

THORACIC DUCT LYMPH FLOW AND ITS DRIVING PRESSURE IN ANESTHETIZED SHEEP

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ABSTRACT

We examined the relationship between thoracic duct lymph flow (TDF) and its driving pressure (DP) in six anesthetized sheep. DP was determined as the thoracic duct pressure (TDP) minus the innominate vein pressure (VP). TDF was measured using an ultrasound transit-time flow meter, placing a flow probe beside the caudal mediastinal lymph node. TDP was measured with a fine needle inserted near the flow probe. TDP increased linearly together with an increase in VP after balloon inflation in the cranial vena cava with a TDP/VP ratio of 0.79. DP decreased, therefore, with an increase in VP and this decrease in DP correlated directly with a fall in TDF. After rapid i.v. fluid infusion, TDF increased but DP varied among the six sheep. Nonetheless, after balloon inflation with expanded volume (i.e., i.v. fluid infusion), DP and TDF were positively correlated. We conclude that DP is the main factor determining TDF when VP rises in conjunction with increased lymph production.

In 1963, the driving pressure between the outflow vein and thoracic duct was measured by Wégria et al in anesthetized dogs (1). They used a bubble flowmeter interposed in the thoracic duct and measured the intralymphatic pressure via a side arm of the flowmeter. They failed to find a direct correlation between lymph flow and thoracic duct

driving pressure although they concluded that the method of pressure measurement probably was inadequate for analysis. In 1971, Browse et al also measured pressure gradients in the canine thoracic duct (2), after introducing small catheters into the thoracic duct through tributaries from the neck and abdomen. They did not, however, measure thoracic duct lymph flow.

In our previous study (3), the response of thoracic duct lymph flow to a stepwise increase in venous outflow pressure showed interindividual variation. In some animals, thoracic duct flow was sensitive to an increase in venous outflow pressure but in others it was resistant in that lymph flow did not decrease until venous outflow pressure rose to high levels (3). Because we could not readily explain the reason(s) for this interindividual variation and because an ultrasound transit time flow meter enabled us to measure thoracic duct lymph flow without cannulation of the thoracic duct, we examined the pressure/flow lymph dynamics in the thoracic duct in the sheep under normal conditions and after rapid infusion of i.v. fluids.

MATERIALS AND METHODS

This study was approved by the University Committee on Animal Resources and conformed to the guiding principles of our institution in the care and use of animals.

Surgery

Six adult sheep of similar size (48 ± 9 kg) were used. After intramuscular injection of ketamine hydrochloride (10 mg/kg), a catheter was introduced into the right external jugular vein by direct puncture, through which thiamilal sodium (10 mg/kg) was injected. Via this catheter, we measured the venous outflow pressure for the thoracic duct using a pressure transducer (Model MPU-0.5, Nihon Kohden, Tokyo, Japan). After the insertion of a cuffed endotracheal tube, general anesthesia was maintained with 0.5-1.5% halothane and 35-40% oxygen in air delivered by a positive pressure ventilator (Model 607, Harvard pump, Natick, MA) with a tidal volume of 400-500 ml, and a respiratory rate of 15-25/min. After the intravenous administration of pancuronium bromide (4 mg), we tracheostomized the sheep to ensure an open airway. Arterial blood pressure was monitored by a pressure transducer (Model LPU-0.1A, Nihon Kohden) and arterial blood gases were determined using a blood gas analyzer (ABL520, Radiometer, Copenhagen, Denmark).

The right external jugular vein was exposed for insertion of a balloon catheter (Cliny catheter 8 Ch/Fr, Create Medic, Yokohama, Japan), and also for a large bore catheter for the rapid infusion of Ringer's lactate. The tip of the balloon catheter was placed in the cranial vena cava. During experiments, a drip infusion of Ringer's lactate (200 ml/h) was maintained through the large bore catheter.

Through a right sixth intercostal incision, the thoracic duct was identified at the level 3-5 cm cranial from the upper edge of the caudal mediastinal node and an ultrasound transit time flow probe (model 2SB, Transonic system, Ithaca, NY) connected to the flowmeter (model T106, Transonic system) was attached to the exposed thoracic duct. For the measurement of thoracic duct pressure, a 22-gauge fine needle was inserted directly into the thoracic duct at a point

approximately 2-3 cm cranial from the flow probe and connected to a pressure transducer (Model MPU-0.5A, Nihon Kohden). Thoracic duct lymph flow was not changed by insertion of this needle.

