Partial Aortic Occlusion and Cerebral Venous Steal
Venous Effects of Arterial Manipulation in Acute Stroke
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Abstract—Acute ischemic stroke therapy emphasizes early arterial clot lysis or removal. Partial aortic occlusion has recently emerged as an alternative hemodynamic approach to augment cerebral perfusion in acute ischemic stroke. The exact mechanism of cerebral flow augmentation with partial aortic occlusion remains unclear and may involve more than simple diversion of arterial blood flow from the lower body to cerebral collateral circulation. The cerebral venous steal hypothesis suggests that even a small increase in tissue pressure in the ischemic area will divert blood flow to surrounding regions with lesser tissue pressures. This may cause no-reflow (absence of flow after restoration of arterial patency) in the ischemic core and “luxury perfusion” in the surrounding regions. Such maldistribution may be reversed with increased venous pressure titrated to avoid changes in intracranial pressure. We propose that partial aortic occlusion enhances perfusion in the brain by offsetting cerebral venous steal. Partial aortic occlusion redistributes blood volume into the upper part of the body, manifested by an increase in central venous pressure. Increased venous pressure recruits the collapsed vascular network and, by eliminating cerebral venous steal, corrects perifocal perfusion maldistribution analogous to positive end-expiratory pressure recruitment of collapsed airways to decrease ventilation/perfusion mismatch in the lungs. (Stroke. 2011;42:00-00.)

Key Words: aortic occlusion □ collateral □ hemodynamics □ ischemia □ stroke □ venous

An observation that aortic manipulation can augment cerebral blood flow (CBF) was directly translated to stroke therapy using a form of partial aortic occlusion.1 However, to develop more targeted stroke treatment methods, we must understand the mechanism through which an acute cardiac afterload augmentation improves CBF. Currently, the effect of partial aortic occlusion is attributed to redistribution of cardiac output from the lower body to the brain. We present an alternative hypothesis that another overlooked effect of acute cardiac afterload augmentation through aortic manipulation is an increase in cardiac preload and propose that this increase might be the primary cause of the observed CBF augmentation. The simple diversion of arterial blood flow from the lower torso and extremities to the leptomeningeal arterial collaterals is unlikely and flow augmentation in the collaterals may be dependent on a venous mechanism.2

Effects of Partial Aortic Occlusion
Hemodynamics in any circulation must consider all segments of the vascular bed, from arterial to venous. Similarly, cardiac output is not a fixed variable, but rather depends on the preload, afterload, and cardiac contractility. Blood flow diversion to the upper torso can occur, but only in the case of fixed cardiac output, as with severe aortic stenosis or in the case of an open circulatory system, such as severe hemorrhage. Partial aortic occlusion is the physiological equivalent to an abrupt increase in afterload. A sudden increase in afterload has 2 immediate effects—decrease of cardiac output and increase in arterial pressure.3 Increase in arterial pressure might be beneficial in some settings, such as systemic hypotension or when CBF depends predominantly on pressure.4 Blood pressure augmentation or induced hypotension may have limited utility for CBF enhancement after stroke in normotensive patients.5 If the hemodynamic effects of partial aortic occlusion after stroke extend beyond blood pressure augmentation, then alternative CBF modulation mechanisms must be implicated.

Cerebral Venous Steal in Stroke
Cerebral venous steal or diversion of blood flow to the periphery of the ischemic territory follows focal venous compression.6 Regional blood flow ceases when the focal tissue pressure (P_e) approaches inflow pressure (P_i). Pressure decreases across the circulatory pathway; highest pressures are exhibited in the arteries and progressively diminish toward the capillary segments. During stroke, an obstruction of the inflow artery decreases pressure to a greater degree, and often pressure is sustained only via the collateral circulation.7 Because of this pressure decrease in the arteries, the inflow pressure at capillary level becomes an even smaller
fraction of the arterial pressure. Therefore, even slight focal tissue pressure increases could significantly reduce capillary perfusion, especially in the presence of a diversion pathway, which has lower effective outflow pressure. Diverted blood flow creates steal in the center and luxury perfusion at the periphery. Increased venous pressure equalizes the effective outflow pressures and diminishes this maldistribution. Conversely, an increase in venous pressure (Pv), as long as it remains below the tissue pressure Pe, does not impede focal penumbral blood flow, but rather enhances it by reversing the cerebral venous steal.

