Understanding of boundary conditions imposed at multiple outlets in computational haemodynamic analysis of cerebral aneurysm

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Abstract Computational fluid dynamics (CFD) is considered to be a promising tool for haemodynamic analysis of the intracranial aneurysm. However, aneurysm CFD is still not regarded as fully reliable mainly because the computational result is influenced by too many factors such as the luminal geometry of the model, spatiotemporal resolutions and boundary conditions. Among the influential factors, this paper focuses on outflow boundary conditions used when the computational domain has multiple outlets. Four outflow strategies found in published articles are reviewed: 1) prescription of constant or zero pressure, 2) flow splitting based on the power law, 3) traction-free and zero velocity-gradient conditions and 4) coupling of CFD with a reduced-order model. None of them has proved definitely superior or inferior to others. For accurate quantification of the haemodynamic state in the aneurysm, it is crucial to incorporate the physiologically correct flow splitting ratio in CFD analysis by means of accurate specification of pressure or flow rate at the outlets. A coupling of CFD and a 0-d model (a subtype of the reduced-order model) appears to be the most promising although further study is necessary to achieve accurate estimation of model parameters.

Keywords haemodynamics, cerebral aneurysm, computational fluid dynamics, outflow boundary condition

Introduction

It is considered that three-dimensional (3-D) haemodynamic analysis of the cerebral aneurysm using computa-

tional fluid dynamics (CFD) will become a powerful tool to assist medical practitioners in day-to-day clinical activity. Many studies with CFD have been conducted on various problems related to cerebral aneurysms from rupture predictions to examinations of the flow-diverter effect. However, even with such efforts, aneurysm CFD is still not regarded as fully reliable. This is mainly due to the fact that the computational result is influenced by too many factors such as the model geometry, blood rheology, numerical scheme, spatial and temporal resolutions, convergence criteria and boundary conditions. For example, the sensitivity of aneurysm CFD to the segmentation method and computational conditions was illustrated in a series of CFD challenges [1–8], in which participating groups calculated flow fields in the same subjects with CFD and produced different results.

Among factors influencing CFD results, this paper focuses on outflow boundary conditions used when the computational domain has multiple outlets, as in an analysis of a bifurcation aneurysm, because outflow boundary conditions seem to attract little attention. There have been a small number of studies which put a special focus upon outflow boundary conditions [9–12], in contrast to inflow conditions which many researchers have investigated [13–23]. The authors inspected articles published in major journals over the recent five years and found that, in the vast majority of them, the outflow boundary condition used was only stated briefly in a sentence with keywords such as “traction-free”, “zero pressure” and “Murray’s law”. It was also noticed that nothing about the outflow boundary condition was mentioned in some articles. Nonetheless, the boundary condition imposed at the multiple outlets is considered to have a significant impact on the haemodynamic state in the bifurcation aneurysm, because the outflow boundary condition

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influences the rate of flow division and, consequently, the amount of blood flowing into and out of the aneurysm.

Four major outflow strategies found in the literature survey are reviewed in this paper after preliminary explanations about boundary conditions are given. Throughout this paper, discussions are limited to the most common setting of aneurysm CFD; a velocity profile is prescribed at the inlet and the arterial wall is treated as rigid.

Boundary conditions for incompressible CFD

Boundary conditions for internal flow

A simple example of internal flow is considered with Fig. 1 which shows a schematic drawing of a rectangular computational domain surrounded by inflow, outflow and rigid wall boundaries. For simplicity, a two-dimensional Cartesian grid is arranged over the domain. The figure also depicts stencils for the case when the 1st order upwind scheme and central difference approximation are used respectively for the convection and viscous terms in the momentum equations. Dotted lines in each stencil represent the connection of nodal points involved in spatial discretisation of the equations. For example, in an algebraic equation derived by spatial discretisation of the x -momentum equation at point P, the velocity component u at point P is expressed in a relationship with u 's at the four neighbouring points located right, left, above and below, i.e. E, W, N and S. This also holds true for pressure because stencils for the pressure correction equation solved in the SIMPLE method [24] are identical to those shown in Fig. 1. Since stencils with the same structure apply to all internal nodal points drawn with white circles in Fig. 1, it follows that the fluid dynamical state at point P is influenced by those at all other points in the domain including boundary points drawn with

dark circles. This important characteristic of incompressible flow is consistent with the fact that the system of the governing equations is classified as elliptic [25].

