The Neglected Leg Lymphatic Vascular Changes in the Pathomechanism of Delayed Onset Muscle Soreness in Runners

Marzanna T. Zaleska, PhD,1 Waldemar L. Olszewski, MD, PhD,2 Andrzej W. Ziemba, PhD,1 and Tomasz Mikulski, MD, PhD1

Abstract

Background: Delayed onset muscle soreness (DOMS) in runners is classified as a leg muscle strain injury and presents with tenderness or stiffness to palpation and movement limitation. Most attention is directed at muscles but not at the mass of other limb soft tissues, including their lymphatic vasculature, although they undergo mechanical stress and bruises, edema, nail destruction, and pains contributing to symptoms.

Methods: The study was done on lower limbs of long-distance runners suffering from DOMS complaints. There were 16 runners, 11 males and 5 females, age 22–28, practicing long-distance running over the last 5 years, with body mass index (BMI) 23–4. Inclusion criteria: three to five marathon runs per year and daily 3–5 km slow runs. Last long distance run 3 to 7 days before the investigation. Controls were six subjects initiating running, of the same age group and BMI. Testing of blood and lymph flow was done before and after standard ergometer 300 W 30 minutes cycling. The measurement methods were leg and big toe venous plethysmography, big toe capillary Doppler, tonometry of skin and deep tissues, lymphoscintigraphy, and indocyanine green (ICG) fluorescent lymphography.

Results: (a) Strain gauge plethysmography of the calf and big toe revealed a two- to three-times higher venous capacity in runners than in controls, (b) the increased toe venous capacity was confirmed by point Doppler recordings showing two- to three-times higher blood capillary flow compared to controls, (c) lymphoscintigraphy revealed retention of tracer in feet, dilated superficial and deep lymphatics, and enlarged popliteal and inguinal lymph nodes, and (d) ICG lymphograms showed confluent of accumulated fluid in foot and calf subcutaneous tissue with fluorescence level reaching 40%–50% compared to 20% in controls.

Conclusion: Our results show that, 3–5 days after run, not only muscles but also skin and subcutaneous tissue reveal major tissue fluid accumulation, an overload bringing about functional lymphatic transport insufficiency. This may be an additional factor responsible for DOMS symptoms.

Keywords: lymphatics, lymph nodes, lower limbs, running, clinical assessment

Introduction

Delayed onset muscle soreness (DOMS) is classified as a type I muscle strain injury and presents with tenderness or stiffness to palpation and/or movement, including: lactic acid, muscle spasm, connective tissue damage, muscle damage, inflammation, enzyme efflux theories, and other proposed models. The intensity and duration of exercise are also important factors in DOMS onset. Up to six hypothesized theories have been proposed for the mechanism of DOMS, namely: lactic acid, muscle spasm connective tissue damage, muscle damage, inflammation, and the enzyme efflux theories.1,2 These exercise-induced perturbations can lead to a decreased physical performance.3

Studies on DOMS have been directed at limb muscles. During running repeated eccentric contractions may lead to muscle damage with disruption of structural proteins in muscle fibers and/or intramuscular connective tissues, followed by subsequent tissue inflammation. However, there is a large mass of skin and connective tissue with fibroblasts, adipocytes, and ground matrix in the epifascial extramuscular compartment of feet, calves, and thighs.4 These tissues play

1Department of Applied Physiology, Mossakowski Medical Research Center, Polish Academy of Sciences, Warsaw, Poland.
2Department of Surgery, Central Clinical Hospital, Ministry of Internal Affairs, Warsaw, Poland.
their own role in running, undergoing thousands of micro-trauma of foot and limb skin and tendon strenuous movements, accompanied by increased blood flow, capillary filtration, and tissue fluid/lymph production. Excess tissue fluid may accumulate in the skin, subcutaneous tissue, and wherever there is connective tissue. Leg edema after run is a common phenomenon in long-distance runners.5–7

