Human thoracic duct in vitro: diameter-tension properties, spontaneous and evoked contractile activity

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Telinius N, Drewsen N, Pilegaard H, Kold-Petersen H, de Leval M, Aalkjaer C, Hjortdal V, Boedtkjer DB. Human thoracic duct in vitro: diameter-tension properties, spontaneous and evoked contractile activity. Am J Physiol Heart Circ Physiol 299: H811–H818, 2010. First published May 28, 2010; doi:10.1152/ajpheart.01089.2009.—The current study characterizes the mechanical properties of the human thoracic duct and demonstrates a role for adrenoceptors, thromboxane, and endothelin receptors in human lymph vessel function. With ethical permission and informed consent, portions of the thoracic duct (2–5 cm) were resected and retrieved at T7–T8 during esophageal and cardia cancer surgery. Ring segments (2 mm long) were mounted in a myograph for isometric tension (N/m) measurement. The diameter-tension relationship was established using ducts from 10 individuals. Peak active tension of 6.24 ± 0.75 N/m was observed with a corresponding passive tension of 3.11 ± 0.67 N/m and average internal diameter of 2.21 mm. The equivalent active and passive transmural pressures by Laplace’s law were 47.3 ± 4.7 and 20.6 ± 3.2 mmHg, respectively. Subsequently, pharmacology was performed on rings from 15 ducts that were normalized by stretching them until an equivalent pressure of 21 mmHg was calculable from the wall tension. At low concentrations, norepinephrine, endothelin-1, and the thromboxane-A2 analog U-46619 evoked phasic contractions (analogous to lymphatic pumping), whereas at higher concentrations they induced tonic activity (maximum tension values of 4.46 ± 0.63, 5.90 ± 1.4, and 6.78 ± 1.4 N/m, respectively). Spontaneous activity was observed in 44% of ducts while 51% of all the segments produced phasic contractions after agonist application. Acetylcholine and bradykinin relaxed norepinephrine preconstrictions by ~20% and ~40%, respectively. These results demonstrate that the human thoracic duct can develop wall tensions that permit contractility to be maintained across a wide range of transmural pressures and that isolated ducts contract in response to important vasoactive agents.

lymphatic system; lymph pump; lymphangion; lymphatic smooth muscle

THE EXCESS FLUID AND PROTEIN of the interstitial spaces in almost all tissues of the body are collected and removed by the lymphatic system. The lymphatic capillaries converge into larger collecting lymphatics, and, ultimately, these terminate into large transport vessels, which return lymph to the blood circulation. The lymphatic system lacks a central pump to drive the transport of lymph. Instead, it is generally accepted that the lymphatic contractility of LSMCs in the collecting and transporting lymphatic vessel wall are responsible for propelling lymph forward by intrinsic contractions. The lymphatic vessels responsible for pumping are comprised of multiple contractile segments separated by unidirectional valves to prevent backflow, termed a lymphangion, and each lymphangion performs much like a cardiac ventricle to provide unidirectional pumping. The contractile part of the lymphatic vasculature can thus be likened to a system of ventricles in series (27).

Tissue preparation. Human thoracic duct tissue was obtained during esophageal and cardia cancer surgery at the Department of Cardiothoracic and Vascular Surgery, Aarhus University Hospital, Skejby, Denmark. The thoracic duct is prophylactically ligated and resected from the midthoracic region as part of the routine cancer resection procedure; thus, the harvesting of the thoracic duct does not

MATERIALS AND METHODS

Address for reprint requests and other correspondence: N. Telinius, Dept. of Physiology and Biophysics, Aarhus Univer., Ole Worms Allé 4, Universitetsparken, DK-8000 Århus C, Denmark (e-mail: telinius@me.com).
represent an additional surgical procedure for the patient. Two highly experienced surgeons performed the surgery. Informed consent was obtained from each patient, and the protocol was reviewed and approved by the ethical committee for the Danish Regional Health Authority (Region Midtjylland Denmark). The study was conducted in accordance with the principles of the Helsinki Declaration. The demographic data of the patients involved in this study are presented in Table 1.

