The importance of monitoring circulating blood volume (CBV) during perioperative management is widely recognized in critically ill patients. The purpose of this study was to investigate the change in CBV following craniotomy by using indocyanine-green pulse spectrophotometry.

**Object.** Circulating blood volume and plasma hormones related to stress and fluid regulation were measured five times: preoperatively, immediately postoperatively, and 1, 2, and 7 days after craniotomy was performed in 17 patients with a brain tumor or an unruptured aneurysm.

The mean value of CBV preoperatively was 82 ml/kg, which decreased to 64 ml/kg (78%) immediately postoperatively and gradually recovered to 82 ml/kg on Day 7 postsurgery ($p = 0.0069$). The mean values of adrenaline, noradrenaline, arginine vasopressin, renin, and aldosterone were highest immediately postoperatively. The mean intraoperative balances of water and sodium were 1090 ml and 113 mEq, respectively. Partial correlation coefficients of CBV to noradrenaline and serum sodium during the entire study were $-0.430 (p = 0.0036)$ and $0.418 (p = 0.0048)$, respectively.

**Conclusions.** Attention should be paid to decreased CBV following craniotomy, which is caused by the shift of fluid to interstitial spaces due to surgical stress. Hypovolemia can be suspected from a postoperative decrease in serum sodium.

**Key Words.** • indocyanine green • pulse spectrophotometry • circulating blood volume • craniotomy • hypovolemia • stress

Clinical Material and Methods

**Patient Population**

Seventeen consecutive patients (eight men and nine women aged 51 ± 14 years [mean ± SD]) were studied in the Department of Neurosurgery, Tokyo Women’s Medical University. The study was approved by the University Ethical Committee, and informed consent was obtained from each patient. Together the patients harbored six benign and seven malignant brain tumors and four unruptured aneurysms. The types of craniotomy performed included frontal in one patient, frontotemporal in eight, temporal in two, temporoparietal in three, and suboccipital in three patients. All patients were in good condition preoperatively. The heights of the patients ranged from 147 to 175 cm (mean 158 ± 10 cm) and their body weights from 41 to 68 kg (53 ± 3 kg).

**Surgical Management**

Isoflurane with phentanyl was used to induce general anesthesia in the patients. Propofol was infused instead of isoflurane during intraoperative physiological monitoring. Crystallloid solution was infused at a rate of 2 to 3 ml/kg to maintain a urinary volume of 1 to 2 ml/kg. Blood pressures above 140 to 150 mm Hg and those below 80 mm Hg were normalized by the administration of nicardipine, diltiazem, or phenylephrine, and ephedrine. Induced hy-
potension was not used during aneurysm surgery. All patients received antibiotic agents intraoperatively. The estimated blood loss was between 150 ml and 800 ml (mean 390 ± 210 ml). Four patients received blood transfusions intraoperatively. Patients received intravenous fluids in amounts ranging from 850 to 7400 ml (mean 2357 ± 1618 ml). Mannitol was infused in five patients to decrease intracranial hypertension. The duration of surgery was 120 to 932 minutes (mean 358 ± 229 minutes).

Postoperatively, no surgery-related complications were observed in the patients. Antibiotic agents, histamine blocker, and crystalloid fluid infusion were used routinely postoperatively. Glycerol and/or steroid medications were used when brain edema was seen on postoperative computerized tomography scanning.

Data Collection
Measurements were performed five times throughout the study: preoperatively (in the ward at 8:00 a.m. at the time of premedication), immediately postoperatively (in the intensive care unit after the patient was transferred from the operating room), and 1, 2, and 7 days following neurological surgery. The following physiological parameters were measured each time: CBV; plasma levels of adrenaline, noradrenaline, AVP, renin, aldosterone, ANP, BNP, total protein, and albumin; COP; RBC count; amount of Hb; hematocrit; serum sodium and potassium levels; and urine sodium levels.

Circulating blood volume was measured using ICG pulse spectrophotometry; adrenaline and noradrenaline by using high-performance liquid chromatography; AVP, renin, aldosterone, ANP, and BNP by using a commercially available radioimmunoassay kit; COP by using a transducer-membrane system (Colloid Osmometer, model 4420; Wescor, Inc., Logan, UT); and other blood and chemical parameters with the aid of an automatic analyzer.

Statistical Analysis
All data were stored on a personal computer and analyzed using a statistical software program (StatView; SAS Institute, Inc., Cary, NC). The sodium balance during surgery was examined using a paired t-test. Data collected sequentially were examined by repeated-measures analysis of variance. Correlations of measured indices to CBV during the entire study and CBV change following craniotomy were examined using a partial correlation coefficient. Unless otherwise noted, data are presented as the means ± SD.