Formation of edema is a function of the capillary filtrating surface.8,9 The basic role in maintaining the physical and chemical environment of tissues is played by the lymphatic system. The capillary filtrate/lymph, generated at the level of venous parts of the microcirculation, moves into the initial lymphatics and flows along the collecting trunks to the inguinal lymph nodes. The lymphatics transport away filtrate containing proteins, erythrocytes, and mononuclear cells, as well as cellular debris and breakdown products of extracellular matrix and penetrating microorganisms. These accumulating components may have an adverse effect on tissue function and be a cause of pathological symptoms. Lymph nodes work as filters for cells and matrix fragments and also create a hydraulic valve for lymph slowing down its flow and facilitating extraction of cells and nonviable elements in the sinuses.10

During long-distance running blood perfusion and, subsequently, capillary filtration rate of plasma and white blood cell transport to tissues increase. Moreover, long-lasting microtrauma of sole skin with breaking matrix and single muscle fibers provide debris in large amounts. The plantar skin surface bacteria penetrate the epidermis. All the accumulating lymph components are taken up and processed in the regional lymph nodes.11,12

Until recently the insight into the function of the limb lymphatic system draining skin, subcutaneous tissue, and muscles was limited. Today, imaging techniques such as lymphoscintigraphy, indocyanine green (ICG) fluorescent lymphography, magnetic resonance lymphography, and ultrasound imaging enable observations of the lymphatic system during limb function.13 Together with plethysmography, capillary Doppler, skin, and deep tissue tonometry techniques provide a thorough insight into the limb tissue events.

Our concept is that DOMS symptoms are caused, beside of those originating from muscles, by stress signals from the skin and subcutaneous tissue. These tissues accumulate during run of excess tissue fluid/lymph with metabolic products and cellular debris. Skin sensory response to the subcutaneous edema has been documented.14 A diversity of mechanosensitive neurons innervate the skin. Light touch is mediated predominantly by Aβ afferents with low mechanical thresholds. The Merkel cells are sensory cells that transduce touch and then communicate with afferents by synaptic transmission. It is quite commonly seen as the “heavy leg” syndrome with chronic soft tissue edema.15

We decided to evaluate the limb skin and subcutaneous tissue venous capacity volume, capillary filtration, lymph formation and flow, tissue water accumulation, and formation of edema fluid flow depicted on lymphograms. The study was done in lower limbs of the long-distance runners with DOMS complaints. Evaluation of the running induced changes was done before and after standard ergometer cycling test using the limb plethysmography and capillary Doppler, tonometry of tissues, lymphoscintigraphy, and ICG fluorescent lymphography.

Materials and Methods

Investigated subjects

We investigated 16 runners, 11 males and 5 females, age 22–28, practicing long-distance running over the last 5 years, body mass index (BMI) 23 ± 4. Inclusion criteria: three to five marathons per year and daily 3–5 km slow runs. Last long distance run 3–7 days before the investigation. Lack of recent leg injuries, no clinically detectable inflammatory skin or muscle changes. No ultrasound detectable superficial and deep venous thrombosis. No medicaments for any local or systemic complaints. Control lymphoscintigraphy showed typical changes for runners as dilatation of lymphatics and enlargement of inguinal lymph nodes with preserved lymph drainage to the inguinal region. As control served six individuals of the same age group and BMI not practicing running. The study received consent of the Warsaw Medical University ethics committee.

Study setting

Frequent long-distance running is followed by increased vascular alertness to sudden muscular effort.16 Since there is a great diversity of the vascular reaction to long runs among individuals, each runner underwent the same ergometer cycling session of 30 minutes up to 300 W. This allowed us to obtain comparable data of blood perfusion, capillary filtration, lymph formation, and flow in the limb in a comparable manner for the whole group of runners and controls. Measurements were taken before and immediately after cycling. The scheme of tests included big toe capillary Doppler test, plethysmography of big toe and calf, skin and deep tissue tonometry, and visualization of the limb lymphatic system on fluorescent lymphography.

