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Transvascular fluid distribution of hyperoncotic Dextran solution

KIYOSHI HORIBA, YOSHIAKI TAKUMI, MITIHARU KANDORI, YASUSUKE INOUE, and HIROSHI NOGUCHI

Department of Anesthesiology and Acute Medicine, Aichi Medical University, Yazako Nagakute-cho, Aichi 480-11, Japan

Abstract

Purpose. The purpose of this study was to confirm the changes in extra- and intravascular fluid distribution during an i.v. infusion of hyperoncotic Dextran solution.

Methods. Twenty-three mongrel dogs with normal capillary integrities were divided into four groups. The R1 and R2 groups received i.v. infusion of Ringer lactate (RL) with a rate of 10 and 30 ml·kg^{-1}·h^{-1}, the D group 6% Dextran 70 solution (DEX) of 10 ml·kg^{-1}·h^{-1}, and the RD group DEX of 10 plus RL of 20 ml·kg^{-1}·h^{-1}. The distribution of infused fluid was assessed with the changes in circulating blood volume (CBV), extravascular fluid volume (EVW), and thoracic duct lymph volume (QL).

Results. In the R1 and R2 groups, EVW increased by 63% and 51%, respectively, of total infusion volume (tInf), while CBV increased by only 10% and 13% of tInf. In the D and RD groups, CBV increased by 103% and 51% of tInf. However, EVW decreased by 21% and increased by 32% of tInf, respectively. In the latter groups, the plasma volume filtered out into the extravascular compartment was less than in the corresponding former group by 52% and 6% of tInf, respectively and the restoration ratio of EVW by lymph was about 3 to 1.8 times greater.

Conclusion. One-fourth to one-third of the plasma expanding effect of 6% Dextran 70 solution was ascribed to direct fluid drawing from the extravascular space, and the rest was due to both the decrease in plasma filtration into extravascular space and the increase in lymphatic restoration of EVW.

Key words: Ringer lactate, Dextran 70, Lymphatic recirculation, Blood volume, Extravascular fluid volume

Address correspondence to: Y. Takumi

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Introduction

It has been widely believed that the intravenous administration of hyperoncotic solution increases plasma volume by drawing fluid from the extravascular compartment by colloid osmotic pressure difference and is beneficial for the resuscitation of hypovolemic shock [1–4]. However, the increase in plasma volume cannot be ascribed only to the direct reabsorption of extravascular fluid on the capillary bed but also to the recirculation through lymph.

The purpose of this study was to confirm the changes in extra- and intravascular fluid volumes during an i.v. infusion of hyperoncotic Dextran solution, and to analyze the quantitative relationship between these two contributing factors.

Materials and methods

This study was approved by the Animal Care and Use Committee of the Aichi Medical University, and the care and handling of animals were performed according to the guidelines of its animal center.

The study was conducted with 23 mongrel dogs weighing 10 to 15 kg each. They were anesthetized and intubated with an i.v. injection of ketamine hydrochloride of 20 mg·kg^{-1} and ventilated with oxygen-enriched air by a respirator (Aika, R-60, Tokyo, Japan). The dogs were immobilized with intravenous pancuronium bromide. The inspiratory oxygen concentration, respiratory rate and end-expiratory CO_2 concentration were adjusted to around the values of 50%, 12·min^{-1}, and 5%, respectively. A 10-F catheter was inserted into the bladder for the measurement of urine volume.

A 7-F balloon-tipped catheter was placed through the femoral vein into the pulmonary artery. Through one of the femoral arteries, a 7-F pigtail catheter (Cordis, Miami, FL, USA) was introduced into the left atrium

via the left ventricle [5], and was used for the measurement of left atrial pressure. Via the other femoral artery, a catheter with a thermistor probe at the tip was placed in the descending aorta for the measurements of the systemic arterial pressure, blood temperature, and cardiac output. Cardiac output was determined with the thermodilution method by injecting 5 ml of cold saline into the left atrium (Kimray, Oklahoma City, OK, USA; Model 3500E Cardiac Output Computer).

