Length-tension relationships of small arteries, veins, and lymphatics from the rat mesenteric microcirculation

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Zhang RZ, Gashev AA, Zawieja DC, Davis MJ. Length-tension relationships of small arteries, veins, and lymphatics from the rat mesenteric microcirculation. Am J Physiol Heart Circ Physiol 292: H1943–H1952, 2007. First published December 15, 2005; doi:10.1152/ajpheart.01000.2005.—The passive and active length-tension relationships of isolated rat mesenteric lymphatics (~150 μm ID), and adjacent small arteries (~240 μm) and veins (~275 μm) were compared under isometric conditions using a wire myograph. About 60% of the lymphatic vessels developed spontaneous contractions in physiological saline solution at nominal preload. To maximally activate smooth muscle, 145 mM K+ + 5 × 10−5 M norepinephrine was used for arteries, and 145 mM K+ + 1 × 10−6 M substance P was used for lymphatics and veins. In response, arteries exhibited monotonic force development to a plateau level, whereas lymphatics and veins showed biphasic force development, consisting of a transient force peak followed by partial relaxation to a plateau over ~5 min. The passive and the active length-tension curves were similar in shape among all three vessels. However, the maximal active tension of arteries (3.4 ± 0.42 mN/mm) was significantly greater than peak active tension (0.59 ± 0.04 mN/mm) or plateau tension (0.20 ± 0.04 mN/mm) in small veins and greater than peak active tension (0.34 ± 0.02 mN/mm) or plateau tension (0.21 ± 0.02 mN/mm) in lymphatics. Maximal active medial wall stress was similar between lymphatics and veins but was approximately fivefold higher in small arteries. For lymphatics, the pressure calculated from the optimal preload was significantly higher than that found previously in isobaric studies of isolated lymphatics, suggesting the capacity to operate at higher than normal pressures for increased responsiveness. Our results represent the first mechanical comparisons of arterial, venous, and lymphatic vessels in the same vascular bed to make comparisons among the three vessel types.

Vascular mechanics; wall stress; strain; isometric; preload; contraction

Maximal active stress is remarkably similar between arterial vessels of different sizes and even among arteries from different species (8, 10, 11, 25). Mesenteric veins differ from their corresponding arteries in terms of wall morphology and contractile properties (42, 47), even though they exhibit comparable expression levels of contractile proteins such as actin, myosin light chain, myosin heavy chain, and calponin (50). Maximal active tension and stress as a function of preload have previously been recorded in mesenteric veins (1, 7, 27). Because mesenteric lymphatics from rat (18) and cow (17, 31) exhibit similar pressure-volume and pressure-radius relationships as peripheral veins (34, 39), we hypothesized that mesenteric lymphatics would exhibit a contractile capacity similar to that of mesenteric veins.

Although a few studies have measured maximal active stress in bovine and porcine lymphatics (2, 15, 16, 32), the maximal contractility of mesenteric lymphatics has not been determined for the rat, which is the model used for many in vivo lymphatic and microcirculation studies (3, 5, 51–53). Furthermore, comparisons between arterial, venous, and lymphatic vessels in the same vasculature do not exist. A recent study (36) demonstrated that muscle cells in rat mesenteric lymphatics have unique contractile machinery composed of both smooth and striated muscle components. Rat mesenteric lymphatic vessels also exhibit contractile characteristics different from lymphatics in other regions of that species (18, 19).

For these reasons, it is important to determine and compare the contractile properties, both in vitro and in vivo, of the three vessel types supplying the rat mesentery. To accomplish this...
goal, length-tension relationships for passive and maximally activated muscle of rat mesenteric arteries, veins, and lymphatics were examined using a wire myograph, and maximal active stress was determined under isometric conditions. The results were compared in terms of the force-diameter, pressure-radius, stress-radius, and stress-strain relationships.

MATERIALS AND METHODS

Isolated vessel preparation. Male Sprague-Dawley rats (100–300 g) were anesthetized with pentobarbital sodium (60 mg/kg body wt). All animal protocols were approved by the Animal Care and Use Committees of University of Missouri School of Medicine and Texas A&M University College of Medicine. A midline abdominal incision was made through the skin, underlying fascia, and abdominal muscle layers. A small loop of intestine with a section of the mesentery was obtained, excised, and placed in 4°C albumin-physiological saline solution (APSS) containing the following (in mM): 145.0 NaCl, 4.7 KCl, 2.0 CaCl₂, 1.17 MgSO₄, 1.2 NaH₂PO₄, 0.02 EDTA, 5.0 glucose, 2.0 sodium pyruvate, 3.0 3-(N-morpholino) propanesulfonic acid, and 1 g/100 ml colloidal bovine serum albumin. Mesenteric artery or vein segments, with accompanying lymphatics, were dissected under a stereomicroscope, and the avascular connective tissue was carefully removed. A 2-mm-long segment was cut from a single artery, vein, or lymphatic and transferred to the myograph chamber.

