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Pressure–Volume Recordings of Human Subcutaneous Tissue: A Study in Patients with Edema following Arterial Reconstruction for Lower Limb Atherosclerosis

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The interstitial fluid pressure–volume relationship was studied in patients who developed leg edema following arterial reconstruction for femoropopliteal atherosclerosis. The increase in subcutaneous tissue volume of the operated limbs was estimated by surface measurements and computed tomography. The subcutaneous interstitial fluid pressure (P_{if}) of the legs was recorded by the wick-in-needle technique and averaged −0.7 mm Hg in healthy controls. Postoperatively, P_{if} was −0.8 mm Hg in patients who did not develop local edema compared to +2.2 mm Hg in patients with postoperative edema. P_{if} increased with increasing subcutaneous tissue volume in patients with moderate edema (0–100% subcutaneous tissue volume increase), but insignificant further increase in P_{if} was observed with additional edema (100 to 600%). A maximal P_{if} of +5 mm Hg was observed in edematous legs indicating a high compliance of the subcutaneous tissue in patients with postreconstructive leg edema.

INTRODUCTION

The compliance of interstitial tissue is defined as the change in the interstitial volume (ΔV) divided by the concomitant change in interstitial fluid pressure (ΔP_{if}). Thus, a high compliance means that interstitial fluid can accumulate with a relatively small increase in P_{if}, whereas a higher increase in P_{if} would be observed with increased interstitial volume in tissues having a low compliance.

The pressure–volume relationship in dog legs was studied by Guyton (1965) who found that the compliance varied significantly at different levels of interstitial tissue hydration. According to his data compliance increased at least 20 times following induction of edema. His results were obtained from pressure recordings in implanted perforated capsules. This method is not suitable for clinical application since an implantation period of 4 to 6 weeks is required. The wick-in-needle technique described by Fadnes *et al.* (1977) seems to meet the requirements for clinical measurement of P_{if} since it can be used acutely with negligible discomfort for the patient.

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Patients undergoing surgery for femoropopliteal arterial occlusive disease often develop leg edema postoperatively (Husni, 1967). The etiology of this edema is probably multifactorial including increased transcapillary filtration and impaired lymphatic drainage due to lymph vessel destruction during the operation (Stranden and Myhre, 1981). Accumulation of fluid in the interstitial space would be opposed by a rise in P_{if}, the magnitude of which depends on the compliance of the interstitium. Thus, increase of leg volume would be restricted with a low compliance, but in case of a high compliance, fluid could more easily be accumulated in the interstitial space.

There have been several studies of the pressure–volume relationship of interstitial tissue based on animal experiments, but such recordings have to our knowledge not been performed in human interstitial space. The purpose of this work was, therefore, to investigate the interstitial pressure–volume relationship in patients with local leg edema following femoropopliteal arterial reconstruction by measuring interstitial fluid pressure and subcutaneous tissue volume increase.

MATERIALS AND METHODS

The group *with leg edema* included 46 patients with a mean age of 67 years (range 41–90) who developed local edema in the operated leg following unilateral bypass grafting for femoropopliteal atherosclerosis. The contralateral leg had no signs of edema as judged from clinical examination. Subcutaneous P_{if} was also measured in 12 patients (mean age 65 years, range 54–80) who underwent the same type of operation *without ensuing local edema* and in 18 *healthy controls* (13 women and 5 men with a mean age of 28 years, range 13–55).

Intramuscular P_{if} of the anterior muscular compartment of the leg was measured bilaterally prior to operation in 5 patients with lower limb atherosclerosis (2 women and 3 men, mean age 69 years), and in 14 patients from the group with postoperative leg edema having a mean leg volume increase close to the average of this group.

In all patients a screening test for deep venous thrombosis was carried out postoperatively by the use of an air-filled plethysmograph (Pulse Volume Recorder, PVR-II, Life Sciences, Inc.). Both venous volume and maximal venous outflow were recorded (Kempczinsky and Rutherford, 1978).

All measurements were performed with the patients' informed consent.

Interstitial Fluid Pressure (P_{if}) Measurements

P_{if} was measured as described by Fadnes *et al.* (1977). Hypodermic needles (0.8 mm o.d., 40 mm length) were provided with a 4-mm side-hole approximately 7 mm from the tip (Fig. 1). The needles were filled with a thread consisting of loosely packed cotton fibers and sterilized by gamma irradiation.