A small skin incision was made on the lateral side of the left external jugular vein, and the thoracic duct was exposed between the jugular vein and carotid artery. The duct was cannulated with a 20-gauge teflon needle in the caudal direction. An extension tube was connected to the needle, and the height of its outflow end was fixed on the level of cardiac atrium. The lymph that dropped from the tube end was caught in a small sterile cup and was returned into the vein every 15 min after measuring the volume. The lymph volume was calculated by summing the volumes of lymph during each measuring interval. The protein concentration was determined with the plasma and lymph at the final 15 min of the measuring interval. To avoid the coagulation of lymph, a small dose of heparin (50 units·kg^{-1}) was given intravenously. The ampulla of the right main lymphatic duct was ligated under skin incision.

The dogs were allowed to stabilize for 60 min under Ringer lactate (RL) infusion of 10 ml·kg^{-1}·h^{-1} and at the end of this period, the baseline measurements were carried out. The measurements consisted of blood temperature in the descending aorta, cardiac output (CO), heart rate (HR), mean arterial and pulmonary arterial

Table 1. Changes in hemodynamic parameters and arterial oxygen tension

	Groups	Baseline	60 min	120 min	180 min
CO (ml·min^{-1}·kg^{-1})	R1	97.7 ± 29.6	90.0 ± 35.5	91.3 ± 32.7	86.5 ± 29.8
	R2	98.5 ± 15.6	102.9 ± 33.7	95.8 ± 29.1	94.4 ± 30.2
	D	100.2 ± 16.0	114.8 ± 35.4	125.1 ± 42.0	131.9 ± 54.9
	RD	86.3 ± 21.9	123.2 ± 23.9[a]	131.4 ± 37.1	155.0 ± 60.3
CBV (ml·kg^{-1})	R1	69.4 ± 8.7	70.7 ± 8.8	72.6 ± 8.3	72.3 ± 10.2
	R2	76.7 ± 17.0	80.5 ± 18.6	84.9 ± 16.9	88.1 ± 19.1
	D	71.0 ± 8.4	80.4 ± 7.3	94.2 ± 9.4[ab]	101.8 ± 8.7[ab]
	RD	68.0 ± 2.4	85.3 ± 6.6[ab]	105.8 ± 5.3[abcd]	114.0 ± 2.6[abcd]
HR (min^{-1})	R1	180.3 ± 30.5	176.7 ± 31.7	172.8 ± 30.9	178.3 ± 27.1
	R2	174.0 ± 27.7	160.0 ± 25.0	156.3 ± 27.6	155.0 ± 30.9
	D	185.7 ± 18.7	179.2 ± 8.7	164.8 ± 8.5[a]	166.2 ± 9.8
	RD	168.5 ± 27.0	164.5 ± 20.9	171.5 ± 17.1	180.8 ± 11.7
MAP (mmHg)	R1	115.9 ± 16.6	115.2 ± 15.5	108.8 ± 14.3	106.0 ± 15.1
	R2	119.3 ± 10.3	109.8 ± 13.5	116.8 ± 15.5	110.5 ± 16.0
	D	95.6 ± 11.7	100.8 ± 19.6	104.5 ± 19.7	102.9 ± 23.7
	RD	103.1 ± 13.9	107.0 ± 20.6	101.1 ± 17.2	106.8 ± 11.7
MPAP (mmHg)	R1	16.7 ± 3.9	16.2 ± 3.3	17.1 ± 2.6	15.5 ± 1.7
	R2	15.1 ± 2.4	17.8 ± 2.6	21.3 ± 6.2	20.8 ± 6.5
	D	15.4 ± 3.7	18.4 ± 4.5	19.4 ± 5.6	20.3 ± 5.7
	RD	14.8 ± 5.3	19.9 ± 5.9	21.2 ± 8.0	27.0 ± 8.8[ab]
LAP (mmHg)	R1	4.2 ± 2.8	4.0 ± 2.7	3.8 ± 1.9	4.5 ± 2.3
	R2	3.5 ± 1.2	5.7 ± 2.5	8.2 ± 4.1[ab]	11.2 ± 7.5
	D	2.3 ± 1.4	3.5 ± 1.5	4.8 ± 2.0[a]	5.5 ± 2.3[a]
	RD	1.8 ± 1.7	3.5 ± 2.6	4.0 ± 2.9	5.3 ± 4.6
CVP (mmHg)	R1	2.7 ± 1.0	3.0 ± 1.7	3.0 ± 2.0	3.0 ± 2.0
	R2	1.8 ± 1.3	3.2 ± 1.5	4.3 ± 1.8[a]	4.8 ± 1.7[a]
	D	0.7 ± 0.6	1.5 ± 0.8[c]	2.0 ± 0.9[ac]	2.5 ± 1.0[ac]
	RD	0.8 ± 0.5	2.8 ± 1.5[a]	2.8 ± 1.5[a]	3.5 ± 2.1[a]
Pao_2 (mmHg)	R1	242.3 ± 18.7	248.5 ± 47.9	262.1 ± 58.6	255.9 ± 51.9
	R2	252.9 ± 33.6	243.3 ± 29.2	238.1 ± 28.6	217.7 ± 27.3
	D	219.3 ± 29.0	217.0 ± 19.7	214.3 ± 24.3	214.7 ± 29.3
	RD	230.2 ± 31.2	234.2 ± 23.4	217.5 ± 28.3	188.8 ± 38.4[b]

