The Importance of Plasma Colloid Osmotic Pressure for Interstitial Fluid Volume and Fluid Balance after Elective Abdominal Vascular Surgery

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The relationships between plasma colloid osmotic pressure (COP_p) and interstitial fluid volume (IFV) as well as postoperative fluid balance were investigated in a prospective study involving 53 patients undergoing elective abdominal aortic reconstruction. The patients were divided into four groups according to pre- and postoperative blood replacement and fluid therapy programs whereby a continuum of postoperative COP_p-values between 33 and 16 mmHg was obtained. Measurements were done before the operation and on days 1 and 4 after surgery. After surgery, COP_p below 20 mmHg led to increased IFV. On day 1, COP_p was linearly correlated to the total amount of fluid retained during the day of operation. A positive fluid balance of 3 L on this day ensured unchanged extracellular fluid volume (ECV). Of the 3 L, 1.5 L was insensible water loss and 1.5 L had moved into the cells. On day 4 after surgery, COP_p below 22 mmHg was associated with increased plasma volume. The authors suggest that COP_p be maintained above 20 mmHg after major surgery, and positive fluid balance should not exceed 5 L during the day of operation.

THE TREND in pre- and postoperative fluid therapy since 1961 has moved towards increasing use of crystalloids on the expense of colloid solutions. Still arguments for and against either proposition are advanced.[1] It is commonly agreed that pulmonary function is relatively insensitive to lowering of plasma colloid osmotic pressure (COP_p).[2-6] Conditions in the systemic circulation after lowering COP_p, however, are not directly comparable to those of the pulmonary circulation but have received less attention, though several indications suggest that edema due to low COP_p may interfere with various functions other than the pulmonary. The aims of the present study were: (1) to obtain a continuum of COP_p values after a standardized major abdominal operation; (2) to relate the concomitant changes in extracellular fluid volume (ECV) and distribution to the COP_p; and (3) to define the limit beyond which a decreasing COP_p leads to an increase in interstitial volume. Determination of such a limit should enable the surgeon to choose a fluid regimen according to the degree of postoperative edema considered acceptable.

Materials and Methods

Fifty-three patients undergoing elective reconstructive surgery on the abdominal aorta were included in this prospective study. ECV, plasma volume (PV), and COP_p were determined before operation and on the first and fourth postoperative days. The informed consent of all patients was obtained according to the guidelines in the Helsinki declaration. Blood substitution and fluid replacement were carried out by four different programs. In *group A* (13 patients), blood loss was replaced quantitatively by whole blood; in addition, albumin was administered to maintain postoperative COP_p at preoperative levels. In *group B* (13 patients), blood loss was replaced, but no extra albumin was given. Also, *group C* (14 patients) had blood loss replaced milliliter for milliliter, and an intraoperative hydration program was followed, giving 15 ml isotonic saline per kg body weight during the first hour of operation and 7.5 ml isotonic saline per kg each of the following 2 hours. *Group D* (13 patients) had blood loss up to 15% of the preoperative blood volume replaced by isotonic saline. Blood loss in excess of this was substituted by whole blood. The same hydration program was followed as in group C. Thus, increased hydration and a decreasing COP_p were obtained. All operations were performed in general anaesthesia using barbiturate induction followed by nitrous oxide-oxygen supplemented by fentanyl and diazepam.

ECV was measured by means of the bolus injection,

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TABLE 1. *Patient Characteristics and Composition of the Four Groups*

	A	B	C	D
Number of patients	13	13	14	13
Women/men	2/11	4/9	3/11	2/11
Age (years)	57 (2.4)*	58 (3.0)	64 (1.6)	60 (2.4)
Body weight (kg)	64.7 (2.5)	63.8 (2.7)	70.1 (3.1)	73.4 (3.0)
Surface area (m^2)	1.74 (0.04)	1.74 (0.05)	1.79 (0.04)	1.85 (0.04)

* Mean values and (SEM).