Each specimen was resected up to 10 cm from the tumor in a separate tissue block at level T7–T9 (thoracic vertebrae), providing us with same part of the duct each time. Upon removal, the tissue was placed immediately in cold (4°C) physiological saline solution (PSS: composition given below). The lymph vessels were subsequently dissected free from surrounding connective tissue and fat under a stereomicroscope. Lymph nodes and side branches were occasionally present in some samples but were not used in these studies.

**Isometric tension measurement.** The portion of the thoracic duct dissected from the tissue block was typically 2–5 cm in length. Ring segments of duct (2 mm long, devoid of valves) were prepared and mounted on 40-μm wires in multichannel myographs (DMT 610M) for isometric force measurements. Up to eight vessel segments for recording were possible from a single duct specimen. The preparation, mounting, and experiments were performed in PSS of the following composition (in mM): 119 NaCl, 4.7 KCl, 1.17 MgSO4, 25 NaHCO3, 1.18 KH2PO4, 0.026 EDTA, 5.5 glucose, and 1.6 CaCl2. The vessels were maintained at 37°C in PSS equilibrated with a mixture of 21% O2 and 5% CO2 throughout the experiments (pH 7.4). Isometric force development (mN) was recorded at 40 Hz with a Powerlab4/25 (ADInstruments) using Chart version 5.5.6 software. Data files were saved for offline analysis. Force data were converted to tension, Newton/meter (N/m), by dividing the force (mN) by two times the segment length (mm). Diameter was calculated by the following equation: [total wire circumference + 2 × wire diameter) + (2 × the distance between the inner edges of the wires)]/2π.

Equivalent pressures were derived from the tension and diameter values using Laplace’s law.

### Table 1. Patient demographic data

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<th>Tumor</th>
<th>TNM</th>
<th>No. of ring segments</th>
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TNM, tumor, nodes, metastases; M, male; F, female. Tissue from the first 10 patients listed contributed to the diameter-tension data, whereas the remaining listed contributed to the construction of concentration-response curves to norepinephrine, U-46619, and endothelin-1. *Patient (M, 75) received neoadjuvant treatment in the form of Fluoracil and cisplatin as did another patient (M, 60) in addition to radiation therapy.
Normalization and pharmacology protocols. The diameter-tension experiments described above provided the average passive wall-tension and equivalent pressure values (see RESULTS) that permitted subsequent vessel segments to be “normalized” using these values. After being mounted, the rings were permitted to equilibrate for 30–60 min at 37°C in PSS gassed with a mixture of 21% O2 and 5% CO2. The segments were then contracted with NE (1 or 10 μM) for 3 min followed by addition of 10 μM acetylcholine (ACh) or 1 μM bradykinin (BK) to assess endothelial-dependent relaxation. Comparison of the average tension during the last 2 min of NE alone was made with that occurring 3 min after the addition of ACh or BK. Following washout and recovery, a cumulative concentration-response curve (CCRC) to NE (1 nM–10 μM) was constructed. Ring segments that produced >0.5 N/m tension after the NE bolus or CCRC were included in this study, and further examined with U-46619 (1 pM–0.1 μM) or endothelin-1 (ET-1; 1 pM–0.1 μM). In this experimental series, 88 rings (from 19 ducts/patients) were investigated, and 45 viable rings (from 16 patients) were studied.

