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A computational model for false lumen thrombosis in type B aortic dissection following thoracic endovascular repair

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ABSTRACT

Thoracic endovascular repair (TEVAR) has recently been established as the preferred treatment option for complicated type B dissection. This procedure involves covering the primary entry tear to stimulate aortic remodelling and promote false lumen thrombosis thereby restoring true lumen flow. However, complications associated with incomplete false lumen thrombosis, such as aortic dilatation and stent graft induced new entry tears, can arise after TEVAR. This study presents the application and validation of a recently developed mathematical model for patient-specific prediction of thrombus formation and growth under physiologically realistic flow conditions. The model predicts thrombosis through the evaluation of shear rates, fluid residence time and platelet distribution, based on convection-diffusion-reaction transport equations. The model was applied to 3 type B aortic dissection patients: two TEVAR cases showing complete and incomplete false lumen thrombosis respectively, and one medically treated dissection with no signs of thrombosis. Predicted thrombus growth over time was validated against follow-up CT scans, showing good agreement with *in vivo* data in all cases with a maximum difference between predicted and measured false lumen reduction below 8%. Our results demonstrate that TEVAR-induced thrombus formation in type B aortic dissection can be predicted based on patient-specific anatomy and physiologically realistic boundary conditions. Our model can be used to identify anatomical or stent graft related factors that are associated with incomplete false lumen thrombosis following TEVAR, which may help clinicians develop personalised treatment plans for dissection patients in the future.

1. Introduction

Thoracic endovascular aortic repair (TEVAR) has been recently established as a viable alternative to open surgery for complicated acute type B distal dissections (Hanna et al., 2014), and has shown promising results for the treatment of both acute and chronic uncomplicated cases (Nienaber et al., 2014; Brunkwall et al., 2014). This minimally invasive procedure involves the placement of an endovascular stent-graft in order to seal the primary entry tear in the hope of reducing pressure in the false lumen (FL), promoting remodelling of the aorta, and inducing complete FL thrombosis, thereby restoring aortic flow. However, complete FL thrombosis is not always achieved. Risk factors such as the presence of distal re-entry tears and visceral vessels arising from the FL can lead to retrograde flow along the stent graft and perpetuate FL flow resulting in incomplete thrombosis (Qin et al., 2012). The latter has been associated with higher mortality rates due to increases in FL mean and diastolic pressure, causing further complications, such as aortic expansion and the formation of stent graft-induced new entry tears (Dong et al., 2010). It is therefore important to understand the hemodynamic and biomechanical consequences of TEVAR and what stent-graft designs and aortic morphologies would favour complete FL thrombosis.

The evaluation of hemodynamic parameters and their links with anatomical features plays an important role in understanding pathogenesis and evolution of vascular diseases and in improving treatment outcomes. In the last decade, computational fluid dynamics (CFD) studies have provided better insights into the hemodynamic environment associated with aortic dissection (AD), and have allowed the estimation of parameters such as wall shear stress (WSS) and pressure, which are difficult to measure *in vivo* (Sun and Chaichana, 2016; Doyle and Norman, 2016). CFD studies have demonstrated that flow in AD is disturbed, with a high velocity jet through the primary entry tear, strong recirculation in the FL and near the tears and large variations in WSS (Tse et al., 2011; Chen et al., 2013; Alimohammadi et al., 2014; Cheng et al., 2013; Wan Ab Naim et al.; 2014, Dillon-Murphy et al., 2015; Ahmed et al., 2016). Several authors have compared flow in pre and post-TEVAR aortas, in order to investigate its effect on AD

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hemodynamics (Karmonik et al., 2010; Midulla et al., 2012; Cheng et al., 2015; Sun and Chaichana, 2016), and a recent study by Nauta et al. (2017) focused on the influence of disturbed flow on the development of thrombus by evaluating platelet activation potential. Although these computational studies have provided valuable insights, little has been done to date to show directly how disturbed flow may lead to the growth of thrombus in the FL, in particular following TEVAR.

In this paper we present the application of a recently developed computational model to three AD cases in order to determine the model's capability to predict thrombus formation under realistic anatomical and flow conditions. The model has been previously tested on idealised AD geometries and validated against experimental data (Menichini and Xu, 2016). It has also been applied to realistic AD geometries based on patient-specific anatomical data, showing good qualitative agreement between the predicted thrombus growth pattern and *in vivo* observations at multiple follow-up stages (Menichini et al., 2016). Here, we further extend the model to patient-specific studies following TEVAR, and evaluate its predictive capability by qualitative and quantitative comparisons with *in vivo* data.