Points adjacent to a boundary such as points Q, R and S refer to their next boundary points. Thus, information about velocity and pressure must be specified at all the boundary points for solution. Such information is called boundary conditions. A boundary condition is either boundary value or mathematical relationship of the parameter in question. Influences of the upstream and downstream flow fields are incorporated into the dynamical state within the computational domain by the boundary conditions imposed at the inlet and outlet, respectively, while restriction on the flow due to the solid wall is embodied by the no-slip condition given at points on the wall surfaces. This discussion can be extended in a straightforward manner to 3-D haemodynamic analysis with an unstructured grid system.

Pressure in incompressible CFD

The term “pressure” usually refers to absolute pressure p_{abs} or gauge pressure p_g . Absolute pressure is real pressure based on actual force and gauge pressure is the difference of absolute pressure from the atmospheric pressure. Nonetheless, pressure p in the incompressible Navier-Stokes (N-S) equations is somewhat ambiguous because it can actually be any relative pressure as expressed in the following equation,

$$p = p_{abs} - p_c \quad (1)$$

where p_c is any constant. Officially, p in the incompressible N-S equations is absolute pressure ($p = p_{abs}$ and $p_c = 0$). However, it should be recalled that p only appears in the form of spatial gradient: $\partial p / \partial x$, $\partial p / \partial y$ and $\partial p / \partial z$. Since p_c is a constant, spatial derivatives of p strictly agree with those of p_{abs} regardless of p_c . Note that p_c makes no contribution to the momentum balance. Thus, in practice, any relative or differential pressure is allowed to be p in the incompressible N-S equations. A typical example of this is found in simple Poiseuille flow, shown in Fig. 2 with a graph of pressure drops for two different flow rates. Solid lines L1 and L2 represent pressure profiles along the conduit for a certain flow rate Q_L . Both pressure profiles are acceptable because they have the same gradient corresponding to the same flow rate Q_L . Similarly, pressure profiles H1 and H2 drawn with dashed lines for a higher flow rate Q_H are fluid-dynamically equivalent to each other since H1 and H2 have the same gradient. The level of the exit pressure (p_1 or p_2) has nothing to do with the flow rate or velocity profile.

What is obtained by incompressible CFD is relative pressure p and, basically, spatial difference or gradient of pressure matters in incompressible flow rather than the pressure itself. Incompressible CFD provides no information about p_{abs} unless a Dirichlet boundary condition for pressure is given in absolute pressure.

Fig. 1 A rectangular computational domain where a Cartesian grid is arranged. The left and right boundaries drawn with dashed lines are an inlet and outlet, respectively, while the top and bottom boundaries represented by thick solid lines are rigid walls. Internal and boundary nodal points are shown by white and dark circles, respectively. Stencils are also depicted with dotted lines.

Fig. 2 Pressure drops in Poiseuille flow at two different flow rates Q_L and Q_H ($Q_L < Q_H$). Gradients of solid lines L1 and L2 are identical because they correspond to the same flow rate Q_L . This is also true for dashed lines H1 and H2, but the gradient of H1 and H2 is steeper because of the higher flow rate Q_H . The level of exit pressure makes no difference in the flow rate or in the velocity profile.

The above discussion is valid only when the wall is rigid. When the arterial wall is deformable, a temporal change in absolute pressure has a significant impact on the flow field.

Incompatibility of boundary conditions

Any outflow boundary condition named in published articles prescribes at least one of the followings at each outlet: pressure, flow rate and velocity gradient. Among these, the pressure and flow rate strategies are incompatible.

