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Capillary Filtration Coefficient (CFC) in Lymphoedema Patients with Normal Lymphangioscintigraphy (LAS).

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Introduction

The diagnosis of lymphoedema is generally based on clinical examination. If supplementary laboratory techniques are required, lymphangioscintigraphy (LAS) is the first choice. LAS gives a fairly good image of the anatomical structures and reveals the function of the lymphatic system. The discriminating ability is, however, not sufficiently strong. In different series the sensitivity is found to be about 0.75 (Weissleder and Weissleder 1988, Bourgeois 1997). This is too low for a good diagnostic test. The reason for this might be:

1. The current LAS methods are incomprehensive. Repeated examinations with different injection sites and an extended observation time might better pick up "borderline" cases (Bräutigam et al. 1993).
2. If the cause of lymphoedema lies in the tissue, (i.e. too dense tissue, occluded prelymphatic channels) any pathology of the transporting system could not be expected (Casley-Smith 1986).
3. Increased net transcapillary filtration exceeding lymphatic transport capacity. This state creates oedema even if the lymphatics have normal function.

We postulate that in some cases the lymphoedema is mainly caused by a capillary dysfunction, enhancing the net ultrafiltration and thereby exceeding a possibly slightly reduced lymphatic transport capacity as a permanent safety valve insufficiency.

The rate of fluid filtration through the capillary wall depends on the capillary permeability, i.e. capillary "leakiness" which may be expressed as the capillary filtration coefficient (CFC) (Cobbold 1963). CFC is the proportionality factor in the Starling equation and is the product of capillary hydrodynamic conductivity per unit area (K_f) and capillary surface area available for filtration (Aukland and Nicolaysen 1981). In other words, both increased capillary "leakiness" and increased capillary surface area may contribute to enhanced capillary transudation.

The aim of this study was to assess transcapillary filtration in patients with lymphoedema and normal LAS. CFC was measured in both legs, and comparisons were made between oedematous and non-oedematous legs. Results from patients were also compared with healthy control subjects.

Material and methods

A small series of 7 patients (one man, 6 women) was examined. The mean age was 46 years (range 37-55). All patients have signs of leg lymphoedema: A typical medical history, localization, signs of thickened skin, bombé appearance, a positive sign of Stemmer and lack of other causes of oedema. Five had primary and 2 secondary (traumatic) lymphoedema. Bilateral affection was present in 3 patients. In all patients LAS indicated normal lymphatic structure and function.

As a control group 9 subjects, 6 women and 3 men, with a mean age of 62 years (44-72) were included. The subjects had no signs or medical history of lymphoedema, venous or arterial insufficiency.

CFC was measured in both limbs by strain-gauge plethysmography using double mercury in silicone strain gauges around the greatest circumference of the calf (Stranden 1983). 8-10 underlying matches prevented indentation of the skin underneath the strain gauge. The plethysmograph ("Strain Gauge Plethysmograph", Stranden) was equipped with electrical calibration permitting repeated calibrations between measurements.

Patients were recumbent for 15-20 minutes prior to the start of measurements. The room temperature was kept between 23-25°C. Cushions under the distal part of thigh and ankle supported the lower limb with the centre calf approximately at heart level. A venous occlusion cuff was applied proximal to the knee (Fig. 1A). Cuff pressure of 50 mmHg was maintained during the measurement. This permitted uninhibited arterial flow into the limb while venous outflow was compromised, resulting in an increased leg volume. Perisoft acquisition and analysis software (Perimed AB, Järfälla, Sweden, www.perimed.se) was used for recording and analysing of foot volume changes and cuff pressure in a computer.

CFC was calculated from the slope of the volume curve in the time period 4-8 minutes after start of venous occlusion, assuming that filtration pressure increased by 50 mmHg. The volume plethysmographic curve was reached to steady state after approximately 3 minutes. The initial relatively steep part of the foot volume recording coincides with the filling of veins. After the volume curve flattens, a secondary very small, but distinct increase of volume is measured which signifies a limb volume increase due to transudation of fluid through the capillary wall (Fig. 1B). This increase of volume over time denotes CFC, and is expressed as ml/min x 100g of tissue x mmHg increase in filtration pressure.

Mann-Whitney and unpaired t-tests were used to compare differences in CFC between oedematous and non-oedematous limbs, and between these and the control group. The results were presented as median values ± standard deviation (SD), with $p < 0.05$ as the level of statistical significance (program Graphpad Instat 3.0, Graphpad Software, Inc., USA, www.graphpad.com).

Results and discussion

Results are given in figure 2. Strain gauge occlusion plethysmography was performed in 10 extremities with typical clinical lymphoedema and normal LAS. There was a tendency, although not statistically significant, of increased CFC in limbs with oedema compared to the non-oedematous limb (0.0060 ± 0.0047 vs. 0.0050 ± 0.0030, $p = 0.23$). However, both values were significantly greater than CFC in healthy controls ($0.0018 \pm$

0.0002, $p < 0.05$).

The significantly greater CFC in patients with lymphoedema than controls points to increased capillary permeability in these patients. The increase was irrespective of development of clinical oedema, and supported our hypothesis of a capillary dysfunction. The large scatter in CFC values in the patient group compared to the narrow range in controls points to a considerable variation in capillary dysfunction in these patients.

