Patient-specific CFD modelling in the thoracic aorta with PC-MRI–based boundary conditions: A least-square three-element Windkessel approach

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Abstract
The increasing use of computational fluid dynamics for simulating blood flow in clinics demands the identification of appropriate patient-specific boundary conditions for the customization of the mathematical models. These conditions should ideally be retrieved from measurements. However, finite resolution of devices as well as other practical/ethical reasons prevent the construction of complete data sets necessary to make the mathematical problems well posed. Available data need to be completed by modelling assumptions, whose impact on the final solution has to be carefully addressed. Focusing on aortic vascular districts and related pathologies, we present here a method for efficiently and robustly prescribing phase contrast MRI–based patient-specific data as boundary conditions at the domain of interest. In particular, for the outlets, the basic idea is to obtain pressure conditions from an appropriate elaboration of available flow rates on the basis of a 3D/0D dimensionally heterogeneous modelling. The key point is that the parameters are obtained by a constrained optimization procedure. The rationale is that pressure conditions have a reduced impact on the numerical solution compared with velocity conditions, yielding a simulation framework less exposed to noise and inconsistency of the data, as well as to the arbitrariness of the underlying modelling assumptions. Numerical results confirm the reliability of the approach in comparison with other patient-specific approaches adopted in the literature.

KEYWORDS
boundary conditions, computational fluid dynamics, patient-specific simulations, thoracic aorta, Windkessel model

1 INTRODUCTION
Patient-specific modelling of cardiovascular diseases has been consolidating over the last two decades as a tool for quantitative analysis to elucidate pathological dynamics or even to design new therapies.1-5 Computational fluid dynamics (CFD) simulations customized in geometries retrieved from patients’ images are moving from a proof-of-concept stage to the clinical practice. In fact, because of the ability of representing in detail hemodynamic patterns (not only in terms of
velocity and pressures but also in terms of derived quantities such as the wall shear stress (WSS) and of predicting possible future scenarios that may support physicians in the decision-making process, it is expected CFD to become a routine clinical tool in the years to come. A crucial role in this scenario is played by the reliability assessment of the numerical results in the general context of uncertainty quantification.

In a patient-specific scenario, these uncertainties might have an origin in each component of a cardiovascular CFD model, such as the equations for fluid dynamics, blood rheology, geometry reconstruction, and boundary conditions. Navier-Stokes equations (NSE) with constant viscosity and density have demonstrated to be a good fit for modelling blood flow in large arteries, and methods for reconstructing vascular geometries interfacing with several different imaging devices are quite well established.6

The customized treatment of boundary data still requires specific investigations due to its major impact in numerical results. On the one hand, one would like to retrieve from specific measures all the data needed by the mathematical model, so to maximize the adherence of the numerical model to the patient-specific data. On the other hand, this is not possible nor appropriate for physical or practical limitations of the measurement process. Devices have limited time and space resolution, and measures are typically affected by noise and inconsistencies,7 so they are not complete and totally trustworthy. In addition, clinical needs require referring to noninvasive and possibly already approved protocols.

To fill the gap and to filter the possible noise of defective and noisy data, we typically need to advocate convenient modelling assumptions. Postulating these assumptions introduces a necessary deviation from the strict patient-specific modelling. From the mathematical point of view, an active field of research is the identification of assumptions whose impact on the final results may be minimized. This requires extensive sensitivity analysis and nonstandard numerical techniques currently under development.8-10 While these solutions are generally rigorous and reliable, they typically require high computational costs. A classical example in this respect is the prescription of flow rates by a Lagrange multiplier approach.11-13 As for now, this high cost may represent a serious drawback when using CFD models in beyond-proof-of-concept contexts, as Computer-Aided Clinical Trials or Surgical Planning. In this case, it is currently more affordable to resort to more engineering approaches that are suboptimal in terms of accuracy yet computationally cost-effective and clinically relevant.

Different pathologies, diseases, vascular districts, and ultimately available measures in this respect lead to different strategies, and the identification of the optimal approach for different problems (and different purposes) is far from being reached, subject of the recent literature.7,14-18 In particular, treatment of boundary conditions shows a wide variety of approaches from an extremely simplified stress-free approach in the outflow boundaries19,20 to sophisticated data assimilation techniques such as Kalman filtering.21

The aim of this article is to present, validate, and test an algorithm for calibrating boundary conditions in thoracic aortic simulations based on the so-called three-element Windkessel model (3WK) and a minimization approach proposed by Toorop et al.22 In fact, the recent article by Pirola et al.,18 though using a different calibration strategy, has confirmed the strength of using 3WK circuits as outflow boundary conditions against other methodologies.

First, we present the mathematical background on boundary conditions and report some approaches currently used in literature. In particular, we recall the Windkessel model with its potentialities and limitations.

Second, we illustrate our novel calibration technique for the parameter identification together with its validation in the general context of possible approaches for the reliable prescription of defective (or missing) data.

Finally, the procedure will be applied to three patients in the framework of a Computer-Aided Clinical Trial dedicated to the investigation of aortic pathologies, called iCardioCloud,5,23 and CFD results compared with parameter calibration techniques proposed by other authors. We focus in particular on velocity, pressure, and WSS results to draw conclusions on the reliability and efficiency of our approach in comparison with other possible techniques. An empirical sensitivity analysis is also performed so as to assess the robustness of the procedure.

2 | NUMERICAL MODELLING OF AORTIC FLOW IN iCardioCloud

2.1 | The mathematical model

We describe hemodynamics in the aorta with a rigid wall model, which is clearly a strong simplification due to the well-known compliance of big vessels. The level of uncertainty in the extraction of wall properties of the patient-specific vascular, as well as the significant increment in the computational costs of fluid-structure interaction (FSI) simulations, make this approximation currently the best trade-off between accuracy and efficiency for clinical purposes.14,24
The patient-specific accuracy of FSI simulations requires a reliable estimate of the structural constitutive parameters (e.g., vessel wall stiffness), which is currently quite hard to achieve in clinics. We focus herein on the fluid dynamics.