Values are mean ± SD. $n = 6$ in R1, R2, and D groups. $n = 5$ in RD group.
CO, cardiac output; CBV, circulating blood volume; HR, heart rate; MAP, mean arterial pressure; MPAP, mean pulmonary arterial pressure; LAP, left atrial pressure; CVP, central venous pressure; Pao_2, arterial oxygen tension.
[a] $P < 0.05$ *vs* baseline; [b] $P < 0.05$ *vs* R1 group; [c] $P < 0.05$ *vs* R2 group; [d] $P < 0.05$ *vs* D group.

pressures (MAP and MPAP), left atrial pressure (LAP), central venous pressure (CVP), arterial blood gases, circulating blood volume (CBV), thoracic duct lymph volume (QL), total protein concentrations in plasma (CP) and lymph (CL), and urine volume (UV). In addition, the changes in extravascular fluid volume (ΔEVW) were calculated by subtracting the UV and changed volume in circulating blood volume (ΔCBV) from the infusion volume during the measurement intervals. Here, the insensible water loss was neglected. The CP and CL were determined by spectrophotometry using the Biuret reaction.

For the measurements of CBV, we have developed a new method using the fluorescein isothiocyanate (FITC) labeled autologous red blood cells as the indicator [6]. The dilution rate of labeled red cells was determined with flow cytometer (Becton Dickinson, FACS-440, San Jose, CA, USA). The average value of CBVs determined by this method on normal mongrel dogs was 76.8 ± 9.2 ml·kg^{-1} (mean ± SD, n = 18) and approximated well the values reported previously [7–9]. This method enables a reproducible measurement of CBV without using radioactive indicators, and is applicable also for the observation of changes in CBV at least for 5 h after an injection of indicator cells [6].

Here, the dogs were divided into four groups. The first group (R1 group, n = 6) received intravenous infusion of RL at a rate of 10 ml·kg^{-1}·h^{-1}, the second (R2 group, n = 6) received RL of 30 ml·kg^{-1}·h^{-1}, the third (D group, n = 6) 6% Dextran 70 solution (DEX) at 10 ml·kg^{-1}·h^{-1}, and the fourth (RD group, n = 5) DEX of 10 ml·kg^{-1}·h^{-1} plus RL of 20 ml·kg^{-1}·h^{-1}. The rate of infusion was controlled by infusion pumps. After the baseline measurements the infusions mentioned above were started, and at every 60 min the same measurements were repeated up to 180 min. They were wrapped in a water blanket, and the temperature of the circulating water was set at 40°C. A fall in blood temperature below 38°C was not found in any of the animals.