Mounting small vessels. Isometric experiments were performed with the use of a single-channel, wire myograph (model 310A, Danish Myo, J. P. Trading, Aarhus, Denmark). In APSS at room temperature, the vessel segment was threaded onto a suitable length of stainless steel wire (diameter = 40 μm for arteries and veins; 25 μm for lymphatics), and the wire was secured to one jaw of the myograph. The second wire was passed gently through the vessel lumen and then anchored to the other jaw. An adjustable micrometer was used to separate the jaws and stretch the vessel between the two parallel wires. A calibrated force transducer (Danish Myo) measured forces between 0 and 30 mN. The force output was digitized with a PCI-6030e A-D card and interface (National Instruments, Austin, TX) using a Pentium 4 computer and LabView (National Instruments). Data were typically collected at 10 Hz.

Microscope system. The mounted segment was transferred to the stage of an inverted microscope (model CK40-F1000, Olympus) coupled to a charge-coupled device camera (model PK-M2U, Hitachi Denshi). A video micrometer (Microcirculation Research Institute, Texas A&M University, College Station, TX) was used to manually measure inner and outer diameters (21), and the experiment was recorded on a digital videocassette recorder (model DMR-E85H, Panasonic). The inner diameter corresponded to the outer edges of the two wires, and the outer diameter corresponded to the outer edges of the vessel, excluding any unremoved pieces of adventitia. To measure wall thickness, we chose at least three places along the length of the vessel and measured the thickness from the outside of one wire to the outside of the medial layer and then averaged these measurements. This was repeated at each preload for subsequent determination of wall stress.

Experimental protocols. After a vessel segment was mounted in the myograph, the bath temperature was raised to 37 ± 0.1°C. The vessel was equilibrated for ~1 h in APSS, with the solution being changed once during the equilibration period. Starting from a completely unloaded state, defined as the maximum diameter associated with zero force, the circumferential length was slowly increased in a stepwise manner by manual adjustment of the distance between the jaws. After a stable level of force was achieved for at least 2 min, the vessel was maximally activated with the appropriate solution. For arteries, the activating solution consisted of KCl substituted for NaCl in APSS (K-PSS) with the addition of 5 × 10⁻⁷ M norepinephrine (4, 25); for veins and lymphatics, 1 × 10⁻⁶ M substance P in K-PSS was used. In initial tests on lymphatic vessels, substance P produced larger and more consistent active force responses than did norepinephrine and other agonists. The time course of active force development was then recorded for 5–10 min. After the vessels were washed twice with APSS, they were returned to an unloaded state, and the force transducer was re-zeroed. After ~5 min, the passive length was increased and the activation protocol was repeated. This procedure was repeated until no further increase in active force (Fₘₐₓ) was recorded. The active length-tension relationship was determined by subtraction of passive force from total force at each preload. Preloads significantly higher than 1.35 times optimal were avoided to prevent damage to the vessels and allow their subsequent use in protocols unrelated to this study.

RESULTS

A total of 12 mesenteric arteries, 14 mesenteric veins, and 15 mesenteric lymphatics were successfully studied. Table 1 summarizes the passive and active mechanical properties of the three vessel types. Although mesenteric arteries, veins, and lymphatics were of the same relative branching order from the same region of the mesentery, the internal diameter of mesenteric lymphatics was ~150 μm, substantially smaller than that of mesenteric veins (~275 μm) or mesenteric arteries (~240 μm).

The time course of force development after activation was quite different for the three vessel types, as shown in Fig. 1. Upon activation, the arteries exhibited a monophasic, sustained force increase, whereas veins and lymphatics showed biphasic force development, consisting of a transient peak followed by partial relaxation to a plateau over a time course of ~5 min (to 60 ± 6.1% of maximal force for veins and to 40 ± 4.8% for lymphatics). In two of the lymphatics, force secondarily returned to 90–95% of peak force at 5 min. The biphasic time course of contraction in veins and lymphatics was not due to the use of substance P as the agonist, because similar responses, albeit to lower levels of maximal active force, were also observed in the same vessels in response to norepinephrine. Nine of fifteen mesenteric lymphatics developed spontaneous contractions in APSS at various levels of preload throughout the experiment. In those cases, force during the relaxation phase of the spontaneous contraction cycle was used to set the passive tension.