Following standard assumptions, we model blood flow as an incompressible fluid with Newtonian rheology. We therefore refer to the classical incompressible NSE as the mathematical model for blood, where \( u(x, t) \) denotes the velocity and \( p(x, t) \) the pressure field. \( \Omega \) denotes the aortic domain of interest, \( x \in \Omega \), and the time \( t > 0 \).

The NSE read
\[
\begin{align*}
\rho \frac{\partial u}{\partial t} + \rho (u \cdot \nabla) u + \nabla \cdot \sigma &= 0, \\
\sigma &\equiv pI - \mu (\nabla u + (\nabla u)^T) \\
\nabla \cdot u &= 0
\end{align*}
\] in \((\Omega, t > 0)\). (1)

Here \( \mu \) is the constant viscosity set to 3.5 cP, \( \rho \) is the blood density set to 1.06 g/cm\(^3\), and \( I \) is the identity tensor.

The equations must be equipped with both boundary and velocity initial conditions. Blood flow can be assumed reasonably periodic over a few heartbeats, and the lack of knowledge of the initial conditions is solved by simulating six heartbeats and eventually focusing on the last one, when the periodic regime has been reached.

The aortic geometry \( \Omega \) is a major factor governing aortic hemodynamics,\(^{15} \) and its 3D subject-specific reconstruction is currently a standard procedure. In our application, it is obtained by an accurate image processing of the patients enrolled in the iCardioCloud project (see Section 2.2). On the boundary of \( \Omega \), hereafter denoted by \( \partial \Omega \), we are supposed to prescribe three scalar conditions to have a correct statement of the mathematical problem. Conditions typically refer to either velocity data (Dirichlet conditions) or traction data (Neumann conditions). The latter conditions prescribe the normal stress \( \sigma \cdot n \equiv p n - \mu (\nabla u + (\nabla u)^T) \cdot n \) as the viscous component is usually considered secondary, these conditions are also often referred to as pressure conditions. In some applications, it may be worth prescribing a combination of velocity and pressure data (Robin conditions).\(^{10} \)

In all the aortic geometries, we can categorize the different portions of the boundary \( \partial \Omega \) as follows (see Figure 1):

1. Wall \( \Gamma_W \): representing the physical wall of the artery;
2. Inlet \( \Gamma_{in} \): representing the main inflow section of the domain, i.e., the ascending aorta (AA) entrance, approximately in correspondence of the sinotubular junction (as reconstructed in our geometrical model);
3. Outlet \( \Gamma_{out} \): representing the set of (not connected) outlet sections (even though the name “outlet” does not exclude that some backflow may occur over the heartbeat) that in our model consists of the brachiocephalic trunk (BCT), the left common carotid artery (LCCA), the left subclavian artery (LSA), and the descending aorta (DA). The supraortic vessels BCT, LCCA, and LSA will be treated in the same way, so for easiness of notation, they will be collectively denoted by \( \Gamma_{sup} \), and we indicate DA outlet with \( \Gamma_{DA} \), so that \( \Gamma_{out} = \Gamma_{BCT} \cup \Gamma_{LCCA} \cup \Gamma_{LSA} \cup \Gamma_{DA} = \Gamma_{sup} \cup \Gamma_{DA} \).

On the aortic wall, boundary conditions stem from the selected physical model. In the case of rigid vessels, these conditions simply resort to enforcing null velocity
\[
u(\Gamma_W, t) \equiv 0.
\] (2)

On \( \Gamma_{in} \), typically, velocity conditions are prescribed, while on the outlets, traction conditions are usually enforced. This is justified by the physical convection, where blood enters the domain in \( \Gamma_{in} \), calling for velocity conditions. However, the data available at the inflow have a finite time-space resolution and are noisy. Processing velocity data as obtained by phase contrast MRI (PC-MRI) is therefore not trivial. Interpolation procedures are made troublesome by the fact that the domain is moving and by the noise of the data. A least-square approach may be pursued, by mapping all the time-dependent inlet sections into a reference one. At the bottom line, one can resort to a constant least-square approximation that amounts to enforcing a value \( u_{in} \) of the velocity such that
\[
rho u_{in}(t)|_{\Gamma_{in}} = \rho \int_{\Gamma_{in}(t)} u_{PC-MRI}(x, t) \cdot nd\gamma = Q_{in}(t),
\] (3)

where \( |\Gamma_{in}| \) denotes the area of the AA section at the time of the heartbeat where the geometry is reconstructed and \( u_{PC-MRI}(x, t) \) is the measured velocity.

This prescription of the flow rate \( Q_{in} \) is quite popular and simple to achieve. The drawback is that the constant profile may be a crude approximation that introduces local errors in the numerical results. A strategy to mitigate this error relies on the introduction of artificial extensions of the physical domain (called “flow extensions”), so that the errors are localized out of the region of interest. This approach is mathematically justified by the theorem proved by Veneziani and Vergara\(^{13} \).
stating that the errors induced by the inaccuracies in the Dirichlet data decay exponentially with the distance from the boundary.

In the following, we will proceed at the inflow with the condition from (3), where the data $Q_{\text{in}}$ are retrieved either from the literature or from patient-specific PC-MRI. Regarding the outflow boundary conditions, their prescription is critical and an accurate and efficient method for elaborating the available data to obtain reliable simulations is exactly the focus of this work. We postpone therefore the discussion to the next section.

