The effect of including increased arterial stiffness in the upper body when modelling Coarctation of the Aorta

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ABSTRACT

Coarctation of the Aorta (CoA) is a congenital narrowing of the aorta and diagnosis can be difficult. Treatments result in idopathic sequelae including hypertension. Untreated patients are known to develop increased arterial stiffness in the upper body, which worsens with time. We present results from simulations with a one-dimensional mathematical model, about the effect of stiffness, stenting, surgery and coarctation severity on blood pressure, Pulsatility and Resistivity Index. One conclusion is that increased stiffness may explain both hypertension in treated patients and why diagnosis can be difficult.

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1. Introduction

Coarctation of the Aorta (CoA) is a congenital heart disease, involving a narrowing in the aorta, which results in increased blood flow to regions of the body that are supplied by arteries upstream of the coarctation (generally the upper body) and decreased blood flow to downstream regions (generally the lower body) (Rao 2005). It is considered a serious disease with a mean age of mortality of 34 years if left untreated (Campbell 1970), and it affects 3–4 in every 10,000 live births (van der Linde et al. 2011). Although several treatments are available that resolve the coarctation, treated patients still experience decreased life expectancies compared to healthy populations, for treatments where data is available (Vriend and Mulder 2005; Nguyen and Cook 2015). Long-term or mortality data for patients treated with some treatments, such as stents, are unavailable as these treatments have only been applied in CoA patients in recent decades; hence, reviews of the treatments for CoA often are unable to recommend a particular treatment as being superior (Pádua et al. 2012).

The cause of CoA is unknown and it typically develops near the junction between the aorta and the ductus arteriosus (Elzenga and Groot 1983), which is an artery present in foetuses that closes shortly after birth. CoA results in modifications to the cardiovascular system, such as the increased artery stiffness that is observed in arteries that are supplied blood from upstream of the coarctation, but not in arteries downstream of the coarctation (Ou et al. 2008; Xu et al. 1997). CoA is also associated with left ventricular hypertrophy (Ou et al. 2008; de Divitiis et al. 2003), and the development of collateral arteries, which act as bypass arteries to provide blood to the lower body through a path that avoids the coarctation (Bramwell and Jones 1941).

The increased arterial stiffness that is observed in patients with CoA correlates positively with age (Lam et al. 2009); however, increased stiffness is observed in all patients, including in children that were treated at a young age (Lombardi et al. 2013).

Previously, it has been shown that, in single untapered (Pathirana et al. 2016) and tapered (Pathirana et al. 2017) arteries, the stiffness in the aorta wall caused by treatments for CoA such as stents or resection and end-to-end anastomosis (REA), may contribute to aneurysms and hypertension, and that the REA treatment may result in fewer long-term complications than stent treatments, after comparing blood flow properties in models of the aorta. This work extends those studies to arterial networks with coortications or treatments in the aorta and examines the effect of upper body arterial stiffness, as well as the effect of coarctation severity and treatment methods.
In this study, one dimensional (1D) blood flow models are used to study the main features of pressure, flow and area in networks of human arteries. Previous studies (Alastruey et al. 2011; Xiao et al. 2014; Boileau et al. 2015) have demonstrated that these models are able to produce many aspects of the fluid dynamics of blood flow in normal and disease conditions, and their results closely match those produced with three dimensional models, as well as matching theoretical results and experiments with networks of silicon tubes.

In this paper, results from arterial networks that include three sets of conditions are presented: coarctations of various severities, to determine the effect of the narrow region of the aorta by itself; coarctations of various severities with various increases in stiffness in the upper body, to determine the effect of the combined symptoms that would be present in patients pre-treatment; and various increases in stiffnesses with representations of either the stent or REA treatments, to determine the effect of conditions that would be present in patients post-treatment.

We provide a description of the mathematical model and numerical method used to simulate blood flow in our model in the Methods section. Systolic and diastolic blood pressure, pressure difference, Gosling’s Pulsatility Index (Gosling et al. 1971), and Pourcelot’s Resistivity Index (Pourcelot 1974) are provided for simulations involving combinations of increased stiffness in the upper body, coarctation severity, and CoA treatments in the Results section. A comparison of these results with previous work, as well as interpretations, are provided in the Discussion section. The Conclusion summarises the main findings of the paper and details future work.