Fig. 3 shows a schematic drawing of a computational domain with an arterial bifurcation. No aneurysm is drawn in the figure for simplicity. Points B and C are located at the ends of the daughter arteries while A_1 and A_2 at the inlet. Fluid elements at inlet points A_1 and A_2 will eventually reach outlets B and C, respectively. The ratio of the flow rates in the two daughter arteries depends on the distal resistance, which is represented by the outlet pressures at points B and C. The higher the pressure at point B becomes, the more blood moves towards point C in the other daughter artery, and vice versa. Thus, for a given geometrical model, the flow division ratio is in a one-to-one relationship with the pressure difference of the two outlets. It is obvious that imposing outlet flow rates and outlet pressures at the same time would be too excessive constraints. If flow rates are given at the distal ends of the daughter arteries, pressures at points B and C must not be specified; those exit pressures will be evaluated by CFD according to the prescribed flow rates. This is the reason why the zero-pressure condition and flow splitting based on a power law are not jointly used.

Fig. 3 A schematic drawing of a computational domain with an arterial bifurcation. Points B and C are located at the ends of the daughter arteries while A_1 and A_2 at the inlet. Point D is far downstream of point C and out of the computational domain. The ratio of the flow rates in the daughter arteries depends on the distal resistance. The higher the pressure at point B becomes, the more blood moves towards point C in the other daughter artery, and vice versa.

Outflow boundary conditions used in aneurysm CFD

In this chapter, four outflow strategies are discussed. Although the traction-free and zero velocity-gradient conditions are usually combined with the zero pressure condition, they are treated separately.

Constant pressure at all outlets

A constant pressure condition fixes pressure at an arbitrary constant value over all outlet sections. In particular, it is called “zero pressure condition” when the constant pressure is zero. As far as the arterial wall is assumed to be rigid, it will make no difference in the calculated velocity field whether the constant pressure is zero or not (see the section entitled “Pressure in incompressible CFD”). A different choice for the outlet constant pressure would only result in a different reference pressure p_c in Eq. (1).

In some studies, pressure wave forms were imposed at outlets for unsteady flow analysis [8, 12, 20, 26, 27]. One should be careful in using this approach. If the identical pressure wave form with the identical magnitude is applied to all outlets, the effect on the velocity field will be the same as the zero pressure condition since there is no temporal derivative of pressure in the governing equations of incompressible flow. In fact, incompressible flow calculation at a certain time step does not refer at all to pressure at any other time steps.

As an outlet boundary condition for pressure specifies nothing about the state of the velocity field, some condition about the velocity at the outlets must be used alongside the pressure condition. In references [6, 28, 29], the zero pressure condition was jointly used with restrictions on velocity gradient such as the traction-free condition and the zero velocity gradient condition. However, in most studies using the zero pressure condition, no outflow condition for velocity (gradient) was named explicitly.

Undoubtedly, giving a constant pressure at all outlets is the most preferred strategy in aneurysm CFD. In the most recent CFD challenge [8], more than a half of the partici-

pating groups chose the zero pressure condition at outlets. The authors' literature inspection also shows that the zero pressure condition is the most prevalently used outflow boundary condition. All these facts show that many researchers still prefer the zero pressure condition despite its drawbacks pointed out by past studies [9, 11].

An unphysical characteristic of the zero pressure condition can be seen in Fig. 3. Pressure can be regarded as almost constant over the inlet cross-section and pressure difference between points A_1 and A_2 is approximately zero, $p_{A1} - p_{A2} \approx 0$, because, otherwise, there would be unrealistically strong secondary flow in the inlet plane. Thus, equating pressures at exit points B and C ($p_B = p_C$) follows that the pressure drop along the path from A_1 to B is almost equal to that from A_2 to C; $p_{A1} - p_B \approx p_{A2} - p_C$. However, this assumption is questionable. It should be emphasised that the amount of total energy loss and resultant pressure drop depend on the route, being subject to the flow rate and the geometry of each daughter artery (calibre, curvature etc.). In particular when the bifurcation harbours an aneurysm, a more complicated haemodynamic state near the bifurcation will make it ever more difficult to prescribe the outlet pressures accurately.

Another problem with the zero pressure strategy is sensitivity to model extension. In Fig. 3, point D is positioned downstream of point C and out of the original computational domain. If the computational domain is extended by stretching the lower artery from C to D and if the zero pressure outflow condition is imposed at outlets B and D, the flow splitting ratio and flow field will be different from those in the original computation with outlets B and C.

Despite the drawbacks mentioned above, the zero pressure condition has not been reported to lead to extremely unreasonable solutions; most computational results produced with the zero pressure conditions seem even reasonable. This will be discussed in chapter "Discussion" in comparison with other outflow conditions.