RESULTS

Diameter-tension relationship. Initial activation of ring segments of the thoracic duct by stretch alone often triggered spontaneous peaks (Fig. 1A). The subsequent addition of NE-KPSS solution induced contraction, with an initial peak occurring within a minute that, after ~10 min, relaxed to a plateau level (Fig. 1A). The average peak active tension at L0 for 39 segments from n = 10 patients (Fig. 1B) was 6.24 ± 0.75 N/m, with a corresponding passive tension of 3.11 ± 0.67 N/m. The equivalent active and passive pressures were 47.3 ± 4.7 and 20.6 ± 3.2 mmHg, respectively. The average diameter-tension relationship revealed a somewhat flat active curve (Fig. 1C) where, at diameters 0.9–1.1 of L0, the vessels produced >80% of the tension at L0. In spite of varied vessel size (2.21 mm; 95% confidence interval: 1.10–3.35 mm), there was no discernable difference in the calculated transmural pressure under passive conditions (Fig. 2). Thus, subsequently assessed duct segments, irrespective of their diameter, were normalized by stretching them until the tension developed corresponded to maximum active tension.

Spontaneous activity. In 7 out of 16 ducts, a total of 19 ring segments were observed to have spontaneous activity (22% of all ring segments). The average amplitude of the spontaneous

Fig. 1. Diameter-tension relationship for human thoracic duct. A: representative recording from the construction of a diameter-tension relationship in human thoracic duct. When stretched (arrow), the vessel displays stretch-induced spontaneous contractions that cease upon maximal activation with high-potassium solution containing 10 μM norepinephrine (NE-KPSS). The segment is maintained in normal (Ca2+-containing) PSS. B: distribution of the maximum active tension values after incubation with NE-KPSS from 39 vessel segments (n = 10 patients). C: the isometric diameter-tension relationship for human thoracic duct in vitro. Total (○), active (■), and passive (▲) wall tension (N/m) is plotted against normalized internal diameter (L0 is diameter corresponding to maximum active tension). Error bars depict SE (n = 10 patients).

Fig. 2. Passive pressure plotted as a function of diameter. No correlation between the two parameters was found.
contractions was 75 ± 6% of the maximal NE-induced contractions. In three rings, fewer than 10 spontaneous contractions were observed; the remaining 16 rings exhibited a stable contractile pattern with a frequency of 1.39 ± 0.35 min⁻¹. Our data do not support that increasing age, within the age span of this study group, affects spontaneous activity [Supplemental Fig. 1 (Supplemental data for this article may be found on the American Journal of Physiology: Heart and Circulatory Physiology website)].

The role of NO and prostaglandins in spontaneous activity was investigated by incubating three ring segments that displayed spontaneous activity in 100 μM N⁵-nitro-l-arginine methyl ester (l-NAME) and then in the presence of 100 μM l-NAME and 1 μM indomethacin. In the presence of l-NAME alone, the spontaneous activity continued but was superimposed on an increase in wall tension (Fig. 3), and the frequency of contractions nearly doubled to 2.52 ± 0.48 min⁻¹. Subsequent addition of 1 μM indomethacin further increased the tension, and the spontaneous contractile frequency increased further to 6.78 ± 1.56 min⁻¹, corresponding to a 4.6 ± 0.4-fold increase from baseline. Interestingly, the effects of l-NAME and indomethacin on frequency and baseline contractility occurred shortly after application to the bath and were maintained throughout the period the compounds were present.

**Endothelium function.** The endothelial function was assessed by addition of ACh (10 μM) or BK (1 μM) to a stable NE-induced contraction (1 or 10 μM). ACh was applied to 39 rings from n = 15 patients and BK to 27 rings from n = 9 patients. On average, the vessel relaxed 25 ± 4% and 41 ± 5% in the presence of ACh or BK, respectively. In some instances, the effect of ACh and BK was compared on the same ring (Fig. 4), and the difference in relaxation produced by them was found to be statistically significant by paired analysis (n = 9; P < 0.05).