Airway, arterial, venous outflow, and thoracic duct pressures and thoracic duct lymph flow were continuously recorded on a polygraph (model R6000, Nihon Kohden). The zero level of each pressure was adjusted at the level of the cranial vena cava at its entrance to the heart. TDF was also displayed on a computer screen and digitally recorded every second on a computer hard disk. The data were analyzed by computer software to calculate a mean thoracic duct lymph flow (ml/min).

Experimental Protocols

(A) After baseline measurement, the cranial vena cava was partially occluded by inflation of the balloon in the vena cava to increase the venous outflow pressure for the thoracic duct. The procedure created a stable pressure elevation at several stages (approximately +10, +20, +30, or +40 cm H₂O from the baseline pressure in a random sequence) for 5 min. Between venous pressure elevations, the balloon was deflated completely for 10 min and all parameters returned to baseline levels, before a different venous pressure elevation was performed.

(B) Baseline lymph flow was increased by rapid i.v. fluid infusion (warm Ringer's lactate solution of 5% body weight) for 30 min. After the baseline, lymph flow was increased and stabilized at a high level, Protocol A was repeated.

Statistics

Data are presented as mean \pm S.D. A paired student's t test was applied for comparisons of measured parameters from baseline values. Correlation was examined by a linear regression analysis. A value of $P < 0.05$ was accepted as statistically significant.

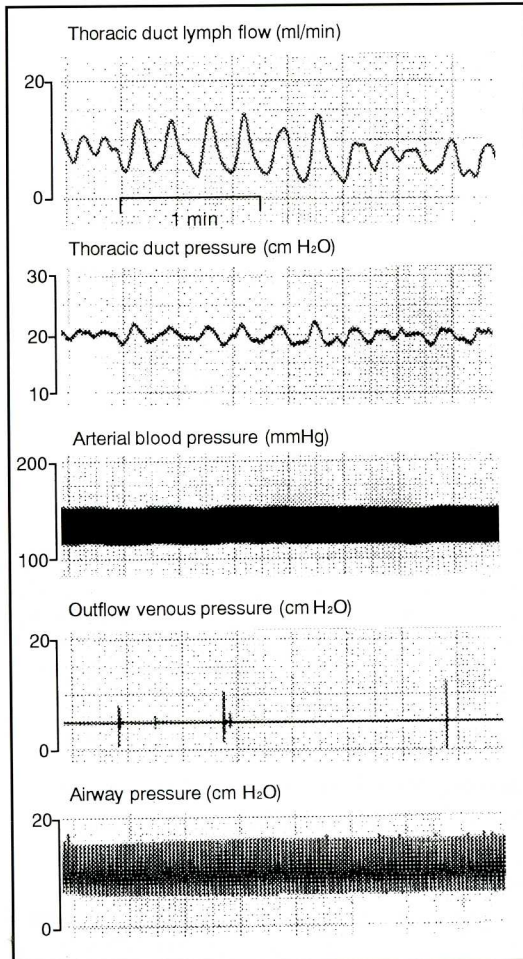


Fig. 1. Actual tracing of measured parameters during the baseline period. Thoracic duct pressure was measured at a point approximately 2-3 cm cranial from an ultrasound flow probe (see Methods).

RESULTS

Fig. 1 shows an actual tracing from a typical experiment during the baseline measurement. Lymph volume flow wave and the pressure fluctuation of the thoracic duct were synchronously pulsatile. There was no relation to arterial blood pulsation or airway pressure fluctuation. During the baseline period the mean lymph flow rate was 4.1 ± 1.3 ml/min, pulsation frequency of the thoracic duct was 5.4 ± 0.8 /min, mean thoracic duct