2.2 | Aortic geometries preprocessing: the iCardioCloud data set

The iCardioCloud project moves from a strong collaboration between the University of Pavia and the medical research hospital IRCCS Policlinico San Donato of Milan with the collaboration of the Department of Mathematics and Computer Science of Emory University. Diseases include thoracic aortic aneurysm, type B dissection, coarctation, penetrating aortic ulcer, and other unclassified diseases that significantly disturb aortic hemodynamics. A dedicated protocol for collecting retrospective patient images and clinical data has been designed together with physicians. Need of patient's written consent was waived by the local ethics committee due to the retrospective nature of the study.
FIGURE 2  Computational domains used for the simulations in three aneurysmatic patients: left, patient 1; center, patient 2; and right, patient 3

(i) Images are retrospectively collected from patients that underwent typical diagnostic studies for thoracic aortic disease. Contrast-enhanced preoperative computed tomography (CT) scans are retrieved for geometry reconstruction (Siemens SOMATOM Definition AS, Siemens Medical Solutions, Erlangen, Germany. Slice thickness, 1 mm; pixel size, 0.8 mm × 0.8 mm; 160-650 mA; 120 kV), and PC-MRI are processed for the evaluation of blood flow velocity in reference cross-sectional slices of specific vessels (Siemens MAGNETOM Aera, Siemens Medical Solutions. TR/TE, 37.1/2.5 ms; 30 samples/beat; pixel size, 2.08 mm × 2.08 mm).

(ii) Follow-up images (either CT or MRI) are collected both for patients that have undergone surgery and for untreated patients for whom periodic pathology evolution monitoring is chosen as best strategy.

(iii) To create the 3D computational domain, we use contrast enhanced CT images. With the software package VMTK, a level-set segmentation procedure is performed. Right after the segmentation, a marching cubes stage is executed to retrieve the zero level of the image, which will be the vessel inner wall. Then, a smoothing filter is applied to correct local imperfections.

(iv) Finally, we add the flow extensions. This step is performed again with VMTK, by mapping a circular section to the portion of boundary to be extended and then extruding a cylindrical region normal to the same section.

As for now, we have enrolled 21 patients in the iCardioCloud program. For our current analysis, we selected three patients with an aneurysm in the vicinity of the aortic arch since they constitute a homogeneous cohort in terms of the location of the enlargement. Furthermore, another reason for this particular choice was the presence of a complete set of postoperative CT and PC-MRI images that could be used for further analyses on the evolution of hemodynamics. Figure 2 shows the surface reconstruction in the three analyzed patients.

2.3 | Computational fluid dynamics

Numerical approximations are required to perform an extensive quantitative analysis of our data set. In particular, we resort to the library LifeV, already validated in the field of computational fluid dynamics. This is a finite element solver particularly developed for hemodynamics as used in the recent work by Xu et al for the numerical investigation of aortic dissections.

As for any finite element solver, after the geometrical domain of interest has been retrieved, segmented, and processed, we need to mesh it (ie, to split it into a number of small elements for the sake of the numerical approximation). Meshing is still computed with VMTK. On the basis of literature studies computing similar hemodynamics in diseased patients, meshes ranged from 3.5 million to 4.5 million elements to ensure result independence. In numerical studies focused on specific quantities like the WSS, it is a good simulation practice the addition of a specific refinement of the mesh in the proximity of the wall—the so-called boundary layer. This guarantees accuracy for the WSS estimation without the computational burden of having an extremely fine mesh everywhere. However, this practice increases the condition number of the matrices to solve. As the WSS is not compared with a quantitative focus here, and the geometrical features of our patient-specific cases determine a disturbed hemodynamics everywhere, we preferred to opt for a uniform fine mesh.
Because of the high Reynolds number in the AA (around 5000), numerical stabilization is performed with streamline diffusion. Using turbulence modelling in this Reynolds range is not strictly necessary, as a fine enough mesh may be sufficient to resolve the velocity field. Recent work incorporated large eddy simulation to model turbulence as a possible strategy for reducing the computational cost in Computer-Aided Clinical Trials, thanks to the use of coarser reticulations. However, here we choose direct numerical solution of the equations, being the number of simulations to run pretty modest. The method presented here is however promptly extended to the case of large eddy simulation turbulence modelling.

3 SELECTION AND ENFORCEMENT OF BOUNDARY CONDITIONS

The major aspects affecting the numerical simulation in hemodynamics are the geometry and the boundary conditions. The prescription of boundary conditions on $\Gamma_{\text{out}}$ is particularly critical for a number of reasons. Data available on $\Gamma_{\text{out}}$ are typically limited, and blood flow is a function of the downstream vasculature that needs to be properly included in the boundary conditions prescription.

When we get to Computer-Aided Clinical Trials as in iCardioCloud, we need an effective strategy for the boundary condition enforcement on a large volume of patients yet with a certified assessment of the CFD reliability. With “effective” we mean that we aim at identifying possible strategies with a minimal data processing yet able of guaranteeing an appropriate reliability for the clinical applications. As many options are available, here we first provide a general framework of possible approaches and discuss strategies available in the literature, before describing in detail our novel proposal.

3.1 General considerations

Even though we focus here on outlet boundary conditions, we first give a general interpretative framework to identify different possible approaches potentially appropriate for any kind of conditions to be prescribed on “artificial” boundaries (ie, boundaries that do not correspond with a physical entity like the arterial wall). As we will see, the prescription of reasonable boundary conditions in practice is all but trivial, and it may be useful to distinguish two steps in the process, namely, what data to prescribe and how.

3.1.1 The direct approach

Following a traditional or “direct” approach, we move from the NSE and then associate a boundary data set. The mathematical features of the problem (second-order differential problem for the velocity) require three scalar conditions on each boundary point. In hemodynamics, it has been recognized for a long time that we typically do not have access to such a complete data set. In the case of the iCardioCloud project, in fact, we have a set of velocity data from PC-MRI that could be used on all the artificial sections ($\Gamma_{\text{in}}$ and $\Gamma_{\text{out}}$). However, this is not recommended for (at least) two reasons:

(i) The domain of interest is actually compliant, so the time-wise balance between the incoming and outgoing flow does not sum up to zero. When sticking to a rigid model, we are assuming that mass conservation ($\nabla \cdot \mathbf{u} = 0$) is instantaneously enforced in the domain $\Omega$. The available PC-MRI data do not fulfil this relation since it is synchronized with the heartbeat and, naturally, the flow waves are shifted in time on the basis of the propagation of the flow along the aorta.

(ii) As we have already pointed out, PC-MRI data are finitely resolved and noisy. If not properly filtered, when velocity is prescribed point-wise, the noise and the errors in the data directly impact the solution in the region of interest. Approximation procedures are necessary, possibly mitigated by the introduction of the flow extensions.