Methods

Continuous big toe and mid-calf circumference and volume measurement. The rate of blood inflow to limbs is measured by plethysmography. Inflation of toe and calf cuffs for 1 minute by pump brings about venous stasis for that period of time, with retrograde dilatation of capillaries by the inflowing arterial blood.17 The circumference and volume of toe and calf increase. This can be recorded by strain gauge plethysmography. Briefly, a plethysmograph (type EC6; Hokanson, Bellevue, WA) in a recording vein mode was applied. Mercury strain gauges of a length of 7.5 and 32 cm were put around the big toe and mid-calf. Elongation of the gauge was read off on the recorder graph scale in mm. It showed increase in circumference brought about by the inflowing blood. A fast 5-second (filling of large veins) and slow 55-second (distension of venous capillaries and plasma filtration) phase curve fragments are obtained. Sequential venous obstruction pressures from 50 to 150 mmHg were used to follow the maximum toe and calf venous volume. The truncated cone formula for measuring toe and calf volumes was applied before and after standard ergometer cycling.

Continuous point Doppler capillary flow in big toe. A single-channel laser Doppler flow meter was used with a specialized fiber optic probe to measure blood cell perfusion in the microvasculature of tissues (Relative Red Blood Cell
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Flux). Class 1 Laser (as per 21 CFR 1040-10 and 1040-11). Relative units (0–5000 Blood Perfusion Units corresponding to 0–5 V output). To obtain the resting capillary flow data the investigated subjects remained in a horizontal position with uncovered limbs, motionless, at room temperature for 15 minutes. Skin capillary blood flow velocity and pulse wave amplitude were recorded. The maximum capillary capacity was recorded at sequential venous obstruction pressures from 50 to 150 mmHg. This allowed to note at which obstruction levels the arterial inflow was still maintained before and after cycling, hence tissue fluid/lymph production. Calf skin point Doppler was applied above the ankle level.

Skin tonometry

Epidermis and dermis in the calves have a vertical dimension of 100–300 μm. Thus, a significant force should be applied to deform skin to move tissue fluid. To estimate how much force to use, the superficial tonometry measuring skin stiffness becomes useful. We applied the recently developed skin fibrometer (Delfin, Kuopio, Finland). This instrument utilizes a small measurement probe (diameter of 23 mm) that is briefly pressed on the skin at all anatomical sites, including curved region. The presence and severity of fibrosis are assessed using a special three-dimensional computational finite element to analyze the biomechanical response of skin tissue to external force. It measures stiffness 1.25 mm deep. Values are expressed in Newtons [force 1 kg/(m·sec^2), one N=0.0981 kg].

Deep tissue tonometry

Tissue tonometry was performed at the same levels as those of girth measurements. A deep tissue tonometer was used. It was composed of a manometer (Wagner, Seattle) connected to a 10 mm long round bottom shape plunger of 1 sq.cm surface area. It was pressed against tissues to the depth of 10 mm within 5 seconds. The applied force was read off on the manometer scale and expressed in g×103/sq.cm.19

ICG near-infrared lymphangiography

Near-infrared fluorescence imaging fills a unique need for simultaneous evaluating of lymphatic architecture and function and edema fluid distribution. ICG is a tricarbocyanine dye that is administered at 785 nm and fluorescence imaged between 820 and 840 nm. A dose of 0.2 mL of 0.5% ICG (Pulsion, Munich, Germany) was injected subcutaneously into the second and fourth toe web or hand interdigital tissue. An ICG fluorescent lymphangiography system (Phodynamic Eye; Hamamatsu Photonics, Japan) was used. The charge-coupled device camera has a fixed focus ranging from 15 to 25 cm, which allows investigation of a 10×10 sq.cm field with one image. Spread of dye in tissue spaces and areas of its distribution in subcutis was evaluated before and after compression. The level of fluorescence was measured using IC-CALC 2.0 software (Pulsion) and presented as a curve from the entire length of the limb.21

Lymphoscintigraphy (isotopic lymphangiography)