The study did not indicate which component in CFC that was increased (capillary surface area, increased "leakiness", or both).

Conclusion. CFC in patients with lympooedema and normal LAS was significantly greater than in healthy controls, in both oedematous and non-oedematous limbs. There was no statistical significant difference in CFC between oedematous and non-oedematous limbs in the patient group, although there was a tendency of increased CFC in limbs with lymphoedema.

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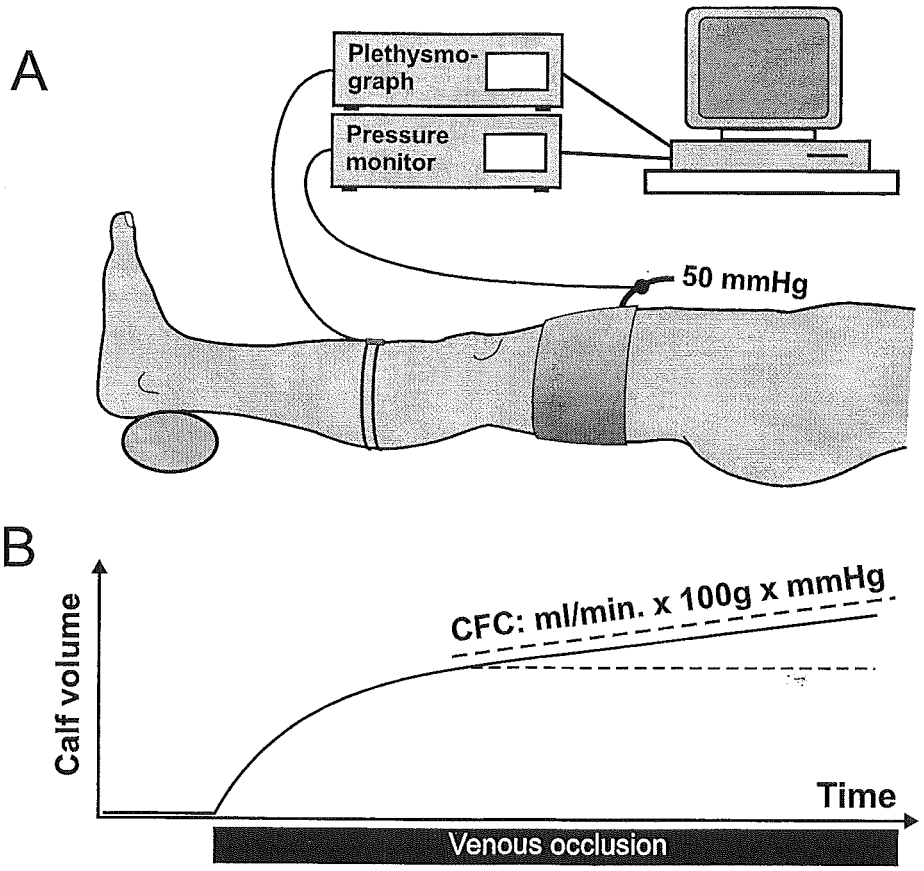
Figure legends

Fig. 1. A: Schematic illustration of the strain gauge plethysmographic set-up for measurements of capillary filtration coefficient (CFC) at the calf level.
B: Schematic illustration of recording of foot volume increase. CFC is calculated from the slope of the volume curve during 4-8 minutes following venous occlusion.

Fig. 2. Capillary filtration coefficient (CFC) in lyphhoedematous lower extremities (n=10) compared to non-oedematous extremities (n=4) and healthy control subjects (n=8). NS: No statistical significant difference.


A
Plethysmo-
graph
Pressure
monitor
50 mmHg
B
Calf volume
CFC: ml/min. x 100g x mmHg
Time
Venous occlusion

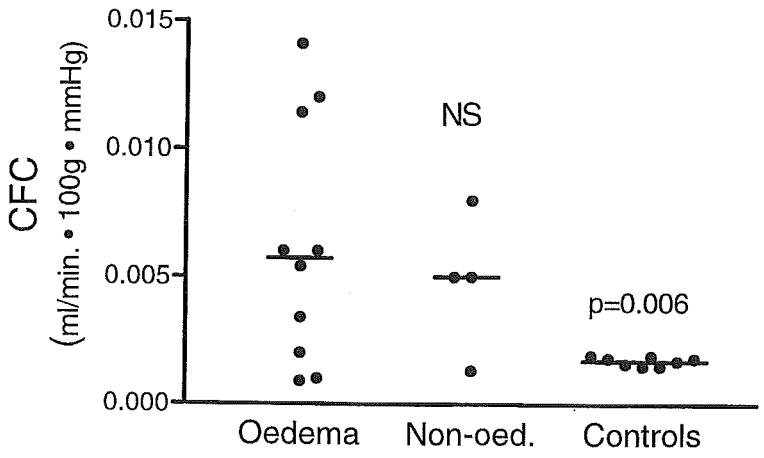

CFC
(ml/min. • 100g • mmHg)
0.015
0.010
0.005
0.000
NS
p=0.006
Oedema
Non-oed.
Controls

Fig 2