In the majority of vessels, the phasic contractions induced by NE continued in the presence of ACh or BK, with a reduction in average NE-induced tension while in a few vessels the phasic contractions ceased after ACh or BK application. To confirm that the effect of ACh and BK was indeed endothelium-mediated, we attempted to mechanically remove the endothelium by rubbing or with air. In some experiments, the relaxation remained most likely indicating that endothelial removal was incomplete. In other experiments, the relaxation was abrogated, but the NE contractile response was also reduced. As an alternative to mechanical disruption, we employed pharmacological inhibition: we repeated the ACh- and BK-induced relaxations with l-NAME (100 μM) present (n = 2). This resulted in an almost complete abolishment of the ACh- and BK-induced relaxation, which decreased from an average 27 to 2% and 25 to 1%, respectively. The combined presence of l-NAME (100 μM) and indomethacin (1 μM) had a similar effect, reducing the ACh relaxation from 37 to 2% (n = 3).

**NE, U-46619, and ET-1.** The NE-induced contractions were observed in two patterns: an increasing tension and phasic contractions with small oscillations of high frequency (>9 min⁻¹) superimposed on them (Fig. 5, A and B) and phasic contractions that quickly transform into small oscillatory contractions (Fig. 5, C and D). From the CCRC analysis, the maximal average tension developed to NE was 2.59 ± 0.36 N/m, resulting in an equivalent transmural pressure of 26.7 ± 4.0 mmHg (45 rings from n = 16 patients), while the absolute maximal tension produced during the NE-CCRC was 4.46 ± 0.63 N/m, equivalent to 39.4 ± 6.3 mmHg. Cumulative addition of the thromboxane A₂ analog U-46619 increased average tension and induced phasic contractions upon which small oscillatory contractions were superimposed (Fig. 6, A and B). In contrast to NE, high concentrations of U-46619 resulted in a tonic contraction. The maximal average tension was 5.62 ± 1.2 N/m, equivalent to 40 ± 7.3 mmHg, and the absolute maximal tension produced was 6.78 ± 1.4 N/m, equating 47 ± 8.1 mmHg (10 rings from n = 8 patients). The contractile pattern observed during activation with ET-1 (Fig. 7, A and B) was similar to that seen with U-46619. The maximum average tension was 5.31 ± 1.3 N/m, equating 54.3 ± 14 mmHg, and the absolute maximal tension produced was 5.90 ± 1.4 N/m, or 60.2 ± 14 mmHg (9 rings from n = 7 patients). The average concentration-response profiles for NE, ET-1, and U-46619 are presented in Fig. 8. Paired statistical analysis was performed for the average data from the patient’s vessel segments that generated curves for both NE and ET-1 or NE and U-46619. Both U-46619 and ET-1 produced significantly higher average tension and pressure than NE, whereas U-46619 also produced significantly higher absolute maximal tension and pressure. Difficulties in washing out the contraction induced by maximal concentrations of ET-1 and U-46619 precluded comparison of these two substances on the same vessel.

**Smooth muscle cell orientation in human thoracic duct.** The number of nonresponders observed in our tension measurements (see MATERIALS AND METHODS) and the observation that
not all segments present spontaneous contractions could be caused by a noncircular arrangement of the LSMCs in the midthoracic region of the adult human thoracic duct. In support of this, and in agreement with a previous investigation of the human duct (8), staining of F-actin fibers with rhodamine-phalloidin revealed that the LSMCs in the media of the midthoracic region of the duct have a heterogeneous arrangement (Fig. 9): LSMCs were observed grouped in bundles that were orientated in the circular, oblique, and longitudinal directions.

