### Computational Fluid Dynamics and Aortic Dissections: Panacea or Panic?

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#### Abstract

This paper reviews the methodology, benefits and limitations associated with computational flow dynamics (CFD) in the field of vascular surgery. Combined with traditional imaging of the vasculature, CFD simulation enables accurate characterisation of real-time physiological and haemodynamic parameters such as wall shear stress. This enables vascular surgeons to understand haemodynamic changes in true and false lumens, and exit and re-entry tears. This crucial information may facilitate triaging decisions. Furthermore, CFD can be used to assess the impact of stent graft treatment, as it provides a haemodynamic account of what may cause procedure-related complications. Efforts to integrate conventional imaging, individual patient data and CFD are paramount to its success, given its potential to replace traditional registry-based, population-averaged data. Nonetheless, methodological limitations must be addressed before clinical implementation. This must be accompanied by further research with large sample sizes, to establish the association between haemodynamic patterns as observed by CFD and progression of aortic dissection.

#### **Keywords**

Computational flow dynamics, aortic dissection, true lumen, false lumen, wall shear stress, endovascular aortic repair, blood flow dynamics

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The traditional approach to investigation and management of aortic dissections has revolved around clinical examination, laboratory tests and a slew of imaging modalities including CT, chest X-ray, MRI, ultrasound and transoesophageal echocardiography.<sup>1</sup>

However, an inherent limitation of these techniques is that they do not consider the temporal dynamicity of aortic blood blow; they capture only a snapshot of the blood flow at single points in time.

Recent research has highlighted the use of computational fluid dynamics (CFD) as a complementary tool to improve our limited understanding of the complex biomechanical behaviour of blood flow in both normal aortas and those with pathology.

The potential application of CFD is widespread, spanning from technological development of new devices to routine clinical decision-making.  $^{\!\!\!\!^{2.3}}$ 

The amalgamation of engineering and medical disciplines has allowed computer simulation to be used to solve numerical equations related to fluid flow. Since CFD's inception in the 1950s by researchers from the Massachusetts Institute of Technology,<sup>4</sup> several studies have attempted to employ CFD techniques to analyse blood flow in different aortic pathologies including aortic aneurysms,<sup>5-7</sup> aortic dissections<sup>5,8-12</sup> and differences before and after endovascular aortic repair (EVAR).<sup>13</sup>

A combination of technological advancements in computing software (ANSYS FLUENT,<sup>14</sup> Open Foam,<sup>15</sup> SIMVascular,<sup>16</sup> ADINA,<sup>17</sup> in-house

coding<sup>18</sup> and the falling cost of supercomputing have paved the way for the use of computing resources to solve mathematical equations in medicine. The Navier–Stokes equation, for instance, allows modelling of intravascular pressure and flow parameters. The use of appropriately framed model parameters gives a realistic picture of blood flow and pressure waveforms in real time, enabling the investigation of blood flow velocity in relation to pressure and density as well as a myriad of other stresses and forces, including ones that cannot be measured, such as wall shear stress (WSS).

Haemodynamics is considered to play a paramount role in the development and progression of all types of aortic dissection aortic dissection but unfortunately remains poorly understood. Hitherto, no clinical consensus has been established as to whether medical, surgical or endovascular treatment is most appropriate for the management of aortic dissection. This has plausibly been attributed to the lack of an imaging criteria to determine the best treatment for individual patients. Therefore, there is burgeoning interest in the use of patient-specific CFD in clinical decision-making.

This review aims to provide an overview of the benefits and challenges of CFD in the management of aortic dissections.

# Haemodynamic Changes in True and False Lumens

Imaging techniques such as CT angiography and MRI have allowed clinicians to accurately visualise the vasculature, which can then be reconstructed by employing various software packages such as Materialise Mimics (Materialise NV) and 3D Slicer (open source). When these are used with a suitable meshing algorithm, CFD software can be applied to the vascular geometry to run simulation tests, along with 4D flow MRI and other imaging modalities such as 2D PC-MRI to provide realistic boundary parameters.<sup>19</sup> It is important to select the correct boundary condition for CFD models as this will improve CFD outcome as highlighted in the literature.<sup>20-22</sup> As stated in a recent publication,<sup>23</sup> it is important to consider the peripheral vascular network as a boundary condition, and model it through different elements of Windkessel Model. This will ensure a comprehensive analysis of blood flow dynamics, which should be useful in the future.

CFD could be employed to investigate haemodynamic changes in both the true lumen (TL) and false lumen (FL), where geometrical changes as a result of the dissection may change the entire flow field significantly. This may provide clues on when to treat an uncomplicated type B dissection. It remains a challenge to identify patients who are at the greatest risk of developing aneurysmal changes and should be given priority for treatment. This could be attributed to the unique geometrical features of the true and false lumen in every patient, which means that changes in the haemodynamic field vary between individuals. Karmonik et al. demonstrated that occlusion of the exit tear can cause an increase in FL pressure, since the geometry is altered after the occlusion. In addition, several studies have showed FL dilation causes a reduction in pressure within the FL.<sup>24</sup> However, some studies have demonstrated that pressure in the TL is generally higher than in the FL. Recent publications with state-of-the-art CFD models have shown that the pressure difference between the TL and the FL is strongly affected by the distensibility of the aortic wall,<sup>25, 26</sup> which should be given consideration when modelling the pressure in aortic dissection.