To obtain lymphoscintigraphic pictures 230–250 MBq of Tc99m-Nanocoll divided into two portions was injected into first and fourth toe webs (to visualize superficial collectors) and posterior part of sole (deep collectors). Continuous acquisition in a whole body mode was carried out using low energy high resolution, matrix 256×1024, zoom 1.0, table speed 15 cm/min. For a semiquantitative evaluation of the area occupied by the tracer, a densitometric method of Microimage (Olympus, Japan) was applied. As another parameter, distribution of radioactivity in soft tissues was measured. The limb surface was divided into three rectangles: One of the inguinal area, one of thigh, and another of the calf, on the edematous and healthy limbs. Data were expressed as percent of area occupied by the tracer in each rectangle and degree of radioactivity in this area. The pre- and post-treatment pictures were compared.

Statistical evaluation

For statistical evaluation of differences of the same patient before and after compression cycle, a double tail Student’s t-test was applied with significance at <0.05 level.

Results

Mid-calf and big toe venous plethysmographic measurement

There was statistically significant difference between runners and controls in the calf venous volume (p<0.01) (Fig. 1). At rest, the plethysmography fast phase curve showed increase in the venous capacity of main veins dependent upon the venous outflow obstruction (Fig. 2a). It rose from a mean 25 to 45 mL/min at the obstruction pressure of 150 mmHg. After cycling, the venous capacity increased from 30 to 55 mL/min. This rise was observed in all subjects (p<0.05). In controls, venous obstruction did not significantly affect the vein volume (Fig. 2b).

The slow phase curve, reflecting capillary distension and permeability, remained at rest at a mean 20 mL/min, did not change at increasing obstruction pressures to drop to 10 mL/min at 150 mmHg (Fig. 3a). Much the same was observed after cycling. The curve remained at 22–25 mL/min to drop to 5 mL/min at 150 mmHg obstruction pressure. This meant that cycling did not increase the permeability of the calf venous capillaries. In controls before and after cycling the plethysmographic curves remained similar to those of runners (Fig. 3b).

In the resting toe the venous blood volume curves remained unaffected by the increasing venous obstruction pressure even at 150 mmHg (Fig. 4a). After cycling the volumes increased 200%–300%, also unaffected by the level of obstruction pressures (Fig. 4a). This meant that the capillary volume increased significantly. In controls at rest, the venous blood volume curves remained unaffected by the increasing venous obstruction pressure even at 150 mmHg. After cycling the volumes increased by 20%–50%, with drop along the rising obstruction pressures (Fig. 4b).

Capillary flow in calf skin and big toe

In the calf skin, values remained within 20–80 mV in both running and control groups.

In the big toe of resting controls, the systolic values ranged between 40 and 100 mV to decrease to zero upon 150 mmHg obstruction of the venous outflow (Fig. 5a). After cycling, the
FIG. 1. An example of plethysmography recording of the skin, subcutis, and muscle arterial blood inflow volume (venous capacity) in a long distance runner leg before and after ergometer cycling. The figure presents measurements of the calf arterial inflow volume at increasing venous obstruction pressures. The calf volume rising curve is composed of a fast and slow phase. The fast phase reflects the increasing blood volume in large veins (large arrow), whereas the slow one depicts dilatation of venous capillaries and rise of plasma filtered volume to tissue (tissue fluid lymph formation) (small arrow). On the calf plethysmographic recording, the lower continuous line runs at peak levels of the increasing vein volume along the rising occlusion pressures (fast phase). The upper continuous line joins peaks of increasing volume in the dilated capillaries and filtered tissue fluid lymph (slow phase). Note that there has been no rise in the capillary permeability (leakage due to capillary damage). In the lower parts of the figure the interrupted lines show range of blood inflow into the big toe under increasing venous obstruction levels. There was no fast and slow phase as toe tissue contains only few large veins. There was no increase of blood volume at rising occlusion pressures.

capillary value rose to 80–120 mV, to drop to zero at 150 mmHg obstruction (Fig. 5b).