Flow splitting based on power law

This class of boundary conditions are used as widely as the zero pressure condition. According to the power law, the flow rate in each daughter vessel downstream of the branch is assumed to be proportional to the n -th power of the inner diameter. Using the power law, one can prescribe flow rates at the outlets with the constraint that the sum of outflow rates over all outlets must agree with the inflow rate. When the inner diameters of the two daughter vessels are d_1 and d_2 , this flow splitting method is denoted mathematically by

$$Q_1 = \frac{d_1^n}{d_1^n + d_2^n} Q_0 \quad Q_2 = \frac{d_2^n}{d_1^n + d_2^n} Q_0 \quad (2)$$

where Q_0 , Q_1 and Q_2 represent the flow rates in the mother and two daughter vessels, respectively. When $n = 3$, the power law is called the cube law or Murray's law. The flow

splitting strategy according to Murray's law is also referred to as the principle of minimal work, because, according to Murray's theory [30], the sum of the metabolic power to maintain the artery and the pumping power to maintain the flow is minimised when $n = 3$.

In Murray's original theory, arterial branching follows the relationship

$$d_0^n = d_1^n + d_2^n \quad (3)$$

where d_0 is the inner diameter of the mother vessel. Flow splitting based on Murray's law is used in CFD even when the actual arterial geometry deviates from the relationship (3) with $n = 3$. It is also important regarding the cube law that the wall shear stress in the daughter arteries will be identical when estimated on the assumption of fully developed Poiseuille flow. Therefore, the outflow condition based on a constant wall shear stress theory [31] is considered to have the same physical meaning as the cube law.

Another strategy used in aneurysm CFD is flow splitting according to the ratio of cross-sectional areas, which corresponds to the power law with $n = 2$. Here, flow speed is assumed to be constant instead of wall shear stress.

It is known that the cube law does not always hold true in actual vasculature. Furthermore, it is likely that the exponent for flow division differs from the junction exponent for the diameter relationship (3). Chnafa et al. [32] investigated terminal bifurcations of internal carotid arteries (ICA) of 31 patients and reported $n = 2.06 \pm 0.44$ (mean $\pm$ standard deviation) for the diameter relationship and $n = 2.45 \pm 0.75$ for flow splitting with $n = 3$ excluded from the confidence interval. Valan-Sendstad et al. [33] recommended $n = 2$ for inflow rate scaling in internal carotid arteries. According to Ingebrigtsen et al. [34], the junction exponent was 2.9 ± 1.2 for middle cerebral artery (MCA) bifurcations while $n = 1.7 \pm 0.8$ for distal ICA bifurcations. Baharoglu et al. [35], who investigated 159 MCA bifurcations, found that the junction exponent fell in the interquartile range 3.26–5.85 at bifurcations harbouring aneurysms. The interquartile range of the junction exponent was lower for patients without aneurysms (2.12–3.06) and patients with aneurysms at locations other than MCA bifurcations (2.52–3.29). Those findings of the past studies suggest that the flow split exponent should change depending on the artery size and the location of the aneurysm. However, researchers in this field do not seem to have reached any consensus on this matter. For example, the square law ($n = 2$) was used in haemodynamic analyses of cerebral aneurysms at various locations from anterior communicating arteries [36–38] through MCA bifurcation [11] to a basilar tip [39].

Conditions on velocity gradient

Any surface in flow receives fluid force. When the surface is strictly planar with the unit normal $\mathbf{n}$, traction or

stress vector $\mathbf{T}$ exerted on the surface is associated mathematically with pressure p and viscous stress tensor $\boldsymbol{\sigma}$ by the following equation [40],

$$\mathbf{T} = (-p\mathbf{I} + \boldsymbol{\sigma})\mathbf{n} = \begin{bmatrix} -p + \sigma_{xx} & \tau_{xy} & \tau_{xz} \\ \tau_{yx} & -p + \sigma_{yy} & \tau_{yz} \\ \tau_{zx} & \tau_{zy} & -p + \sigma_{zz} \end{bmatrix} \begin{bmatrix} n_x \\ n_y \\ n_z \end{bmatrix} \quad (4)$$

where $\mathbf{I}$ is the unit tensor and

$$\boldsymbol{\sigma} = \begin{bmatrix} \sigma_{xx} & \tau_{xy} & \tau_{xz} \\ \tau_{yx} & \sigma_{yy} & \tau_{yz} \\ \tau_{zx} & \tau_{zy} & \sigma_{zz} \end{bmatrix} \quad \mathbf{n} = \begin{bmatrix} n_x \\ n_y \\ n_z \end{bmatrix} \quad (5)$$