As a work-around to problem (i), we may retain all the PC-MRI data apart from one artificial section, where we need to prescribe other conditions. This is a reasonable approach yet subject to the arbitrariness of the choice of the specific nonvelocity section. The final solution will generally depend significantly on the choice of the differently treated section. As for problem (ii), we will later show how noise is automatically filtered by using pressure conditions based on the 3WK. This filtering would be impossible to achieve with direct prescription of flow data.

3.1.2 The inverse approach

We introduce a different perspective to the boundary enforcement for computational hemodynamics. We can call this an “inverse, variational” approach. In fact, we center our method on the boundary conditions and not in the equations...
to solve. Assume generically that we have a data set \( D \) referring to physical quantities \( \mathcal{P}(\mathbf{u}, p) \), function of velocity, and pressure fields. We introduce the mismatch \( J \) as a quantification of the difference between \( D \) and \( \mathcal{P}(\mathbf{u}, p) \),

\[
J(\mathbf{u}, p) \equiv ||D - \mathcal{P}(\mathbf{u}, p)||^2.
\]

We can formulate then the following problem: Find \( \mathbf{u} \) and \( p \) that minimize \( J(\mathbf{u}, p) \) under the constraint of the NSE. This approach was advocated\(^8\) for the enforcement of flow rates (in both rigid and FSI problems); however, it is much more general and attains to the field of data assimilation.\(^31-33\) In practice, one may identify some parameters of the solution that serve as control variables to obtain the minimal mismatch. The advantage of this approach is that it is general and automatically enforces the data in a “least-square” sense, so to manage the presence of noise. The main drawback is the high computational cost, since the identification of the minimum is based on iterative methods that require solving several times the NSE. For the current state of methodology and computational power, this option in clinical routines is now out of reach. However, it provides a general mathematically rigorous framework that can be approximated for the sake of the computational efficiency. This is exactly what we do here, with the identification of a surrogate optimization problem to enforce the data.

### 3.1.3 Pressure conditions: the “do-nothing” and the geometrical multiscale approaches

When pressure data are available, typically in the form of a scalar function \( P_d(t) \) (corresponding to an approximate value of the pressure in a specific point of the domain), a popular and easy method for the direct enforcement is the so-called do-nothing approach.\(^34\) This basically corresponds to the condition

\[
p_n - \mu (\nabla \mathbf{u} + \nabla^T \mathbf{u}) \cdot \mathbf{n} = P_d \mathbf{n},
\]

and it is promptly included in the weak formulation of the NSE required by the finite element method. In fact, the traction on the left-hand side is assumed to be constant (as \( P_d \) is independent of space), and the rationale is that the viscous component is secondary. When no pressure is available, this often resorts to the so-called traction-free condition

\[
p_n - \mu (\nabla \mathbf{u} + \nabla^T \mathbf{u}) \cdot \mathbf{n} = 0.
\]

As the sensitivity of the NSE solution to the traction data is much lower than to the velocity data, the prescription of an arbitrary null traction has less impact on the solution. However, when applied to multiple outlets, this condition may resort in a nonphysical flow splitting among the branches, whose pressure is erroneously set to be the same.

In the absence of available/usable data, a much better approach consistent with the physiology of the arterial network relies on the construction of surrogate models of the downstream circulation. As the downstream circulation has, in fact, an impact on the region of interest, a surrogate model may provide realistic relations connecting velocity and pressure at the artificial section. This approach was introduced in the biomedical engineering literature a long time ago. However, since the surrogate models are in general ordinary differential systems or one-dimensional partial differential equations, the coupling to the 3D NSE in a numerical solver is not trivial. This has been called the “geometrical multiscale approach,” elucidated in a number of papers.\(^10,30\) In particular, here we refer only to a specific yet popular surrogate model, the so-called three-element Windkessel. In Section 3.1.4, we recall its mathematical formulation as it is critical in the presentation of our method.

### 3.1.4 The three-element Windkessel lumped parameter model

The name Windkessel stems from a German firemen tool to convert periodic into continuous flow, as happens in human vasculature. The original idea of Frank\(^35\) was refined several times over the years. The most popular Windkessel model features three parameters, two resistances, and one compliance, as illustrated in Figure 3.

With the notation of Figure 3, the equations describing the peripheral circulation read

\[
P = R_1 Q + P_p
\]

\[
\frac{dP_p}{dt} + \frac{P_p}{CR_2} = \frac{Q}{C}.
\]
By a standard application of the method of integrating factors, we promptly obtain the relation

$$P(t) = R_1 Q(t) + P_p(0) e^{-t/\left(C R_1\right)} + \frac{e^{-t/\left(C R_2\right)}}{C} \int_0^t Q(\tau) e^{\tau/\left(C R_2\right)} d\tau. \tag{7}$$

This is a relation between pressure $P(t)$ and flow rate $Q(t)$ that can be assumed to be valid at the downstream sections $\Gamma_{\text{out}}$ to surrogate the peripheral circulation. Each section of $\Gamma_{\text{out}}$ has its own set of parameters $R_1, R_2$, and $C$. The original two-element Windkessel model (2WK) is formally obtained by taking $R_1 = 0$.

In the frequency domain, the quotient between pressure and flow can be described in terms of their Fourier transforms $\hat{P}(\omega)$ and $\hat{Q}(\omega)$ and is named impedance, $Z(\omega)$

$$\hat{P}(\omega) = Z(\omega) \hat{Q}(\omega), \quad Z(\omega) = \frac{R_1 + R_2 + \omega^2 C^2 R_1 R_2}{1 + \omega^2 C^2 R_2^2} - j \frac{\omega C R_2^2}{1 + \omega^2 C^2 R_2^2}. \tag{8}$$

where $\omega$ is the frequency and $j = \sqrt{-1}$.

To finalize the 3WK model as a boundary condition generator for the mathematical model of the aortic flow, we simply plug the pressure $P(t)$ in Equation 7 as $P(t) = P_0(t)$ in Equation 4, following the “do-nothing” approach. In this way, we resort to a Robin boundary condition.