Cheng et al. showed that altered flow patterns in FL and TL may affect disease progression, and this is best explained by changes in wall shear stress (WSS). WSS exerted on the cell surface causes morphological deformation of the cells in the direction of blood flow, triggering rapid cytoskeletal remodelling and activating signalling cascades with the consequent acute release of nitric oxide and prostacylin followed by activation of transcription factors including NF- $\kappa$ B, c-fos, c-jun and SP-1.<sup>27</sup>

Low WSS is also associated with endothelial dysfunction, reduced nitric oxide production, increased oxidative stress, atheroma/ neointima formation and a propensity for vasoconstriction rather than vasodilatation.<sup>28</sup> In contrast, high and moderate WSS is associated with good endothelial function, reduced expression of adhesion molecules, increased expression of endothelial nitric oxide synthase and reduction in oxidative stress.<sup>29,30</sup> However, the threshold for low and high WSS appears controversial, and varies between studies. While Cheng et al. showed that WSS can go up to 17.98 Pa in the true lumen,<sup>31</sup> Karmonik et al. showed that maximum WSS can decrease from 0.9 to 0.4Pa,<sup>32</sup> and low WSS was determined to be less than 0.4 Pa. However, the authors believe that WSS can be geometry dependent, and might serve as an invaluable marker of vessel wall health, and thus, may help surgeons to prioritise patients for treatment.

### Haemodynamics of Exit and Re-entry Tears

Wan Ab Naim and colleagues showed that a re-entry tear can provide a return path for blood flow back to the TL during systole and an extra outflow path into the FL during diastole, which may alter the progression of a dissected aorta.<sup>33</sup> A high velocity profile located at the entry tear may result in high WSS. On the one hand, high time-averaged WSS (TAWSS) values have been found<sup>8,34</sup> to increase the progression of the entry tear. Elevated WSS depends on the site of entry. On the other, a reduction in shear stress can minimise the propagation of dissection. However, because each patient has a unique anatomical structure, there is a large range of WSS values across various types of tears. For example, the TAWSS exceeded 5 Pa in a study by Alimohammadi et al.<sup>8</sup> but twice this value was given (10 Pa) in a study by Karmonik et al.

### Haemodynamic Differences Before and After Endovascular Aortic Repair

Improvements in haemodynamic patterns within the aorta are expected after endovascular aortic aneurysm repair but this varies from patient to patient depending on the specific pathology and boundary conditions.

Unfortunately, some patients develop thrombosis in the false lumen after EVAR, and this is postulated to be due to haemodynamic factors. Menichini et al., for instance,<sup>35</sup> showed how turbulent flow in the aorta may promote thrombus formation in the FL, particularly following thoracic endovascular aneurysm repair (TEVAR). In addition, Wan Ab Naim et al. demonstrated that geometrical factors such as a re-entry tear and abdominal branches may cause the development of complete and incomplete FL thrombosis after stent graft repair.<sup>36</sup> These studies show that haemodynamic changes should be monitored closely to assess the risk of thrombus formation in the FL. The use of computational flow dynamics may accurately provide crucial information about WSS and change in velocity patterns, allowing clinicians to assess the risk of thrombus formation in every patient.

#### **Stent Design**

In addition, CFD offers a platform for stent design optimisation, with the primary aim of reducing the haemodynamic impact (reduced sscillatory shear index, renal replacement therapy and TAWSS) of the stent on the vessel. Simulation tests allow for assessment of the stent's mechanical and hemodynamic parameters that influence its performance. Strut thickness, for instance, has been found to be an important factor in predicting a stent's performance.<sup>37-39</sup>

A benefit of CFD is it makes it possible to accurately analyse the myriad of factors that cause potentially devastating stent-related complications, including malpositioning, neointimal hyperplasia and collapse.<sup>40,41</sup> Vascular surgeons are then able to identify patients at high risk of such complications, and can decide to implement prophylactic interventions.

## Clinical Integration of Computational Flow Dynamics

CFD may prove to be an invaluable tool across the different stages of clinical management for patients who present with aortic dissection. However, much needs to be done to integrate CFD in virtual treatment planning and patient-specific risk prediction. Ideally, there should be smooth integration of a patients' vasculature (cardiovascular imaging) with patients' clinical data (baseline characteristics) before running a CFD simulation. However, once this has been attained, surgeons would have a comprehensive understanding of the condition they are dealing with, and can decide on the optimal treatment option.

Research wise, this may also represent a paradigm shift from populationbased data to digital patient representations,<sup>42,43</sup> the former of which is severely limited because it requires large participant numbers and clinical trials to establish evidence. Instead, the combination of (Bayesian) machine-learning methods and CFD virtual data would enable continuous predictions of outcomes, thereby reducing the cost, time and resources associated with large-scale clinical trials. However, data are insufficient at present to establish a multidimensional database for machine-learning methods to be conducted appropriately.44

#### Limitations

The benefits of CFD must be viewed in the context of known limitations. First, the sample sizes in published studies are small, given that most analyse a cohort of fewer than 30 patients. Ideally, a large cohort of patients should be recruited with long-term follow-up (1 year), to establish the association between progression of a dissected aorta and haemodynamic factors such as disturbed flow and elevated WSS.

Secondly, the CFD technique itself is limited by its failure to consider biochemical interactions, although this is understandable because it

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boundary conditions.

should be addressed.

Conclusion

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methodological and logistical challenges are paramount before implementation into clinical practice.

was first used to model kinetics.<sup>45</sup> Therefore, CFD should never be used

in isolation and improvements are warranted in terms of setting the

Finally, CFD can never be entirely accurate in modelling the actual aortic

environment, including pulsatile blood flow and vascular structure.

Moreover, simulations may not be that specific to the individual patient given the continuous physiological fluctuations, which are

affected by a host of factors such as lifestyle, medication or genetic

predisposition. Integration of patient-specific data is lacking and

The adoption of CFD modelling is a new era in vascular surgery. While

potentially highly useful in the diagnosis, prediction and prognostication of aortic dissections, the application remains in its infancy. Addressing

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