In the big toe of resting runners, the systolic values ranged between 40 and 100 mV to decrease to zero upon 150 mmHg obstruction of the venous outflow (Fig. 5c). After cycling, the systolic values rose to over 250 mV and were still recorded after arterial inflow obstruction at 150 mmHg (Fig. 5d). There were large differences in the individual response to effort; however, in each case cycling increased the capillary level and amplitude by at least 50%. The difference between runners’ and control values were evident ($p<0.05$); however, individual variations in the Meyer’s capillary physiological waves made evaluation of the statistical significance difficult.

**Tissue tonometry**

In runners skin tonometry before cycling was $0.6\pm0.23$ kg/sq.cm to increase after cycling to $0.72\pm0.32$ kg/sq.cm ($p<0.05$). Deep tissue tonometry was $0.9\pm0.13$ and $0.99\pm0.18$ kg/sq.cm ($p<0.05$), respectively.

In controls skin tonometry before cycling was $0.6\pm0.48$ kg/sq.cm to increase after cycling to $0.62\pm0.32$ kg/sq.cm non significant (NS). Deep tissue tonometry was $1.0\pm0.12$ and $0.95\pm0.28$ kg/sq.cm (NS), respectively.

**Lymphoscintigraphic imaging of limbs**

In all investigated cases there was retention of the tracer in the feet (Fig. 6b), dilatation of the superficial and deep lymphatic collectors, and slight to abundant enlargement of inguinal lymph nodes (Fig. 6c). Numerical evaluation of differences in the lymphatic shadow area with normal subjects is relative due to great individual variations. In our evaluation there was an increase by 150%–250% (runners vs. controls).

ICG lymphographic imaging

This method enables a direct following of lymph flow and opacification of the lymphatic vessels and nodes. In case of lymph excess, the tracer spreads at the site of injection and there is a delay in its flow away. The runner’s and control images from the foot and mid-calf are shown on Figures 7 and 8. An evident difference in the area occupied by the tracer fluorescence could be observed in the runners (Fig. 9). Most dye was spread in feet and lower parts of calves. Moreover, the levels of fluorescence can be quantitated along the limb axis before and after runs. The numerical differences before and after cycling were estimated (Fig. 10).

**Discussion**

DOMS is routinely classified as a muscle strain injury. However, limbs have also a large epifascial space containing skin, subcutaneous tissue, blood and lymphatic vessel, tendons, and nerves. The bulk of edema fluid developing after strenuous efforts accumulates in the foot where blood perfusion and capillary filtration with tissue fluid formation are most pronounced. The question arises which changes develop in this compartment and whether they may add to the DOMS symptoms.

We decided to evaluate the limb skin and subcutaneous tissue venous capacity volume, capillary filtration rate, lymph formation and flow, tissue stiffness, formation and site of accumulation of excess tissue fluid/lymph flow shown on lymphograms in a group of long distance runners. The lower limb vascular reactivity of runners is adjusted to an extreme effort. An ergometer cycling can imitate running in these cases. This is why we used it as substitute of run and took measurements before and after cycling.

This study has provided the following results: (a) strain gauge plethysmography of the calf revealed a two- to three-times higher venous capacity in runners than in controls, (b) significant increase in venous capacity in runners but no such reaction in controls, (c) no increase in the calf tissue venous capillary permeability, (d) evidently higher big toe venous volume in runners compared with controls, (e) rather limited increase in big toe venous volume upon cycling, (f) confirmation of the increased toe venous volume by point Doppler recordings showing a two- to three-times higher blood capillary flow compared to the control values, (g) tonometry of calf tissues was increased by 10%–15%, (h) lymphoscintigraphy showed retention of tracer in the feet, dilated superficial and deep lymphatics, and enlarged popliteal and inguinal lymph nodes, and the ICG lymphography showed confluent pictures of the accumulated fluid in the foot and calf subcutaneous tissue with fluorescence level 40%–50% compared with 20% in controls. Taken together, these data show
FIG. 2. Numerical data of the calf fast blood volume increment curves in mL/min for each obstruction pressure level before (continuous curves) and after (interrupted curves) ergometer cycling in (a) 16 runners and (b) 6 normal subjects. Note an increase in the runners' calf venous volume dependent on the obstruction pressure level after cycling ($p < 0.05$). There were no differences in control subjects. Statistically significant difference was noted between runners and controls in calf venous volume even at rest ($p < 0.01$). Data are mL/min, mean ± standard deviation of 16 mL.