Figure 2 shows the passive, total, and active length-tension relationships for mesenteric arteries, veins, and lymphatics. In each plot, the curve depicted by open squares represents the relationship between passive wall tension and length, where tension = force/(2 × segment length). Internal circumference of the vessel (L) was calculated as the wire circumference plus 2 times the wire diameter plus 2 times the distance between the inner edges of the wire (24, 44). The curve represented by solid squares depicts the total length-tension relationship. The difference between these two curves (dashed lines) denotes the active tension developed at each preload. To compare the maximum active tension among vessels of different sizes, L was normalized to the optimal internal circumference (Lₒ) at which vessels generated maximal active force (Fₘₐₓ).

A number of interesting differences in the mechanical properties of the three vessel types were apparent. The optimal preload of mesenteric arteries, at which maximal active tension was achieved, was 0.69 ± 0.03 mN/mm (Fig. 2A). For mesenteric veins, maximal peak active tension (Fig. 2B) was achieved at a preload of 0.08 ± 0.01 mN/mm, which is lower than the optimal
Mechanical characteristics of rat mesenteric arteries, veins, and lymphatics

<table>
<thead>
<tr>
<th>Vessel</th>
<th>Mesenteric Artery</th>
<th>Mesenteric Vein</th>
<th>Mesenteric Lymphatic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diameter, μm</td>
<td>238.9±9.7</td>
<td>275.4±8.3</td>
<td>149.1±4.1</td>
</tr>
<tr>
<td>Number</td>
<td>12</td>
<td>14</td>
<td>15</td>
</tr>
<tr>
<td>Thickness of the wall of vessels, μm</td>
<td>14.4±1.3</td>
<td>5.9±0.7</td>
<td>6.0±0.7</td>
</tr>
<tr>
<td>Volume of the wall of vessels, μm²</td>
<td>11,479</td>
<td>5,505</td>
<td>3,268</td>
</tr>
<tr>
<td>Passive tension at (L_o), mN/mm</td>
<td>0.69±0.03</td>
<td>0.38±0.01</td>
<td>0.08±0.01</td>
</tr>
<tr>
<td>Maximal peak active tension, mN/mm</td>
<td>0.59±0.04</td>
<td>0.34±0.02</td>
<td></td>
</tr>
<tr>
<td>Maximal plateau active tension, mN/mm</td>
<td>3.34±0.22</td>
<td>0.20±0.04</td>
<td>0.21±0.02</td>
</tr>
<tr>
<td>Passive pressure at (R_o), cmH₂O</td>
<td>59.6±3.9</td>
<td>28.0±0.7</td>
<td>9.4±0.4</td>
</tr>
<tr>
<td>Maximal peak active pressure, cmH₂O</td>
<td>57.8±3.1</td>
<td>42.3±1.9</td>
<td></td>
</tr>
<tr>
<td>Maximal plateau active pressure, cmH₂O</td>
<td>308.2±15.9</td>
<td>15.6±2.2</td>
<td>24.8±2.1</td>
</tr>
<tr>
<td>Passive stress at (R_o), (10^5) N/m²</td>
<td>0.55±0.04</td>
<td>0.73±0.09</td>
<td>0.13±0.01</td>
</tr>
<tr>
<td>Maximal peak active stress, (10^5) N/m²</td>
<td>1.48±0.19</td>
<td>0.60±0.03</td>
<td></td>
</tr>
<tr>
<td>Maximal plateau active stress, (10^5) N/m²</td>
<td>3.25±0.18</td>
<td>0.53±0.12</td>
<td>0.38±0.04</td>
</tr>
</tbody>
</table>

Values are means ± SE. Values of tension, pressure, and stress are calculated from the basal force reading on the myograph. The optimal internal circumference (\(L_o\)) at which vessels generated maximal active force (\(F_{max}\)) was calculated from the distance between the wires plus their diameters, with the assumption of elliptical geometry. \(D_o\) and \(R_o\) corresponding to optimal diameter and radius, respectively, were measured by \(L_o\).