Fig. 1. Graph showing serial changes in CBV following craniotomy preoperatively (pre OP), immediately postoperatively (post OP), and on Days 1, 2, and 7 postsurgery. Values are expressed as the means ± SD (vertical bars). There is a significant change over time (p = 0.0069).

Fig. 2. Graph depicting serial changes in plasma adrenaline (ADR) and noradrenaline (NOR) levels following craniotomy. There are significant changes over time in ADR (p = 0.0022) and NOR (p < 0.0001) values.

Fig. 3. Graph demonstrating serial changes in plasma AVP, renin, and aldosterone levels following craniotomy. There are significant changes over time in the values of AVP (p < 0.0001) and aldosterone (p = 0.0002) but not in renin levels.
Circulating blood volume following craniotomy

Results

The mean preoperative value of CBV was 82 ml/kg, which decreased to 64 ml/kg (78%) immediately postoperatively and gradually recovered to 82 ml/kg on Day 7 following craniotomy (Fig. 1). The change in CBV between the preoperative and postoperative states was not related to the duration of surgery, type of anesthesia, blood pressure, agents used during surgery, water balance, estimated blood loss, or the presence or absence of mannitol. Sodium intake was 222 ± 152 mEq and output was 109 ± 64 mEq during surgery. The mean sodium balance was 113 ± 137 mEq (p = 0.0151). Urine sodium was 67 ± 30 mEq/L during surgery.

The mean values of adrenaline and noradrenaline were highest immediately postoperatively. Adrenaline levels decreased rapidly, whereas noradrenaline decreased gradually to Day 7 following craniotomy. These changes over time were significant (Fig. 2). The mean values of AVP, renin, and aldosterone changed similarly to those of adrenaline and noradrenaline (Fig. 3).

The mean values of ANP had two peaks: immediately postoperatively and on Day 2 following craniotomy. The mean value of BNP was highest on Day 2, but the change over time was not significant (Fig. 4).

The mean values of the RBCs, Hb, and hematocrit decreased gradually to Day 2 and increased on Day 7 following craniotomy. The change over time was significant (Fig. 5). The mean value of serum sodium (141 mEq/L preoperatively) was lowest immediately postoperatively (136 mEq/L) and then increased. It was 138 mEq/L on Day 1, 140 mEq/L on Day 2, and 139 mEq/L on Day 7 postsurgery. The change over time was significant (Fig. 5).

The mean values of total protein, albumin, and COP decreased immediately postoperatively and on Days 1 and 2 in the same degree. The values increased on Day 7 postsurgery. The changes over time were significant (Fig. 6).

Table 1 shows partial correlation coefficients of CBV to measured indices. Those of noradrenaline and serum sodium were −0.43 (p < 0.0036) and 0.418 (p < 0.0048), respectively. Moderate correlations were also seen between CBV and total protein, and between CBV and the hematocrit. However, there were no correlations between CBV and albumin or between CBV and RBCs. There was also no correlation between CBV and COP.

Discussion

The CBV decreased postoperatively to approximately four fifths of its preoperative value and gradually increased and returned to its preoperative value on Day 7 following craniotomy. The reduction in CBV 2 days after cardiac surgery has been reported to be 11.8%. Postoperative hypovolemia should be noted even in a small surgical field such as craniotomy. Judging from the positive water and sodium balance, the amount of decreased CBV may move to the interstitial compartment. A more general application of these observations is preferable to replication of the results under a more stringently controlled series of patients in which the anesthesia regimen is identical.

Fig. 4. Graph showing serial changes in plasma ANP and BNP levels. There is a significant change over time in ANP levels (p = 0.0442) but not in BNP levels.

Fig. 5. Graph demonstrating serial changes in RBC and serum sodium levels following craniotomy. There are significant changes over time in RBC (p = 0.0001) and sodium levels (p < 0.0001).

Fig. 6. Graph depicting changes in COP and in the plasma albumin (Alb) level following craniotomy. There are significant changes over time in the values of COP (p < 0.0001) and Alb (p = 0.0003).
The endocrine–metabolic response to surgical and anesthetic stress includes release of adrenocorticotropic hormone, cortisol, growth hormone, prolactin, adrenaline, noradrenaline, antidiuretic hormone, renin, and aldosterone, which cause a catabolic state designed to stimulate and increase the healing process. All of the stress hormones measured in our study were elevated during the postoperative state and soon decreased. Of these hormones, the change in noradrenaline over time was adversely correlated with CBV. Plasma noradrenaline levels result from an overflow of noradrenaline released from sympathetic nerves, whereas adrenaline levels are derived from adrenergicergic secretion. The increased sympathetic activity may be related to the reduction in CBV. It depends on an increase in filtration pressure between the intravascular and extravascular compartments. Capillary pressure is sensitive to changes in postcapillary resistance: the increase in venous pressure produced by adrenaline or noradrenaline, as reflected by a rise in venous tone, results in a loss of fluid to the extravascular space. Cytokine release and systemic inflammatory response occurring during surgery promote an acute-phase response by endocrine, metabolic, and systemic changes including alteration of capillary permeability. This may also be a mechanism of the promotion of fluid shift.