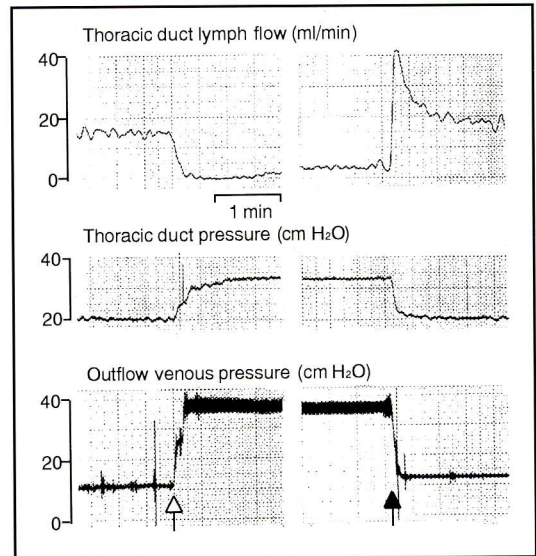


Fig. 2. Actual tracing of a typical experiment of increasing venous outflow pressure. The balloon in the cranial vena cava was inflated (white arrow) and later deflated (black arrow).

pressure was 13.5 ± 3.9 cm H₂O and mean venous outflow pressure was 10.3 ± 4.1 cm H₂O.

Response of Thoracic Duct Pressure to Increased Venous Outflow Pressure

Fig. 2 shows a typical tracing when venous outflow pressure was increased by inflation of the balloon in the cranial vena cava. Lymph flow decreased and thoracic duct pressure increased immediately after venous outflow pressure was increased. After deflating the balloon, thoracic duct pressure promptly returned to the baseline level in conjunction with a sudden increase in flow of lymph.

Venous outflow pressure was increased by inflation of the balloon in the cranial vena cava with several new incremental stable venous pressure levels (baseline 10.3 ± 4.1 ; 1; 20.5 ± 4.2 ; 2; 30.2 ± 5.4 ; 3; 40.8 ± 5.8 ; 4; 46.5 ± 1.5 cm H₂O). Fig. 3A shows individual data on thoracic duct pressure and venous outflow pressure. Thoracic duct and venous outflow

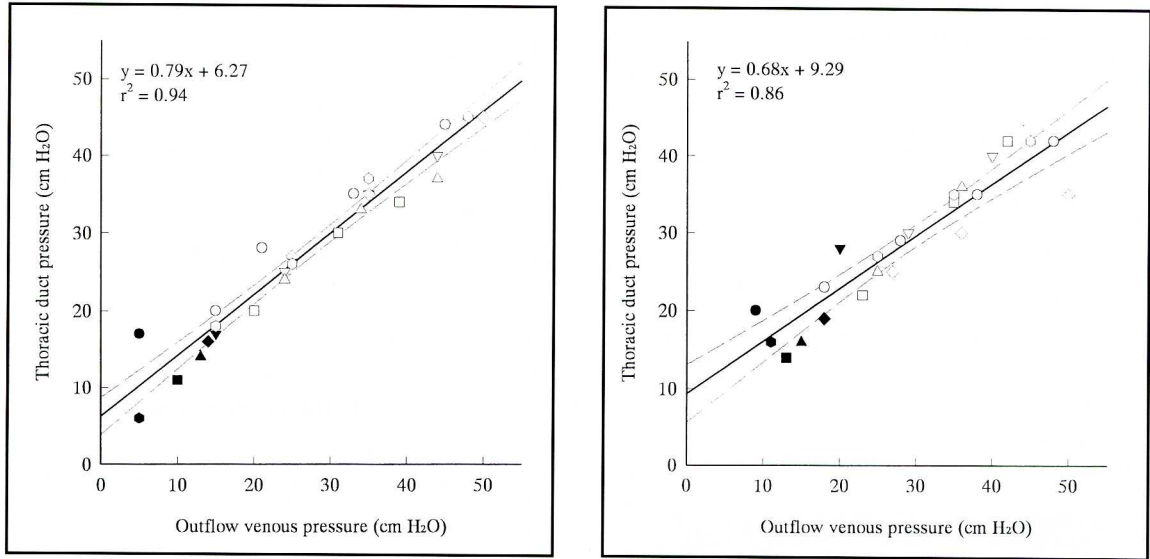


Fig. 3. Individual data on thoracic duct pressure response to increases of venous outflow pressure before (A) and after (B) rapid fluid infusion in 6 sheep. Thoracic duct pressure and venous outflow pressure was significantly correlated ($P < 0.01$). A regression line with a 95% confidence interval was obtained from all the data. Each symbol signifies an individual sheep. Closed symbols show baseline values and open symbols show values after balloon inflation in the cranial vena cava.