**DISCUSSION**

This in vitro study investigated the biomechanical and pharmacological properties of ring segments of mediastinal human thoracic duct. From our isometric myograph recordings of the human thoracic duct, we have determined that LSMCs produce maximal active tension when stretched to a diameter equivalent to a transmural pressure of $\frac{1}{21}$ mmHg. The maximal active tension produced by LSMCs and the equivalent transmural pressure describe the muscular limit for contractions and the maximal limit for pressure that the vessel can pump against, respectively. Our calculated value of $\frac{1}{21}$ mmHg parallels well with in vivo recordings of healthy human thoracic duct pressures around 20 mmHg (5, 6, 26, 30, 44). In the current study, the total tension generated after maximally activating human thoracic duct rings with NE-KPSS would produce an equivalent transmural pressure as high as $68 \pm 5.3$ mmHg. From previous reports of isolated human superficial groin and leg lymphatics, it is possible to calculate the wall tension and equivalent pressure under baseline conditions. Ring segments from groin lymphatics were stretched at baseline to a wall tension with 32–38 mmHg of equivalent transmural pressure, and these segments could produce 42–57 mmHg after maximal activation with potassium (35, 36). Likewise, isolated leg lymphatics had an equivalent pressure of 28 mmHg at baseline and could produce an estimated 55 mmHg when exposed to high potassium (38). Inflating a cuff on the upper portion of a healthy individual’s arm will decrease the lymphatic drainage from that limb with total cessation when cuff pressures reach the range of 40–70 mmHg (13, 23). In the leg, cuff obstruction inhibits flow at 55–70 mmHg (13). Cannulated healthy collecting lymphatics demonstrate resting pressures of 30–50 mmHg (37) and 55 mmHg and higher when deliberately obstructed (25). Acute compression of the thoracic duct during surgical conditions has been reported to result in developed pressures of 30–50 mmHg (15). In general, it seems that human collecting lymphatics and the thoracic duct can pump against and generate high transmural pressures.

It has previously been reported that ring segments of human thoracic duct are reactive to NE and U-46609 and that these agonists induced both phasic and tonic constrictions (39).

**Fig. 5.** Representative concentration-response curves to NE depicting the two major contractility patterns observed in the human thoracic duct. A: phasic contractions with oscillatory contractions superimposed and increasing average tension (31 vessel segments). B: an expanded view of a phasic contraction from A. C: phasic contractions quickly transforming to oscillatory contractions upon increasing average tension (14 vessel segments). D: detailed view of the small high-frequency oscillatory contractions from C.

**Fig. 6.** Example recording of a U-46619 concentration-response curve in human thoracic duct. A: the whole curve where average tension increases with increasing concentrations and the phasic contractions transform into a tonic contraction at the highest concentrations. B: the phasic contractions in A (at 1 nM) have a small oscillation with high frequency superimposed upon them.
However, these seminal observations by Sjöberg and Steen (39) in 1991 were obtained on two ring segments from a single patient only. Our data demonstrating the constrictive effect of NE, U-46619, and ET-1 in human thoracic ducts from a larger sample group thus confirm and extend upon that observation. Furthermore, our observations are in agreement with in vitro studies from other human and animal lymphatics (3, 21, 34, 36, 38). We observed the order of contractile efficacy ET-1 \(\approx\) U-46619 \(>\) NE in the human thoracic duct. In general, all three substances initiated large, phasic contractions at low agonist concentrations, and with higher concentrations the total contractile force and frequency of the phasic behavior increased until stable contractions were achieved. In human lower leg lymphatics, this pattern to NE was observed in 86% of ring segments tested while the remaining produced stable constrictions only (38). However, in human isolated groin lymphatics, NE had almost no contractile effect while only 50% of experiments with U-46619 displayed the phasic-to-tonic contractile pattern with increasing concentrations of agonist (36). This disparity in reactivity to agonists likely reflects differences in sympathetic innervation as well as distinct receptor subtype expression along the lymphatic vascular tree. Analysis of the \(\beta\)-adrenoceptors, thromboxane A2, and endothelin receptor subtypes expressed in the human thoracic duct was beyond the scope of the current study. However, the present findings illustrate the importance of these agents for thoracic duct contractility.