residue detection method.[7] After injection of 5000 mg polyfructosan-S (Inutest®, Laevosan Gesellschaft, Linz, Austria) through a central venous catheter, blood samples were taken from the same catheter at intervals between 5 and 240 minutes. The concentration of polyfructosan-S in plasma water was determined and plotted semilogarithmically against time. Non-compartmental analysis was applied and ECV calculated. PV was measured concomitant with ECV by means of ^{131}-I-labelled albumin (IK 20 S, Kjeller, Norway) using the semiautomatic apparatus Volemetron® (Ames Lab-Tek Inc., Billeria, MA).[8] Interstitial fluid volume (IFV) was determined by subtracting the PV from ECV. Plasma colloid osmotic pressure was measured at the same time as body fluid volumes using the Hansen osmometer.[9]

From the morning of the operation, fluid and electrolyte intake were registered, and urine output and concentration of electrolytes in urine were measured daily. Patients in diuretic therapy before the operation were maintained on diuretics; otherwise, diuretics were avoided. The patients were weighed on all days of measurement.

Non-parametric statistics were used as tests for significance. The Wilcoxon signed rank test for pair differences was used to compare pre- and postoperative data and the Mann-Whitney test to compare values from different groups.

Results

Table 1 shows the mean age and the sex distribution in the four groups as well as preoperative body weight and surface area. The baseline values for COP_p, ECV, PV, and IFV before and after correction to 1.73 m^2 body surface area are shown in Table 2. No statistically significant differences were found between the groups. In Figure 1, the changes in IFV/1.73 m^2 are plotted against the COP_p for all patients on both postoperative days of measurement. The preoperative mean COP_p for all patients was 27 ± 2.4 mmHg (mean ± SD). The change in IFV for values above 22.2 mmHg (*i.e.*, preoperative mean minus 2 SD) was evenly distributed between increased and decreased IFV. COP_p values below 22.2 mmHg lead to increased IFV in 28 patients and decreased IFV in four patients. All COP_p values below 20 mmHg were accompanied by increased IFV. No linear correlation was found.

On the first postoperative day, 35 patients had an unchanged PV, defined as PV being within ±10% of the preoperative value. In these patients, the fluid balance was increasingly positive with decreasing COP_p. Figure 2 depicts the relation between COP_p on the first postoperative day and standardized fluid balance, *i.e.*, fluid balance/1.73 m^2 ($Fbal_{st}$) of the day of operation. The equation for the regression line of the 35 patients with unchanged PV was $Fbal_{st} = -0.34 \times COP_p + 11.8$ ($N = 35$; $r = -0.80$; $p < 0.0001$). The corresponding relationship for the patients with either increased or decreased PV is shown in Figure 3. The regression line equation was: $Fbal_{st} = -0.31$

TABLE 2. *Baseline Values of the Measured and Calculated Variables before and after Correction to 1.73 m^2 Body Surface Area*

	A	B	C	D
COP_p (mmHg)	26.2 (0.7)*	28.3 (0.7)	26.4 (0.5)	27.0 (0.6)
ECV (L)	9.3 (0.5)	8.3 (0.3)	10.0 (0.7)	9.1 (0.3)
ECV (L/1.73 m^2)	9.2 (0.4)	8.2 (0.4)	9.7 (0.5)	8.5 (0.3)
PV (L)	3.2 (0.1)	2.8 (0.1)	3.6 (0.2)	3.6 (0.1)
PV (L/1.73 m^2)	3.1 (0.1)	2.8 (0.1)	3.5 (0.1)	3.3 (0.1)
IFV (L)	6.1 (0.4)	5.5 (0.3)	6.4 (0.6)	5.6 (0.3)
IFV (L/1.73 m^2)	6.1 (0.4)	5.4 (0.4)	6.2 (0.4)	5.2 (0.2)

COP_p = plasma colloid osmotic pressure; ECV = extracellular fluid volume; PV = plasma volume; IFV = interstitial fluid volume.
* Mean values and (SEM).
No statistically significant differences among the groups.

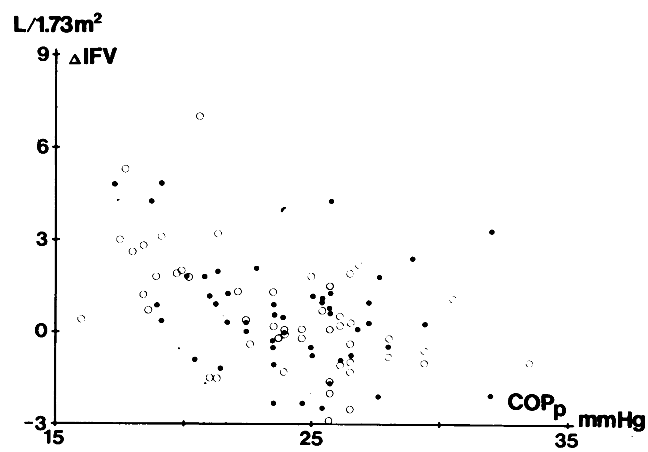

FIG. 1. Postoperative relation between COP_p and change in interstitial fluid volume. Open circles: first postoperative day. Closed circles: fourth postoperative day.