The means and standard deviations were calculated for each of the measured parameters. The significances of difference in parameters within the same group were assessed by paired Student t-tests. The differences between the groups at the same timepoints were analyzed by Welch t-test. A P value of less than 0.05 was regarded as significant.

Results

Table 1 presents the values of hemodynamic parameters (CO, HR, MAP, MPAP, LAP, and CVP), CBV and arterial Po_2 during the experiment. After the start of infusion, LAP and CVP increased in three of the groups except R1. CBVs in the two Dextran groups (D and RD) showed significant increases at 120 and 180 min after the start of infusion. Compared with the R1 group, the increases in CBVs were significant in the D and RD groups. CO increased also in the two Dextran groups but their increases were not significant. MPAP increased with time in all groups, and in the RD group it was significantly higher than in the R1 group at 180 min. However, LAP in the RD group did not increase as much as MPAP. Pao_2 fell in both high-dose infusion groups (R2 and RD), but the significant fall when compared with the R1 group was found only in the RD group.

In Table 2, the values of ΔEVW, ΔCBV, cumulative urine and thoracic duct lymph volumes during 3 h (tUV and tQL), CL, CP, and the CL/CP ratio are presented. The tUVs in the R2 group (high-dose RL group) were significantly larger than in the other three groups. The tQLs in the two Dextran groups (D and RD) were significantly higher than in the R1 group, and its increase in the RD group was also significant compared with the R2 group. The EVW decreased in the D group while it increased in the other three groups. The most dominant increase was found in the R2 group (high-dose RL group). At 180 min after the start of infusion, the increases in EVW in the R2 and RD groups and its decrease in the D group were significant compared with the R1 group. However, its increase in the RD group was less than in the R2 group, although both groups received the same volume of fluid (30 ml·kg^{-1}·h^{-1}).

The CP decreased during the 3 h in all groups, and the decreases were significant in the three groups except R1. Their decreases were almost parallel to the increases in CBV. On the other hand, the CL also showed gradual reduction with time in all groups, and its decrease at 180 min was significant in the R2 and RD groups (high-dose infusion groups). The decrease in CL was smallest in the D group. Because of the more marked fall of CP than of CL, the calculated CL/CP ratios in the two Dextran groups increased during the experiment and became larger than 1.0 after 60 min. As explained later, this strange phenomenon seems to result from the faster transfer of plasma protein through the vascular wall rather than from the effect of Dextran 70.

Table 3 presents the ratios of tUV and tQL during the 3 h and ΔCBV and ΔEVW at 180 min to the cumulative infusion volume during the 3 h (tInf). The tUV/tInfs in the RL groups (R1 and R2) were 28% to 37%, but those in the Dextran groups (D and RD) were less and remained under 20%. The tQL/tInfs were significantly more in the Dextran groups than in the RL groups (D *vs* R1 and RD *vs* R2). The ΔCBV/tInf was 51% in the RD group and over 100% in the D group, contrasting to 10%–13% in the RL groups (R1 and R2). The ΔEVW/

Table 2. Changes in circulating blood volume and extravascular fluid retention, cumulative urine and thoracic duct lymph volumes, and protein concentrations in the plasma and lymph

