

## The Clinical Significance of Lympho-Venous Anastomoses in Malignant Disease

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### Summary

Pedal lymphangiography has revealed lympho-venous anastomoses (LVA) in 62 patients with malignant disease. The LVAs were caused by obstruction of lymph flow and the obstruction was secondary to surgery in 23 patients, abnormal lymph nodes in 16 and a combination of surgery and abnormal nodes in 14. In 16 patients the LVA led to portal radicals giving opacification of the liver.

Chest X-ray examination was normal in 41 patients. In 5 patients the initial chest examination was normal, but lung metastases or widening of the mediastinum developed 1-5 years later. Twelve patients had lung metastases or widening of the mediastinum at the time of the diagnosis of LVA.

Clinical follow-up was available in 47 patients, of whom 30 died 1-60 months after diagnosis of LVA.

It is concluded that the prognosis of a patient with LVA is poor, provided the cause is not a negative lymph dissection or an unrelated surgical procedure. In patients with pathological lymph nodes the presence of LVA indicate an advanced involvement. Relatively few patients with LVA had or developed lung metastases indicating that the biology of the tumor and the patient is more important than LVA to develop lung metastases.

Lympho-venous anastomoses (LVA) are normally present in lymph nodes of animals as well as in man. They are seldom demonstrated by lymphangiography, and then only in case of obstruction of the lymph flow. The obstruction may be due to lymph node metastases, previous surgery, inflammatory or infectious disease.

The clinical significance of LVA, demonstrated by lymphangiography is not well known. It has been suggested that in malignant disease the risk of lung metastases is increased if a LVA is demonstrated (1, 2, 3, 4) and that the prognosis of these patients is poor (5).

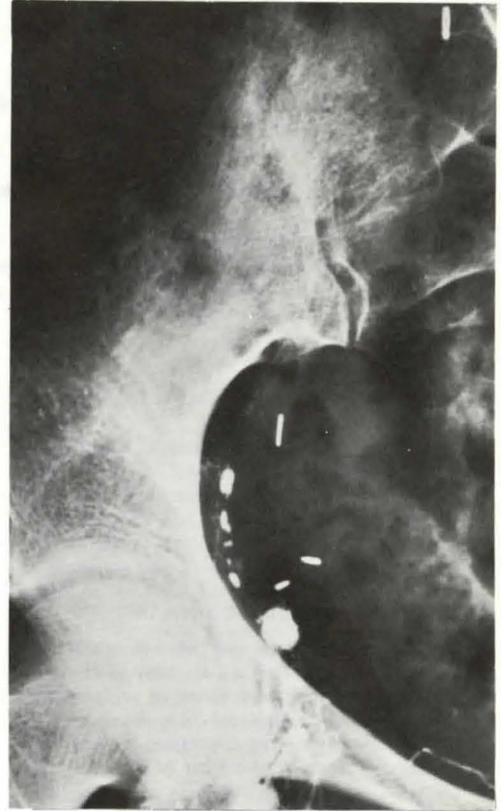
The present report will account for our experience of LVA demonstrated by pedal lymphangiography in patients with malignant disease. Special interest has been devoted to the cause of LVA, incidence of lung metastases, incidence of extremity edema and survival.

### Methods

Pedal lymphangiography was performed according to a technique previously described (6). Soon after the start of injection of contrast medium, films were obtained of the inguinal and pelvic areas during injection. These films were taken after the injection of 2-5 cc of Ethidol on each side, or until the lymph vessels of the pelvis and para-aortic regions were opacified.

### Material

The material was collected from lymphograms performed from January 1969 to May 1977. Clinical information was collected from the patient files. The material consists of 42 females aged 26-74, mean 51 and 20 males, aged 16-71, mean 41. The primary tumors of the females were: carcinoma of the cervix 22, ovary 5, vagina 2, urethra 1, uterus 1,



**Fig. 1** The patient is a 39 year old female, who at the age of 35 was operated on with hysterectomy and lymph node extirpation because of carcinoma of the cervix. At operation metastasis was found in one lymph node. Repeat lymphangiography was

performed because of obstruction of the left ureter and suspected recurrence. A) In the right iliac region multiple "pearls" of Ethiodol are seen in veins during injection. B) After completed injection the veins are empty of contrast medium

malignant melanoma 2, unknown primary 2, non-Hodgkin lymphoma 6, and Hodgkin lymphoma 1. The primary tumors of the males were: carcinoma of testicle 9, prostate 2, scrotum 1, bladder 1, non-Hodgkin lymphoma 2, and Hodgkin lymphoma 5.

### Results

The lymphangiographic contrast medium (Ethiodol) has a characteristic appearance in blood vessel with collections of small droplets (Fig. 1). The LVAs led to inguinal and/or pelvic veins in 54 patients, to para-aortic or paravertebral veins in 5 and into veins in the middle or distal end of the extremity in 3.

In all patients an obstruction of the lymph flow, either general or local was apparent, giving rise to the LVA. In 3 patients, however, the LVAs were located in the extremity, one due to local trauma and the others of obscure origin probably disease or previous surgery in pelvic nodes.

The obstruction of lymph flow was secondary to surgery in 23 patients, and in these there were no lymphangiographic evidence of lymph node metastases or lymphoma. The LVA was secondary to pathologic lymph nodes in 22 patients, 16 with metastatic disease and 6 with lymphoma, apparent on the lymphangiograms. In 14 patients, 8 with metastatic disease and

6 with lymphoma there were previous surgery and also pathologic lymph nodes and it was not possible to exactly establish the reason for the LVA.

