Carotid Artery Diameter, Plaque Morphology, and Hematocrit, in Addition to Percentage Stenosis, Predict Reduced Cerebral Perfusion Pressure during Cardiopulmonary Bypass: A Mathematical Model

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Abstract: Cerebral complications after cardiac surgery are a significant cause of morbidity, mortality, and financial cost. Numerous risk factors have been proposed to explain the risk of cerebral damage. Carotid artery disease has an important role. Percentage carotid artery stenosis is the only measure of carotid artery disease that is used by cardiac surgeons to determine the need for either a carotid endarterectomy and/or a higher pump perfusion pressure. Identification of patients through their carotid plaque morphology who might benefit from higher pump perfusion pressures or concomitant carotid endarterectomy may reduce cerebral morbidity and mortality. A mathematical model using finite element analysis was created to model the carotid artery vessel and its stenotic plaque. Analysis showed that the degree of carotid artery stenosis, the length of the carotid artery plaque, the diameter of the carotid artery, and the blood hematocrit all independently significantly affect the required pump perfusion pressure to maintain adequate cerebral perfusion during cardiopulmonary bypass (CPB). The results from a mathematical model showed that carotid artery diameter, carotid artery plaque length, and hematocrit, in addition to percentage stenosis, should be included in any thought process involving carotid artery stenosis and cardiac surgery. Estimating cerebral risk during CPB should no longer rely on only the percentage stenosis. Keywords: carotid artery stenosis, hematocrit, cardiac surgery, cardiopulmonary bypass. JECT. 2009;41:92–96

Cerebral vascular accidents (CVAs) after cardiac surgery remain an important cause of mortality, morbidity, and financial cost (1). Numerous causative factors have been associated with CVAs secondary to cardiac surgery (2): ascending aortic atheromatous disease (3), carotid artery disease, age, diabetes, hypertension, cardiopulmonary bypass (CPB) length, previous cerebrovascular events (4), and perfusion pressure (5). Cardiac surgeons have adopted several strategies to reduce the incidence of CVAs including single episode aortic clamping (6), systemic cooling (7), ascending aortic replacement/atherectomy (8), concomitant carotid artery surgery (9), off-pump no aortic touch, axillary cannulation, and raising pump perfusion pressure (10,11). Opinion is divided on all of the above maneuvers.

Concomitant carotid artery stenting (12) or surgery (13) has been recommended in patients who have >70% occlusion of the carotid arteries as assessed by Doppler ultrasound or angiography. Raising the cerebral perfusion pressure has not produced conclusive results, although it is generally agreed that a pressure in excess of 50 mmHg is necessary to reliably protect cerebral function, in the absence of carotid artery disease, during prolonged periods of bypass (14,15).

To date, only the degree of the maximal carotid artery stenosis has been included in the estimation of CVA risk (16). This paper, through simplified mathematical fluid dynamic theory, includes the length and degree of the stenosis along with the vessel diameter and blood viscosity during bypass, so that the optimal CPB pressure and need for concomitant carotid endarterectomy can be more accurately assessed. This study was deliberately limited to studying only the above characteristics, even though it is
appreciated that many other factors are important, such as temperature, oxygen delivery, collateral flow, and emboli.

MATERIALS AND METHODS

A mathematical model using finite element analysis was created. Finite element analysis is a numerical technique that mathematicians and engineers use to find solutions to complex fluid or structural problems with variables in time and space, by assuming a three-dimensional (3D) structure can be analyzed in thin slices “finite element analysis.” Variables in the mathematical model included percentage carotid artery stenosis, length of plaque, carotid artery diameter, and blood viscosity. These variables were varied independently to assess their individual contribution to the required cerebral perfusion pressure to maintain adequate cerebral perfusion. Flow was assumed to be non-pulsatile, as occurs on bypass, and the venous pressure was assumed to be a constant 0 mmHg.