2. Methods

2.1. The ADAN56 model

The ADAN56 model used in this study is a reduced version (Boileau et al. 2015) of the anatomically detailed arterial network model developed by Blanco et al. (2015). It comprises the 56 largest human arteries. Bifurcations within arteries are managed by splitting arteries into multiple domains, such that bifurcations exist at the ends of these domains. This results in a total of 77 domains in the model (Figure 1). The length of each artery, its radius at its proximal and distal ends, and the three-element Windkessel model parameters (for terminal arteries in the model), are tabulated in a paper by Boileau et al. (2015) and are reproduced in the supplementary material for this paper.

2.2. Fluid simulation details and numerical method

Simulations of the ADAN56 model with our modifications, as detailed in the Introduction and in Section 2.3, were run with the 1D blood flow package Nektar1D (Alastruey et al. 2012).

Briefly, conservation of mass and momentum for incompressible fluid flow in an axisymmetric vessel with constant cross-sectional pressure yields the equations (Alastruey et al. 2012)

\[
\frac{\partial}{\partial t} A(x, t) + \frac{\partial}{\partial x} [A(x, t)u(x, t)] = 0
\]

and

\[
\frac{\partial}{\partial t} [A(x, t)u(x, t)] + \frac{\partial}{\partial x} [\alpha(r, x, t)A(x, t)u(x, t)^2] = - \frac{A(x, t)}{\rho} \frac{\partial P(x, t)}{\partial x} + \frac{f(x, t)}{\rho},
\]
where \( x \) is the position along the longitudinal axes of the artery, \( t \) is time, \( A \) is the cross-sectional area of the artery, \( u \) is the blood flow velocity, \( a \) is the momentum flux correction factor that allows for Poiseuille type flow patterns, \( r \) is the position along the radial axis of the aorta, \( P \) is the blood pressure, and \( f \) is the frictional force per unit length.

A velocity profile,

\[ u(x, r, t) = U \frac{r}{R(x, t)} \left[ 1 - \left( \frac{r}{R(x, t)} \right)^\zeta \right], \]

is used to match in vivo measurements that show that flow velocity is non-uniform across cross-sections of blood vessels (Seed and Wood 1971), where \( U \) is the average blood velocity through a cross-section of the aorta, \( \zeta = \frac{2}{3} \) and \( R(x, t) \) is the radius of the artery lumen (assumed to be circular).

Blood viscosity, \( \mu \), is incorporated in the frictional force per unit length term,

\[ f(x, t) = 2\mu\pi R \left[ \frac{\partial u}{\partial r} \right]_{r=R}. \]

Fluid-structure interaction is accounted for by a Voigt-type visco-elastic law (Alastruey et al. 2011),

\[ P_e(A, x) = P_{ext} + \frac{\beta(x)}{A_0(x)} \left( \sqrt{A} - \sqrt{A_0(x)} \right) \]

and

\[ \beta(x) = \frac{4}{3} \sqrt{\pi E(x) h(x), \quad \Gamma(x) = \frac{2}{3} \sqrt{\pi \psi(x) h(x)}, \]

where \( P_{ext} \) is external (extramural) pressure, \( A_0 \) is the cross-sectional area when \( P = P_{ext} \) and \( \frac{\partial A}{\partial t} = 0 \), \( P_e \) is the elastic component of pressure, \( h \) is the aorta wall thickness, \( E \) is the Young’s modulus of the aorta wall and \( \psi \) is the wall viscosity, which is the property of artery walls that dampens or dissipates pulse waves (Bia et al. 2005). This visco-elastic law assumes thin, isotropic, homogeneous, incompressible, impermeable artery walls that deform axi-symmetrically with circular cross-sections (Alastruey et al. 2012). The prescribed inflow condition (Figure 2) was interpolated from that used by Boileau et al. (2015) for their work with the ADAN56 model, which in turn was adapted from an inflow reported by Murgo et al. (1980).

The three-element Windkessel model is used to account for compliance and resistances in the artery network. Windkessel and other parameter values for each of the arteries in the model are provided in Boileau et al. (2015).

The numerical method used in Nektar1D is the discontinuous Galerkin method, and full details of the implementation have been documented by Alastruey.
et al. (2012) and on the Nektar1D website. Briefly, the discontinuous Galerkin method is a spectral method, with Legendre polynomials used as the basis functions. Solutions to the governing equations are approximated in finite elements, then Riemann problems are solved to produce a continuous solution across the domain and implement the boundary conditions. The Adams-Bashforth scheme is used for time steps. Simulations were run for several heartbeat cycles to remove transient effects.