	Groups	Baseline	60 min	120 min	180 min
ΔCBV (mg·kg^{-1})	R1		+1.3 ± 5.1	+3.2 ± 4.9	+2.9 ± 5.5
	R2		+3.8 ± 10.2	+8.2 ± 9.8	+11.4 ± 10.4
	D		+9.4 ± 4.5^{b}	+23.2 ± 5.1^{bc}	+30.8 ± 4.9^{bc}
	RD		+17.3 ± 3.1^{bcd}	+37.8 ± 2.6^{bcd}	+46.0 ± 1.6^{bcd}
ΔEVW (ml·kg^{-1})	R1		+6.1 ± 3.0	+11.5 ± 2.4	+18.9 ± 4.8
	R2		+20.3 ± 7.8^{b}	+34.7 ± 13.4^{b}	+45.7 ± 18.4^{b}
	D		−0.8 ± 3.6^{bc}	−6.5 ± 7.0^{bc}	−6.2 ± 7.2^{bc}
	RD		+8.9 ± 6.8^{cd}	+12.4 ± 10.8^{cd}	+29.0 ± 7.7^{bd}
tUV (ml·kg^{-1})	R1		2.7 ± 1.5	5.4 ± 2.4	8.3 ± 5.7
	R2		5.9 ± 4.9	17.1 ± 9.2^{b}	33.0 ± 16.2^{b}
	D		1.4 ± 0.8	3.4 ± 2.9^{c}	5.6 ± 2.8^{c}
	RD		3.7 ± 2.8	9.6 ± 8.2	14.9 ± 8.4^{c}
tQL (ml·kg^{-1})	R1		4.3 ± 1.1	9.1 ± 2.8	14.2 ± 2.8
	R2		4.9 ± 0.8	11.1 ± 1.6	18.3 ± 3.8
	D		6.9 ± 2.5	14.4 ± 4.8^{b}	23.5 ± 8.0^{b}
	RD		7.6 ± 3.0	17.5 ± 5.8^{b}	29.4 ± 6.4^{bc}
CP (g·dl^{-1})	R1	5.13 ± 0.81	4.89 ± 0.83	4.65 ± 0.92	4.70 ± 1.06
	R2	4.88 ± 0.53	4.21 ± 0.59	4.00 ± 0.63^{a}	3.61 ± 0.49^{a}
	D	5.15 ± 0.33	4.75 ± 0.49	3.85 ± 0.59^{a}	3.25 ± 0.72^{ab}
	RD	4.87 ± 0.80	4.33 ± 0.76	3.50 ± 0.56^{ab}	2.49 ± 0.71^{abc}
CL (g·dl^{-1})	R1	4.30 ± 0.80	4.20 ± 0.73	4.04 ± 0.69	3.83 ± 0.87
	R2	4.43 ± 0.78	3.58 ± 0.78	2.91 ± 0.72^{ab}	2.69 ± 0.87^{ab}
	D	4.79 ± 0.45	4.95 ± 0.80^{c}	4.42 ± 0.67^{c}	4.18 ± 1.17^{c}
	RD	4.62 ± 0.69	4.48 ± 0.79	4.04 ± 1.02	3.27 ± 1.03^{a}
CL/CP	R1	0.84 ± 0.09	0.86 ± 0.08	0.88 ± 0.05	0.82 ± 0.07
	R2	0.91 ± 0.13	0.86 ± 0.19	0.73 ± 0.17	0.75 ± 0.26
	D	0.93 ± 0.07	1.05 ± 0.23	1.19 ± 0.38^{c}	1.42 ± 0.79
	RD	0.95 ± 0.04	1.04 ± 0.05^{ab}	1.15 ± 0.20^{bc}	1.31 ± 0.21^{abc}

Values are mean ± SD. $n = 6$ in R1, R2, and D gruops. $n = 5$ in RD group.
ΔCBV and ΔEVW, changes in blood volume and extravascular fluid volume from baseline; tUV and tQL, cumulative urine and thoracic duct lymph volume from baseline; CP, total protein concentration in plasma; CL, total protein concentration in lymph.
[a] $P < 0.05$ *vs* baseline; [b] $P < 0.05$ *vs* R1 group; [c] $P < 0.05$ *vs* R2 group; [d] $P < 0.05$ *vs* D group.