Components of the viscous stress tensor $\boldsymbol{\sigma}$ are expressed by the following relations,

$$\begin{aligned} \sigma_{xx} &= 2\mu \frac{\partial u}{\partial x} - \frac{2}{3}\mu \cdot \text{div } \mathbf{u} & \sigma_{yy} &= 2\mu \frac{\partial v}{\partial y} - \frac{2}{3}\mu \cdot \text{div } \mathbf{u} \\ \sigma_{zz} &= 2\mu \frac{\partial w}{\partial z} - \frac{2}{3}\mu \cdot \text{div } \mathbf{u} \end{aligned} \quad (6)$$

$$\begin{aligned} \tau_{xy} &= \tau_{yx} = \mu \left(\frac{\partial u}{\partial y} + \frac{\partial v}{\partial x} \right) & \tau_{yz} &= \tau_{zy} = \mu \left(\frac{\partial v}{\partial z} + \frac{\partial w}{\partial y} \right) \\ \tau_{zx} &= \tau_{xz} = \mu \left(\frac{\partial w}{\partial x} + \frac{\partial u}{\partial z} \right) \end{aligned} \quad (7)$$

Divergence of the velocity field $\text{div } \mathbf{u}$ vanishes for incompressible flow due to the continuity equation. After inserting Eqs (6) and (7) into (4), traction $\mathbf{T}$ is described by pressure and velocity gradient.

The traction-free condition assumes $\mathbf{T} = \mathbf{0}$ over the cross-sectional area of the outlet. This condition is usually combined with the zero pressure condition. The resultant outflow condition is

$$\boldsymbol{\sigma}\mathbf{n} = \begin{bmatrix} \sigma_{xx} & \tau_{xy} & \tau_{xz} \\ \tau_{yx} & \sigma_{yy} & \tau_{yz} \\ \tau_{zx} & \tau_{zy} & \sigma_{zz} \end{bmatrix} \begin{bmatrix} n_x \\ n_y \\ n_z \end{bmatrix} = \mathbf{0} \quad (8)$$

The outlet condition that prescribes zero stress vectors [41] is considered to be the same as Eq. (8).

When the outward normal of the outlet surface points in the x -direction, the following simple expression of the traction-free condition is obtained from Eqs. (6–8),

$$\frac{\partial u}{\partial x} = 0 \quad \frac{\partial u}{\partial y} + \frac{\partial v}{\partial x} = 0 \quad \frac{\partial w}{\partial x} + \frac{\partial u}{\partial z} = 0 \quad (9)$$

Poiseuille or Womersley flow in which the secondary flow components v and w vanish does not satisfy the condition (9). It might be inappropriate to impose the traction-free condition onto cases when daughter arteries are extended by adding straight pipes because flows are being developed in the straight pipes. In fact, researchers using the traction-free condition simply truncated distal arteries, not applying

the outlet extension to their 3-D models [28, 41–44]. Xu et al. [29], instead, adopted zero velocity-gradient in the normal direction for models with extended outlets. The zero velocity-gradient condition is derived from Eq.(9) by eliminating the in-plane gradient terms of u ,

$$\frac{\partial u}{\partial x} = \frac{\partial v}{\partial x} = \frac{\partial w}{\partial x} = 0 \quad (10)$$

The meaning of “traction-free” is literally “no pulling force”. However, the traction-free condition needs to be interpreted with a little caution because, in incompressible CFD, p is not absolute or real pressure but relative pressure. Real traction $\mathbf{T}$ evaluated with absolute pressure can never be zero because the magnitude of viscous stress in human cerebral arteries is much smaller than absolute blood pressure ($\approx 10^5$ Pa). The traction-free condition is actually a viscous-stress-free condition, as seen in Eq. (8). It prevents unnatural acceleration and deceleration due to viscous stress so that blood can flow out smoothly and, consequently, the calculation can be stabilised. However, it is questionable whether viscous stress is really zero over the outlet cross-section. On the other hand, the zero velocity-gradient condition (10) seems reasonable for fully-developed flow.