Optimal Venous Pressure
According to the parallel Starling resistor model, penumbral flow is maximized when venous pressure approaches tissue pressure; any venous pressure increase beyond the tissue pressure will decrease cerebral perfusion pressure. The only question remaining is what is the local penumbral tissue pressure? Local penumbral tissue pressure Pe is virtually impossible to measure in the clinical setting, but it can never be lower than intracranial pressure if brain edema is present. Hence, intracranial pressure can be used as a marker of the level to which venous pressure can be safely increased without the fear of decreasing global cerebral perfusion pressure; critical closing pressure, which can be estimated noninvasively, also can be used as an alternative surrogate measure. As venous pressure reaches the level of critical closing pressure or intracranial pressure, it has no effect on these variables. Alternatively, an optimization of venous pressure after stroke can be performed in the same way cardiac preload is optimized with respect to the cardiac output: an incremental venous pressure increase/decrease until the target perfusional blood flow reaches peak.

Aortic Occlusion Redistributes Blood Volume to the Upper Body
Redistribution of the systemic blood volume from the splanchnic circulation is a well-known effect of partial aortic occlusion. Although most of what we know about redistribution of blood volume after aortic occlusion comes from animal studies, this knowledge is used widely to manage patients undergoing surgery requiring aortic cross-clamping. The splanchnic organs contain nearly 25% of the total blood volume stored in the venous vasculature. After aortic occlusion, nearly two-thirds of this volume (>800 mL) is autotransfused into the systemic circulation within seconds, causing an instantaneous increase in central venous pressure. In a previous study, aortic cross-clamping in dogs resulted in marked increases in mean arterial pressure by 84% and end-diastolic left ventricular pressure by 188%, whereas simultaneous cross-clamping of the aorta and inferior vena cava resulted in no significant change in preload or in mean arterial pressure. Cardiac stroke volume was reduced by 74%. Interestingly, by transfusing blood during clamping of the inferior vena cava, the investigators re-established the hemodynamic effect of thoracic aortic cross-clamping alone. This study also demonstrated that thoracic aortic cross-clamping, similar to partial aortic occlusion adjacent to the renal arteries, is associated with a dramatic increase (155%) in blood flow above the clamp level, whereas no such change occurred with simultaneous aortic and inferior vena cava occlusion. Another study demonstrated that aortic cross-clamping at the diaphragmatic level was associated with significant increases (by 8%–38%) in the γ-emission in all organs and tissues above the level of aortic occlusion. These studies support the hypothesis that cross-clamping of the aorta at the diaphragmatic level is associated with an increase in blood volume, not necessarily blood flow, in the organs and tissues proximal to the level of cross-clamping.

The effects of aortic cross-clamping also have been assessed with respect to intracranial hemodynamics. Cerebral blood volume was assessed in 8 pigs undergoing cross-clamping of the descending thoracic aorta for 30 minutes using MRI before cross-clamping, during cross-clamping, and after declamping. Ventricular volume decreased after cross-clamping of the descending thoracic aorta. Because no cerebral edema was observed, the decrease of ventricular volume could only be attributed to increased intracranial blood volume and an increase in intracranial outflow pressure. Clamping of the thoracic aorta alone (n=10) was accompanied by severe arterial hypertension, a dramatic decrease in inferior vena cava flow, and a dramatic increase in superior vena cava flow. Simultaneous clamping of the thoracic aorta and inferior vena cava (n=13) was accompanied by no significant change in arterial pressure or superior vena cava flow.

Yet, how may increased blood volume in the upper part of the body exert a potential beneficial hemodynamic effect in stroke? It is important to consider that an increase in blood volume is inevitably associated with venous pressure elevation. Such venous pressure elevation may equalize effective outflow pressure throughout the brain and abolish a steal-like phenomenon, previously termed “cerebral venous steal.” Even limited ischemic tissue injury after arterial occlusion may cause intraparenchymal pressure gradients. These pressure gradients are transmitted from parenchyma to the cerebral vasculature, determining effective outflow pressure if it is higher than venous pressure (West zone II). Figure 1 illustrates how venous pressure affects regional CBF in regions with normal tissue pressure (Pe=0, Ohms resistor); homogeneously increased tissue pressure (Pe=constant >0, Starling resistor) and heterogeneously increased tissue pressure (Pe variable, >0, venous steal prone anatomy). Equalizing venous and focal tissue pressures equilibrates effective outflow pressure in the perifocal area. When this occurs, cerebral venous steal is abolished, heterogeneity in the cerebral tissue perfusion is reduced, and blood flow is restored to the areas of increased tissue pressure, possibly translating into improved clinical outcomes. An idealized Starling resistor model predicts that blood flow can be re-established from zero to >50% of normal simply by increasing venous pressure (Figure 2). One of the simplest means of restoring flow without decreasing cerebral perfusion pressure is head-down tilt, whereas head-up tilt may decrease cerebral perfusion pressure because of cervical venous collapse.
Pharmacological Alternatives to Partial Aortic Occlusion