In spite of some inaccuracies that led to the introduction of possible refinements like the four-element Windkessel, this model is quite popular as a reasonable trade-off between accuracy and complexity. With “complexity” we mean here specifically the reliable identification of the parameters. The quantification of $R_1, R_2$, and $C$ in a patient-specific setting based on clinically available measures is, in fact, quite critical and challenging. We detail possible procedures present in the literature later on, followed by our specific approach, that represents the main novelty of this work.

### 3.1.5 3WK parameter estimation

A critical step when using a surrogate model like the 3WK is the identification of the parameters $R_1, R_2$, and $C$. Having more parameters generally allows a better tuning of the impedance to the physiology. However, this is effective in a patient-specific setting only after their appropriate identification, usually complicated by the fact that those parameters surrogate a complex system in a way that may be hardly correlated to measurable variables.

Generally speaking, we identify two general strategies for the parameter tuning. We consider an interpolation strategy, when the parameters are tuned for fitting some landmark values of the impedance promptly related to measurable variables. For instance, since the time average of the pressure and the flow rate by definition correspond to $\hat{P}(0)$ and $\hat{Q}(0)$, respectively, and $Z(0) = R_1 + R_2$ from Equation 8, we can estimate the total peripheral resistance as

$$R_1 + R_2 = Z(0) = \frac{\hat{P}(0)}{\hat{Q}(0)} = \frac{1}{T} \int_0^T P(t) dt \frac{1}{T} \int_0^T Q(t) dt. \tag{9}$$

where $T$ is the duration of the heartbeat.

In general, these interpolation procedures rely on available data. Regarding the estimation of $R_1$, Westerhof et al. and Xiao et al. proposed to use the local pulse wave velocity, or PWV, which is the speed in which the arterial pulse propagates
along a certain vessel. The choice was based on the fact that $R_1$ represents the impedance of the big vessels and is associated with the wave transmission characteristics of a certain segment. The value of $R_1$ that minimizes the magnitude of the reflected wave is

$$R_1 = \frac{PWV \rho}{A},$$

where $A$ is the vessel cross-sectional area.

Other empirical approaches suggest that $R_1$ can be calculated as a fixed fraction of $R_2$. The interpolation procedures do not filter possible noise in the data and, generally, require measurements, which are not always available in clinics.

As an alternative, with a least-square approach, we tune the parameters by minimizing a functional quantifying the mismatch between an estimated value and a target. For instance, Toorop et al tune their parameters to minimize the least-square error between a target pressure wave, $P_T$, as invasively measured in the aorta and the estimated pressure, $P_e$, as predicted by the 3WK. As multivariable optimization may be computationally intensive, some authors performed suboptimal procedures where the optimization is done only for $C$, having previously calculated $R_1$ and $R_2$.

The approach we propose here is based on an optimization procedure to include available PC-MRI velocity data in a least-square sense, so to reduce the impact of the noise and the inconsistency of the measures with the rigid wall assumption.

**Remark 1.** The electrical analog of the systemic vasculature was born with a 2WK where $R_1$ was absent. Naturally, the 2WK is easier to calibrate since there is one parameter less to estimate. As proposed by Stergiopulos et al, $R_2$ is calculated with Equation 9 by setting $R_1 = 0$. Then, $C$ is found with the pulse pressure method by iteratively modifying its value until the estimated pulse pressure matches the target one (we will use this method for 2WK parameter estimation herein).

Other alternatives for finding $C$ associated with a 2WK circuit have been proposed. Importantly, we point out that the meaning and value of $C$ in a 2WK circuit is not the same as in a 3WK model for given pressure and flow data. Indeed, the 3WK compliance tends to be lower than the 2WK. In these articles, the discussion revolved around finding the “physical” compliance value. For our purpose, the physiological meaning of $C$ is not of core importance, as we wish to fit the model according to the minimization of the $L^2$-norm as explained in the next section.

### 3.2 Boundary conditions tuning by least-square minimization

When dealing with medical studies, as we mentioned in Section 1, required data to fit a numerical model are not always available. We will describe herein the “exact” approach as the mathematical model that would use a complete data set and then the “inexact” approach will detail how to fill the gap between the required and available information.

#### 3.2.1 The “exact” approach

Equation 7 states a relation between the pressure $P(t)$ and the flow rate $Q(t)$ at the outlet sections, which we rewrite as

$$P(t) = f_{3WK}(Q(t), R_1, R_2, C).$$

In the *iCardioCloud* data set, we have PC-MRI measures of $Q(t)$. As we pointed out, unfortunately, these data cannot be used immediately as velocity data. If we had accurate pressure measures, we could prescribe those directly via a “do-nothing” approach. If the measured $P(t)$ is too noisy to be enforced directly, we can use the 3WK surrogate model and use the data to tune the parameter according to the least-square approach. We set the target pressure $P_T$ to be the measured data, and then we solve the problem

$$(R_1, R_2, C) = \arg \min \sum_{k=1}^{N} (P_T(t_k) - f_{3WK}(Q_{PC-MRI}(t_k), R_1, R_2, C))^2,$$

where $k$ is a time index when discretizing the pressure and flow waves, $t_k$ are the observation times, and $N$ is the total number of measures. In this way, the parameters are set to minimize the mismatch between the available pressure $P_T$ and the 3WK estimated pressure $P_e = f_{3WK}(Q_{PC-MRI}, R_1, R_2, C)$. "width="100%" style=""/>
To validate the approach, we tested this method against invasively measured flow and pressure from humans retrieved from Stergiopulos et al.\textsuperscript{36} Both adult (or type A) and child (or type C) waveforms were used for validation. The $L^2$-norm of the relative error for pressure estimation in time was calculated as

\[
\| \epsilon \|_{L^2} = \sqrt{ \frac{1}{N} \sum_{k=1}^{N} (P_e(t_k) - P_T(t_k))^2 },
\]

which yielded errors of 3.1\% and 2.4\% for the type A and type C waves, respectively. Figure 4 illustrates the measured and approximated pressures with our approach.