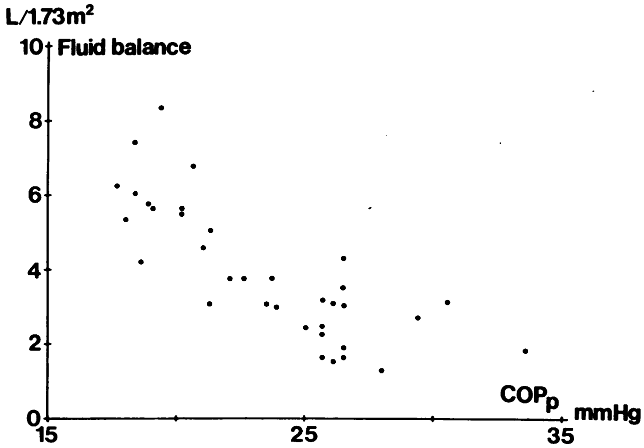

FIG. 2. Plasma colloid osmotic pressure *vs.* fluid balance on the first postoperative day in patients with unchanged plasma volume.

$\times$ COP_p + 10.5 ($N = 18$; $r = -0.80$; $p < 0.0001$). The slopes and interception values of two regression lines were not significantly different.

The changes in extracellular fluid volumes/1.73 m^2 and the fluid balance/1.73 m^2 on day 1 after surgery not corrected for insensible water loss are shown in Table 3 for all groups. A positive linear relationship was found between fluid balance/1.73 m^2 on the day of operation and the change in interstitial fluid volume/1.73 m^2 (ΔIFV) from before operation to day 1. The equation was $\Delta IFV = 0.77 \times Fbal_{st} - 2.05$; ($N = 53$; $r = 0.667$; $p < 0.001$). To determine how the mean fluid balance affected the ECV in the four groups, we subtracted the changes in IFV and PV from the mean fluid balance. In the groups having less than 3 L positive fluid balance, a decrease in ECV was found, whereas fluid balance above 3 L resulted in

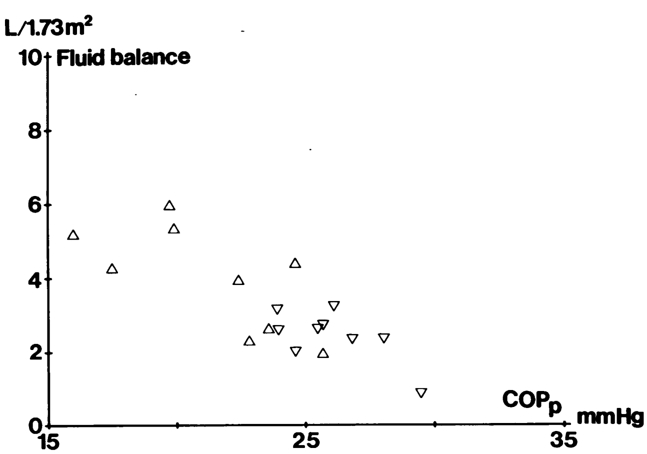

FIG. 3. Plasma colloid osmotic pressure *vs.* fluid balance on the first postoperative day in patients with either increased or decreased plasma volume. Triangles pointing up: increased plasma volume. Triangles pointing down: decreased plasma volume.

