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ARTERIOVENOUS SHUNTS IN PERIPHERAL LYMPHEDEMA: HEMODYNAMIC FEATURES AND ISOTOPIC VISUALIZATION

F Solti, M Iskum, C Banos, F Salamon

Cardiovascular Surgical Clinic, Budapest, Hungary

ABSTRACT

The hemodynamic characteristics of peripheral lymphedema were studied in 28 patients with uni- or bilateral leg swelling. Leg blood flow was measured by venous isotope dilution (a technique for nutritive — capillary blood flow) and arteriovenous shunts were visualized by perfusion scintigraphy using radiolabelled macroaggregated albumin. Arteriovenous communications were uniformly detected in lymphedema, with a calculated "shunt flow" of 200 to 600 ml/min. Other features in the lymphedematous leg included an elevated limb blood flow rate and narrowed arteriovenous oxygen difference.

Accumulation of protein-rich interstitial fluid accompanies longstanding insufficiency of the peripheral lymph circulation. Characteristically a lymphedematous limb is inelastic or stiff. In the late stages, however, fibrous-sclerotic tissue replaces proteinaceous interstitial fluid, and with progressive collagen deposition "elephantiasis" appears. It is noteworthy that despite profound swelling, development of trophic lesions (e.g. skin ulceration, gangrene) is exceptional with lymphedema. Other clinical and experimental data suggest that the peripheral blood circulation and oxygen supply is also altered in extremity lymphedema. Previously, we provided evidence that arteriovenous communication develop in the course of lymph stasis, and this study further extends these concepts in peripheral lymphedema.

MATERIALS AND METHODS

Investigations were carried out in 28 patients with longstanding lymphedema. In 16, lymphedema affected only one leg while in 12 others lymphedema was bilateral. In 11 patients lymphedema was primary (i.e. idiopathic) while in 17 lymphedema was secondary (i.e. recurrent lymphangitis, iatrogenic-surgical). There were 12 males and 16 females; age varied from 18 to 61 years (mean 44 years). Of the primary lymphedemas, 8 patients had lymphedema precox, 2 lymphedema tarda and 1 congenital. Of the 17 patients with secondary lymphedema 2 also had essential hypertension, one cardiomyopathy and 1 diabetes mellitus.

Total limb blood flow (TLBF) was determined using the venous isotope-dilution method as previously described (1). In brief, the "counter flow isotope principle" was used wherein the femoral vein was doubly punctured in its proximal portion. One needle was introduced 3 cm below the inguinal ligament with the tip directed inferiorly. The other needle was introduced just beneath the inguinal ligament with the tip directed superiorly. Thus the distance between needles was greater than 3 cm. Via the distal needle 4 to 6μc NaI^{131} diluted into 200-300 cc was rapidly infused over one minute under pressure using a highly calibrated infusion pump. Via the proximal needle multiple (28) blood samples were taken after beginning the infusion and the radioactivity determined. Femoral

venous flow was calculated from: Iv = Ii (Ci/Cv-1) where Iv = venous flow (ml/min); Ii = infusion flow (ml/min); Ci = infusions solution isotope cc (CpNa/ml) and Cv = recovered venous blood isotope.

The arterial and venous oxygen content of leg blood was measured after direct puncture of the femoral artery and vein. The leg O_2 consumption (LO_2C) was calculated by the ratio of TLBF and the femoral arteriovenous blood O_2 difference. Nutritive (i.e. capillary) blood flow of the leg and presence of arteriovenous shunts were visualized by peripheral isotope perfusion scintigraphy using tracer doses of technetium-labelled human macroaggregated albumin 99mTc HSA MAA (2). In brief, 99mTc HSA MAA (160mC) was administered by direct puncture of the femoral artery and detected in a scintillation detector (gamma camera) and photographed with polaroid film[6]. Normally, intraarterial administration of radioactive particles (20-100μm diameter) uniformly distributes throughout the leg consistent with capillary perfusion whereas inactive or "spotty" distribution suggests bypassing of capillaries or arteriovenous shunts.

Cardiac output was determined by rapidly infusing Evans blue (50 mg) intravenously, sampling femoral arterial blood every second for 30 seconds for Evans blue concentration and calculating blood flow rate by extrapolating from the dye-dilution.

In patients with unilateral lymphedema, the peripheral hemodynamic data obtained in the lymphedematous leg was compared to the contralateral unaffected leg whereas in bilateral leg lymphedema the findings were compared to similar hemodynamic data in 52 patients of similar age without peripheral arterial, venous or lymphatic disease (controls).

Data was statistically evaluated by using both paired and unpaired students T-test. Lymphangiography was performed in five patients.

RESULTS

In the normal leg, blood flow was in the range of 330-420 ml/min, a value similar to the mean of 355 ml/min previously obtained (1). By comparison, in unilateral leg lymphedema total limb blood flow was elevated and the femoral arteriovenous oxygen difference narrowed compared to the contralateral healthy leg. Leg O2 consumption was unchanged (Fig. 1).