FIG. 3. Numerical data of the calf slow blood volume increment curves in mL/min for each obstruction pressure level before (continuous curves) and after (interrupted curves) ergometer cycling in the same group of (a) 16 runners and (b) 6 normal subjects. At rest no significant differences between runners and controls. After cycling evident increase in runners with the capillary volume at venous obstruction pressures of 50–100 mmHg ($p < 0.05$) with a sudden drop at higher pressures. There was a sudden decrease of arterial inflow at 120 mmHg obstruction pressure, as it was in the slow calf phase. This could be accounted for by accumulating lymph obstructing venous capillaries. Data are mL/min, mean ± standard deviation of 2.0–4.5 mL.
that long-distance running predisposes to a rapid increase in skin and subcutaneous tissue capillary filtration and lymph formation and limb functional lymphatic insufficiency.

The most important original observation was finding a two- to three-times higher calf venous capacity in runners than in controls and significant increase in venous capacity in runners during cycling but no such reaction in controls. This could be accounted for by venous dilatation due to continuously high blood flow through limb tissues during running. Luckily, there was no increase in the calf tissue venous capillary permeability. Had it happened, large edema of calf could have developed. In concert with the runners’ high calf venous capacity, we found evidently higher big toe venous volume in runners compared with controls. This was corroborated by Doppler detected high toe blood flow. Large number of open blood capillaries leads to profuse plasma filtration to tissues. This mobile fluid is directed to initial and further collecting lymphatics. The transport capacity of lymphatics can be limited, and the result would be local edema.

Was there any specific correlation observed between increased venous capacity and lymphatic insufficiency? We showed a two- to three-times higher venous capacity in calves and big toes of runners than in controls, and lymphoscintigraphy depicted retention of tracer in the feet, dilated superficial and deep lymphatics, and confluent pictures of the accumulated fluid in the foot and calf subcutaneous tissue with fluorescence level 40%–50% compared with 20% in controls. These are indirect proofs of interdependence of the venous and lymphatic systems in formation and transport away of excess tissue fluid/lymph, revealing in case of runners insufficient transport capacity of lymphatics.

The feet and calves hidden edema detected only by tonometry and overt one seen as pitting swelling are the products of excessive tissue capillary filtration. The bulk of tissue fluid/lymph is produced in the foot soft tissues. Its excess forms edema of the subplantar and dorsal part reaching lower parts of the calf. How much lymph is generated depends on the blood capillary filtration area. The more open capillaries the larger it is. The capillary density in foot skin is high and ranges from 30 to 100/sq.mm.8,9 The average resting blood flow in the young adult male foot ranges from 0–2 mL/100 mL tissue per minute to 16–5 mL/100 mL/min at increased temperature.22 The potent local stimulating factors are limb posture23 and mechanical stimuli from the foot skin hitting the surface. During running the plantar skin undergoes multiple microtrauma. This reaches around 60,000 hits during a marathon run. Fortunately, cutaneous vascular adaptation develops that partly limits capillary filtration.24

All these factors are responsible for the volume of the foot extracellular fluid formation. We found that upon foot exercise there was a two- to three-times increase of the big toe blood capillary flow compared to the mean control values. It can be extrapolated from this observation that a similar increase could have been seen in the entire sole skin. Increase in blood perfusion is the product of enlarged filtration area by opening more capillaries. This was seen on the Doppler and plethysmographic recordings.

