the chylothorax was on the right side)
- Transvenous retrograde intubation of the thoracic duct [8].
- Direct percutaneous puncture of the cervical thoracic duct

After the intervention, our patients usually received parenteral nutrition for two days before gradually returning to normal food.
The chyle/lymph output via the drains was recorded before and after the intervention.

Results

Sufficient lymphatic vessel visualization was not possible in two patients (one patient with HIV-related lymphoma and one multimorbid patient with pronounced leg edema).
The following procedures were performed in the 19 treated patients:
- 17 thoracic duct embolizations (15 transabdominal, 1 transcervical, and 1 retrograde transvenous)
- 2 lymphatic vessel destructions
- 1 CT-guided injection of ethanol at the left main branch of a duplicated thoracic duct after the right main branch was occluded by transabdominal embolization, which was however not clinically sufficient despite the right-sided chylothorax.

The interventions were clinically successful in 15/19 (78.9 %) patients.

14 of the 17 (82.3 %) technically successful embolizations of the thoracic duct resulted in clinical cure of the chylothorax. The postoperative chylothorax was also successfully treated in the patient who received an injection of ethanol next to the left-sided duct portion following an insufficient response to transabdominal embolization of the right main branch of the thoracic duct.
The intervention was not clinically successful in one of the two patients with lymphatic vessel destruction. Nothing is known about the course in the other patient.
The intention-to-treat analysis thus yields a success rate of 15/21 (71.4 %).
The lymph/chyle output via the drains stopped in some cases shortly after the intervention and in some cases only over the course of 5 – 7 days.
Minor postinterventional pain for approx. two days was described in almost all patients with transabdominal accesses. This is to be viewed as a side effect rather than as a complication and responded well to conventional pain medication. Persistent and progressive pain was observed in one patient who developed bile peritonitis that had to be treated surgically.
We observed worsening of the clinical situation as a further intervention-associated complication in a patient with pulmonary lymphangioleiomyomatosis. After clinically successful thoracic duct occlusion, increased and faster chyle accu-

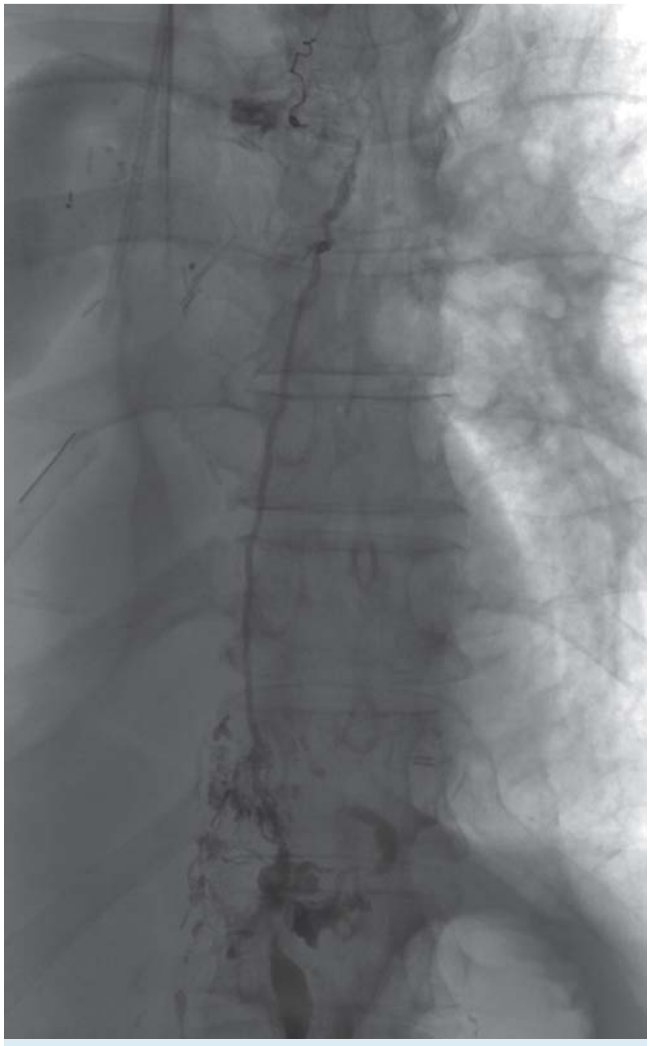

Fig. 4 Final follow-up after thoracic duct embolization. A microspiral was implanted cranially in the thoracic duct. The duct was completely filled with Lipiodol-marked Histoacryl. A large cisterna chyli is visible at the lower edge of the image.

mulation in the pleural space compared to the initial finding was seen. This results in a complication rate of 2/19 (10.5 %). The method-associated mortality was 0 %. However, one patient with Marfan syndrome died of a rerupture of the aorta within 30 days after uncomplicated thoracic duct embolization. In this patient the successfully treated chylothorax occurred as a result of an aortic replacement.

Discussion

A leak of thoracic lymphatic vessels, usually of the thoracic duct, can result in accumulation of chyle in the pleural cavity. By etiology, traumatic (nowadays most frequent) chylothoraces are to be differentiated from non-traumatic chylothoraces. [3, 4, 9].

Initial treatment is usually conservative. This includes drainage of the effusion as well as a medium-chain triglyceride diet, or complete parenteral nutrition. In addition, the administration of somatostatin/octreotide can be considered but their effectiveness is controversial [4]. The goal of conservative measures is to reduce the lymph flow so that a lymph leak site can spontaneously close.

