Lymphatic and Transcapillary Forces in Patients with Edema Following Operation for Lower Limb Atherosclerosis

Einar Stranden and Karin Kramer

Department of Vascular Surgery (Head: Professor S. Vasil) and Department of Radiology (Head: Professor I. Enge), Aker Hospital, University Clinic, Oslo, Norway

Summary

Intralymphatic end pressure and Starling pressures (interstitial fluid pressure ($P_{if}$), plasma and interstitial fluid colloid osmotic pressures ($COP_{pl}$ and $COP_{if}$)) were measured in leg subcutaneous tissue in 5 patients with local leg edema following femoropopliteal reconstruction for lower limb atherosclerosis. Superficial lymphatics were cannulated proximal to the ankle and the catheter was connected to either syringes for determination of lymph flow and colloid osmotic pressure ($COP_p$), or to a pressure transducer for measurement of intralymphatic end pressure. Samples of interstitial fluid were collected by implantation of nylon wicks and $P_{if}$ was measured by the "wick-in-needle" technique.

In all patients normal end pressure waves with maximum values ranging between 30 and 40 mmHg were recorded, indicating that the ischemia prior to surgery had not significantly affected the intrinsic mechanism for lymph propulsion. $COP_{if}$ of the operated leg averaged 5.7 mmHg ± 1.0 which was 0.9 mmHg ± 0.7 higher than the corresponding $COP_p$. This supports the theory of "preferential channels" between the capillaries and the lymphatics.

There was a statistically significant correlation between lymph flow and estimated capillary pressure (reabsorption pressure), capillary filtration coefficient, calf blood flow and $P_{if}$. According to this study the capillary pressure should at least be 11 mmHg before production of lymph occurs.

Introduction

The edema commonly seen following arterial reconstruction for lower limb atherosclerosis (1) is mainly located within the subcutaneous tissue (2) and may last for several months.

The etiology of this edema is proposed to be disruption of lymph channels during the operation with resultant lymphedema (3, 4, 5, 6) and increased filtration from the capillaries which are suddenly exposed to high pressure (7, 8, 9).

Olszewski and Engestøl (10, 11) have demonstrated intrinsic contractility of leg lymphatics. This intrinsic pumping mechanism is supposed to be the dominant factor for propulsion of lymph from lower limb subcutaneous tissue against a hydrostatic gradient.

In addition to operative dissection trauma in patients operated for lower limb atherosclerosis the ischemia prior to surgery may have influenced the function of the lymph vessels. A general perturbation of lymph vessel contractility and ensuing reduction in lymph flow capacity may increase the risk of developing functional lymphatic obstruction and edema formation. In patients operated on for lower limb atherosclerosis this could be of special importance because increased transcapillary fluid filtration (increased capillary filtration coefficient, CFC) is generally found in these patients (12) increasing the need for lymphatic drainage capacity.

The aim of the following investigation was to evaluate the lymph vessel function and study the transcapillary forces (Starling forces) in patients with local leg edema following reconstructive surgery for lower limb atherosclerosis.

Supported by grants from Anders Jahres Fund for the Promotion of Science and J.L. Tiedemanns Tobaksfabrik, Joh. H. Andresens Medical Fund.

0024-7766/82 040148-08 $ 02.00 © 1982 Georg Thieme Verlag Stuttgart · New York

Permission granted for single print for individual use. Reproduction not permitted without permission of Journal LYMPHOLOGY.
Material and Methods

The study includes 5 female patients with a mean age of 70 years (67–75). They all had local leg edema following femoropopliteal arterial reconstruction for lower limb atherosclerosis.

All patients received intraoperative anticoagulation consisting of 3000 IE Heparin® but no colloids as Dextran or albumin were given. The day of operation they received an average of 4000 ml of crystalloids usually consisting of 1000 ml isotonic saline solution (155 mMol/l) and 3000 ml Ringer’s Lactate (130 mMol/l).

The patients were mobilized on the second postoperative day, and were given regular p.o. diet prior to the operation and from the first postoperative day. All measurements were performed with the patient’s informed consent.

Lymph vessel cannulation

One of the subcutaneous lymphatics were cannulated approximately 15 cm above the ankle joint as described by Engeset and co-workers (13). Using microsurgical technique a lymph vessel was dissected for approximately 1 cm using local anaesthesia (Xylocain®, adrenalin, Astra, 5 mg/ml + 5 µg/ml) following visualization with Patent Blue-Violet. Cannulation was performed with a 20–25 cm polyethylene tube with an outer diameter of 1.1 mm (PP 60, Portex Limited, Hythe Kent, England). Before use one end of the tube had been heated, pulled out to decrease its diameter and siliconized. It was then sterilized in 2% cetyl pyridinium chloride (Pyrisept®) for at least 24 hours. Prior to insertion the tubes were flushed with sterile isotonic saline solution.