Maximal active pressure was estimated by subtracting the passive curve (Fig. 3, open squares) from the total curve (Fig. 3, solid squares). This represents an estimate of the pressure required to maintain a pressurized vessel isometric during maximal activation with the respective agonist. The active pressure-diameter relationships of all three types of vessels were nonlinear and convex to the preload axis, with a broad ascending limb. For mesenteric arteries (Fig. 3A), a maximal active pressure of ~300 cmH₂O was achieved at a preload of 0.85 \(L_o\) (~60 cmH₂O), whereas the maximal active peak (~60 cmH₂O, Fig. 3B) and plateau (~15 cmH₂O, Fig. 3C) pressures for mesenteric veins were reached at 0.75 \(L_o\) (~12 cmH₂O passive stretch) and 0.90 \(L_o\) (~20 cmH₂O passive stretch), respectively. For mesenteric lymphatics, the optimal peak (Fig. 3D) and plateau distending pressures (Fig. 3E) were very consistent with the optimal tension at 1.0 \(L_o\) (6.7 cmH₂O at 0.93 \(L_o\) and 9.4 cmH₂O at 1.0 \(L_o\), respectively). When compared with the maximal distending pressure of mesenteric veins, lymphatics had a lower peak pressure (~42 cmH₂O) but a larger plateau pressure (~25 cmH₂O).

Figure 4 compares wall stress as a function of initial length for the three vessel types. To compare the mechanical properties of vessels with remarkably different sizes, the contractile force can be normalized to the muscle mass, as reflected by the medial wall thickness (24, 44). Wall thick-
ness data were obtained from direct dimensional measurements during the experiments, and wall stress was computed by dividing wall tension by wall thickness of the media layer at each point on the length-tension curve. Wall stress was then plotted as a function of the normalized radius, $R/R_o$, where $R$ and $R_o$ were the internal radii calculated from $L$ and $L_o$. Maximal active wall stress was estimated by subtracting the passive curve from the total tension curve. $L/L_o$, length normalized to optimal internal circumference. Error bars, ± SE.

For all three vessel types, the optimal preload corresponding to maximal active stress (Fig. 4) shifted slightly to the right in comparison with the optimal preload for maximal active tension (Fig. 2). Maximal active stress of mesenteric arteries was obtained at a preload of $1.07 L_o$ (Fig. 4A), whereas the maximal active peak (Fig. 4B) and plateau (Fig. 4C) stress of mesenteric veins were produced at $1.12 L_o$ and $1.32 L_o$, respectively. For mesenteric lymphatics, both the maximal peak (Fig. 4D) and plateau stress (Fig. 4E) corresponded to a preload of $1.10 L_o$. The maximal active peak stress of mesenteric lymphatics ($\sim 0.60 \times 10^5$ N/m²) was approximately twofold lower than that of small veins ($\sim 1.48 \times 10^5$ N/m²) and about eightfold lower than that of small arteries ($\sim 3.25 \times 10^5$ N/m²). Maximal active plateau stress of mesenteric lymphatics was $\sim 0.38 \times 10^5$ N/m², in the same range as that of small veins ($\sim 0.53 \times 10^5$ N/m²).
$10^5$ N/m$^2$). Similar relationships were apparent when stress was plotted as a function of strain (Fig. 5).

**DISCUSSION**

The present study represents the first quantitative measurements of maximal active force development in rat mesenteric collecting lymphatics ($\sim 150 \, \mu$m ID, in situ) and provides a systematic evaluation of the length-tension relationship of rat lymphatic muscle relative to that of smooth muscle in arterial and venous vessels from the same vascular bed.

Length-tension relationships of mesenteric lymphatics. An aim of the present study was to compare the passive and active length-tension relationships of lymphatics with those of arterial and venous vessels in the same vascular region. As lymph pump activity is believed to serve as an intrinsic mechanism to propel lymph flow (6, 43, 48, 53), a basic knowledge of the mechanical characteristics of collecting lymphatic vessels is essential for understanding lymph transport.