When prepared for measurements, the needles were connected to a Statham P 23 Db pressure transducer via a polyethylene tube (PORTEX manometer line, 60 cm, 200/490/060). The transducer was provided with a specially built Perspex dome having a single outlet and a rubber O-ring as a seal against the transducer. The P_{if} system was checked for leaks by sealing the holes of the needle and increasing the pressure by tightening a screw clamp on the polyethylene tube. A steady pressure level following this procedure indicated absence of leaks. The

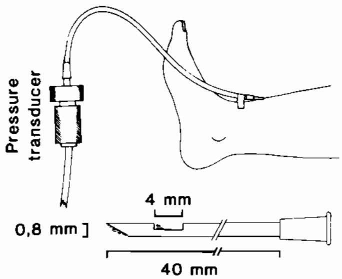

FIG. 1. Schematic illustration of the interstitial fluid pressure (P_{if}) recording system (wick-in-needle technique), with a needle shown in high magnification below. The pressure transducer (Statham P 23 Db) is connected via an amplifier unit to a pen recorder. When prepared for measurements careful attention was given to avoid leakage artifacts at the connecting points.

compliance of the total measuring system was 0.7 μl/100 mm Hg. P_{if} was recorded by a Beckman Dynograph.

The system was calibrated to zero pressure by leveling the needle at the site of measurement and adjusting the pressure amplifier until zero pressure was obtained. After each recording zero pressure was checked by placing the needle at the same level. To prevent dehydration of the wick during the calibration procedure it was moistened with drops of saline solution (9 mg/ml).

Immediately after insertion of the needle a negative pressure in the range of −10 to −20 mm Hg was usually recorded (insertion artifact). However, the pressure increased rapidly and stabilized after 1–10 min. The patency of the fluid phase between interstitium and needle lumen was checked by slight compression and decompression of the polyethylene catheter by means of a 10-mm-wide screw clamp (Fadnes *et al.*, 1977). The clamp was tightened to induce a pressure rise of approximately 5 mm Hg caused by injection of a small volume of saline solution into the interstitial space. The pressure was then usually reestablished at the original level within 1–2 min. Loosening the clamp gave the opposite response. If the pressures did not return to the original values after these procedures, the measurements were discarded ($n = 3$) and not included in the study.

In the operated patients the measurements of subcutaneous P_{if} were performed once from 1 to 16 days postoperatively (mean 7 days). The examination was carried out with the subjects in supine position following a resting period of 15–20 min. The air temperature of the room varied between 22 and 24°. The needle was inserted on the distal anterolateral aspect of the leg approximately 15 cm above the malleolus.

Leg Volume Measurements

The leg volume (V) was quantified by surface measurements and calculated according to the formula describing the volume of a truncated cone: $V = \pi h(R^2 + Rr + r^2)/3$. R is the largest radius as calculated from circumference measurements (radius = circumference/2 π), r is the smallest radius proximal to the ankle and h the calculated length of the truncated cone. The leg edema was calculated as the difference in volume between the edematous and the contralateral leg (Stranden, 1981).

In a separate study using computed tomography (CT) in 10 patients from the same group of patients having postoperative edema it was shown that 98% of the leg volume increase took place within the subcutaneous tissue. According to this study there was a statistically significant positive correlation between subcutaneous tissue volume increase (CT measurements) and total leg volume increase (surface measurements, $P < 0.001$). Subcutaneous tissue volume increase was, therefore, calculated from the leg volume measurements by the equation,

$$\text{subcutaneous tissue volume increase (\%)} = 11.8x - 93.1, \qquad (1)$$

where x ($x > 8\%$) is percentage leg volume increase, $r = 0.85$ (Stranden and Enge, 1982).

The results were analyzed according to standard statistical methods with 5% as the level of significance. Student's t test for paired data was used for comparing subcutaneous and intramuscular P_{if} in the same patients. Unpaired t test was used when subcutaneous P_{if} of controls and patients without and with edema were compared.

RESULTS

No postoperative complications like bleeding, infection, or early reocclusion occurred, and no deep venous thrombosis were detected plethysmographically.