If this is not successful, more invasive measures, such as pleurodesis or surgery, are necessary. Today usually open or thoracoscopic ligation of the thoracic duct is performed. The main problem of operative duct ligation is its intraoperative identification and the recognition of any variants. Therefore, it can occur that a lymphatic vessel is ligated but the chylothorax persists [4].

Percutaneous embolization of the thoracic duct was developed as an alternative to surgical duct ligation [1, 2]. For the procedure, abdomino-thoracic lymphatic vessels are visualized with lymphography by injecting oily contrast agent (Lipiodol Ultra Fluid, Guerbet). If a lymphatic vessel with a diameter that allows puncture and that seems suitable for intubation with a microcatheter is seen in the upper abdomen, it is punctured under fluoroscopy (CT guidance has also been reported) with a fine needle; afterwards a microcatheter is introduced over a coaxially inserted guide wire. Direct transabdominal or transhepatic access is possible. We prefer the transabdominal approach [3, 11, 12].

Thoracic duct embolization can also be successful after unsuccessful surgery, as we experienced in three of our patients. [3]. We cured a chylothorax in three patients wirth ihtorax gree.

On the other hand, intubation of the thoracic duct is not always feasible (17/21 (80.9 %) of our cases). The main cause for failure are anatomical variations; i. e., there is no lymphatic vessel suitable for puncture or no cisterna chyli in almost one third of cases [11, 13 – 15].

In such a case surgical treatment can still be possible and effective.

However, before surgery other forms of interventional treatment can also be attempted in these cases. If there is no larger abdominal lymphatic vessel that can be intubated but rather multiple smaller prevertebral lymphatic vessels can be identified, an attempt can be made to damage them mechanically e. g. via repeat puncture or "scratching". The resulting scarring can cause a decrease in lymph output and ultimately closure of the lymph/chyle leak [11, 13, 16].

The technical success rate of lymphatic vessel destruction is specified as up to 72 % [17] but is usually significantly lower [9, 11] thus making it substantially lower than that of direct embolization. If intubation and embolization of the thoracic duct are successful, success rates of up to 90 % are achieved [3, 6, 7, 9]. We treated only two patients by lymphatic duct destruction. In one patient this procedure was unsuccessful, the other patient was lost to follow up.

In selected cases, direct non-transabdominal duct puncture can be helpful, e. g. in cervical leaks, or transvenous retrograde duct intubation may be successful [8]. Regardless of the access path, the principle approach in duct occlusion is the same.

CT-guided percutaneous injection of sclerosing agents or tissue adhesives next to lymphatic vessel, may also be perfomed, and reduce the lymph flow via the resulting scarring or adhesive occlusion. This was successfully performed in one patient. Compared to thoracic duct embolization the experience with such procedures is however very limited.

The success of thoracic duct embolization depends not only on anatomical conditions but also on the underlying disease and output rate. In general, post-traumatic/postoperative

chylothoraces can be treated with greater success [3, 9]. For example, a lymph leak caused by tumor arrosion is less effectively stopped and is not healed by occlusion of upstream lymphatic vessels.

For approximately two days after transabdominal intervention, mild but regressive upper abdominal pain is normal and is therefore to be considered a side effect rather than a complication. However, it is important to ensure that this (mild!) pain does not persist or worsen.

Peri-interventional complications of thoracic duct embolization are reported in 0 – 6.7 % of cases [3, 9, 16]. Among other things, asymptomatic pulmonary embolisms caused by dislocated tissue adhesive, a contralateral chylothorax, chylous ascites due to insufficient occlusion of the access path, a perihepatic hematoma, and a bile leak in two patients with a transhepatic access path were described [3, 9, 12, 17, 18]. We observed complications in 2 of our 19 (10.5 %) patients. Bile peritonitis was seen in one patient. In this patient the transabdominal access path ran through the gallbladder in an extremely adipose patient. While the exit point of the transcystic access path closed sufficiently, bile seeped out of the catheter insertion site at the gallbladder and necessitated surgical intervention.

In one patient with lymphangioleiomyomatosis, the clinical situation worsened after successful uncomplicated duct embolization. The reason was unknown. Altogether despite the unusual access path, thoracic duct embolization is a rather safe procedure.

The lymph/chyle drainage does not stop immediately after successful intervention. This can take several days. The lymphatic vessel may only become completely occluded after a few days, also it takes some time for existing lymph accumulations to be drained. However, the end result is achieved after approx. 5 – 7 days.

Swelling of the legs (8 %) and diarrhea (12 %) were reported as late complications of percutaneous thoracic duct occlusion as determined by a follow-up after an average of 34 months [19]. However, these complications are not specific for the percutaneous approach but are also observed after surgical duct ligation.

After lymphography alone a lymph leak can close over the course of days to weeks and a chylothorax can heal without further intervention [20]. However, the success of the measure is difficult to predict and decreases with more pronounced output of a lymph/chyle fistula. In the case of more than 500 ml/d, success was reported in only approx. one third of patients [22].

In light of the more successful and more reliable options, lymphography alone is only rarely indicated for the treatment of a chylothorax nowaydays. On the other hand, it is an integral part of percutaneous lymphatic interventions. Such interventions should be included early in differential-therapeutic considerations in the case of a treatment-resistant chylothorax. According to current data, these interventions have a lower morbidity compared to surgical treatment and deaths have not yet been reported [3, 4, 14 – 17]. When technically feasible, they definitely represent an alternative to surgery [23] and can achieve successful treatment of a chylothorax even after unsuccessful surgical attempts.

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