Mathematical Model

The stenosis in a carotid artery can be represented diagrammatically as in Figure 1. The resistance to blood flow (Rcap) combined with the cerebral vascular resistance (Rcv) represents the total resistance to flow through the carotid artery (Rtot; Equation 1).

\[ R_{\text{tot}} = R_{\text{cap}} + R_{\text{cv}} \] (1)

The cerebral blood flow (Fc\text{cv}) depends on the cardiopulmonary perfusion pressure (BP\text{cpb}) and the central venous pressure (BP\text{cvp}; Equation 2).

\[ F_{\text{cv}} = \frac{(BP_{\text{cpb}} - BP_{\text{cvp}})}{R_{\text{tot}}} \] (2)

A cerebral perfusion pressure >50 mmHg is thought to be essential for cerebral protection during a significant period of bypass. This depends on BP\text{cpb} and the blood pressure drop across the carotid artery plaque (Bpcap; Equation 3).

\[ BP_{\text{cpb}} - BP_{\text{cap}} > 50 \] (3)

According to Poiseuille’s formula, the resistance offered by a pipe (Rp) to a fluid of viscosity \( \eta \), of length L, and diameter d is given in Equation 4.

\[ R_{p} = \frac{8\eta L}{\pi (d/2)^4} \] (4)

If an infinitely thin representative section of the carotid artery is taken (thickness \( \delta x \)), the resistance offered by this (R\( \delta x \)) is given in Equation 5.

\[ R_{\delta x} = \frac{8\eta \pi (d/2)^4}{\delta x} \] (5)

If all of these thin sections are added together to calculate the total resistance of the stenotic carotid artery (Rcap), Equation 6 results.

\[ R_{\text{cap}} = \sum R_{\delta x} \] (6)

Combining and rearranging Equations 3 and 6 results in Equation 7, where F\text{cv} is carotid blood flow.

\[ BP_{\text{cpb}} > 50 + F_{\text{cv}} \times R_{\text{cap}} \] (7)

Plaque Model

To simplify finite element analysis, the plaque was modeled as in Figure 3, with the plaque having two defining characteristics: length and height. The leading and trailing edges of the plaque were each assumed to comprise 10% of the full plaque length. The leading and trailing edge height protrusion (y) into the carotid artery was represented by a quadratic equation (Equations 8 and 9, respectively).

\[ y = 20hx/L - 100hx^2/L^2 \] (8)

\[ y = h - 100hx^2/L^2 \] (9)

The remaining 80% of the plaque was assumed to have uniform height (y = h).

Computer Model

All calculations were performed in Excel version 7.0 (Microsoft, Redmond, WA) on a 120-mHz Pentium. A finite element thickness of 1 \( \mu \text{m} \) was used, which resulted in between 500 and 50,000 element analysis depending on the length of the plaque. The following mathematical formula was used in the finite element analysis to calculate the height (y) at a distance (x) along the carotid plaque.

\[ y = |20hx/L - 100h(x/L)^2|_{x < L/10} + |h - 100h(x - 9L/10)|_{x > 9L/10} \times (x - 9L/10)/L^2|_{x > 9L/10} + |h|_{x < 9L/10} \]

RESULTS

Table 1 shows the calculated perfusion pressures required during CPB to maintain a cerebral perfusion pressure of 50 mmHg for various percentages of carotid artery stenosis. For 100% carotid artery stenosis, it is impossible to calculate the required perfusion pressure because it is entirely dependent on the adequacy of the collateral circulation.

Figure 2 is a graphical representation of Table 1 for carotid stenosis between 40% and 90%. As expected, the
greater the percentage stenosis of the carotid artery, the greater the required perfusion pressure. It can be seen that the length of the stenosis makes a significant difference to the required perfusion pressure. It can be seen that, with a carotid artery stenosis of 75%, the required perfusion pressure varies between 54 and 86 mmHg, depending on the length of the stenosis. Thus, the length of a carotid stenosis can have a significant effect on the required pump pressure to maintain adequate cerebral function.

