

# Aggressive Zero Balance Ultrafiltration on CPB in Patients with Renal Failure May Cause Cerebral Edema: A Theoretical Analysis

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**Abstract:** The objective of this study was to determine the brain volume changes that occur secondary to hemofiltration during cardiopulmonary bypass in patients with renal failure. We hypothesized that in patients with elevated urea levels, quick aggressive hemofiltration could be associated with cerebral edema. We constructed a simple two-compartment model similar to the urea kinetic model developed by Depner. Intracellular urea exit was assumed to be minimal based on known urea redistribution times. Calculations were based on a 70-kg patient, with an intracellular volume of 25 L, extracellular volume of 15 L, and a preoperative urea of 40 mmol/L filtered to a post-procedure urea of 6 mmol/L. Analysis showed that a standard size 1500-mL

human brain filtered from a preoperative urea of 40 to 6 mmol/L over a short period will expand by 59 mL secondary to the osmotic disequilibrium secondary to hemofiltration ( $p < .05$ ). The higher the preoperative urea, the larger the fluid shift. This figure does not include the cerebral edema component that is known to arise secondary to cardiopulmonary bypass. Significant cerebral edema theoretically occurs secondary to hemofiltration during cardiopulmonary bypass. More detailed mathematical urea kinetic analysis and clinical correlation are needed. **Keywords:** dialysis, bypass, renal failure, brain. *JECT. 2008;40:234–235*

Hemofiltration during cardiopulmonary bypass (CPB) is used to correct hemodilution and correct electrolyte imbalance of patients with renal failure (1). Hemofiltration on or off CPB in the setting of renal failure can result in osmotic changes caused by rapid changes in serum urea concentrations. Large osmotic changes in extracellular compartments can potentially lead to cerebral edema. Cerebral edema is assumed to be the cause of dialysis disequilibrium syndrome characterized by headache, disorientation, nausea, seizures, and coma (2). Animal studies have shown that the resulting cerebral edema could be caused by the “reverse urea effect,” in which brain urea remains relatively high despite rapid decrease in plasma urea (3). We therefore set out to analyze the potential effect of aggressive filtration during CPB on brain volume.

## MATERIALS AND METHODS

A simplified two-pool urea kinetic model similar to that described by Depner was used (4). We assumed that the intracellular exit of urea to be negligible in accordance to known urea distribution times during a 1-hour period of CPB. The scenario of zero balance ultrafiltration (Z-BUF) was studied. Osmotic volume changes were calculated as previously described (5). The calculations were done for a 70-kg patient with an intracellular volume of 25 L, an extracellular volume of 15 L, a blood volume of 5 L, and an interstitial volume of 10 L, and filtered from a preoperative urea of 40 mmol/L to a postoperative urea of 6 mmol/L. The model assumes that the patient does not undergo significant cooling during the procedure—this is impossible to quantify exactly, but patient temperature remains  $>24^{\circ}\text{C}$ .

## RESULTS

The resultant increase in brain volume from being filtered at varying levels of preoperative urea to a postop-

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erative urea of 6 mmol/L is shown in Table 1. With a preoperative urea of 40 mmol/L, a standard 1500-mL brain would increase in size by 59 mL as a result of osmotic disequilibrium from aggressive hemofiltration. These calculations do not take into account the resulting cerebral edema known to occur with CPB.

## DISCUSSION

It seems that significant cerebral volume changes occur, in theory, after the aggressive filtration of renal failure patients to a normal postoperative urea. It is not known to what extent this theorized increase in brain volume has on the clinical picture.

Causation of cerebral dysfunction after CPB is difficult to determine because of the multiple confounding effects of bypass, emboli, cardiovascular status, anesthetic drugs administered, and whether filtered for renal failure during CPB cerebral edema.

The brain and spinal cord are enclosed in a rigid bony box with very little compliance. Cerebral swelling can initially be compensated for by reduction in cerebrospinal fluid volume (CSF), negating any rise in intracranial pressure. Despite a normal intracranial pressure, cerebral swelling can result in neurologic symptoms that potentially could be permanent. This argument parallels the case of CSF drainage in patients undergoing thoracoabdominal aneurysm repair (6).

Previous work has shown an increase in brain volume, averaging 32.8 mL in patients undergoing routine nonaggressive hemodialysis, using MRI to assess brain volume changes (7). These findings have been confirmed by other groups (8). The volume calculations on the extent of cerebral edema were performed before urea distribution took place but correlate very closely with these clinical studies. Because the technique of Z\_BUF was used, the volume filtered is immaterial; it is the osmotic changes that are important.

Urea is a major contributor to plasma osmolarity ( $2[\text{Na}^+] + [\text{glucose}]/18 + [\text{urea}]/2.8$ ), hence the importance in changing its level slowly to reduce osmotic fluid shifts. Sodium flux across membranes is quick, and because se-

vere hyponatremia is rare, urea concentration changes dictate the osmotic fluxes.

Little consensus exists on filtration during bypass, especially with regard to filter pressure (frequently through a three-way tap from arterial return line with no actual direct pressure measurement), filter flow, fluid volume removal, or the effects of pre-procedural blood chemistry.

We recommend, based on the findings of this study, that elective patients in renal failure are dialyzed preoperatively, so that their urea during cardiac surgery is near normal. If patients are unstable or present as emergencies, they may benefit from continuous filtration after the procedure to try and reduce rapid osmotic changes. The relative use of hemodialysis and peritoneal dialysis depends on geographical location and logistical factors, but generally, peritoneal dialysis is thought to be inferior (9). We observed that patients undergoing cardiac surgery receiving peritoneal dialysis are more likely to have very elevated urea levels compared with patients undergoing hemodialysis.

In summary, fluid shifts caused by filtration of patients in renal failure undergoing CPB may potentially be associated with deleterious effects on cerebral function. Further work is needed in conjunction with a more detailed urea kinetic model.

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**Table 1.** Change in brain volume after filtration on bypass.

Pre-Filtration Urea (mmol/L)	Post-Filtration Urea (mmol/L)	Volume Change in Brain (mL)
40	6	59
30	6	42
20	6	25
10	6	7
6	6	0