The surgical procedures previously performed were lymph node dissection in 20, lymph node biopsy in 7, hysterectomy and/or salpingo-oophorectomy in 9 and inguinal varices operation in 1.

The time between operation and the lymphangiographic diagnosis of LVA was one month to 20 years. In 16 patients, 14 females and 2 males the LVA led to a portal radical and caused opacification of the liver. Chest radiographs at the time of lymphangiography was available in 58 patients and missing in 4. Of 14 patients with lymphoma, 8 had a normal chest radiogram, while 3 had widening of the mediastinum or pulmonary nodules. In 2 patients the initial examination was normal but widening of the mediastinum appeared 1 and 5 years later. Information concerning chest radiography was missing in one patient with lymphoma. Of the remaining 44 patients, 33 had a normal chest examination, 9 had lung metastases and information was missing in 2. In 3 patients the initial examination was normal, but lung metastases developed 1, 3 and 5 years later.

The patients with lung metastases developed their LVA secondary to surgery in 6, metastatic lymph nodes in 2 and the combination of surgery and metastases in 1. Of those 3 patients who later developed lung metastases 2 got the LVA secondary to surgery and one to surgery and lymph node metastases.

Sixteen patients had opacification of the liver. Of these only 2 were examined with liver scan, both negative. In one of these patients also ultrasound examination of the liver was normal. Exploratory laparotomy in one patient revealed no liver metastases and liver biopsy in another patient was negative. Autopsy revealed liver metastases in one patient (with carcinoma of the cervix), 3 months after lymphangiography. In the remaining 11 patients no examinations of the liver were recorded.

In 5 patients with liver opacification chest examination revealed lung metastases or mediastinal adenopathy.

Edema of the lower extremity was obvious in 17 patients. The cause of the LVA was surgery in 3, abnormal lymph nodes (metastases or lymphoma) in 9 and both abnormal nodes and surgery in 5. Slight extremity edema was apparent in another 4 patients, but they had all extremity varices, which may have caused the edema. No clinical evidence of edema was present in 36 patients and in these the cause of LVA was surgery in 18, abnormal nodes in 11, surgery and abnormal nodes in 6 and trauma in 1. Information concerning edema was missing in 5 patients.

### *Discussion*

Embryologically the lymphatics are formed as buds from the veins and this creates the potential for lympho-venous anastomoses. Such LVA have been demonstrated in experimental animals (1, 7, 8, 9, 10, 11, 12, 13), but only under conditions where an increased pressure of the lymph flow was achieved, i.e., obstruction due to previous ligation, surgery or inflammatory reaction.

LVA have been demonstrated in human cadavres (14). Clinical reports on LVA in patients with obstruction of the lymph flow have usually described only one or a few cases (2, 3, 4, 5, 15, 16, 17, 18, 19). This is probably due to the fact that they are infrequently demonstrated by the common technique. The collection of contrast medium in veins empty rapidly and in order to demonstrate the LVA, at least the small ones, it is necessary to take films while the contrast medium is still running in (Fig. 1). An unusual heavy oil embolization to the lungs may indicate the presence of an LVA although it may be difficult to visualize. The LVA may be obvious only as small droplets in paravertebral veins, and it may be difficult to observe them, unless aware of the possibility.

The diagnosis of LVA to portal radicals with opacification of the liver is more obvious, although the LVA may not be localized. The problem of such LVA have been described and discussed by others (20-26).

The clinical significance of LVA has been discussed in a previous communication (27). Several authors have postulated that the presence of LVA, when due to lymph nodes metastases (1-4) increases the risk of lung metastases. The present material does not justify this suspicion. Relatively few patients had lung metastases at the time of lymphangiography and a still smaller number developed such metastases during the follow-up time. In 5 patients with LVA opacifying the liver, lung metastases were present at the time of diagnosis. Most of the patients with lung metastases had had surgery and the lymphangiogram was negative for lymph node metastases. The surgical procedure may have obscured the demonstration of lymph nodes metastases, but it appears as if the risk of lung metastases is more due to the biology of the tumor and the patient rather than the presence of an LVA.

MDAH is a referral hospital and after the patients have been investigated and/or treated they are sent back to their local hospital or to the care of a family doctor. This explains the poor follow-up concerning the significance of lympho-portal anastomoses. Only a few patients had examination of the liver after the diagnoses. Only one autopsy report was available, although 8 patients with LVA to the liver died within one year after diagnosis. The present report can thus not give any information concerning the risk of liver metastases when a lympho-portal anastomosis is present.

Although all the 62 patients had more or less obstruction of lymph flow from the lower extremity, only 17 had an obvious lower extremity edema. The majority of these were secondary to pathological lymph nodes and only 3 seemed to be secondary to surgery. This is well in line with the experience of retroperitoneal lymph node dissection in patients with non-seminomatous testicular tumors (4). The present results indicate that a LVA is an important pathway to take care of the lymph flow when there is a disturbance of the lymph dynamics.

It has been stated that the presence of LVA in patients with Hodgkin's disease indicate a poor prognosis (5). The survival rate of the present material confirms this statement. The presence of LVA in a patient with lymph node metastases or lymphoma indicate an advanced lymphatic involvement of the disease, and those who died within one year after the diagnosis of LVA, 16 out of 20, had lymphangiographic evidence of metastases.

Thus, the present investigation indicates that there is no definite correlation between lung metastases and LVA in patients with malignant disease. The patients with LVA usually have advanced disease with a low survival rate. Lower extremity edema may be avoided thanks to the development of LVA, but the risk of edema is far more pronounced when the LVA is due to abnormal lymph nodes than to surgery.

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