Figure 3 shows the pressure drop across the plaque for carotid artery stenosis between 50% and 80%. It can be seen that, as carotid artery diameter decreases from 10 to 5 mm, the pressure drop across the plaque markedly increases. It can be seen that for a fixed 65% carotid artery stenosis, the pressure drop across the plaque varies between 4, 12, and 60 mmHg for carotid artery diameters of 10, 7.5, and 5 mm, respectively.

Figure 4 shows the influence that hematocrit has on the pressure drop across the plaque, depending on length of the carotid plaque stenosis, for a carotid artery stenosis between 50% and 90%. It can be seen that, as the hematocrit rises, the pressure drop across the plaque increases exponentially for a given carotid artery stenosis. It can be seen that for a 1-cm-long stenosis of 80%, hematocrit has virtually no effect, with the pressure drop across the plaque being <15 mmHg. However, for a 5-cm-long stenosis of 80%, the pressure drop across the plaque ranges from 35 to 90 mmHg as the hematocrit increases from 15% to 40%. Thus, the hematocrit can have a significant effect on the required pump pressure to maintain adequate cerebral perfusion.

The length of the carotid artery plaque results in a significant increase in the pressure drop across the plaque. This means that the higher the hematocrit and the longer the stenosis, the higher the required perfusion pressure.

**DISCUSSION**

Our results showed that the percentage carotid artery stenosis, length of the carotid artery plaque, the blood...
hematocrit on bypass, and the diameter of the carotid artery significantly affect cerebral perfusion pressure during CPB. To date, only the percentage carotid artery stenosis has been included in the thought process of deciding the pump perfusion pressure and the need for concomitant carotid endarterectomy in patients who are about to undergo CPB.

Carotid artery diameter and plaque lengths are readily obtainable data; they are easily available from either Doppler ultrasound, magnetic resonance angiography, or conventional angiography.

Some of the calculated perfusion pressure data are supraphysiologic. This implies that either the brain has to adapt to a lower blood flow or collateral cerebral perfusion must occur if cerebral damage is to be averted. Collateral cerebral flows occur through the circle of Willis. Unfortunately, this is incompletely developed in >50% of patients (17). Thus, this cannot be relied on as a source of collateral blood flow to protect the brain during CPB, because it is only fully developed in 18% of patients (18). Of these patients, atherosclerosis causes an additional decreased functionality.

The percentage carotid artery stenosis is conventionally the only indicator of carotid artery disease that is taken into account. The data showed that, for stenotic lengths <2 cm, the required perfusion pressure does not alter significantly for carotid artery stenosis <50%, regardless of the blood hematocrit or carotid artery diameter. This correlates with previous clinical studies and present clinical practice (19). However, the length of the carotid artery stenosis can play a significant part in determining the required perfusion pressure required during CPB. The length of the stenosis plays an exponential role in determining the required perfusion pressure when the degree of the carotid artery stenosis exceeds 55%.

Blood hematocrit values are routinely monitored during bypass; thus, no additional blood samples are needed. Blood hematocrit, which partly determines viscosity, has been studied extensively during CPB. The mathematical model used in the above calculations does not take into account the potential hazardous sequelae that can result from an excessively low hematocrit, resulting in inadequate cerebral oxygen delivery. The model does confirm previous studies that a moderate degree of hemodilution could have stability, irregularity, temperature, oxygen delivery, collateral flow, or embolic load.

Benefits of Mathematical Model
To study patients clinically with all of the permutations of percentage stenosis, carotid artery diameter, blood viscosity, and length of stenosis with just six patients per group would need a study size in excess of 3000 to be necessary, assuming that the patients were not normally distributed for these factors (which they are). Thus, to take into account a patient population that is normally distributed so that every permutation can be studied just six times would require a study population in excess of ~30,000, which is clearly unobtainable. This shows the power of a
mathematical model as a risk predictor tool for a population but not an individual.

**Future Work**

Three-dimensional reconstruction using magnetic resonance scanning of carotid arteries with computational fluid dynamic calculation of estimated pressure drop needs to be developed and correlated with clinical outcome.

**REFERENCES**