### 2.3. Artery network modifications

In this work, modifications were made to introduce coarctations, treatments for CoA, and increased upper body arterial stiffness into the ADAN56 model. Increased arterial stiffness in the upper body that is present in CoA patients was modelled by adding a multiplier to the stiffnesses in the normal ADAN56 model, while coarctations of various severities were modelled as modified artery radius (Figure 3) and stiffness (Figure 4), where stiffness was also modified to represent treatments for CoA, in the region where coarctations or these treatments typically occur (Figure 1). These stiffness modifications are similar to those used previously to represent treatments for CoA (Pathirana et al. 2016) and to compare the treatments in a model of the aorta (Pathirana et al. 2017). The modifications are hereafter referred to with codes for prefixes and suffixes that are described in Table 1.

### 2.4. Blood flow velocity indices

The following two indices that involve blood flow velocity were used to measure the effect of coarctation severities, arterial stiffnesses and CoA treatments on blood flow: (1) Gosling’s Pulsatility Index (Gosling et al. 1971), which is given by

\[
Pulsatility\ Index = \frac{\text{Systolic velocity} - \text{Dystolic velocity}}{\text{Mean velocity}},
\]

where “Mean velocity” is calculated as the average velocity in the final heartbeat period of the simulation when transient effects are minimal; (2) Pourcelot’s Resistivity Index (Pourcelot 1974), which is given by

\[
\text{Resistivity Index} = \frac{\text{Systolic velocity} - \text{Dystolic velocity}}{\text{Systolic velocity}}.
\]

The Pulsatility Index (Gosling et al. 1971) has been associated with cardiovascular disease risk (Pase et al. 2012), aneurysmal subarachnoid haemorrhage (Soehle et al. 2007) and pre-eclampsia (Takata et al. 2002). The Resistivity Index (Pourcelot 1974) is a similar calculation that has also been associated with aneurysmal
subarachnoid haemorrhage (Soehle et al. 2007), as well as kidney damage (Ikee et al. 2005).

3. Results

3.1. Coarctation severity and its effect on blood flow properties

CoA is commonly diagnosed by measuring the difference in systolic (maximum) blood pressure from the upper to the lower body, such as in the brachial artery in the right arm and in the popliteal artery in the right leg (Boutsikou et al. 2016; Nguyen and Cook 2015). In this study, coarctations of a range of severities were simulated using the ADAN56 human artery network model. Figure 5 shows the ranges of blood pressure in the brachial artery in the right arm for each of these simulations. Systolic blood pressure can be read as the top value of each bar in the figure, and diastolic blood pressure can be read as the bottom value.

The stent and REA treatments, normal aorta, and C25 and C50 coarctations all had similar systolic blood pressures near 120 mmHg. Systolic blood pressure increased in coarctations ranging from C70 to C94, compared to normal, with a greater coarctation severity resulting in a greater increase. A similar plot for blood pressure in the popliteal artery in the right leg is given in Figure 6. In this artery, the systolic blood pressure for the normal aorta, stent, REA treatment, and C25 coarctation had similar values near 160 mmHg, whereas systolic blood pressure in coarctations of a greater severity increased with coarctation severity up to C70, and then decreased.

The difference between systolic blood pressure in the brachial and popliteal arteries is plotted in Figure 7. Coarctations of a severity up to C82 have negative pressure differences between these two arteries, as do the normal aorta, and the stent and REA treatments. Coarctations of a severity greater than C82 result in an increased pressure difference, and the difference is positive for coarctations of a severity above C84.

Diastolic (minimum) blood pressure is also an important predictor of cardiovascular disease (Stamler et al. 1993). In the brachial artery (Figure 5), the

| Prefixes | CNo | CRe | CSt | C## |
|----------|-----|-----|-----|-----|
| Suffixes | SNo | S## |