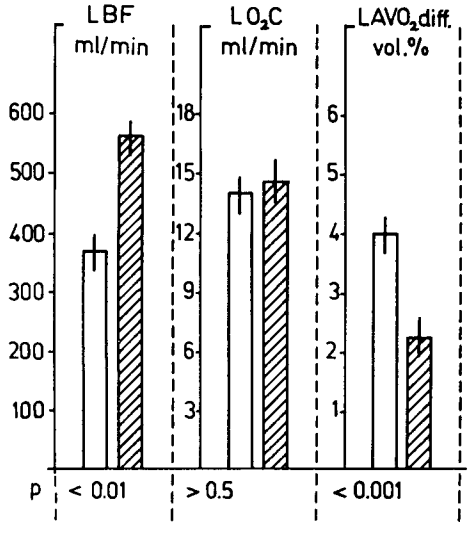

Fig. 1: Increased leg blood flow and narrowed femoral arteriovenous oxygen content in 16 patients with unilateral leg lymphedema (crossed-hatched columns) compared with contralateral intact leg (empty columns). LBF — Total Blood Flow; LO_2C = Leg O_2 Consumption; $LAVO_2$ diff = Leg Arteriovenous O_2 Consumption; $LAVO_2$ diff = Leg Arteriovenous O_2 difference

In bilateral leg lymphedema similar hemodynamic findings were observed. Leg blood flow was about 60% higher and femoral arteriovenous oxygen difference approximately 50% less than normal (Fig. 2). These findings were corroborated in five patients by extrapolation from isotope pulmonary scintigraphy. Initially a small dose of 99mTc macroaggregated albumin (MAA) (approximately 1/5 of that used for peripheral isotope scintigraphy) was administered intravenously and the isotope

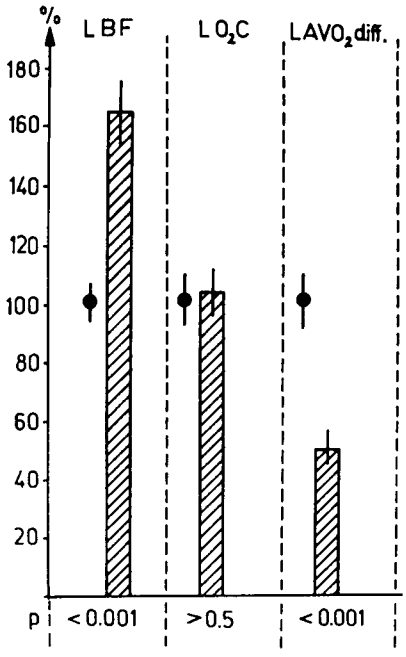

Fig. 2: Alteration of blood flow and O_2 content in lymphedematous leg (bilateral lymphedema-12 patients) compared with controls (52 patients). See Fig. 1 legend for abbreviations. Data are expressed as percentage of normal (100%).

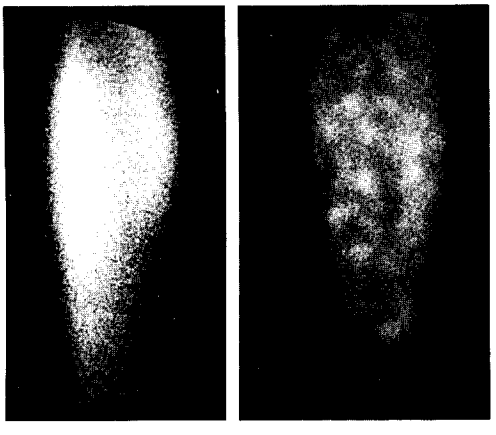

Fig. 3: Peripheral perfusion isotopic scintiscan in unilateral lymphedema (right) compared with normal leg (left). In contrast to the uniform, regular distribution of radioactivity in the thigh of the healthy leg, the lymphedematous leg showed spotty, irregular radioactivity suggesting lack of capillary perfusion or arteriovenous shunts.

accumulation in one portion of the lung determined. Ten minutes later, an isotope lung scintigraphy in this area was repeated after administering 99mTc MAA into the femoral artery of the lymphedematous leg. By determining the increase in radioactivity in the selected area of the lung and taking into account the difference in quantity of 99mTc MAA appearing in the lung after intravenous compared with intraarterial injection, the percent isotope traversing arteriovenous shunts was calculated. In these individuals leg blood flow was 600-800