Results show that the parameter optimization for the 3WK model may be a viable alternative for the prescription of boundary conditions if high-quality pressure measurements are available since it accurately represents the target waveform.

### 3.2.2 The “inexact” approach

The iCardioCloud protocol does not include invasive pressure measurements although they are required to calibrate the 3WK. The only available information is the cuff systolic, $P_s$, and diastolic, $P_d$, pressures.

The strategy we propose is to use a baseline pressure (denoted $P_T$) from the literature, more precisely the human type A pressure wave we propose in Stergiopulos et al.\textsuperscript{36} Then, this waveform data is scaled in order to match the mean and pulse pressures for the given patient.

As a first step, the pressure wave is rescaled in time to ensure that the duration of each patient’s heartbeat is respected. This is done by arbitrarily sampling the information retrieved from Stergiopulos et al\textsuperscript{36} to a fixed number of samples (e.g., 1024 to speed up the computational calculation of the fast Fourier transform\textsuperscript{45}) and then assigning $\Delta t = T/1024$ as the temporal distance between samples for subsequent analysis.

We can then compute the brachial mean pressure\textsuperscript{46} $P_{m,b}$ and brachial pulse pressure\textsuperscript{47} $P_{p,b}$ respectively as

\[
P_{m,b} = \frac{1}{3} P_s + \frac{2}{3} P_d, \quad P_{p,b} = P_s - P_d.
\]

In fact, we need to evaluate the mean and pulse pressures in the central aorta, $P_{m,c}$ and $P_{p,c}$, to rescale the available pressure waveform. While the former does not undergo major changes along the arterial tree,\textsuperscript{48} the latter scales according to an empirical augmentation index advocated in Nichols et al\textsuperscript{49} as a function of the age $a$ of the patient, so we set

\[
P_{m,c} = P_{m,b}, \quad P_{p,c} = P_{p,b}/(-0.012 a + 1.97).
\]

The generic pressure wave $P_T(t)$ is then scaled to match these landmark values: First, it is multiplied by a constant to reach $P_{p,c}$, and then another fixed value is added/subtracted to attain $P_{m,c}$. The resulting scaling is shown in Figure 5. After the customized $P_T$ is obtained, we proceed as described for the “exact” approach.
In this section, we present a number of numerical results to demonstrate the relevance of our method for calibrating the 3WK parameters. Firstly, we investigate the impact of the optimization approach, in particular the importance of a complete multivariable optimization vs suboptimal strategies when only one parameter at a time is obtained by the optimization approach.

Secondly, we illustrate how our approach compares with other possible strategies available from the literature. We test three iCardioCloud cases and assess the quality of the results by using the available measures.

Then, grounded on the noisy nature of PC-MRI acquisition, we perform a sensitivity analysis following Bozzi et al to assess the impact of uncertainties in our parameter estimation.

Finally, we check the velocity and pressure profiles, as well as the time averaged wall shear stress (TAWSS).

4.1 Multivariable vs single-variable optimization

As univariate optimization is easier to perform, we first tested suboptimal strategies leading to the optimization for just one variable of the 3WK. More precisely, we considered three possible strategies in our cohort of patients:

- **SubOpt 1**: \( R_1 \) is calculated from Equation 10 and \( R_2 \) from Equation 9. Therefore, only \( C \) is found by minimization.
- **SubOpt 2**: \( R_1 \) is calculated as the average of the 3rd to 10th harmonics of \( Z(\omega) \) as empirically chosen in Stergiopulos et al. for representing the high frequency range of the impedance. \( R_2 \) is calculated from Equation 9. Only \( C \) is found by minimization.
- **Opt** or multivariable optimization: All \( R_1, R_2, \) and \( C \) are calculated by minimization, as for our original approach.

In addition, for the sake of completeness, we compare the parameters obtained with the three strategies against the parameters obtained with a 2WK.

Table 1 shows the parameter models calculated in each of the output vessels in the three patients selected from our database where the aforementioned strategies have been used. Relative errors from \( P_c \) to \( P_T \) are calculated with Equation 13.

Note that using the optimization approach and as predicted by Stergiopulos et al., \( R_1 \) is systematically lower in Opt compared with SubOpt 2. Also, \( C \) is systematically higher in Opt than in the estimation with 2WK.

4.2 Validation of the calibration strategy in a cohort of patients

To assess the performances of our “inexact” 3WK-based optimization approach, we performed several numerical tests on three iCardioCloud patients by using four different boundary conditions. We are particularly concerned on comparing literature-based vs patient-specific tuning.

The first tested option, which we call BC1, reproduces a scenario in which only the geometry has been retrieved from patient-specific imaging. Since there is no information on the flow, both the inflow waveform and the outflow 3WK values were taken from literature. The second approach, BC2, represents the case for which, besides the aortic morphology, only the inflow is known and patient specific.
<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
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<th>SubOpt 2</th>
<th>Opt</th>
<th>Patient 2</th>
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<th>Opt</th>
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<td>6.39%</td>
<td>6.56%</td>
<td>6.38%</td>
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<td>5.71%</td>
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<td>12.07%</td>
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</table>

Abbreviations: BCT, brachiocephalic trunk; DA, descending aorta; LCCA, left common carotid artery; LSA, left subclavian artery; 2WK, two-element Windkessel model; 3WK, three-element Windkessel model. DA/Sub: flow wave for calibration corresponded to subtraction of flow enforcing mass conservation. DA/MRI: flow wave for calibration corresponded to phase contrast MRI slice.
Two other sets of BC represent an application of our optimization strategy. We considered two variants for treating the flow rate data. As we pointed out, the PC-MRI data are inconsistent with the rigid wall assumption. While this is critical for a direct prescription of the boundary conditions, a reasonable question is whether the same inconsistency is critical when estimating the parameters in the least-square framework. For this reason, we checked the performance of our method when the flow rate in the DA is (i) computed as the algebraic sum of the flow rates at the other sections (consistent mass conservation strategy or “subtraction”) or (ii) retrieved directly from PC-MRI.