Although the bulk of tissue fluid is formed in the foot, there is also increase of capillary filtration in the calf tissues, however, mostly in the muscles but not skin. We showed that the venous capacity of the calf increased by 35–45 mL/min. This could also slightly contribute to the excess fluid during running. Interestingly, the slow phase curve reflecting increased capillary

![FIG. 4. Numerical data of the big toe blood volume increment curves in mL/min for each obstruction pressure level before (continuous curves) and after (interrupted curves) ergometer cycling in the same group of (a) 16 runners and (b) 6 normal subjects as on Figure 7. Significant difference between runners and controls both before and after ergometer cycling (p<0.05). No effect of cycling in runners. Data are mL/min, mean ± standard deviation of 1.2 mL.](image-url)
FIG. 5. Point Doppler recordings of the toe blood capillary flow before and after a 30-minute 250 W ergometer cycling under various venous outflow obstruction pressures of 50, 80, 100, 120, 150, and 180 mmHg (large dots on recordings). Capillary flow values on the graph are expressed in mV reflecting the summarized erythrocyte flow speed. (a) Control subject, under rest venous obstruction pressures, brings about capillary flow decrease to zero at all obstruction levels, recovering after release of the obstruction chamber to 50 mV. (b) Same subject, after cycling during obstruction flow, remained at 10–20 mV and increased to 80–100 mV upon release of the obstruction. (c) Marathon runner, at rest obstruction, the capillary flow ranged between 20 and 80 mV and remained at around 20 mV at high venous obstruction pressures. (d) After cycling the flow was found high around 300 mV, didn’t decrease to zero even at obstruction pressure of 180 mmHg. These recordings point to the reactive dilatation of toe skin capillaries in runners by a simple cycling test.
FIG. 6.  Lymphoscintigrams of lower limbs showing the subcutaneous and subfascial collecting trunks in a control subject and a long distance runner. (a) Normal pattern of collectors and small inguinal lymph nodes in a nonrunning male. (b) Dilated collectors and enlarged inguinal and iliac nodes in a long-distance male runner. (c) Dilated collectors and pathological enlargement of inguinal, iliac, and popliteal nodes in a professional long-distance runner.

FIG. 7.  ICG lymphography picture of the foot dorsum. (a) Normal size collecting lymphatics. Arrow points to the contracted lymphangion and dilated ones above and below. This proves active lymph flow by spontaneous contractions of lymphangions. (b) Large spots of dye at the injection site and multiple dilated lymphatics above in a runner foot. This is a sign of excess lymph in the foot tissue and an overloaded network of collectors conducting lymph away to the groin. ICG, indocyanine green.
FIG. 8. ICG lymphography picture of the mid calf. (a) Normal size collecting lymphatic collectors. Arrows point to the contracted lymphangions, with dilated ones above and below. (b) Multiple largely dilated lymphatic collectors in a runner. This is a sign of excess tissue produced lymph flowing from the foot to the upper parts of the limb.

FIG. 9. An example of numerical evaluation of the ICG lymphograms in the lower limb of a long-distance runner. The curves present mean pixel intensity of fluorescence along the limb. They reflect accumulation of excess tissue fluid/lymph at various limb levels. The upper curve shows fluid distribution level before a long run. The middle curve depicts increase of tissue fluid accumulation on day 5 after a 75 km run. The lower curve was obtained 6 months after the run. It still shows an above normal tissue fluid/lymph volume in the resting limb, despite recent cessation of running.
permeability rose only in proportion to the increased obstruction pressure. This meant lack of damage of the calf tissue capillary walls as an eventual source of excess tissue fluid.

The toe capillary flow and plethysmographic data in runners were at rest evidently higher than in controls, however, after cycling did not differ significantly. The conclusion could be drawn that there was similar increase in the capillary filtration and tissue fluid/lymph formation. Otherwise, large increase in volume after cycling would have occurred.

Moreover, what we found in runners compared to the control group was extensive dilatation of lymphatics in foot and calf. This was certainly adaptation to the excess tissue fluid/lymph. Images of ICG tissue spread and outlining of dilated lymphatics proved the high degree lymphatic transport insufficiency. The isotope lymphographies showed dilatations along the entire limb with retention in foot. In addition, enlargement of inguinal lymph nodes pointed at a reaction to the cellular debris transported from the foot tissues. The literature no reports on lymphographies in the DOMS suffering subjects could be found.