TABLE 3. *Fluid Balance/1.73 m^2 and Associated Changes in ECV on Postoperative Day 1*

	A*	B*	C*	D*
Fluid balance	+2.2 (0.3)†	+2.7 (0.2)	+3.8 (0.3)	+5.5 (0.2)
ΔIFV	−0.8 (0.4)	0.0 (0.4)	+0.9 (0.5)	+2.3 (0.4)
ΔPF	−0.1 (0.1)	−0.2 (0.1)	0.0 (0.1)	+0.2 (0.05)
Fluid balance-ΔECV	+3.1 (0.5)	+2.9 (0.4)	+2.9 (0.4)	+3.0 (0.4)

* L/1.73 m^2.
† Mean values and (SEM).

increased ECV. The difference between fluid balance and the sum of changes in IFV and PV was found to be 3 L for all four groups. The distribution of this surplus fluid necessary to maintain unchanged ECV was also analyzed. Plotting the fluid balance (Fbal) *versus* change in body weight (ΔBW) leads to a positive linear correlation given by the equation: $\Delta BW = Fbal \times 1.08 - 2.02$ ($N = 53$; $r = 0.8672$). Solving this equation for $\Delta BW = 0$ gives $Fbal = 1.87$ L. This amount of fluid corresponds to the unmeasured weight losses and can be accounted for by the insensible water loss plus the weight loss by catabolism.

The change in ECV plotted against change in BW revealed a positive linear correlation with the equation: $\Delta ECV = \Delta BW \times 0.71 - 0.83$ ($N = 53$; $r = 0.7300$). Solving this equation for $\Delta ECV = 0$ leads to a $\Delta BW = 1.2$ kg. Thus 1.2 L of the retained fluid was not found in the ECV on the first postoperative day. Table 4 shows the effect of fluid balance/1.73 m^2 on the ECV. Some scatter on the results is seen but the pattern is clear: fluid balance below 2 L was associated with a decreased ECV. A positive fluid balance of 2–4 L led to an unchanged ECV while fluid accumulation above 5 L inevitably led to an increased ECV. The mean fluid balances of patients with increased, unchanged, or decreased ECV were 4.6 ± 1.8 L/1.73 m^2, 3.2 ± 0.7 L/1.73 m^2, and 2.4 ± 1.2 L/1.73 m^2, respectively. Each value is significantly different from the others ($p < 0.05$).

The cumulative fluid balance on day 4 was plotted against the COP_p and the resultant PV change was recorded (Fig. 4). It was found that all COP_p values below

TABLE 4. *Effect of Fluid Balance/1.73 m^2 on ECV on the First Postoperative Day*

Fluid Balance	No Patients with Increased ECV	No Patients with Unchanged ECV	No Patients with Decreased ECV
<2 L/1.73 m^2	1	1	6
2–4 L/1.73 m^2	6	16	4
4–5 L/1.73 m^2	2	2	2
>5 L/1.73 m^2	13	0	0
Total	22	19	12

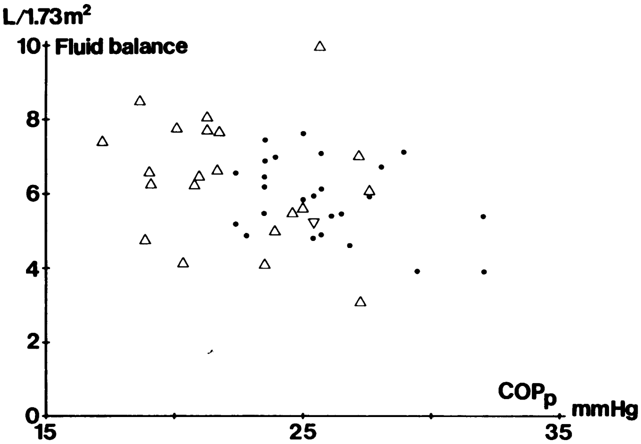

FIG. 4. Plasma colloid osmotic pressure *vs.* cumulative fluid balance on the fourth day after surgery. Circles: unchanged plasma volume. Triangles depict changed plasma volume as in Fig. 3.

22.2 mmHg were associated with increased PV. For values above 22.2 mmHg, 25 patients had unchanged PV, eight had increased PV, and one patient had a lower PV on the fourth day than before operation.

Discussion

The present study appears to be the first dealing with the relationship between COP_p and IFV after major elective surgical procedures. It is shown that COP_p can be lowered to about 20 mmHg before interstitial edema occurs and that COP_p values below this limit invariably lead to interstitial edema. No linear correlation was found between the COP_p and change in IFV either the first or the fourth postoperative day, but all COP_p values below 20 mmHg were associated with increased IFV. This can hardly be explained by a simple dilution of the plasma proteins as PV was unchanged in most patients with decreased COP_p on day 1. The findings are in accordance with computer simulation results,[10] and consistent with the proposition of an edema-preventing washout of plasma proteins from the interstitium, as described by Fadnes[11] and Reed.[12] This mechanism was shown to be exhausted in the rat when the COP_p was lowered more than some 5–10 mmHg; in the present study, the safety margin appears to be about the same order of magnitude.