The mean subcutaneous P_{if} in patients with edema was 2.2 ± 2.0 mm Hg (mean $\pm$ SD, $n = 46$). This was significantly higher than healthy controls ($P < 0.001$) who had a slightly negative P_{if} (-0.7 ± 1.3 mm Hg, $n = 18$). The mean value in patients without postoperative edema was not significantly different from the controls (-0.8 ± 0.9 mm Hg, $n = 12$, $P = 0.41$).

The intramuscular P_{if} of the anterior compartment in 14 patients with edema averaged 3.1 ± 2.8 mm Hg which was not significantly different from intramuscular P_{if} measured preoperatively in 5 patients (10 measurements: 2.6 ± 1.3 mm Hg, $P = 0.30$).

The mean leg volume increase in patients with edema was 25.5% corresponding to an increase in subcutaneous tissue of 210% as calculated from Eq. (1). The relationship between subcutaneous P_{if} and calculated subcutaneous tissue volume increase in patients with postoperative leg edema is shown in Fig. 2. There was some scatter in the recorded values and for this reason it was difficult to assign a particular fit to the data. In patients with moderate leg edema (0–100% subcutaneous tissue volume increase) P_{if} increased significantly, and in this interval the equation of the calculated regression line was $P_{if} = 0.027x - 0.63$, where x is percentage increase in subcutaneous tissue volume, $r = 0.51$, $P < 0.05$. In the group with edema corresponding to 100–600% subcutaneous tissue volume increase mean P_{if} was significantly increased (2.7 ± 1.7 mm Hg, $P < 0.001$). In this interval, however, there was no significant correlation between P_{if} and subcutaneous tissue volume increase. The calculated regression line was described by the equation: $P_{if} = 0.001x + 2.5$, $P > 0.05$. Subcutaneous P_{if} did not exceed +5 mm Hg even in patients with massive edema, indicating that large amounts of interstitial fluid can be accumulated in the subcutaneous tissue of edematous legs while P_{if} is rather unaffected.

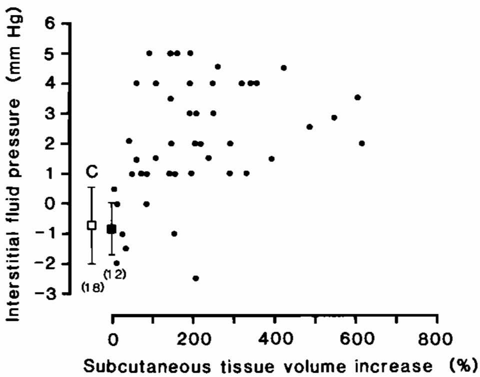

FIG. 2. Relationship between subcutaneous interstitial fluid pressure (P_{if}) and calculated subcutaneous tissue volume increase in patients following reconstructive femoropopliteal surgery for lower limb atherosclerosis. Patients with postoperative edema are represented by ●. Mean P_{if} ± SD of patients without edema is represented by ■, whereas mean P_{if} ± SD of healthy controls (C) is given to the left □. Number of subjects in each group is given in the parentheses below.

DISCUSSION

The pressure–volume relationship observed in the present study to some extent corresponds with previous animal experiments (Guyton, 1965; Eliassen *et al.*, 1974; Wiig and Reed, 1981). In the early phase of edema formation there was a significant increase of P_{if}. Therefore, the initial accumulation of fluid into the interstitial space may be counteracted by a concomitant increase in P_{if}. Furthermore, the transudate will tend to dilute the interstitial fluid with reduction of interstitial fluid colloid osmotic pressure, thereby opposing transcapillary filtration additionally.

In the later phase of edema development the compliance of the interstitial space seems to increase considerably permitting large quantities of fluid to transude from the capillaries without any significant increase in P_{if}.

Depending on which part of the pressure–volume curve was used for the calculation, a high variability of compliance has been observed by other investigators. Guyton (1965) found an increase of at least 20 times following experimental induction of edema. Wiig and Reed (1981) measured the pressure–volume relationship in rat subcutaneous tissue. When calculating compliance at 75% subcutaneous tissue volume increase they found that it had increased severalfold compared to values calculated at 0–20% subcutaneous tissue volume increase.

The pressure–volume relationship observed in the present study may not be readily comparable to results from animal experiments since the amount of volume changes and the composition of tissues included in the experiments are different. Apart from our study the experiments by Wiig and Reed (1981) and Brace and Guyton (1979) are the only investigations which include only subcutaneous tissue.

