**Supplementary Table 4**

**Studies utilizing changes in the volume and viscosity state to alter cardiac output**

*CBF, cerebral blood flow; CI, cardiac index; CO, cardiac output; CPP, cerebral perfusion pressure;CVO, central venous pressure; CVR, cerebrovascular resistance; ETCO2, end-tidal carbon dioxide; MAP, mean arterial pressure; MCA, middle cerebral artery; PAC, pulmonary artery catheter; PWA, pulse wave analysis; rCBF< regional cerebral blood flow; TBI, traumatic brain injury; TCD, transcranial Doppler; Vmca, middle cerebral artery flow velocity; Xe, xenon*

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| **Author (Year)**  **[Reference #]** | **N** | **Subjects** | **Method of CBF measurement** | | **Method of CO measurement** | **Intervention** | **Change in CO/CI** | **Change in MAP** | **Change in pCO2 (measure)** | **Change in CBF** |
| Keller (1982) [55] | 8 | 8 adult Rhesus monkeys with surgical right MCA occlusion | Hydrogen clearance | PAC | | 4 received IV colloid infusion until CO plateaued. 4 (control) underwent exchange transfusions (hemodilution without changing the volume state).  Hematocrit fell an average of 20%. | CO rose between 100-200% above control levels in the experimental arm. | MAP did not vary significantly with volume expansion. | No Data | CBF increased in those receiving volume expansion.  Significant increases occurred only in the region of ischemia.  CBF remained stable in those that received isovolumetric infusion. |
| Bouma (1990) [53] | 35 | 35 patients with severe TBI | Inhaled or intravenous 133Xe | PAC | | Mannitol was infused as an intravenous bolus of 0.66 gm/kg as a  20% solution to assess rheological effect.  Patients were grouped by intact or defective autoregulation, with intact defined as dCPP/CVR being >0 and ≤2 | CO did not change significantly with mannitol load in either the defective autoregulation group (+1±9%) nor the intact group (+17±40%). | MAP did not change significantly with mannitol (intact 101±14 to 100±15; defective 94±9 to 90±11 mmHg) | No data | CBF did not change significantly from baseline/ CBF change 0±21%  With defective autoregulation, CBF had substantial (but not statistically significant changes) with mannitol +40±34% |
| Davis (1980) [54] | 70 | 40 cats | Intraarterial 133Xe | PAC | | Controlled hemorrhage was performed | Controlled hemorrhage led to a reduction in CO by 32%.  Hematocrit fell from 0.435±0.013 to 0.316±0.026 after hemodilution | Controlled hemorrhage led to a mild increase in MAP (no quantitative data). CVP decreased in most (no quantitative data). | CBF, MAP and CO remained responsive to CO2 changes (no quantitative data). | Controlled hemorrhage led to a reduction in CBF of 24%. |
| Tu (1996) [57] | 13 | 13 pituitary or spinal surgery patients | Inhaled 131Xe-CT | PAC | | Isovolumetric hemodilution by repeated withdrawal of 250 mL blood and replacement with 175 mL low-molecular-weight dextran until hematocrit level reached 0.31 to 0.33 | CI increased with hemodilution from 3.7±0.2 to 4.6±0.2 (p<0.05) | MAP was unchanged (92.2±4.1 to 92.3±2.2) with hemodilution | No data | rCBF increased significantly at 3 hours after  isovolemic hemodilution. The average increase in rCBF was 40.7% in the cortex, 27.6%  in the white matter, 36.8% in the putamen, and 34.9% in the thalamus |
| Tranmer 1992 [59] | 8 | 8 Macaques | Hydrogen clearance | PAC | | Proximal MCA occluded.  Incremental IV colloid infusion. The subjects were then hemorrhaged to return CO to baseline levels. | CO increased from baseline (0.9±0.2 L/min) with volume expansion (2.6±1.0L/min) and decreased with exsanguination (1.2±0.3L/min)  Hematocrit decreased from baseline of 44±%5 to 28±4% with infusion, then to 23±5 with hemorrhage. | MAP remained constant from baseline (114±11 mmHg) with volume expansion (116±18) and decreased (not statistically significantly) with exsanguination (101±29) | pCO2 was maintained between 35-40 mmHg as per study protocol. Actual measures of pCO2 are not given.  ICP did not alter (5±4 mmHg) with volume expansion (4±3) and exsanguination (4±3) | CBF in non-ischaemic brain did not alter from baseline (65±30ml/100g/min) with volume expansion (66±32) or exsanguination (61±31).  CBF in ischemic brain (20±11) increased with volume expansion (34±15). CBF decreased with exsanguination (18±4). |
| Wood 1984 [60] | 16 | 16 splenectomised dogs | 85Kr washout | PAC | | Infusion of autologous plasma equivalent to 40% of the total blood volume in 7 dogs | CO at baseline (1.7±0.1 L/min) increased with volume expansion (2.9±0.3).  Hematocrit decreased from 45±3% to 35±3%. | MAP remained around baseline (123±9 mmHg) | paCO2 was maintained at 37-42 mmHg | Regional CBF increased from 72±8ml/100g/min to 83±9 (although not reaching statistical significance) |
| Ogawa (2007) [41] | 12 | 12 healthy volunteers | TCD Vmca | Impedance cardiograph | | Infusions of 0.9% saline (15 mL/kg and further 15 mL/kg). | CO increased with 30ml/kg NS infusion (4.16±0.79 to 5.08±1.05) (p<0.05). | MAP did not change with NS infusion (80±9 to 82±10) | ETCO2 did not change with NS infusion (41±3 to 40±3mmHg) | Vmca increased with 0.9% saline infusion (+8.5±8.9%). |
| Ogoh (2005) [42] | 7 | 7 healthy volunteers | TCD Vmca | Aceytlene re-breathing technique | | Rapid changes in blood volume were achieved LBNP (-8 and -16 mm Hg), both with and without cycling and infusions of colloid to raise CVP to 2.5±0.4 mmHg above baseline. | CO increased with colloid infusion (6.5±0.3 to 8.5±0.4) (p<0.05).  CVP increased with colloid by 2.5±0.4 mmHg at rest, and 4.9±1.0 mmHg during exercise after colloid infusion.  Hematocrit decreased from 49.5±2.9% to 42.7±3.6%. | Colloid infusion did not change MAP compared to control in resting (96±3 to 91±3mmHg) or exercising subjects (109±5 to 106±5mmhg) | Colloid infusion did not change paCO2 in resting (42±1 to 41±1mmHg) or exercising (41±1 to 41±1 mmHg) subjects. | Colloid infusion did change Vmca compared to control in resting (66±4 to 73±4mmHg) but not in exercising subjects (70±5 to 74±4mmhg) |