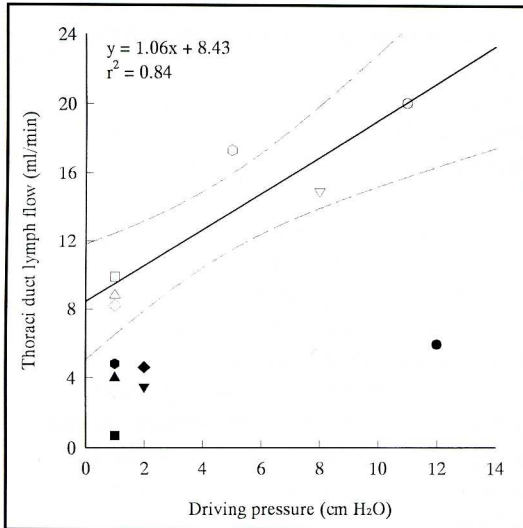


Fig. 4. Driving pressure and thoracic duct lymph flow of each sheep ($n=6$) during the baseline period before (closed symbols) and after rapid i.v. fluid infusion (open symbols). There was a significant correlation between thoracic duct lymph flow and the driving pressure after rapid fluid infusion ($P < 0.01$). A regression line with a 95% confidence interval was obtained from the data after rapid i.v. infusion. Each symbol signifies an individual sheep.

pressures were linearly correlated ($r^2=0.94$, $P < 0.01$).

After rapid fluid infusion of Ringer's lactate solution (5 ml/kg/30 min), venous outflow pressure increased significantly from 10.3 ± 4.1 to 14.3 ± 3.9 cm H₂O ($P < 0.01$). Baseline lymph flow increased from 4.4 ± 1.8 to 11.3 ± 4.1 ml/min ($P < 0.01$). Thoracic duct pressure increased from 13.5 ± 3.9 to 18.8 ± 4.6 cm H₂O ($P < 0.05$). Pulsation frequency of the thoracic duct changed from 5.4 ± 0.8 to 6.1 ± 0.8 /min but not significantly. In this high baseline flow condition, thoracic duct pressure responded immediately to inflation of the balloon in the cranial vena cava similarly to that under baseline flow conditions. Venous outflow pressure was incrementally increased (baseline; 14.3 ± 3.8 ; 1; 24.5 ± 3.5 ; 2; 35.0 ± 3.6 ; 3; 43.8 ± 4.4 ; and 4; 48.0 cm H₂O). Fig. 3B shows individual data on thoracic duct and venous outflow pressures after rapid fluid infusion. Thoracic duct and venous outflow pressures were linearly correlated ($r^2=0.86$, $P < 0.01$).