Table 3. Ratios of cumulative urine and lymph volumes during the 3 h, and the increases in circulating blood volume and extravascular fluid retention at 180 min to the cumulative infusion volume during the 3 h

		Group			
		R1	R2	D	RD
tInf	ml·kg^{-1}	30.0 ± 0.0	90.0 ± 0.0	30.0 ± 0.0	90.0 ± 0.0
tUV/tInf	%	27.7 ± 19.0	36.7 ± 18.0	18.7 ± 9.3	16.6 ± 9.3^{b}
tQL/tInf	%	47.3 ± 9.3	20.3 ± 4.2^{a}	78.3 ± 26.7^{ab}	32.7 ± 7.1^{abc}
ΔCBV/tInf	%	9.7 ± 18.3	12.7 ± 11.6	102.7 ± 16.0^{ab}	51.1 ± 1.8^{abc}
ΔEVW/tInf	%	63.0 ± 16.0	50.8 ± 20.4	−20.7 ± 24.0^{ab}	32.2 ± 8.6^{ac}
tQL + ΔEVW	ml·kg^{-1}	33.1 ± 5.6	64.0 ± 18.8^{a}	17.3 ± 10.8^{ab}	58.4 ± 10.0^{ac}
(tQL + ΔEVW)/tInf	%	110.3 ± 18.7	71.1 ± 20.9^{a}	57.7 ± 36.0^{a}	64.9 ± 11.1^{a}
tQL/(tQL + ΔEVW)	%	42.9 ± 8.5	28.6 ± 5.9^{a}	135.8 ± 46.2^{ab}	50.3 ± 11.0^{bc}
ΔCBV − tQL	ml·kg^{-1}	−11.3 ± 6.2	−6.9 ± 11.1	+7.3 ± 9.4^{ab}	+16.6 ± 6.6^{ab}
(ΔCBV − tQL)/tInf	%	−37.7 ± 20.7	−7.7 ± 12.3^{a}	+24.3 ± 31.3^{a}	+18.4 ± 7.3^{ab}

Values are mean ± SD at the end of the experiment.
tInf, tUV, and tQL, cumulative infusion volume, cumulative urine volume, and cumulative thoracic duct lymph volume; ΔCBV and ΔEVW, increases in circulating blood volume and extravascular fluid volume during the 3 h.
[a] $P < 0.05$ *vs* R1 group; [b] $P < 0.05$ *vs* R2 group; [c] $P < 0.05$ *vs* D group.

tInfs in the R1, R2, D, and RD groups were 63%, 51%, −21%, and 32%, respectively. The ratio of ΔEVW to tInf decreased due to the Dextran infusion. However, there was no significant difference between the R2 and RD groups.

Discussion

The 6% Dextran 70 solution used in this study is Macrodex (Pharmacia, Sweden), and the solvent of Dextran is normal saline. Therefore its crystalloid osmotic pressure is the same as RL. The mean molecular weight of Dextran 70 is 70000, larger than that of albumin (66000). On this account, the passage of the albumin molecules through the capillary wall is expected to be faster than Dextran 70, and the share of albumin in extravascular fluid should have been larger than in plasma. This might be the cause of the peculiar increase in CL/CP of over 1.0 in the two Dextran groups.

Regrettably, we could not determine the colloid osmotic pressures (COPs) in lymph and plasma in this study. However, the COP of canine serum with the total protein concentration of $5\,g\cdot dl^{-1}$ (mean CP of the four groups at the baseline: Table 2) can be derived as 13.1 mmHg with the equation after Navar and Navar [10]. On the other hand, the average COP of Macrodex is reported as about 59 mmHg [11]. Therefore, the COP of 1:2 mixture solution of Macrodex and RL was about 20 mmHg. As a result, the animals in the D and RD groups received colloidal solutions with about 4- and 1.5-times stronger oncotic pressure than in plasma.

We have determined the lymph volume with the outlet height fixed on the level of cardiac atrium. Because the lymphatic outflow into the vein is impeded by venous pressure, the QLs obtained in this study may overestimate the real volume. However, as presented in Table 1, there were no significant differences in the CVPs between the groups which received the same volumes of infusion (R1 *vs* D and R2 *vs* RD). For this reason, we regarded this possible over-estimation of tQLs as negligible, at least in assessing their shares in the tInfs.