Reduced-order models

3-D flow analysis with CFD can reveal details of the blood flow in arteries. However, CFD requires such high computational cost that application of CFD to a large arterial system is practically impossible. It is, therefore, a reasonable approach that 3-D modelling is performed only for a region of interest while the adjacent arteries are represented by a reduced-order model.

Reduced-order models are derived by simplification of the N-S and continuity equations and a dramatic reduction in computational cost can be achieved. There are mainly two types of reduced-order model used for haemodynamic analysis, depending on the degree of simplification: one-dimensional (1-D) and zero-dimensional (0-D) models.

Equations for 1-D models are derived by integration of the N-S and continuity equations over an arterial cross-section with deformability of the wall taken into consideration [45–47]. In the resultant system, variables for pressure, flow rate and cross-sectional area are solved in 1-D space at every time step. Different 1-D models exist due to variations on the assumed velocity profile and pressure-area relationship. 1-D models can treat arterial bifurcations by introducing the assumption that the total pressure is conserved [45].

0-D or lumped-parameter models are based on the analogy of a vessel system with an electric system with elements such as a resistor, capacitor and inductor, which represent arterial resistance, compliance and inertance, respectively. Among 0-D models, a class of Windkessel

model is well-known. The first Windkessel model proposed by Frank [48, 49] is a so-called two-element model because it consists of a resistor and capacitor. Westerhof et al. [50] developed a three-element model by adding another resistor which represents upstream impedance. Fig. 4 shows a three-element Windkessel model in the electrical form. Adding an inductor to a three-element model, Stergiopoulos et al. [51] used a four-element model so that inertia of blood flow could be expressed. The four-element Windkessel is usually applied to large vessels like aorta.

As 0-D models are less costly than 1-D models, a Windkessel model is often used to provide boundary conditions for 1-D blood flow simulation [46, 47, 52]. A coupling of a 1-D and 3-element Windkessel model proposed by Raymond et al. [47] was adopted in several studies on aneurysm CFD for the purpose of specifying boundary conditions [53–55]. Another way to utilise a 0-D model is to acquire outflow boundary conditions for 3-D haemodynamic simulation directly, not via any 1-D model. An important assumption used here is that blood pressure drops to the same level in the peripheral arterial bed regardless of the route as shown in Fig. 5, where terminals of each Windkessel model is earthed.

Fig. 4 A three-element Windkessel model shown in electric form. R_1 and R_2 are resistors while C represents a capacitor.

The strategy using a reduce-order model appears to be less popular than the constant pressure and flow splitting strategies discussed in the previous sections. 0-D models were used by only 2 in 26 participating groups in the 2013 CFD challenge [3] and 2 in 17 in the 2018 CFD challenge [8].

Distinct superiority or inferiority of 0-d models has not been reported. Baek et al. [56] compared the zero-pressure condition and the outflow condition by a RC model (variant of the Windkessel) on ICA aneurysms and concluded that instability of the aneurysmal flow was not affected by choice of the outflow boundary condition. Torii et al. [57] coupled a fluid-structure interface model of an MCA aneurysm with a 0-D model based on a recursive structural tree assumption of the peripheral vasculature [58] and found that use of the 0-d model made no significant difference in the computational result. Meanwhile, Xu et al. [59] performed 3-D haemodynamic analysis of distal bifurcations of the common carotid artery with three outflow conditions including a three-element Windkessel model and compared computational results with the measurement by ultrasound Doppler velocimetry (UDV). They reported that a slightly better result was obtained with the Windkessel than with the other two outflow strategies: a structural-tree model for the distal resistance [58] and a fully-developed flow model based on Murray's law.

0-d models are capable of accounting for the behaviour of the downstream or peripheral vasculature when the model parameters are properly estimated. As distal haemodynamic states are not directly considered in the other outflow strategies discussed in the previous sections, it can be said that 0-D models have the potential to provide a better outflow condition. Further study on 0-d models is necessary so that accurate estimation of the model parameters can be achieved.