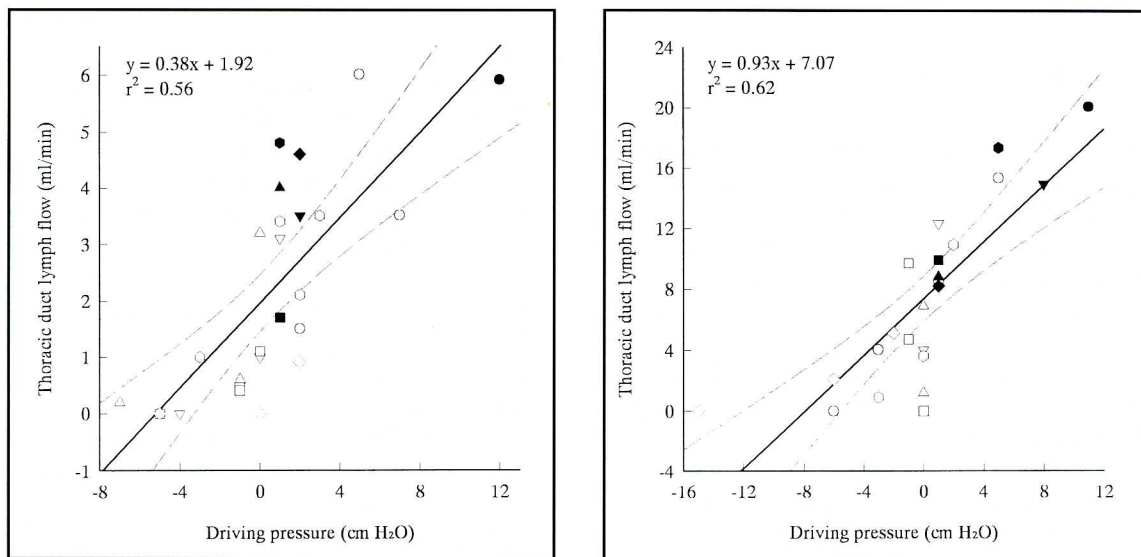


Fig. 5. Individual data on thoracic duct lymph flow and the driving pressure before (A) and after (B) rapid i.v. fluid infusion in 6 sheep. Baseline values are shown by closed symbols. After incremental inflation of a balloon in the cranial vena cava, thoracic duct lymph flow and driving pressure uniformly decreased (open symbols) ($P < 0.01$). A regression line with a 95% confidence interval was obtained from all data. Each symbol signifies an individual sheep.

Driving Pressure and Lymph Flow

Thoracic duct pressure minus venous outflow pressure was considered the driving pressure for thoracic duct lymph. The driving pressure of each sheep at the baseline before rapid fluid infusion is shown in Fig. 4 by closed symbols. Five sheep showed low driving pressures (1-2 cm H₂O). One sheep showed a high driving pressure (12 cm H₂O). A correlation between thoracic duct lymph flow and thoracic duct driving pressure was not observed. After rapid fluid infusion, thoracic duct lymph flow uniformly increased (Fig. 4, from closed symbols to open symbols). However, the driving pressure increased only in two sheep (from 1 and 2 cm H₂O to 5 and 8 cm H₂O, respectively). In two other sheep, the driving pressure decreased 1 cm H₂O and in the final two sheep the driving pressure was unchanged (Fig. 4, from closed symbols to open symbols). Although there was no correlation between thoracic duct lymph flow

and its driving pressure before rapid fluid infusion (closed symbols), there was a significant correlation between the two after infusion (open symbols, $r^2 = 0.84$, $P < 0.01$).

Fig. 5 shows individual data on thoracic duct lymph flow and the driving pressure before (A) and after (B) rapid i.v. fluid infusion and after progressive inflation of the balloon in the cranial vena cava. Both thoracic duct lymph flow and its driving pressure decreased after balloon inflation ($r^2 = 0.56$, $P < 0.01$) (Fig. 5A). After rapid i.v. fluid infusion (Fig. 5B), balloon inflation yielded similar correlation between lymph flow and driving pressure ($r^2 = 0.62$, $P < 0.01$). There was still some lymph flow even with a calculated negative driving pressure at both normal and high baseline flow conditions (Figs. 5A and 5B). Note that in Fig. 2, lymph flow was also recorded during negative driving pressure, i.e., 3ml/min after balloon inflation.

DISCUSSION

In 1963, Wégria et al (1) measured pressures in the thoracic duct and the left innominate vein, along with the rate of lymph flow in the thoracic duct in anesthetized dogs. They used a bubble flowmeter interposed in the thoracic duct and measured the pressure with a side arm of the flowmeter. They exposed an upper portion of the thoracic duct through a left thoracotomy. Pressure gradients between the upper portion of the thoracic duct and the innominate vein ranged from 11 to 24 mm H₂O. It is of interest that we observed a similar pressure gradient in the lower portion of the thoracic duct in sheep. Although the species differed, the pressure gradient in the thoracic duct is probably determined at its junction with the innominate vein.

In 1971, Browse et al (2) systematically measured the pressure gradients in the canine thoracic duct while preserving normal lymph flow into the jugular vein. These investigators introduced small catheters into the thoracic duct through tributaries from the neck and abdomen, but they did not quantify thoracic duct lymph flow rate. They reported that the pressure gradients were no more than 0.5-2.0 mmHg along the entire length of the thoracic duct. Our measurement of the driving pressures between the thoracic duct at the level of the caudal mediastinal node and the jugular vein was 1-2 cm H₂O (5 of 6 sheep) during baseline before rapid fluid infusion (see closed symbols, *Fig. 4*). Our findings were thus similar to Browse et al (2) with small pressure gradients along the whole thoracic duct under normal lymph flow conditions.