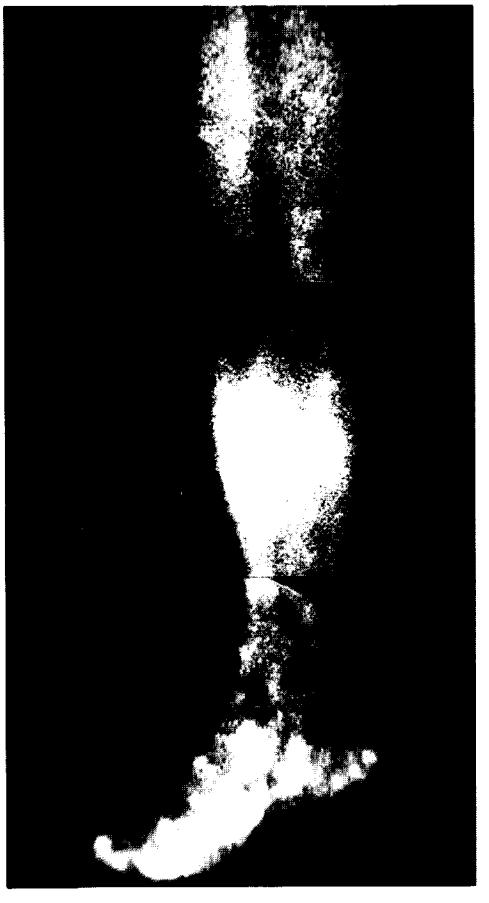

Fig. 4: Perfusion isotope scintiscan from the lower leg in a lymphedematous extremity. Many empty (black), "dropout" areas in the thigh, ankle and foot are suggestive of poor capillary perfusion or arteriovenous shunts.

ml/min (using Evans blue dye dilution) with 30-40% or 180-350 ml/min estimated as passing directly via arterial-venous communications. Taken together, we estimated that 200-600 ml/min of blood flow in a lymphedematous leg was "shunted".

In each of 14 patients with peripheral lymphedema cardiac output was elevated (range 6.5-11.0 l/min; cardiac index = 4.0-7.8 l/min).

Leg perfusion isotope scintigraphy using 99mTc HSA MAA in 15 patients with lymphedema uniformly showed empty, spotty perfused areas of radioactivity suggestive of bypassed capillary beds or multiple arteriovenous shunts (Fig. 3,4).

In five patients dorsal pedal lymphangiography confirmed abnormal lymph circulation.

DISCUSSION

Peripheral lymphedema consists of both primary (i.e. idiopathic) and secondary lymphedema (3-6), and both types are present in our patient group. The hemodynamic and isotopic studies suggest in longstanding lymphedema, that the blood circulation is also altered with inhomogeneous capillary perfusion and development of peripheral arteriovenous communications. Previously we demonstrated bypassed capillary blood flow in experimental lymphedema using polyvinylchloride injection in corrosion preparations to visualize arteriovenous connections (7). Of note, similar arteriovenous shunts develop in conjunction with cardiac lymph stasis (8). An increase of total limb blood flow and greater O_2 content in lymphedematous extremity venous blood was previously observed by us (9) and of high oxygen saturation in femoral venous blood in leg lymphedema by Esterly and Wood (10). These earlier data had suggested arteriovenous shunting in peripheral lymphedema and are further corroborated by the narrow femoral arteriovenous oxygen difference and isotopic perfusion studies described here. Development of lymphatic-venous anastomoses in response to lymph stasis is generally accepted (11-14) and it appears that development of arteriovenous shunts are also a common accompaniment of lymph stasis. Whereas Calnan et al (16) and Quarfordt et al (17) found decreased circulation rate in peripheral lymphedema, Jacobson (15) and Mayall et al (18) support heightened blood flow rate in this condition. It should it noted, however, that Calnan et al's patients also had stenosis or restriction to blood flow in the iliac vein, whereas Quarfordt et al used isotopic Xenon to measure leg blood flow before and after exercise. Because this latter technique primarily measures nutritive muscular capillary blood flow and although with exercise the increase in blood flow in the leg and lymphedema was less than in the normal extremity, it does not preclude that total leg blood flow overall with arteriovenous shunting was augmented in lymphedema. Despite these discrepancies our findings substantiate that in lymphedema, peripheral blood flow is elevated, arteriovenous O_2 difference narrowed and in conjunction with intraarterial isotopic "spotty" perfusion and heightened cardiac output, the presence of arteriovenous shunts is favored. On the other hand, limb O_2 consumption in lymphedema is unchanged, and thus nutritive blood flow despite "shunted blood flow" is adequate at least at rest. Of note six of our patients with lymphedema had cardiac enlargement, a finding consistent with peripheral arteriovenous shunting and elevated cardiac output.

Because nutritive blood flow is seemingly adequate at least at rest in lymphedematous legs, it remains unclear whether these "shunts" need treatment. On the other hand, these arteriovenous shunts are multiple and not readily visualized (i.e. microscopic) and thus they are not amenable to conventional operative obliteration. Of interest, in experimental lymphedema, these arteriovenous connections diminish with resolution of lymph stasis. Whereas further clinical studies are necessary to determine the pathophysiologic significance of arteriovenous shunts in lymphedema, it is nonetheless apparent that

blood circulatory dynamics are altered in this condition.

Professor Dr. Francis Solti DMSCI
Cardiovascular Surgical Clinic
Budapest
Varosmajor Str. 68
H-1122, HUNGARY

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