Two different experimental approaches, isobaric and isometric protocols (31–33, 45), are often used to quantitate the mechanical properties of lymphatic muscle. In vitro, isobaric
preparations allow monitoring of lymphatic diameter changes at relatively constant diastolic pressure, whereas wall tension can be calculated from diameter and pressure by using the Laplace relationship. One limitation of the isobaric approach is that maximal activation is difficult to achieve without luminal closing, and muscle shortening during activation can potentially lead to partial deactivation of the contractile apparatus and underestimation of the possible maximal force generation (13, 26, 40). Another limitation of isobaric methods is that localized increases in systolic pressure occur during strong lymphatic contractions (3, 17, 31), and, because luminal pressure is not typically measured under those preparations, uncertainty is added to any subsequent tension calculations. Thus the contractions are neither isometric, isotonic, nor perfectly isobaric. An advantage of isometric preparations is that they allow for direct measurement of force and allow contractions to be measured at constant length, assuming that negligible displacement of the force transducer is required to detect force during contraction. Isometric preparations are sometimes preferable for mechanical studies; however, in the case of the wire myograph method, the cross-sectional geometry of the vessel lumen is not circular as it would be in vivo. To date, the

Fig. 4. Wall stress as a function of normalized internal radius for rat mesenteric arteries (A), veins (B–C), and lymphatics (D–E). R/\(R_o\) is the normalized internal radius, where \(R_o\) is the radius associated with maximal active force. Active stress (dashed line) was obtained by subtracting the passive curve from the activated curve. Error bars, ±SE.
The majority of information on the contractile properties of collecting lymphatics comes from pressure-diameter and pressure-volume data obtained using in vivo isobaric preparations. Only a few studies (15, 16, 32, 45) have been conducted under isometric conditions—from mesenteric lymphatics of cow, pig, and sheep (diameter ~0.5–3.0 mm) and from the thoracic duct of rat (diameter ~400 μm).

However, the active length-tension curves for the three types of vessels show dramatic differences. When tension is normalized to $F_{\text{max}}$, active tension at 0.8 $L_o$ is about 80% to 90% of $F_{\text{max}}$ in small arteries and small veins but is only 50% to 60% of $F_{\text{max}}$ in lymphatics. This feature of the active length-tension relation in mesenteric lymphatics suggests that lymphatic vessels are relatively less compliant, with an increased tissue elastic modulus. The time course of maximal force development in lymphatics was biphasic and similar to that in veins; both contrasted with the monophasic force development in mesenteric small arteries. In this respect, the behavior of lymphatics and small veins resembles that of phasic visceral smooth muscle (29). Our previous molecular analyses of the contractile apparatus demonstrated that mesenteric lymphatic muscle appears to have more organized contractile elements and different expression levels of contractile proteins, especially myosin heavy chains and actin, than do mesenteric arteries (36). This distinctly different composition of lymphatic contractile machinery in mesenteric lymphatics as well as the composition of the extracellular connective tissue matrix (14, 23, 38) might also contribute to the differences in the active length-tension relationship between arterial, venous, and lymphatic vessels. Alternatively, differences in the mechanisms that regulate the contraction cycle, such as $Ca^{2+}$ mobilization processes and differential phosphorylation of contractile protein elements (12, 41, 45), might affect the shape of length-tension relationship of the three vessel types. However, the underlying mechanisms of these processes are virtually unknown for lymphatics. Clearly, additional morphological, functional, and molecular analyses of the contractile apparatus of lymphatics need to be performed to identify the
underlying mechanisms and the physiological impact of the possible differences.

**Maximal active wall tension and wall stress in mesenteric lymphatics.** The second aim of the present study was to define the maximal contractile capacity of mesenteric lymph vessels with a view to understanding how their activation contributes to regulation of lymph propulsion. Although several of our previous studies compared lymphatic contractile activity in different regions using in vitro and in vivo methods (3, 18, 19), maximal wall tension and wall stress of lymphatics must be determined under isometric conditions where muscle activation state and preload can be precisely controlled. Since a strong isobaric contraction might induce closure of the lymphatic lumen, a limitation of previous studies to determine the maximal contractile reserve in lymphatics was that the vessels could only be partially activated by agonists for the limited range (1–10 cmH2O) over which luminal pressure could be varied (18, 19, 31). For this reason, we activated the vessels with the combination of elevated K+ and substance P under isometric conditions. Our aim was to permit a more accurate evaluation of the maximal contractility of lymph muscle and allow comparisons between lymph vessels and blood vessels under nearly identical in vitro conditions.