More precisely, in BC3, we hypothesize that the apparent mass loss within a cardiac cycle occurs along the DA, so we replace available measures of flow rate in DA with the algebraic sum of the other available data. In fact, while the measures are generally less accurate in supraortic vessels for their smaller diameter, the flow in the DA is also affected by several intercostal vessels, which we got rid of, for poor imaging evidence. We guess therefore that the PC-MRI flow rate in the DA is the most inconsistent with our geometrical assumptions.

Conversely, the idea behind BC4 is to avoid any a priori assumptions regarding the conservation of mass as we did for BC3. In BC4, we rely on the computational model (ie, the incompressible NSE) and the geometry to satisfy the incompressibility constraint. As in our approach, measures are used only for calibrating the parameters; modelling inconsistencies while data are not affecting the mathematical correctness of the partial differential equation system.

To summarize, the following scenarios are tested:

- **BC1**: Literature inflow profile taken from Morbiducci et al and literature outflow 3WK BC taken from Kim et al.
- **BC2**: Patient-specific inflow extracted from patient’s PC-MRI and literature outflow 3WK BC taken from Kim et al.
- **BC3**: Patient-specific flow as extracted from PC-MRI directly imposed in the AA and 3WK calibrated with our strategy in the outlets. In the DA, parameters were tuned enforcing mass conservation (consistent mass conservation strategy).
- **BC4**: Patient-specific flow as extracted from PC-MRI directly imposed in the AA and 3WK calibrated with our strategy in the output vessels. In the DA, parameters were tuned using flow directly from PC-MRI.

To compare the various methods, we are interested first at looking at the flow split since each strategy will dictate a different flow distribution. This impacts the overall velocity field and is thus of primary interest. Furthermore, to show how the different strategies impact the solution, we will also look at clinically relevant quantities such as the velocity field and the TAWSS.

We recall that WSS is defined as

$$\tau = \sigma \cdot n - (n \cdot \sigma \cdot n) \cdot n,$$

where $\sigma$ is the stress tensor. The corresponding TAWSS reads

$$TAWSS = \frac{1}{T} \int_0^T |\tau| dt.$$

To summarize, we will compare

1. flow rate and pressure profiles at the outlet sections,
2. velocity in the domain $\Omega$, and
3. TAWSS.

The relative error of the volume of blood through each vessel along one single cycle is calculated as

$$\Delta Q% = \frac{\sum_{k=1}^{N} Q(t_k)_{SIM} - Q(t_k)_{MRI}}{\sum_{k=1}^{N} Q(t_k)_{MRI}},$$

where $Q(t_k)_{SIM}$ is the flow wave resulting from each simulation and $Q(t_k)_{MRI}$ is the flow extracted from the PC-MRI.

The $L^2$-norm of the error between each simulated waveform and its MRI counterpart is calculated as
\[ \|e\|_2^2 = \frac{\sum_{k=1}^{N} \|Q(t_k)_{\text{SIM}} - Q(t_k)_{\text{MRI}}\|^2}{\sum_{k=1}^{N} \|Q(t_k)_{\text{MRI}}\|^2}. \] (19)

### 4.3 Flow and pressure profiles at the outlets

Figures 6 to 8 show the flow and pressure waves computed in the CFD simulations with the different types of BC in each vessel. The PC-MRI data and the adjusted pressure wave, used for calibration, were included as reference as well as the subtraction flow used for tuning BC3. It is worth noting that PC-MRI measurements, as mentioned in Section 1, are significantly affected by noise.

Comparison between flow waves in the simulation and the PC-MRI are reported in Tables 2 and 3 calculated by means of Equations 18 and 19, respectively. Because of its impact in the error quantification, the relative mass difference calculated by simply replacing \(Q_{\text{SIM}}\) with \(Q_{\text{subtraction}}\) in Equation 18 is also shown.

Regarding the flow split error, BC3 appears to be the method of choice yielding the lowest error both in the supraortic vessels and in the DA/Sub scheme. This result confirms that the 3WK tuning is accurate at representing the required flow split. Since the 3WK parameters in the DA in BC4 were tuned using directly PC-MRI data, we would expect the DA/MRI error to be in the same order of magnitude as DA/Sub. However, not only the trend is opposite but also the supraortic vessels yield a higher error. Interestingly, flow split errors in BC4 are positively correlated with the mass difference between the subtraction and the PC-MRI flow defined previously. When the gap is lower (as the case of patient 3), BC4 gets closer to BC3.

**FIGURE 6** Flow and pressure waves in four different models of boundary conditions for each input and output vessel in patient 1. AA, ascending aorta; BCT, brachiocephalic trunk; DA, descending aorta; LCCA, left common carotid artery; LSA, left subclavian artery; PC-MRI, phase contrast MRI
Comparable $L^2$ errors in flow were found between BC3 and BC4. This might be attributed to the noisy waveform of the PC-MRI, which is the landmark value used for this comparison. Another source of this error is the time shift present in the PC-MRI, which is absent in the simulated waveforms since they feature instantaneous wave propagation.

In the case of the pressure waves, mixed results were found. Both mean and pulse pressure from the calibration were respected in BC3 and not in BC4, where values were higher than expected. In patients 1 and 2, pressure wave difference between BC3 and BC4 was only a constant (different mean pressure) whereas its shape and pulse pressure remained equal. In patient 3, not only the mean pressure differed but also the waveform was different. We suspect that this difference is due to the variety of mass loss in our patients.

BC3 appears to be the method of choice that gives the best results against the set of assumptions used to define the problem.

### 4.4 Sensitivity to noise from PC-MRI

The PC-MRI flow acquisitions, which were used as gold standard to quantify errors, are known to be intrinsically noisy. Therefore, we need to estimate whether this uncertainty in the raw data is propagated when tuning the 3WK parameters. To do so, we performed a sensitivity analysis on the basis of the noise description by Tresoldi et al.