The present investigation only includes single observations from different patients. Repeated measurements in the same animal have been used by others for the study of pressure–volume relationship in experimental models (Guyton, 1965; Strømme *et al.*, 1969; Eliassen *et al.*, 1974). Although the present measurements did not cause any significant discomfort for the patients, we found it difficult to perform repeated recordings in the postoperative period, even though such measurements would have been of considerable interest.

The relatively moderate increment in P_{if} found in patients with edema could to some extent be explained by "stress–relaxation" of the subcutaneous tissue (Guyton *et al.*, 1971). The postoperative edema developed during several days with a mean increase in P_{if} of approximately 3 mm Hg. In contrast, when edema was produced in animal experiments by acute injection of fluid into the tissue, P_{if} could be as high as +15 to +20 mm Hg initially. The pressure decreased rapidly even though the same degree of edema was maintained by continuous injection of fluid (Guyton, 1965; Guyton *et al.*, 1971).

The moderate increase in subcutaneous P_{if}, even with subcutaneous tissue volume increase up to 600%, is in accordance with a recent study in patients with nephrotic syndrome and leg edema having a maximal P_{if} of +5 mm Hg (Noddeland *et al.*, 1982). In their study no volume measurements were included. The moderate increase in P_{if} found in both investigations is obviously due to a relatively high distensibility of the skin and subcutaneous tissue. However, in tissue surrounded by a nonelastic fascia or eschar formation as seen in burn injuries, the development of edema may cause a considerable increase in P_{if} (up to 50–100 mm Hg) (Hargens *et al.*, 1977; Saffle *et al.*, 1980).

P_{if} in controls corresponded well to the pressure in subcutaneous tissue of rats found by Fadnes *et al.* (1977), and in human control legs using the wick-in-needle technique (Noddeland, 1982). It is, however, higher than found in dogs by the perforated capsule technique by Guyton (1963) and in subcutaneous tissue of rats and dogs by the Scholander wick technique (Scholander *et al.*, 1968; Strømme *et al.*, 1969). Recent experimental investigations have shown a good correlation between the wick-in-needle technique and micropuncture of the subcutaneous tissue with a servocontrolled counterpressure system (Wiig *et al.*, 1981). Furthermore, a study using a modified wick-catheter technique has shown the same P_{if} of human subcutaneous tissue as in the present investigation (-0.7 ± 0.4 mm Hg) (Hargens *et al.*, 1981).

The assumption that most of the leg edema in our patients was located subcutaneously was confirmed by CT measurements (Stranden and Enge, 1982). For practical reasons it was not possible to obtain CT measurements in all patients included in this study. Indirect measurement of leg volume increase corresponds well with the CT measurements and is easier to perform in clinical routine. From such measurements subcutaneous tissue volume increase could be calculated according to Eq. (1).

Another indication that the edema fluid was mainly located subcutaneously in our patients was that the postoperative intramuscular P_{if} was not significantly higher than the preoperative values. Any larger accumulation of subfascial fluid would have increased P_{if}, because of the surrounding nonelastic fascia. Furthermore, no patients had symptoms of compartment syndrome which may occur if the subfascial pressure increases considerably (Hargens *et al.*, 1977). The intramuscular P_{if} measurements were performed in the anterior compartment, since the fascia of both posterior compartments were left open in connection with dissection of the popliteal artery below the knee and performance of the distal arterial anastomosis. Due to this fasciotomy it is unlikely that P_{if} could have been increased in these compartments. The possibility still exists that the pressure might have been increased in the lateral compartment which was not included in the investigation.

In summary, P_{if} increased with increasing subcutaneous tissue volume in patients with moderate edema (up to 100% subcutaneous tissue volume increase). In this part of the pressure–volume curve the increase in P_{if} may oppose further transudation. When the subcutaneous tissue volume increase was excessive (more than 100%) there was no significant further increase in P_{if} even with an additional subcutaneous tissue volume increase of 500%, allowing a great amount of fluid to accumulate in the tissue. This finding supports the theory of Aukland (1973) and Fadnes (1975) that at least in subcutaneous tissue, alterations in P_{if} is probably not the most important edema-preventing factor operating.

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