After Browse et al (2), Campbell and Heath in 1973 (4) measured the lymph flow rate and pressure of a lumbar lymphatic trunk in sheep. They introduced a cannula directly into the lumbar trunk and drained lymph to the outside of the body for flow determination. They calculated the measured pressure of the pulsatile portion of the measured lymphatic pressure, expressed the

phenomenon as contractility and determined that lymphatic contractility increased after intravenous fluid infusion. Campbell and Heath (4) demonstrated a linear relationship between lymphatic contractility and lymph flow rate in the sheep lumbar trunk and recognized that contractility was an intrinsic force to propel lymph to the jugular vein. In our study of 6 sheep after rapid i.v. fluid infusion, the baseline driving pressure increased in two, decreased in two, and was unchanged in two other sheep (*Fig. 4*). In each sheep, thoracic duct lymph flow increased after i.v. fluid infusion. Whereas there was no correlation between the driving pressure in lymph flow rate before i.v. fluid infusion (closed symbols in *Fig. 4*), a significant correlation occurred after i.v. infusion (open symbols in *Fig. 4*). These findings suggest that a higher driving pressure is needed to propel lymph forward with excess lymph production.

We recorded a negative driving pressure between the thoracic duct and the jugular vein (*Figs. 2,5*), a phenomenon noted by other investigators (2,5). Previous workers interpreted this finding as suggesting that lymph flow occurred only when the gradient became positive between the two neighboring lymphatic compartments (lymphangions) and that centripetal lymph flow was maintained by competent lymphatic valve action. Whereas this explanation is reasonable, it is also possible that some lymph flows into tributaries of the thoracic duct and is absorbed by blood capillaries in lymph nodes at the time of negative driving pressure. Lymph propulsion from a lymphangion to a neighboring lymphangion in the thoracic duct is likely regulated by intrinsic contractile activity, as supported by the findings of Reddy and Staub (6). The latter workers confirmed increased lymph flow through a doubly cannulated (proximal and distal end) canine thoracic duct when both cannulated ends were elevated to an equal height (zero driving pressure).

Thoracic duct pressure responded

immediately after the changes in venous outflow pressure (*Fig. 2*). Wégria et al (1) also demonstrated that an acute rise of pressure in the innominate vein was followed by a parallel increase of thoracic duct pressure in anesthetized dogs. This finding suggests that the thoracic duct has high pressure conductivity throughout its length despite numerous intraluminal valves. Reddy et al (6) examined the gross anatomy of the thoracic duct and showed a 16 cm thoracic duct in the dog contained 12 valves. We observed 18 valves in an excised 22 cm long thoracic duct segment between the portion of the flow probe and the outlet to the jugular vein. It is noteworthy that despite these valves that pressure conducts without time delay.

Drake et al (7) and Szabø et al (5) demonstrated that the pressure gradient between the intestinal lymphatics and the outflow portion was positive under normal conditions but readily became negative when outflow pressure was increased. In our study, thoracic duct pressure remained higher than venous outflow pressure until the latter exceeded 30 cm H₂O (*Fig. 3*), suggesting that the driving pressure remained positive until outflow pressure was very high. Perhaps pressure conductivity was "free" in the thoracic duct where the valves were less competent. Nonetheless, pressure from the outflow portion was diminished to the level of the intestinal lymphatics where pressure may have been dissipated into the abdominal lymph cisterns. Valves in the intestinal lymphatics are probably more competent and thus maintain lymph flow in a centripetal direction against the pressure differential.

Drake et al (8) increased neck vein pressure by i.v. fluid infusion and measured the pressure in the intestinal lymphatics. With this technique, intestinal lymphatic pressure was also slightly higher than neck venous pressure. A positive pressure gradient was preserved when lymph production was increased, as we similarly observed in the thoracic duct of the sheep (*Fig. 4*).

Although thoracic duct lymph flow

increased after rapid fluid infusion in each sheep, the driving pressure varied considerably. Nonetheless, overall there was a significant correlation between thoracic duct lymph flow and its driving pressure (*Fig. 4*). Perhaps higher lymph flow requires higher driving pressure when lymph flow exceeds a threshold level.

In our previous study (3), the response of thoracic duct lymph flow to the stepwise elevation of venous outflow pressure showed interindividual variation, and there was no direct correlation between thoracic duct lymph flow and venous outflow pressure. In this study, however, we demonstrated a significant correlation between thoracic duct lymph flow and its driving pressure when lymph dynamics were altered by balloon inflation in the cranial vena cava in conjunction with rapid i.v. fluid infusion (*Figs. 4, 5*). From these data we conclude that driving pressure is the main factor determining thoracic duct lymph flow.

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