Fig. 5 An example of 3-element Windkessel models coupled with 3-D haemodynamical simulation. The outflow conditions for the 3-D simulation can be acquired with the peripheral resistance and compliance taken into consideration.

Discussion

Comparison of four outflow strategies

Characteristics of the four outflow strategies reviewed in the previous chapter are summarised in Table 1 where disadvantages are distinctly shown by shaded cells.

Among the four strategies, the third one specifying the outlet velocity gradient has only a secondary effect on the flow splitting ratio, because a velocity gradient condition imposed at an outlet only affect the local haemodynamic state near the outlet, which is usually positioned far downstream of the bifurcation and aneurysm. This strategy is only used in combination with one of the other three strategies which work as determinants of the flow splitting ratio. Therefore, which to choose from these three strategies is a key to a better approximation to the flow splitting ratio. The three outflow strategies that determine the flow splitting ratio can be further classified in two according to the parameter handled; the flow splitting ratio is directly specified by the second strategy (power law) while pressure at each outlet is given by the first (constant pressure) and fourth (reduced-order model) strategies.

It is not too much to say that little physiological or physical grounds can be found about the constant pressure strategy. It is another concern that this strategy is highly sensitive to model extension. On the other hand, the constant pressure strategy is easy to implement in CFD software and does not require high computational cost.

Reduced-order models are considered more physiological than the constant pressure strategy and, perhaps, the flow splitting with the power law, because only this approach can take the influence of the peripheral vasculature into account. However, reduced-order models have some drawbacks, i.e. uncertainty of model parameters, high computa-

tional cost and rather complicated implementation.

The flow splitting strategy with the power law is based on the observation of real arterial branches, while it takes no influence of the peripheral vasculature into account in a direct manner. Therefore, this strategy is considered to have moderately good physiological grounds. Being similar to the constant pressure condition, the power law is easy to implement and characterised by low computational cost. However, it is practically difficult to obtain the exact value of the exponent unless a patient-specific flow measurement is conducted.

Table 1 suggests that the power law strategy attains a good balance between the physiological reality and cost, while use of a reduced-order model should be recommended for the pursuit of higher accuracy. However, these theoretical characteristics have not been embodied in real computing because, according to published articles, none of the existing outflow strategies has proved definitely superior or inferior to others. It is understandable that researchers would rather choose the least costly zero pressure condition from outflow strategies of seemingly similar performances.

Reasons for similar performances

It is difficult to determine adequate values for model parameters: the exponent in the power law, and resistance R and compliance C in Windkessel model. Due to this difficulty, the capacities of the two promising strategies (power law and reduced-order model) have not been used to their maximum potential. Meanwhile, the zero pressure condition might not be as bad as you might think. Suppose that the zero pressure condition is imposed at outlets B and C in Fig. 3 and that $d_B < d_C$ where d_B and d_C are diameters of the respective daughter arteries. The zero pressure condition at both outlets means that pressure drops in the two daughter

Table 1 Comparison of the four outflow strategies. Disadvantageous points are indicated by shaded cells

	Strategy	Keywords	Determinant of flow splitting	Parameter specified at outlet	Physiological grounds	Practical disadvantage	Computational cost	Implementation
1	Constant pressure	zero pressure	Yes	Pressure	Ambiguous	Sensitivity to model extent	Low	Easy
2	Power law	Murray's law, principle of minimal work, cube law, square law	Yes	Flow rate	Moderate	Uncertainty of exponent	Low	Easy
3	Velocity gradient	Traction-free, zero gradient	No – jointly used with another strategy	Velocity gradient	Not fully confirmed	None	Low	Easy or slightly complicated
4	Reduced-order model	1-d model, 0-d model, Windkessel model	Yes	Pressure	Good	Uncertainty of model parameters	High	Rather complicated

arteries are equal, $\Delta p_B = \Delta p_C$ where Δp_B and Δp_C represent pressure drops from the bifurcation to points B and C, respectively. If simple Poiseuille flow is assumed in each daughter artery, the pressure drops will be expressed by

$$\Delta p_B = \frac{32\mu L_B u_B}{d_B^4} \quad \Delta p_C = \frac{32\mu L_C u_C}{d_C^4} \quad (11)$$