Moderate venous pressure increases, although counterintuitive, may improve cerebral ischemia in animal studies. Ischemia improves with the enhancement of venous pressure in humans, too, as recently demonstrated in 2 case reports in which clinical improvement and middle cerebral artery flow velocity increases were observed after creation of upper body venous congestion with chest-high antigravity suit inflated with 10 to 20 mm Hg pressure. The effects of phenylephrine on blood flow in poststroke perifocal penumbra suggest that mild induced hypertension increases collateral cerebral blood flow and oxygenation and improves cerebral metabolic rate of oxygen in both the core and the penumbra. Shin et al induced hypertension with phenylephrine infusion starting 10 or 60 minutes after ischemia to increase blood pressure by 30% for the duration of ischemia. Similarly, Chi et al demonstrated that acute phenylephrine infusion increased the number of veins with $SvO_2>40\%$ in a rat model of middle cerebral artery occlusion. Phenylephrine is an $\alpha$-1 adrenergic agonist that constricts arterioles and directly increases afterload and also redirects blood from bowel and muscle to the central circulation and, as such, enhances cardiac preload and cardiac output. Central venous pressure increased during infusion of phenylephrine in men. An additional study by Appleton et al examined $\alpha$-adrenergic control of the venous circulation in dogs in which heart rate was controlled with atropine. To eliminate reflex changes in vascular tone, 8 dogs received ganglionic blockade with trimethaphan. Increased central blood volume resulted in an increase of mean circulatory filling pressure and, as such, pressure gradients for venous return ($P<0.025$). These authors concluded that phenylephrine reduces peripheral vascular capacitance and shifts blood from peripheral to the central vascular compartment. Phenylephrine, similar to partial aortic occlusion, therefore may cause a redistribution of blood volume rather than augmentation of blood flow through arterial hypertension.

In summary, one must consider the venous effects of any direct arterial intervention because hemodynamics results from complex interactions among all aspects of the vascular system. Future vascular approaches for acute occlusion of an intracranial artery may be advanced by this conceptual perspective. Furthermore, promising approaches such as partial aortic occlusion may require further study to determine optimal treatment protocols that enhance key venous effects.

Figure 1. Venous pressure augmentation affects regional cerebral blood flow (rCBF) in 3 ways: (a) like an Ohm resistor in the regions with normal tissue pressure (external tissue pressure $[Pe]<0$): flow decreases proportional to venous pressure $[Pv]$ and stops when $Pv$ equals arterial pressure $[Pa]$; (b) like a Starling resistor in the regions with homogeneously increased tissue pressure ($Pe>0$, spatially homogenous): flow decreases only when $Pv$ exceeds $Pe$; and (c) like a Starling resistor with steal in the regions with heterogeneously increased tissue pressure ($Pe>0$, spatially heterogeneous): flow is diverted to the pathway of least resistance ($Pe=0$). When inflow resistance $[Ri]$ is high, pressure at microcirculation level $Pi$ decreases and flow completely ceases when inflow pressure $[Pi]<Pe$. Increasing $Pv$ augments $Pi$ and re-establishes flow when $Pi \geq Pe$. This is marked as point of no reflow (PONR): minimal venous pressure required to re-establish flow in the compressed regions. Regional flow is maximized when $Pv$ reaches $Pe$. Further increase in $Pv$ decreases regional flow to the same extent as in Ohm or Starling resistors. $Pa$ is scaled to 100. $Pv$ varied from 0 to $Pa$.

Figure 2. Arterial pressure increase does not augment regional cerebral blood flow (rCBF) in regions with venous steal until venous pressure exceeds point of no reflow (PONR), ie, minimal venous pressure required to re-establish flow in the presence of steal.

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