In the present study, the maximal active wall stress of mesenteric arteries (3.25 × 10^5 N/m^2) agrees quite well with values (2.3–3.9 × 10^5 N/m^2) determined by other investigators using different experimental techniques for arteries of different sizes (10). By the same approach, we determined the maximal active stress to be −0.53–1.48 × 10^5 N/m^2 in small mesenteric veins and −0.38–0.60 × 10^5 N/m^2 in mesenteric lymphatics. There have been only a few measurements of maximal active stress reported for small veins (1, 7, 27). At least one of these (27) agrees quite closely (143 kN/m^2) with the present results (148 kN/m^2). There are only a few previous reports (15, 16, 32) of maximal active tension and wall stress in lymphatics. In the latter, the medial wall stress of maximally activated lymphatics ranged from 0.27 to 0.36 mN/mm^2 for much larger lymphatic vessels (bovine and porcine mesenteric lymphatics with outer diameters between 0.5 and 3.0 mm). The value for maximally active medial wall stress determined in the present study was slightly higher but still within the same range as the larger lymphatics, indicating that there may be an optimal maximal wall stress common to lymphatic vessels of any size. One caveat of such comparisons is that calculations of wall tension and stress might need to be corrected for muscle cell pitch. Preliminary measurements in our studies indicate ~6% cell pitch (from perpendicular to the flow axis) for mesenteric lymphatics (unpublished results), suggesting that over 99% of the developed muscle force would be transmitted circumferentially (49). Because cell pitch was relatively small and was not reported in the other lymphatic studies, no correction was made in the calculations of wall tension and wall stress reported here.

The present study also assessed mesenteric lymphatic responsiveness as a function of wall tension and stress. The range of optimal preload (pressure) was 43–82 cmH2O in small mesenteric arteries, 9–16 cmH2O for the maximal peak pressure in small veins, and 16–24 cmH2O for the maximal plateau pressure in small veins. Our data are quite consistent with values of 68–109 cmH2O for arteries and 34–54 cmH2O for the plateau preload of veins that have been measured by other investigators (37). The in vivo pressure in this branching order of rat mesenteric arteries is normally 108–129 cmH2O (Davis MJ and Gore RW, unpublished results), whereas pressure in rat mesenteric veins is ~11–14 cmH2O (9), suggesting that the in vivo preload of mesenteric arteries and veins may be slightly less than that at which the vessels would generate maximal active force (Fmax). For mesenteric lymphatics, the optimal transmural pressure was determined to be 3–5 cmH2O under isobaric conditions (18, 19); at higher pressures (7–9 cmH2O), mesenteric lymphatic vessels showed reductions in contraction amplitude. However, results from the present study suggest that the optimal preload for peak and sustained active force development ranges from 5.1 to 12.9 cmH2O. This indicates that mesenteric lymphatics are also normally operating on the ascending slopes of their active length-tension curves in vivo and have the capacity to significantly shift upward for increased responsiveness. Another implication is that mesenteric lymphatics produce maximal force under higher than normal pressures even though the amplitudes of the phasic contractions are known to be decreased at those pressures (18). With consideration that the pump activity of lymphatics consists of phasic and tonic components (18, 43), the data suggest that the decreased amplitude of phasic contractions may not necessarily be associated with a decrease in tonic constriction or with a decrease in total flow through a given lymphatic vessel.

**Conclusions.** Our results are consistent with the idea that lymphatic vessels have the potential capacity to regulate lymph transport by at least two mechanisms. First, with the increase of active pump activity under physiological conditions (at comparatively low transmural pressures and low or moderate levels of extrinsic flow (20)), lymphatic vessels must contract phasically to maintain lymph flow toward central lymphatics and veins. As transmural pressures increase up to critically high levels, e.g., during edemagenic stress (3), lymphatic vessels would be able to maintain strong tonic constrictions to prevent their own overdistension, to decrease the rate of lymph formation, and to regulate local lymph flow according to the abnormally high levels of extrinsic flow (20).

Finally, our data indicate striking contractile differences among the three vessel types. When their respective physiological tasks are taken into account, it should not be unexpected that arterial smooth muscle is capable of intense, tonic constriction at maximal tension and stress. Lower levels of maximal active tension and stress in mesenteric veins are consistent with their primary function as capacitance vessels. Lymphatic vessels generate the least active tension and stress among the three types of vessels. However, the distinct mechanical properties (elastic as well as both phasic and tonic constrictions) of lymphatic muscle allow lymphatic vessels to play an important role in the maintenance of the normal transport of nutrients and metabolites as well as in protection against the formation of gross edema. It is anticipated that further investigation of the contractile response of lymphatic muscle in response to physical, neural, and humoral factors will provide insights into the altered mechanisms of lymphatic pumping in lymphedema and certain inflammatory diseases.
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GRANTS

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REFERENCES