Prefixes indicate no coarctation or treatment (CNo), a REA treatment (CRe), a stent treatment (CSt) or coarctations that involve a reduction in the radius of the artery by a percentage specified as the number (##) in C##. Suffixes indicate either no change to the stiffness in the upper body (Figure 1) arteries (SNo), or an increase by a multiplier that is specified as the number (##) in S##.
normal aorta, stent, REA treatment, and coarctations of a severity up to C82, had similar diastolic blood pressures of between 72 and 75 mmHg, although diastolic blood pressure in coarctations decreased in small amounts with coarctation severity up to C75, then increased in small amounts up to C82. From C82 onwards diastolic blood pressure increased more significantly with greater coarctation severities.
In the case of diastolic blood pressure in the popliteal artery in the right leg (Figure 6), the normal aorta had slightly greater diastolic pressure than the REA treatment, which had slightly greater pressure than the stent treatment. Diastolic blood pressure decreased with coarctation severity up to C75, then increased up to C84, while coarctations with severity C84-C92 had a diastolic blood pressure in the range

![Figure 7](image-url)  
**Figure 7.** Difference in the systolic blood pressure values over a cardiac cycle between the brachial (right arm) and popliteal (right leg) arteries, in the ADANS6 model with various coarctation severities, a stent, and the REA treatment.

![Figure 8](image-url)  
**Figure 8.** Pulsatility Index (Equation 1) in the brachial artery in the right arm from simulations of coarctations of a range of severities, a stent, and the REA treatment in the ADANS6 model.

In the case of diastolic blood pressure in the popliteal artery in the right leg (Figure 6), the normal aorta had slightly greater diastolic pressure than the REA treatment, which had slightly greater pressure than the stent treatment. Diastolic blood pressure decreased with coarctation severity up to C75, then increased up to C84, while coarctations with severity C84-C92 had a diastolic blood pressure in the range
of 74-76 mmHg, followed by a large drop for C94 to about 59 mmHg.

The Pulsatility Index (Equation 1) in the brachial artery in the right arm for coarctations of a variety of severities is plotted in Figure 8. Increases in Pulsatility Index are seen in all coarctations up to the C92 severity, compared to no coarctation. A similar result is seen when the Resistivity Index (Equation 2)
is plotted (Figure 9), except that the increases are relatively smaller.

In the popliteal artery in the right leg, there is a small increase in Pulsatility Index (Figure 10) for coarctations up to the C75 severity, compared to no coarctation. As coarctation severity increases above C75, the Pulsatility Index decreases, and is also decreased compared to no coarctation. The Resistivity Index (Figure 11) for coarctations with C25 or C50 severity is similar to no coarctation; however, coarctations between C70 and C84 severities have an increased Resistivity Index compared to no coarctation. Coarctations with the C86 severity or greater have a decreased Resistivity Index compared to no coarctation, and as the severity increases above the C86 severity, Resistivity Index decreases.

3.2. Effect of pre-treatment CoA on blood flow properties

Coarctation of the aorta can result in increased artery wall stiffness in the upper body, which persists after direct repair of the coarctation. Increased artery wall stiffness has been observed in the brachial (de Divitiis et al. 2001) and carotid (Vriend et al. 2006) arteries, as well as the section of aorta that is proximal (upstream) of the coarctation (Vitarelli et al. 2008; Vogt et al. 2005; Xu et al. 1997). In this section, and the next, increased stiffness in the arteries in the upper body was simulated to identify the effects of this symptom on blood flow properties for both pre- and post-treatment of the coarctation. A range of increases in stiffness was simulated, combined with a range of coarctations, to represent the pre-treatment case. Simulations with increased stiffness are indicated by a suffix that is either S02, S05 or S10, which represents 200%, 500% and 1000% stiffness, respectively. The suffix SNo indicates normal, or 100%, stiffness.

Results for systolic blood pressure in the brachial artery in the right arm are plotted in Figure 12, and in the popliteal artery in the right leg in Figure 13, on the top of the bars, for a range of stiffnesses from 200% to 1000%, combined with a range of coarctations with a 25%–82% reduction in radius, as well as for a normal aorta. For every coarctation severity, and the normal aorta, systolic blood pressure increased with increased artery wall stiffness. Systolic blood pressure in the popliteal artery in the right leg (Figure 13) followed the same pattern, except for coarctations with severity C70, C75 and C80, which had the highest systolic blood pressure at S05.