A positive fluid balance of 1.87 L in surplus of the measured losses resulted in an unchanged body weight. Insensible water loss on the day of operation has been estimated to be approximately 1500 ml,[13] leaving some 300 gm to catabolic weight loss[14] and eventual underestimation of operative blood loss. Out of the 3000 ml fluid surplus needed to ensure an unchanged ECV, 1200 ml of fluid are retained on the day of operation. Adding the endogenous water production of about 300 ml/24 h, there is a total of approximately 1500 ml of extra fluid that cannot directly be accounted for. Considering that plasma osmolality decreased in all groups of patients, despite hyperosmolality of the retained fluid, and the fact that cells gain sodium and lose potassium following surgical trauma,[15–18] it seems a reasonable suggestion that these 1500 ml of fluid have moved into the cells.

The linear correlation between COP_p and fluid balance on the first day after surgery corresponds to experimental results with colloid and crystalloid priming solutions in cardiopulmonary bypass.[19] This reflects the well known fact that more fluid is needed to maintain circulating volume when crystalloid solutions are used.

In discussing consequences of a low COP_p, distinction should be drawn between the effect on the pulmonary and the systemic circulation. Accumulated clinical evidence now favors the concept that extravascular fluid shift in the lung is relatively insensitive to lowering of the colloid osmotic pressure in plasma. This apparent conflict with the Starling equation is explained by two physiological properties of the pulmonary circulation. Firstly, the pulmonary lymphatics have the ability to increase fluid transport up to tenfold[5,20] and, thus, to cope with an increased amount of fluid across the capillary membrane. Secondly, as the interstitial protein concentration in the lungs reaches up to 70–80% of that of plasma,[5,20,21] the colloid osmotic pressure difference across the capillary endothelium is relatively small and the hydrostatic pressure difference becomes the main factor determining transcapillary fluid transport. Further, as pointed out by Civetta,[22] the high interstitial protein concentration acts as an effective safety mechanism against edema formation by offsetting increases in the pressure gradient through a decrease in interstitial protein concentration caused by dilution and washout. In patients to be resuscitated from hypovolemic or septic shock, conditions may be different. A recent report on pulmonary edema in such cases seems to indicate that the maintenance of a normal COP_p may be of greater importance in the critically ill patients.[23]

In the systemic circulation, on the other hand, transcapillary fluid transport is to a greater extent governed by the Starling equilibrium forces.[24] Thus, lowering of COP_p below 20 mmHg exposes the tissues to edema formation, which in divers ways may interfere with normal functions. A number of reports have described adverse effects of interstitial edema in several regions, including the cardiac muscle[19,25–28] and intestines.[19,29–34] Also peripheral oxygen transport has been reported to suffer,[35,36] with eventual retarded wound healing and increased susceptibility to wound infection as consequences.[37–40] Less tangible, though not less relevant, is the concern expressed by Shackford et al.[41] that overhydration makes mobilization of the patients more difficult. Possible advantages of a low COP_p, as opposed to maintaining COP_p at preoperative level by supplemental albumin infusion, may be facilitated lymphatic drainage from the overhydrated interstitium[21] and increased stimulation of hepatic protein synthesis, including the acute phase proteins.[42,43] In the authors' opinion, COP_p should not be allowed to go below 20 mmHg, corresponding to a total protein concentration of 50 g/L, and the fluid balance should not exceed 5 L per 1.73 m^2 surface area on the morning of the first postoperative day. If routine fluid administration regularly exceeds this limit in a clinic, the patients should be weighed and COP_p controlled.

On the fourth postoperative day after uncomplicated major elective surgery, the total circulating protein mass had attained the preoperative level in these patients.[42] As the present study shows (Fig. 4), a decrease in COP_p at this time is likely to be a dilution phenomenon associated with increased PV and IFV. In the clinical setting this observation is of consequence for the treatment. If the decreased protein concentration is treated with infusion of albumin or whole blood under these circumstances, it may well result in overloading of the circulation and eventually pulmonary stasis or edema.

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