Activation of the renin–angiotensin–aldosterone system leads to sodium retention, causing a shift of fluid into the circulation. Arginine vasopressin is also involved in the conservation of body water by favoring the reabsorption of solute-free water. In spite of the increase in these hormones in our study, CBV decreased. The responses of these hormones during surgery may be complex, affect each other, and influence the fluid retention in the body but not in the circulation.

What could be an indicator of CBV change in routine examinations? Hypovolemia could be suspected from a postoperative decrease in serum sodium. Serum sodium correlated well with CBV following craniotomy during the entire study. Hypotensive hypovolemia may be induced by the shift of fluid and sodium to the interstitial space due to surgical stress. The fluid stored in the interstitial compartment may move to the intravascular space with a decrease in filtration pressure. Diuresis may be activated by ANP and BNP, which were elevated during the postoperative period. On postoperative Day 7 the balance of fluid and sodium between the intravascular and interstitial compartments may have returned to that of the preoperative state.

Measurement of CBV may be useful for monitoring fluid distribution. Radioactive isotopes have been used to measure CBV, but these methods are not suitable for routine bedside use. The integrated pulse spectrophotometry monitoring system is less invasive and can be repeatedly applied within a short period without blood sampling. This method is useful for estimating the CBV of neurosurgical patients with a single bolus injection of ICG.

Hypovolemia has been shown to increase the incidence of cerebral ischemia and cerebral infarction in patients with SAH. Depression of CBV after surgery may accelerate ischemia caused by cerebral vasospasm. Hypervolemia and hypertensive therapy can prevent ischemic neurologic deficits. However, no monitoring system has been used for estimating CBV other than the Swan–Ganz catheter. Indocyanine-green pulse spectrophotometry could be a powerful tool for the management of patients with SAH.

### Conclusions

We should pay attention to decreased CBV following craniotomy, which is caused by the shift of fluid to the interstitial space due to surgical stress. Hypovolemia can be suspected from a postoperative decrease in serum sodium.

### References


### Table 1

<table>
<thead>
<tr>
<th>Factor</th>
<th>Correlation Coefficient</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>noradrenaline</td>
<td>-0.430</td>
<td>0.0036</td>
</tr>
<tr>
<td>serum sodium</td>
<td>0.418</td>
<td>0.0048</td>
</tr>
<tr>
<td>total protein</td>
<td>0.364</td>
<td>0.0159</td>
</tr>
<tr>
<td>hematocrit</td>
<td>0.364</td>
<td>0.0159</td>
</tr>
<tr>
<td>renin</td>
<td>-0.350</td>
<td>0.0208</td>
</tr>
<tr>
<td>aldosterone</td>
<td>-0.302</td>
<td>0.0488</td>
</tr>
<tr>
<td>antidiuretic hormone</td>
<td>-0.244</td>
<td>0.1152</td>
</tr>
<tr>
<td>BNP</td>
<td>0.235</td>
<td>0.1293</td>
</tr>
<tr>
<td>adrenaline</td>
<td>-0.227</td>
<td>0.1444</td>
</tr>
<tr>
<td>albumin</td>
<td>0.210</td>
<td>0.1784</td>
</tr>
<tr>
<td>Hb</td>
<td>0.168</td>
<td>0.2831</td>
</tr>
<tr>
<td>ANP</td>
<td>0.108</td>
<td>0.4923</td>
</tr>
<tr>
<td>serum potassium</td>
<td>-0.107</td>
<td>0.4968</td>
</tr>
<tr>
<td>COP</td>
<td>0.053</td>
<td>0.7377</td>
</tr>
<tr>
<td>RBC</td>
<td>0.047</td>
<td>0.7683</td>
</tr>
</tbody>
</table>
Circulating blood volume following craniotomy


Manuscript received October 19, 1999. Accepted in final form June 5, 2000.

This work was supported in part by a grant-in-aid for scientific research (C) from the Japanese Ministry of Education, Science, Sports and Culture to Dr. Kasuya.

Address reprint requests to: Hidetoshi Kasuya, M.D., Department of Neurosurgery, Tokyo Women’s Medical University, Kawada-cho 8-1, Shinjuku-ku, Tokyo 162–8666, Japan. email: hkasuya@nij.twmu.ac.jp.