Lymph was collected in sterile syringes which were taped to the leg at approximately the same level as the cannulation. The syringes were changed several times a day and the lymph flow per hour was measured. The results in this study are referring to the measurements of the second or third day after cannulation.

Intralymphatic end pressures were recorded by connecting the catheter to a pressure transducer (Statham P 23 Db). The signals were amplified and recorded by a Watanabe Mark V linear recorder. Pressure measurements were standardized to a zero baseline at the level of the internal opening of the cannula. Lymphatic pressures were measured with the subjects in supine position.

Interstitial fluid hydrostatic pressure (Pif) was measured on the distal antero-lateral aspect of the leg with the “wick-in-needle” technique (14, 15). Hypodermic needles (0.8 mm OD, 40 mm length) were provided with a 3–4 mm side-hole about 7 mm from the tip, filled with a loosely packed cotton tread and sterilized by gamma irradiation. During measurement the needles were connected via a polyethylene tube to a pressure transducer with a small volume displacement (Statham P 23 Db).

The edema was quantified from surface measurements regarding the leg as a truncated cone. The method has previously been compared with direct water volumetry (16). The technique is based on the assumption that the edema is unilateral and that initial volume of the two legs are equal. Edema is then expressed as percentage increase in leg volume.

Interstitial fluid colloid osmotic pressure (COPif) was measured by the “wick method” previously described (17, 18). Four double-stranded nylon wicks (0.8 mm, 210 fibers) were sewn subcutaneously at a length of 3–4 cm on the distal antero-lateral aspect of the leg approximately 10 to 15 cm above the ankle. A small dose (0.05 ml) of local anaesthesia (Xylocain®, Astra, 20 mg/ml without adrenaline) was given where the needles were inserted and pulled out. After an implantation period of 1 hour the wicks were pulled out and the wick fluid isolated as described by Johnsen (19). The colloid osmotic pressure was measured by a small sample oncometer active to proteins with a molecular weight above 30000 dalton.

Plasma colloid osmotic pressure (COPpl) was obtained by cannulating a cubital vein and a plasma sample was transferred to the oncometer.
The force opposing filtration (reabsorption pressure, \( P_f \)) is defined as: \( \text{COP}_{\text{pl}} - \text{COP}_{\text{ir}} + P_{\text{if}} \). At filtration equilibrium (i.e. filtration equals reabsorption) \( P_f \) should be of the same magnitude as the capillary pressure (\( P_c \)) (20, 21).

Colloid osmotic pressure of lymph (\( \text{COP}_l \)) was measured in lymph samples from the collecting syringes. The values therefore represent an average from each collecting period. The values referred to in Table 1 represent the lymph obtained at the time of the \( \text{COP}_{\text{ir}} \)-measurements.

Calf blood flow and capillary filtration coefficient (CFC) were measured by strain-gauge plethysmography (22) using a double mercury in rubber strain-gauge (Loosco Plethysmograph, G.L. Loos & Co., Amsterdam, Holland) encircling the thickest part of the leg. To prevent deformation of the skin underneath the strain-gauges these were supported by 15–20 regular matches. A venous occlusion cuff placed at the thigh was rapidly inflated to a pressure of 50 mmHg and leg volume increase was recorded (Watanabe Mark V linear recorder). From the initial slope of the volume curve arterial blood flow was calculated. CFC was calculated from the volume increase following 3–6 minutes of venous stasis and expressed as ml/min \( \cdot 100 \) g of tissue \( \cdot \) mmHg increase in filtration pressure.

In two of the patients only one of the two parameters CFC and \( P_{\text{if}} \) was obtained because of technical problems connected with the measurements.

All measurements were carried out in a room with an air temperature of 23–25 °C.

Statistics

The results were analyzed according to standard statistical methods including Student's t-test for paired data with 5% as the level of significance. Regression lines were calculated with the least squares method.

Results

In all subjects the maximum (systolic) intralymphatic end pressure waves ranged between 30 and 40 mmHg. The pattern of the pressure waves varied from one patient to another (Fig. 1 and 2) as well as with time in the same patient. When the cannula was connected to the pressure transducer the intralymphatic pressure gradually increased. After the pressure had reached a threshold, rhythmic pulsations appeared. The threshold pressure varied between 5 and 15 mmHg. The intralymphatic pressure was not significantly influenced by voluntary muscle contractions producing only small artifacts on the pressure curves (Fig. 3).