2. Methods

Two patient-specific post-TEVAR models were included: (i) one for a patient who developed complete FL thrombosis following TEVAR (TEVAR-P1), (ii) one for a patient who developed partial FL thrombosis (TEVAR-P2). Both patients were classified as complicated, and were treated with TEVAR in acute phase. Patient TEVAR-P1 was treated with a Gore TAG device (W. L. Gore & Associates, Flagstaff, Arizona; proximal diameter: 31 mm, distal diameter: 31 mm, endoprosthesis length: 20 cm), while patient TEVAR-P2 was treated with a Medtronic Valiant Captivia device (Medtronic/AVE, Minneapolis, Minnesota; proximal diameter: 34 mm, distal diameter: 34 mm, endoprosthesis length: 20 cm). A third uncomplicated patient who was under medical treatment and did not show any signs of FL thrombosis during follow-up was also included as a benchmark case (BMT). All patients were kept under CT surveillance. Formal ethical approval was not required for this retrospective study, as prior agreement was made to undertake computational modelling work using totally anonymised images without requiring further specific ethics committee agreement for individual patients. All data were analysed anonymously and patient information was de-identified prior to analysis.

The patient-specific models were reconstructed using Mimics (Materialize HQ, Leuven) from CT images acquired within one month after TEVAR. All CT scans were performed with a Philips Mx8000 IDT 16 scanner, with voxel sizes in the range of (0.75–0.92) × (0.75–0.92) × 2 mm^3 and FoVs between 382 and 477 mm. As the focus of this study was to predict thrombosis within the FL, all branches were excluded from the analysis. The models were meshed using ICEM 15 (Ansys Inc.), and mesh sensitivity tests were performed to ensure mesh independence for each case. As the growth of thrombus is driven by hemodynamic parameters, the sensitivity test was focused on ensuring mesh independence of the flow field. Three meshes were tested for each geometric model, and differences in peak wall shear stress and velocity below 2% were considered acceptable. The final grids represented a compromise between accuracy and computational cost and comprised approximately 3 million elements each, with a tetrahedral core and 10 prismatic layers near the walls. A fine resolution in the boundary layer is essential to guarantee accuracy in WSS predictions and smooth thrombus propagation. Larger element size was used in the core region, while gradual changes were made to avoid sudden jump in mesh size, which could compromise thrombus growth patterns.

Thrombus formation was simulated using the hemodynamics-based model developed by Menichini and Xu (2016) and modified by Menichini et al. (2016). The computational model identifies regions of thrombus growth through the evaluation of time-averaged WSS and shear rates, as well as the distribution of activated and resting platelets and fluid residence time. The growth of thrombus is tracked through the local concentration of a species denoted as bound platelets (BP), which is used as a surrogate for thrombus. Thrombus growth is predicted through a feedback mechanism which controls the formation of thrombus by allowing BP to accumulate in regions of high concentration of activated platelets, low shear and long residence times, and by stopping thrombus growth when these conditions are not satisfied. The full set of equations for the thrombus growth model and all model parameters can be found in the Appendix (Anand et al., 2003; Diamond, 1999; Ghirelli and Leckner, 2004; Harrison et al., 2007; Nesbitt et al., 2009; Wootton et al., 2001). As in our previous studies, the rate of thrombus growth was artificially accelerated in order to allow predictions to be obtained in a feasible time frame (Menichini and Xu, 2016).

The patient-specific models were implemented in Ansys CFX 15 with a high-resolution spatial discretisation scheme. Blood was treated as a non-Newtonian fluid described by the Quemada model (Quemada, 1978) and the flow was assumed to be laminar. A realistic flow waveform extracted from the literature (Cheng et al., 2014) was applied at the inlet of each model with a flat velocity profile. This boundary condition was deemed appropriate as our region of interest is located distal to the aortic arch (Cheng et al., 2014). Realistic 3D inlet velocity profiles would be needed for faithful prediction of flow in the ascending aorta, but these were found to have a negligible effect on flow in the descending aorta (Morbiducci et al., 2013). The walls were assumed to be rigid with no slip conditions. The flow split between the iliac arteries in the two post-TEVAR models was regulated by a 3-element Windkessel model (3EWM) outlet boundary condition (Dillon-Murphy et al., 2015), which describes the relationship between pressure and flowrate based on the analogy between electrical circuits and the cardiovascular system (Ruel and Lachance, 2010). For the BMT model, a pressure waveform calculated through a 3EWM was applied at the only outlet. Values for the 3EWM parameters were extracted from the literature (Xiao et al., 2014), as no patient-specific data was available. The boundary conditions applied in the three models are summarised in Fig. 1, with the respective outlet flows derived from the 3EWM. A fixed time-step of 0.005 s was adopted based on previous time-step sensitivity test (Menichini and Xu, 2016) and numerical simulations were carried out until thrombus growth stopped, which occurred after 20 cardiac cycles for TEVAR-P1, 42 cycles for TEVAR-P2, and 10 cycles for BMT. Simulation results were post-processed using CEI Ensight 10 and predictions of thrombus growth over time were validated against follow-up data.

3. Results

3.1. Model geometries

Fig. 2 shows the reconstructed geometries based on initial CT scans for all three patients together with the stent graft coverage for the TEVAR cases. In TEVAR-P1, the stent graft starts from below the left subclavian artery and covers the entire thoracic aorta and part of the abdominal aorta up to the celiac artery. Below the stented region, only one re-entry tear is observed, which has an area of around 20 mm^2 and is located at the iliac bifurcation level. The remaining FL extends upwards towards the celiac artery and downwards towards the iliac bifurcation. TEVAR-P2 presents a different stent configuration, with the stent graft covering the left

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