Diastolic blood pressure in the brachial artery in the right arm are plotted as the bottom of the bars in Figure 12, where it can be seen that the pattern of results is different from the systolic pressure results. In the model with a normal aorta, and at each
coarctation severity except C82, diastolic blood pressure generally decreased with increased artery wall stiffness in the upper body. In the popliteal artery in the right leg (Figure 13), this pattern occurs in the C50, C70, and C75 coarctations, but not the C25, C80 and C82 coarctations.
The pressure difference from the brachial artery in the right arm to the popliteal artery in the right leg, for coarctations of various severities, with various increases in stiffness in the arteries in the upper body, is plotted in Figure 14. This shows the effect that stiffness increases, as a CoA patient ages, have on the pressure difference, which is a significant indicator for CoA. For coarctations with a severity of C75 or greater, the pressure difference increases as the stiffness increases, with C80 and C82 exhibiting a positive pressure difference at the higher stiffnesses of S05 and S10.

3.3. Effect of post-treatment CoA on blood flow properties

As described in the previous section, stiffness in the arteries in the upper body is known to persist in patients that have been treated for CoA. In this section, results for the combined effect of increased stiffness with treatments for CoA are presented. A stent and the REA treatment were incorporated into the ADAN56 model and simulated with a variety of increases in stiffness in the arteries in the upper body (Figure 1). Results for systolic blood pressure in the brachial artery in the right arm are plotted as the top of the bars in Figure 15 for no treatment (CNo), a stent (CSt), REA treatment (CRe), combined with a 100% (indicated by a label with the suffix SNo), 200% (S02), 500% (S05) and 1000% (S10) stiffness in the arteries in the upper body. At each stiffness, there is a small increase in blood pressure in simulations with the REA treatment, compared to the normal aorta, and a further increase with the stent treatment. Larger increases in blood pressure occur across treatments when comparing simulations with 200% stiffness (S02) to simulations with 100% stiffness (SNo), and similarly when comparing 500% (S05) to 200% (S02) stiffness.

Systolic blood pressure in the popliteal artery in the right leg from simulations of the post-treatment conditions is presented in Figure 16. The results are similar to those described for systolic blood pressure for the same conditions in the brachial artery in the right arm (Figure 15), with small increases in blood pressure from CNo to CRe, and from CRe to CSt, treatments at each stiffness, and larger increases across treatments from SNo to S02, and from S02 to S05. Compared to the brachial artery in the right arm, all systolic blood pressures in the popliteal artery in the right leg are higher, and the increases in blood pressure in the popliteal artery, due to treatments or increased stiffness, is also greater than in the brachial artery, with the range of systolic blood pressures in the popliteal artery (about 20 mmHg, from CNoSNo to CStsS10) about twice that in the brachial artery (about 10 mmHg).
Diastolic blood pressure in the brachial artery in the right arm is also plotted as the bottom of the bars in Figure 15. The increases in systolic blood pressure between specific treatment-stiffness combinations in the brachial artery, as described above, are mirrored as decreases in diastolic blood pressure of a similar.
magnitude between the same treatments. Diastolic blood pressure (Figure 16) similarly mirrors increases in systolic blood pressure between treatments in the popliteal artery in the right leg; however, compared to the decreases in diastolic blood pressure in the brachial artery, the decreases between treatment-stiffness combinations in the popliteal artery are greater in magnitude.

4. Discussion

In this paper, we investigated the effect of pre- and post-treatment conditions of CoA patients on blood flow properties, by simulating coarctations to represent the early stages of the disease, coarctations with increases in the arterial stiffness in the upper body to represent later stages of the disease, and treatments with increases in the arterial stiffness in the upper body to represent treated patients.

When we simulated coarctations of various severities, we found that both diastolic and systolic blood pressure in the brachial artery in the right arm increase as coarctation severity increases above C75 (Figure 5), in the brachial artery in the right arm; however, the increases in diastolic blood pressure were relatively small up to C88. This suggests that CoA may result in either isolated systolic hypertension, which involves only increased systolic blood pressure, or hypertension that involves increases in both systolic and diastolic blood pressure, depending on the severity of the coarctation.

This is consistent with studies that show that CoA may produce isolated systolic hypertension proximal to the coarctation (Allen et al. 2016) and a gradient in the blood pressure between the upper and lower limbs of a neonate (Hoschtitzky et al. 2010), although use of this gradient to diagnose CoA may have a high false positive rate (Crossland et al. 2004). Our finding of an increased diastolic blood pressure in the brachial artery in the right arm in artery networks with a severe coarctation appears to be unreported in the literature.