Manual compression of the foot did, however, usually produce increased intralymphatic pressure and flow as visualized by increased number of droplets per time unit at the catheter opening when disconnected from the pressure transducer.

---

Permission granted for single print for individual use. Reproduction not permitted without permission of Journal LYMPHOLOGY.
During a 24-hour period lymph flow ranged between 0.6 and 2.8 ml/h (mean 1.24 ml/h ± 0.9 (SD), Table 1). There was, however, diurnal variation related to the level of physical activity as seen in Fig. 4. Upright position or walking was generally associated with a lymph flow 3 to 4 times the value obtained when the patient was relaxing in horizontal position. There was a statistically significant positive correlation between lymph flow and CFC, \( P_{if} \), calculated capillary pressure (\( P_r \)) and arterial calf blood flow (Fig. 5A, B, C and E). The correlation between calf blood flow and CFC was also statistically significant (5D). According to the regression line in Fig. 5E the capillary pressure should be at least 11 mmHg before any lymph flow occurs. COP\(_1\) of the operated leg averaged 5.7 mmHg ± 1.0 which was 0.9 mmHg ± 0.7 higher than the corresponding COP\(_1\) (\( p = 0.02 \)), but not significantly different from the contralateral leg. COP\(_1\) varied somewhat during the day (Fig. 4). A period with low lymph flow was generally associated with or followed by increased COP\(_1\) but the variation was moderate. To obtain comparable results the measurements of COP\(_{if}\) and COP\(_1\) were therefore performed at the same time, usually between 2 p.m. and 4 p.m.

**Discussion**

The intralymphatic pressure recordings revealed values similar to those reported from healthy controls (11). In patients operated for atherosclerosis both threshold pressure (the intralymphatic pressure necessary to produce spontaneous contractions) and systolic pressure were normal. All pressure recordings were performed in horizontal position and hence no hydrostatic pressure component was present. Thus, the results from the present investigation do not support the hypothesis that affec-
Table 1 Transcapillary and lymphatic forces in five female patients with edema after femoro-popliteal reconstruction for lower limb atherosclerosis. The values in parenthesis represent measurements from the contralateral leg.

<table>
<thead>
<tr>
<th>Pat. no.</th>
<th>Days after surg.</th>
<th>Edema</th>
<th>P_if COP_pl</th>
<th>COP_if COP_pl</th>
<th>P_r COP_pl- COP_if</th>
<th>COP_l COP_pl</th>
<th>CFC</th>
<th>Calf blood flow</th>
<th>Lymph flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>70</td>
<td>11</td>
<td>24%</td>
<td>+1.0 (-0.5)</td>
<td>25.5 (6.4)</td>
<td>19.8 (18.6)</td>
<td>5.0</td>
<td>1.7</td>
<td>2.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.4</td>
</tr>
<tr>
<td>2</td>
<td>67</td>
<td>9</td>
<td>60%</td>
<td>+2.0 (-1.0)</td>
<td>28.7 (4.9)</td>
<td>26.0 (22.7)</td>
<td>3.4</td>
<td>1.3</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.8</td>
</tr>
<tr>
<td>3</td>
<td>75</td>
<td>14</td>
<td>18%</td>
<td>+1.0 (-1.0)</td>
<td>17.7 (5.8)</td>
<td>14.0 (10.9)</td>
<td>4.8</td>
<td>-0.1</td>
<td>0.6</td>
</tr>
<tr>
<td>4</td>
<td>69</td>
<td>11</td>
<td>20%</td>
<td>+0.5 (-0.5)</td>
<td>24.5 (5.8)</td>
<td>24.0 (10.3)</td>
<td>5.5</td>
<td>0.8</td>
<td>2.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.8</td>
</tr>
<tr>
<td>5</td>
<td>69</td>
<td>9</td>
<td>15%</td>
<td>+0.5 (-0.5)</td>
<td>19.7 (6.3)</td>
<td>13.9 (12.9)</td>
<td>5.3</td>
<td>1.0</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.6</td>
</tr>
</tbody>
</table>

P_if = interstitial fluid pressure (mmHg)
COP_pl = colloid osmotic pressure of plasma (mmHg)
COP_if = colloid osmotic pressure of interstitial fluid (mmHg)
P_r = calculated reabsorption pressure = COP_pl - COP_if + P_if (mmHg)
COP_l = colloid osmotic pressure of lymph (mmHg)
CFC = capillary filtration coefficient (ml/min • 100 g • mmHg) • 10^3
Calf blood flow (ml/min • 100 g)
Lymph flow = average value during 24 hours (ml/h)

Fig. 4 Measurement of lymph colloid osmotic pressure and lymph flow during a period of 40 hours in a patient with local leg edema (pat. no. 1). Lymph flow was positively correlated to the indicated level of physical activity: at rest in horizontal position, standing (orthostatic load) and walking within the hospital ward. The interrupted line represents the average lymph colloid osmotic pressure. In the period 14–16 hours (2 p.m.–4 p.m.) the colloid osmotic pressure of the subcutaneous interstitial fluid near the site of cannulation was measured, and the value was 1.7 mmHg higher than in the lymph.