The plasma volume that was filtered out into the extravascular compartments may be derived as the sum of tQL and ΔEVW, if it is assumed that the insensible water loss was zero. At the end of the experiment, they were 33.0, 63.9, 17.1 and $58.5\,ml\cdot kg^{-1}$ and their ratios to tInf were 110%, 71%, 57% and 65%, respectively, in the four groups (Table 3; (tQL + ΔEVW) and (tQL + ΔEVW)/tInf). The differences of these values between R1 and D or R2 and RD (15.9 and $5.4\,ml\cdot kg^{-1}$, respectively) were the reductions in the filtration caused by the infusion of Dextran solutions with 4- and 1.5-times stronger oncotic pressures than in plasma. These values amounted to 53% and 6% of tInfs during the 3 h.

Of these filtered fluid volumes, the volume of lymph was restored again in the intravascular space. The ratio of lymph to the filtered volume (Table 3: tQL/(tQL + ΔEVW)) presents a restoration ratio via lymph. These ratios in the D and RD groups at 180 min were 136% and 50%, respectively, and about 3- and 1.8-times more than in the R1 and R2 groups (43% and 29%, respectively). In the D group it was over 100%, suggesting that more fluid than the filtered fluid returned to the intravascular space. The lymphatic restoration of interstitial fluid to intravascular space was improved clearly by hyperoncotic Dextran infusion.

It has been suggested that the administration of colloidal solution can facilitate the formation of edema [12,13]. This suggestion seems to originate from the hypothesis that the colloid molecules are trapped in the coil structure in the matrix of interstitial ground substance and are hardly washed out into lymph [14,15]. This hypothesis may be true only when the interstitial matrix is hydrated and swollen. In this study, we preferred to infuse fluid of $30\,ml\cdot kg^{-1}\cdot h^{-1}$ for swelling the interstitial matrix (R2 and RD groups). By this high-dose infusion, EVW increased markedly in both the R2 and RD groups. However, the lymphatic restoration ratio increased more in the RD group than R2. We could not obtain any evidence for this suggestion.

The reason why the infusion of hyperoncotic Dextran solution increases the lymphatic restoration of interstitial fluid is unknown. The CLs in the two Dextran groups did not decrease as in the RL groups, and the ΔEVWs in the former groups did not increase as in the latter groups (Table 2). These results may suggest that the expansion and swelling of interstitial ground substance is restricted when the oncotic pressure of the fluid filtered out into the interstitial space is high. For the interstitial fluid to lodge in that compartment stably, there must be sufficient numbers of coils with enlarged diameter, which allow the capture of colloid molecules in them.

As in the case of Dextran groups in this study, if the oncotic pressure in the filtered fluid is high, the volume of filtered fluid which hydrates the interstitial ground substance and expands the coils in its matrix might be less, depending on the strength of oncotic pressure in the filtered fluid. This might have been the cause of increasing effects on the lymphatic drainage of the hyperoncotic Dextran solution.

The difference between ΔCBV and tQL may fit either the volume of infused fluid not filtered out into the extravascular space, or the volume reabsorbed directly from the extravascular compartment into the capillaries. This fluid volume was 24% and 18% of tInf in the D and RD groups (Table 3: ΔCBV − tQL and (ΔCBV −

tQL)/tInf). On the other hand, this value was negative in the R1 and R2 groups (−38% and −8%, respectively), suggesting that this volume of lymph was lost in urine. Because the ΔCBV/tInfs in the former groups were 103% and 51%, respectively, about 1/4 to 1/3 of the plasma-expanding effect of 6% Dextran 70 solution consists either in the direct fluid reabsorption from the extravascular compartment into blood or its direct intravascular retention.

In conclusion: (1) Infusion of hyperoncotic Dextran solution not only reduced the plasma volume filtered out into extravascular space by 53% to 6% of tInf depending on the strength of oncotic pressure, but also increased the lymphatic restoration ratio of interstitial fluid to intravascular space by 3- to 1.8-times more. (2) In the Dextran groups, a larger increase in blood volume over the lymph volume fitted 24% and 18% of tInf, and consisted either of the fluid directly reabsorbed from the extravascular compartment into the capillaries or of direct retention of the infused fluid in the intravascular compartment. One-fourth to one-third of the plasma expanding effect of 6% Dextran 70 solution was ascribed to these two direct effects.

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