The role of the endothelium in modulating lymphatic contractile behavior was investigated using ACh and BK. NE-preconstricted ducts relaxed upon addition of ACh and BK, most likely through endothelium-mediated effectors, since their action on the duct was affected with mechanical and chemical disruption of the endothelium. A similar vasorelaxant effect of ACh via nitric oxide is well described in animal lymphatics, including canine thoracic duct (41), guinea pig mesenteric lymphatics (43), and rat iliac lymph node afferent vessels (22). Cyclooxygenase inhibition by indomethacin or aspirin application has been reported to suppress both spontaneous and evoked changes in lymphatic pumping in isolated animal lymphatics (2, 10, 14, 17), and in vivo administration of indomethacin to volunteers with catheterized subcutaneous lymphatics does not alter measured end pressures or rhythmic pressure waves (37). L-NAME and indomethacin administration to the human thoracic duct, to inhibit NO and prostaglandin production, respectively, did not inhibit spontaneous activity, suggesting that these factors modulate pumping frequency but are not of importance for the generation of this activity.

The human thoracic duct has been observed to be spontaneously contractile in situ in anesthetized patients with an inherent frequency of 4 – 6 min\(^{-1}\) (7, 16). However, only a small proportion of the duct vessel segments studied here were spontaneously active: spontaneous contractions had a frequency of 1.4 min\(^{-1}\), which was increased \(\approx\)4.5-fold in the presence of L-NAME and indomethacin to a level equivalent of that observed in vivo. The spontaneous contractions analyzed were those observed after normalization during the 30- to 60-min equilibration period before initiating the pharmacological protocol. However, the number of vessels displaying...
spontaneous activity increased after the viability check with NE and the subsequent washouts. Because a NE standard-start protocol is commonly employed in wire myography studies of arteries but not lymphatic vessels, we chose to analyze spontaneous activity occurring before the NE test for viability. Thus the levels of spontaneous activity reported in the initial equilibration period may reflect a lower-than-expected level. In the well-performed studies by Sjöberg and colleagues (35, 36, 38, 39), none of the isolated human lymphatics studied were spontaneously active. It is vital to note that, in our study, 44% of all ducts had at least one spontaneous segment, and 51% of the segments were capable of phasic contractions in response to agonist stimulation. Similar observations have been made in previous studies of isolated human lymphatics (36, 38), suggesting that isolated segments are capable of oscillatory activity but that only certain regions can initiate the contractile wave. It has previously been suggested that “pacemaker” cells drive this activity (19), and this could explain the disparity in human thoracic duct spontaneous and evoked reactivity. Whether the LSMCs constitute the pacemaker system themselves or it is initiated by a specialized pacemaker cell requires further experimentation. An alternative hypothesis and one that we briefly examined here was that ring segments containing more circular LSMC bundles than its neighbor would have a greater likelihood to have spontaneous activity detected in the myography. Ultrastructural and histological analyses of monkey and human thoracic ducts have reported an organization of LSMCs into longitudinal, oblique, and circular (8, 18, 32, 33). From phalloidin-staining experiments, we confirmed that the arrangement of LSMCs in the human thoracic duct is not only circular, as seen in blood vessels. Our observation of a varied organization of LSMCs is additionally supported by our diameter-tension data, which do not present a sharply decreasing length-tension active curve produced by a circular fiber arrangement (45). In another study of isolated rat thoracic duct, using an isobaric approach, 40% of the vessels included in the study were not phasically active (11) so the use of pressure myography per se may not improve the chances of observing spontaneous activity. Nonspontaneously active zones may be an inherent characteristic of the wall of the thoracic duct. Other groups studying human lymphatics have suggested the lack of contractility to reflect irregular LSMC distribution in the wall (35). Because our data reflect a distinct population with an average age of 63 years and cancer-afflicted, one could presume that our observations on the LSMC arrangement may apply only to this group. However, histological analysis of human ducts from a broad range of ages (newborn to 90 years of age) suggested that the major changes associated with aging are a thickening of the intima with degeneration of the internal elastic lamina, increased collagen in the media, and no significant reduction in the musculature (29). In that same study, the LSMCs “tended” to appear in the inner half or two-thirds of the wall as opposed to the “evenly dispersed” distribution in ducts from younger individuals; however, no observations of the total numbers of LSMCs or their bundle arrangement were provided (29). The overall contribution of cancer and aging to the data presented here can only be fully understood when a larger population group including young and healthy individuals can be studied.