Flow obstruction caused by the recording device. The values thus probably represent the maximum pressures that could be produced in the lymphatics. Lateral pressures recorded when both lymphatic endings are cannulated and free flow is allowed through a T-tube.
Lymphatic and Transcapillary Forces in Patients with Edema

The average lymph flow was almost twice the value previously measured in control subjects by Engeset and co-workers (13, 0.78 ml/h). The measured lymph flow does not necessarily represent the flow in that particular vessel before cannulation. If the lymphatics had been disrupted at the knee or the groin level during the operation, there could be a negligible flow before the system was opened during the cannulation. On the other hand the close correlation between lymph flow and the filtering promoting factors (calf blood flow and capillary pressure) contradicts that the observed flow is merely drainage of the accumulated subcutaneous edema. The statistically significant correlation between lymph flow and CFC supports this view, indicating that the increased lymph flow is the result of increased fluid transport across the capillaries. The lower colloid osmotic pressure of lymph compared to interstitial fluid found in this study does not support the theory of concentrating ability of the lymphatic vessels (23).

It is, however, in favor of the idea of "preferential channels" which was first postulated by McMaster and Parsons (24, 25) and later by Bill (26). According to their hypothesis, continuous, unrestricted channels leading from the capillaries to the lymphatics may transport a fluid with a protein concentration different from the fluid in the interstitial gel matrix. However, no final conclusion about these theories can be drawn from the present investigation since COP1 and COPif may have been measured in fluid samples obtained from different areas. Major lymphatics proximal to the ankle drain skin, subcutaneous tissue and presumably muscular fascia of the foot and ankle (27), whereas the wick fluid in our measurements mainly represents subcutaneous tissue fluid proximal to the ankle. Furthermore, the wick fluid probably reflects the mean colloid osmotic pressure of both interstitial gel matrix and the hypothetical "channel fluid".

Because of the relatively low velocity of lymph transported through the cannula, the fluid collected in the syringe represents interstitial events somewhat earlier. COP1 does, however, vary little throughout the day so this "time error" is small (in Fig. 4 when measurement of COPif was performed COP1 actually equalled the preceding period).

The calculated Pr is at filtration equilibrium (filtration equals reabsorption) assumed to be equal to Pc. Actually Pc > Pr, but the difference is estimated to be in the order of 0.5 mmHg at normal conditions (28). In a situation with net transcapillary filtration the underestimation of Pc is larger. Consequently the lower value of Pc where net filtration oc-
curs (i.e. lymph is produced) may therefore be above 11 mmHg.

The positive correlation between $P_{lf}$ and lymph flow may indicate that this pressure plays an important part in the filling of initial lymphatics.

Arterial calf blood flow is affecting lymph flow formation probably by its influence on $P_c$ and CFC (29). Two factors are of major importance for CFC: The permeability (hydrodynamic conductivity) of the capillary wall and the capillary surface area. Although changes in capillary permeability may be present in tissues being exposed to ischemia (30), the increased CFC is probably due to increased capillary surface area caused by a reduction in precapillary resistance following the arterial reconstruction (31).

In conclusion the mechanism for lymph propulsion in patients with edema following arterial reconstruction seems to be intact. If edema is produced by insufficient lymph transport capacity, this is likely the result of lymph vessel destruction during the surgical procedure.

Acknowledgments

The authors are indebted to A. Engeset M.D. and W.L. Olszewski M.D., Lab. of Hematology and Lymphology, The Norwegian Radium Hospital, Oslo, Norway, for their kind instruction in the technique of lymph vessel cannulation and valuable discussions during the study.

References

22 Whitney, R.J.: The measurement of volume changes in human limbs. J. Physiol. 121 (1953) 1–27
23 Taylor, A., H. Gibson: Concentrating ability of lymphatic vessels. Lymphology 8 (1975) 43–49
25 McMaster, P.D., R.J. Parsons: Physiological conditions existing in connective tissue. II. The state of the fluid in the intradermal tissue. J. exp. Med. 69 (1939) 265–282

Einar Stranden, Dept. of Vascular Surgery, Aker Hospital, Oslo 5, Norway

Permission granted for single print for individual use.
Reproduction not permitted without permission of Journal Lymphology.