The outcomes for patients that have been treated for CoA are generally worse when treated at an older age; for example, risk factors for late hypertension and premature death increase, although the risk factor for recoarctation decreases (Brouwer et al. 1994; Daniels 2001). The fact that the coarctation itself may narrow over time if left untreated (Elzenga and Groot 1983), suggests that CoA should be treated at an early age.

Increased stiffness has been observed in the brachial (de Divitiis et al. 2001) and carotid (Vriend et al. 2006) arteries, as well as the section of the aorta that is proximal to the coarctation (Vitarelli et al. 2008; Vogt et al. 2005; Xu et al. 1997), in CoA patients. In this study we found that only severe coarctations produce a blood pressure difference of at least 20 mmHg between the upper and lower body (Figure 7), but less severe coarctations can produce this pressure difference if the stiffness in the arteries in the upper body is increased (Figure 14). The increased stiffness in the aorta is known to increase with the age at treatment of the patient (Lam et al. 2009). This suggests that arteries that are proximal to the coarctation have increased stiffness, and that this stiffness increases as untreated CoA patients age, consequently this increased stiffness can contribute to an increased blood pressure difference when patients are older. This may explain why early detection of CoA can be difficult (Ing et al. 1996). We also found that the increased stiffness resulted in increased systolic blood pressure in the upper and lower body (Figures 15 and 16). This may explain why the hypertension in adult CoA patients can persist after being treated for CoA (Daniels 2001; Bhat et al. 2001).

Patients with less severe coarctations may be asymptomatic and remain undiagnosed until adulthood (Kaemmerer 2011). Our findings suggest that a reason why patients may be undiagnosed is that these coarctations do result in increased blood pressure in the upper body (for example, C84 in Figure 5), but do not produce a sufficient pressure difference required for diagnosis (C84 in Figure 7). High blood pressure can contribute to arterial stiffening (Zieman et al. 2005), hence the higher blood pressure in the upper body may result in higher arterial stiffness in the upper body, which can contribute to a pressure difference that results in a diagnosis of CoA later in life.

As discussed earlier in the section, early treatment of CoA can improve outcomes for patients; however, early diagnosis can be difficult in some patients who do not present with signs or symptoms early. We found that some less severe coarctations, which did not result in a pressure difference between the upper and lower body of at least 20 mmHg, did produce differences in Gosling’s Pulsatility Index and/or Pourcelot’s Resistivity Index. While both indices may be useful, measuring the Pulsatility Index in the brachial artery in the right arm may provide greater differences between patients with or without CoA, because it produces a large percentage increase for coarctations with a severity between C70 and C90 when compared with no coarctation (CNo).

5. Conclusion

In this study we investigated the effect of CoA alone, CoA with increased upper body arterial stiffness, and
treatments with increased upper body arterial stiffness, on blood pressure and indices of blood flow in the brachial artery in the right arm and the popliteal artery in the right leg of a simulated arterial network.

We found that severe coarctations produce the 20 mmHg blood pressure difference between the upper and lower body that is often used to diagnose CoA; however, we also found that less severe coarctations, which did not produce the 20 mmHg pressure difference, can produce systolic hypertension, which can contribute to increases in arterial stiffness in the upper body over time (Zieman et al. 2005). We showed that increased upper body arterial stiffness can produce the 20 mmHg pressure difference in these less severe coarctations, which may explain why some CoA patients do not present with signs and symptoms until adolescence or adulthood. We also found that this increased stiffness can explain the systolic hypertension that is observed in patients post-treatment, as treatments target the coarctation itself, and not increased arterial stiffness in the upper body. Measuring arterial stiffness in the upper body arteries may help inform treatment choice for hypertension in CoA patients post-treatment. Finally, we found that early detection of less severe CoA may be possible by calculating Gosling’s Pulsatility Index or Pourcelot’s Resistivity Index in the upper and lower body.

In future work, arterial stiffness in the upper body and blood pressure could be measured in CoA patients post-treatment to validate the relationship between these two parameters that this paper describes. Other complications that are associated with CoA, such as left ventricular hypertrophy and the development of collateral arteries, may be implemented in the model to investigate their effects and whether they can explain complications that are observed in untreated or treated CoA patients. The Pulsatility Index or Resistivity Index can also be compared between CoA patients pre-treatment and humans without CoA to determine whether these indices can help to diagnose CoA.

Disclosure statement
No potential conflict of interest was reported by the authors.

Notes
1. http://haemod.uk/nektar
2. http://haemod.uk/nektar

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