where L and u stand for the length and mean flow velocity of the daughter artery specified by the subscript, respectively, and μ represents blood viscosity. Equating the two pressure drops in eq.(11) results in

$$\frac{Q_B}{Q_C} = \frac{L_C}{L_B} \cdot \frac{d_B^4}{d_C^4} \quad (12)$$

where $Q_B (= \pi d_B^2 u_B / 4)$ and $Q_C (= \pi d_C^2 u_C / 4)$ are the flow rates in the respective daughter arteries. If $L_B = L_C$, eq. (12) will agree with the power law with $n = 4$. However, a situation where $L_B < L_C$ is more likely, because the extent of the computational model along the larger daughter artery C tends to be longer than along the smaller B. In such a situation, eq. (12) corresponds to a power law with the exponent smaller than 4. In particular when $L_B:L_C = d_B:d_C$, eq. (12) is identical to the cube law ($n = 3$). It is, therefore, presumed that, in many applications of aneurysm CFD, the zero pressure condition has the same effect as a power law with the exponent smaller than 4 ($n < 4$). Although eq. (12) does not strictly hold true in real arterial bifurcations, it can be concluded that the zero pressure condition is unlikely to cause an excessive deviation from the cube law, which has more physiological grounds.

The fractions on the right hand sides in the power law formulae (2) represent the ratios of flow division. Fig. 6 shows the flow division ratios versus the ratio of diameters of the daughter arteries for different exponents from 2 to 4. Here, a percentage of 100% corresponds to the flow rate in the mother artery. It is seen in Fig. 6 that the gap between

flow division ratios of $n = 2$ and 4 hits the maximum of approximately 20% when d_1/d_2 is around 0.6, which falls in the normal range of the diameter ratio in cerebral arteries. However, it is presumed that this level of flow rate variation in daughter arteries does not change the intra-aneurysmal flow structure dramatically. Thus, different outflow strategies might appear to produce similar computational results unless a severe quantitative comparison is made.

Perspective on future

Quantitative discussion on haemodynamics in cerebral aneurysms will be made more actively based on CFD results. In particular, it is important to evaluate low wall shear rate or stress accurately. For example, as pathologically low wall shear stress (WSS) could prevent normal physiological functions in the arterial wall and might lead to aneurysmal rupture [60], difference in the computational results caused by different outflow conditions should not be overlooked. Furthermore, in prediction of thrombus formation or embolisation using CFD [61–63], regions of interest are characterised by extremely low shear rate. In terms of the fibrin coagulation kinetics, Tipple and Müller-Mohnssen [64] reported a shear rate lower than 15 s^{-1} as the condition necessary for blood-clotting. Ogawa et al. [65] reported that more platelets could adhere to endothelial cells at a lower shear rate and suggested that the upper limit of shear rate at which platelet adhesion could occur was slightly higher than 16.8 s^{-1} . These extremely low shear rates may not be reproduced by CFD when a crude outflow condition is used. It is, therefore, important to be careful in choosing the outflow boundary condition. From this point of view, a coupling of CFD and a 0-d model is considered to be the most promising although further study is necessary to achieve accurate estimation of model parameters.

Conclusion

Four outflow strategies used in aneurysm CFD with multiple outlets were reviewed. For accurate quantification of the haemodynamic state in the aneurysm, it is crucial to incorporate the physiological flow splitting ratio in CFD analysis by means of accurate specification of pressures or flow rates at the outlets; it should be noted that the constant or zero pressure condition has less physiological grounds. Although, in practice, no existing outflow strategy has proved definitely superior to others, a coupling of 3-D CFD with a 0-d model is considered to be the most promising, because it has the potential for providing a more physiological relationship between the outflow rate and outlet pressure with the peripheral haemodynamic state taken into account. Further study on 0-d models is necessary so that accurate estimation of the model parameters can be achieved.

Fig. 6 Percentages of flow division by power laws with different exponents from 2 to 4. A percentage of 100% corresponds to the flow rate in the mother artery. Diameters of the two daughter arteries are d_1 and d_2 , respectively. The graphs are only drawn for the case when $d_1 < d_2$.

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