There is a large body of evidence on efforts to decrease the intensity of DOMS or even to prevent its occurrence. Most of them are directed at the muscle damage, their swelling, and contractile impairment. Reports are available on the necessity of enabling a reduction in the space available for muscle edema formation, thereby limiting fluid diffusion into the interstitial space and facilitating the transport of metabolites/neutrophils/damage proteins from the muscle to the blood through changes in blood and edema fluid flow from the subfascial muscular compartment. Limb tissue massage and compression garments are recommended.

Trials on applying compression garments during running have also been reported. Some other methods have also been applied for treatment of DOMS with variable results like water immersion, electrostimulation, stretching, and anti-inflammatory interventions relying on cold exposure, such as cryotherapy.

Our observations confirmed the commonly accepted view of edema negatively affecting the function of muscles. The obtained data on the calf deep tissue tonometry showed slight increase in stiffness after cycling, although it should have been low because of pumping out the muscle venous blood. Increased tonometry is an indirect proof of excess extravascular fluid contained in the subfascial region. However, this is only a part of the pathological picture of DOMS hydromechanics changes, leaving behind the large epifascial compartment of skin, subcutaneous tissue, and other limb functional structures. Our studies enrich the picture of edema in DOMS by adding the new findings on excess capillary filtrate in foot and calf epifascial tissues. The bulk of the epifascial fluid is formed in the front foot and lower calf tissues. Studies in runners showed enhanced foot but not calf capillary blood flow on Doppler test, dilatation foot and calf veins proved plethysmographically, abnormal diffusive spread of ICG and Tc99 lymphographic markers in the tissues of the most dependent parts of limb and dilatation of the subcutaneous lymphatics with enlargement of inguinal lymph nodes. The effects of tissue fluid/lymph stagnation in foot and calf are the "heavy leg," tiredness, and decreased limb movement capacity.

The question arises whether it is possible to prevent formation of excess accumulation of physiologically generated tissue fluid during and its transport away after running. The literature data are not unequivocal. The applied techniques are diverse and outcomes not comparable. Limiting the stretching capacity of foot and calf epifascial tissues during muscle contractions during running by external compression would theoretically decrease the vein volume and subsequently capillary overload with excess filtration. There are at least two question marks. The first is where is compression to be applied as fluid accumulates in the front-foot, sole, and ankle region but not the upper calf areas. How to design the compression material with diversified pressure capacity at various levels? The second is whether compression would not negatively affect muscle contraction during run. After run the situation is simpler and a pressure gradient bandaging or stocking may be applied, higher in foot and decreasing upwards in the calf and thigh.

**FIG. 10.** Fluorescence level in lower limb tissue fluid/lymph of 16 runners measured 1–3 months after the last long-distance run (upper curve) and 6 control subjects (lower curve) at rest. Evidently high levels in runners. Significant differences between groups at all limb levels. *p < 0.05.
The main limitation of the study is a great difference in the physiological reactivity of the vascular system of the studied subjects dependent on inherent features as the rest blood flow, the level of capillary Mayer’s waves, rise of capillary flow, volume of limb veins (venous capacity), as well as the total number of miles run in the past, previous foot injuries, days from the last run, last run distance, reactivity to ambient temperature, and alert reaction to the carried out study.

In summary, studies of capillary filtration and lymph formation in feet of the long-distance runners showed 3–5 days after run dilatation of skin blood capillaries, excess fluid in skin and subcutaneous tissue with dilated lymphatics, and enlarged lymph nodes. This is the first ever study showing that not only muscles but also skin and subcutaneous tissues undergo major fluid exchange changes during and may be co-responsible for DOMS symptoms.

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Address correspondence to:
Waldemar L. Olszewski, MD, PhD
Department of Surgery
Central Clinical Hospital
Ministry of Internal Affairs
Woloska 137
Pawinski 5
Warsaw 02106
Poland

E-mail: waldemar.l.olszewski@gmail.com