Approximately one-half of the vessel segments in this study were excluded based on low force development. Exclusion was based on an arbitrary cut-off value as is often employed in wire myography of both arteries and lymphatic vessels (24, 35). Nonresponders have been observed in the order of 25–35% for human groin and leg lymphatics (35, 38). The repeated finding of nonresponders in isolated human lymphatics suggests, as mentioned above, that heterogeneity in the LSMC structure may underlie some of this. Alternatively, and more difficult to quantify, is damage occurring during the surgical process. Although the majority of patients included in this study had a T-status less than or equal to three (no infiltration of neighboring structures), we cannot exclude that local chemokine changes or other cancer-related changes from the proximally located tumor could disturb thoracic duct function. However, the thoracic ducts in this study had an average diameter that is in agreement with published data for healthy subjects. Magnetic resonance lymphography has determined the mean diameter of thoracic ducts in healthy volunteers to fall in the range 0.5–4.0 mm (12) and 2.6–5.6 mm (40), according to the region of the duct measured. Ultrasonography of the cervical thoracic duct from >500 control subjects determined the average diameter to be 2.5 mm, which was independent of the subject’s age (31). In congestive heart failure, the cervical thoracic duct diameter can enlarge 2.5- to 6-fold (31, 44). On average, the maximum diameter has been observed to enlarge by 50% in alcoholic cirrhosis and 10% in nonalcoholic cirrhosis (40) but does not change with malignancy, chronic hepatitis, or inflammatory bowel disease (31, 40). Our diameter values from the midthoracic region of the duct suggest that the cancer status of these patients did not result in thoracic duct distension and support the notion that, in spite of cancer affliction, these vessels appear normal. Furthermore, because the patients included in our study do not demonstrate lymphedema, lymphocytopenia, ascites, malabsorption, or other lymphatic system dysregulation, we suggest that it is fair to consider the thoracic ducts investigated here as reasonably representative of a “normally” functioning lymphatic system. What is of interest, but outside the scope of this study, is why thoracic duct ligation does not create the downstream lymphatic disturbances observed when obstructing lymphatic drainage in the limbs. This could be explained by anatomical variation of the thoracic duct, with the existence of duct bifurcates, parallel multiple ducts, and lymphaticovenous communications in the thorax and abdomen that would permit lymphatic return in spite of a “ligated” duct.

The current study emphasizes that the largest human lymphatic vessel possesses the capacity to generate spontaneous activity. The isolated thoracic duct can develop wall tensions that correspond to a wide range of transmural pressures, much higher than generally expected from the lymphatic system. The vasoconstrictors NE, U-44619, and ET-1 are all effective agents in the thoracic duct and evoke pump-like phasic contractions. Theoretically, high concentrations of these three substances in vivo would stimulate spasm-like vasoconstriction that would decrease lymphangion stroke volume and impair lymph flow. However, low concentrations would increase pump frequency and promote lymph flow although stroke volume would be reduced. If catecholamines, prostaglandins, and/or endothelin levels were upregulated during high lymph flow conditions, one could hypothesize, in analogy to heart failure and the ordination of β-blockers to improve cardiac pumping, that blocking the receptors for these sub-
stances could improve lymphatic pumping and improve lymph clearance. Whether the pharmacologically generated increases in contractile activity seen in the thoracic duct from the current patient group translate to increased lymph propulsion in vivo in a broader population is deserving of further investigation.

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DISCLOSURES
None.

REFERENCES