In their work, authors measured the signal to noise ratio (SNR) in PC-MRI, which quantifies the quality of the signal against its noise. Signal to noise ratio is defined for a given measurement with certain variability, characterized by a probability distribution (ie, Gaussian), as $\text{SNR} = \frac{\mu}{\sigma}$, where $\mu$ is the mean and $\sigma$ the standard deviation of the bell curve. The higher its value, the less predominant is the noise and the cleaner is the data set.

Grounded on this description and following the approach by Bozzi et al., we generated a set of 1000 “noisy” flow waves drawing independent samples from a Gaussian distribution. The mean value was our original PC-MRI flow information whereas the standard deviation was $\sigma = \mu/16$.

Then, we calculated 1000 sets of “noisy” $R_1$, $R_2$ and $C$ for each vessel based on these flow samples with embedded uncertainty. The SNR of these output parameters based on uncertain measures resulted between 100 and 400, one order
FIGURE 8  Flow and pressure waves in three different models of boundary conditions for each input and output vessel in patient 3. BC2 is absent since the simulation crashed. AA, ascending aorta; BCT, brachiocephalic trunk; DA, descending aorta; LCCA, left common carotid artery; LSA, left subclavian artery; PC-MRI, phase contrast MRI

TABLE 2  Flow split error in all the vessels

<table>
<thead>
<tr>
<th>Mass Diff</th>
<th>Integral Error %</th>
<th>Patient 1 (74%)</th>
<th>Patient 2 (99%)</th>
<th>Patient 3 (20%)</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>BC1</td>
<td>BC2</td>
<td>BC3</td>
</tr>
<tr>
<td>BCT</td>
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<td>109</td>
<td>137</td>
<td>2</td>
</tr>
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<td>LCCA</td>
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<td>172</td>
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<td>LSA</td>
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<td>119</td>
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<tr>
<td>DA/Sub</td>
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<td>DA/MRI</td>
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Abbreviations: BCT, brachiocephalic trunk; DA, descending aorta; LCCA, left common carotid artery; LSA, left subclavian artery. Results in the DA are compared against flow resulting from the consistent mass conservation constraint (DA/Sub) as well as to PC-MRI flow (DA/MRI).

of magnitude higher than the original PC-MRI information. Consequently, the tuning procedure acted as a filter to the noise in flow data, not propagating variations into the parameter estimation.

4.5  Velocity contours

Velocity contours are shown in Figure 9 at the systolic peak (17% of the cycle) and the early diastole (44% of the cycle) in all the four schemes for patient 1. Phase contrast images are also illustrated with matching profiles of acceleration. The various choices of parameters showed significantly different hemodynamic patterns in the aneurysmatic sac and DA. An accurate choice of boundary conditions is therefore crucial to have meaningful results in these zones, as well as in the supraortic vessels.
### TABLE 3 $L^2$-error in all the vessels

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<th>BC2</th>
<th>BC3</th>
<th>BC4</th>
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<td>3</td>
<td>20%</td>
<td>236</td>
<td>46</td>
<td>94</td>
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<td>236</td>
<td>46</td>
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<td>292</td>
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Abbreviations: BCT, brachiocephalic trunk; DA, descending aorta; LCCA, left common carotid artery; LSA, left subclavian artery. Results in the DA are compared against flow resulting from the consistent mass conservation constraint (DA/Sub) as well as to PC-MRI flow (DA/MRI).

**FIGURE 9** Volume rendering of the velocity in the systolic peak (top) and the early diastole (bottom) in the four BC schemes. PC-MRI through slices are shown with coincident acceleration patterns (A) within the aneurysm and (B) in the descending aorta.

**FIGURE 10** Time averaged wall shear stress (TAWSS) in the four BC schemes.
4.6 | Wall shear stress

Figure 10 depicts the TAWSS along a cardiac cycle calculated with all the BC schemes. Time averaged wall shear stress is an important indicator of plaque formation, and results show that a change in the boundary conditions significantly impacts both its qualitative and quantitative nature.

5 | DISCUSSION

Boundary conditions for computational hemodynamics are an active area of research (see previous studies\(^7,9,11,17,18\)). The complexity of choosing a boundary condition scheme is intrinsically related to the availability of the data.

Historically, lumped models have been primarily used to assess physiological parameters such as vessel compliance, cardiac output, and peripheral resistance. Then, only in the last decades, lumped models were adopted as boundary condition systems for CFD. Because of their relevance in the clinical practice, most of the literature has focused on the quality of the parameter estimation with different methodologies.\(^3\)

In this work, we pick a lumped model known to be a good approximation of the physical system (ie, the 3WK for aortic flow), and we find its parameters in a least-square fashion rather than relying in their formal definition. This difference was early proposed by Stergiopulos et al\(^4\) but apparently overlooked by the computational mechanics community.

Indeed, as pointed out in Section 4.1, an optimization approach gives much better results with respect to the given data than fixing \(R_1\) and \(R_2\) separately, eg, due to measurement error in high frequency. For us, the physiological value of the parameters is not as relevant as having the system to fit well the input data, and this is the message we try to convey here on three patient-specific simulations.

Another critical aspect of the choice for a lumped model is to weakly impose the flow (opposed to a Dirichlet scheme, for example, as in Gallo et al\(^17\)). The rationale behind this choice is that we can account for the mismatch between the data and the model created when introducing modelling assumptions, such as the rigid wall constraint. Additionally, with this method, we also account for the diastolic and systolic pressure that can be easily known from patient-specific data.

In Section 1, we have stated many of the weaknesses of imposing flow data as velocity boundary conditions. Alongside with the development of our tuning strategy, we analyzed how would uncertainty of the PC-MRI acquisition impact the CFD outcomes as described by Bozzi et al.\(^5\) The reduction of the SNR by one order of magnitude constitutes yet another strength of using lumped models through constrained optimization: Even if the acquisition is noisy, the impact in the solution of the NSE would be negligible.

Assumptions were made on the data for calibration rather than the model, making the minimization approach versatile enough to accommodate further elements in the lumped circuit, as is frequently used in other vascular districts.\(^5\) Recent studies performing CFD in the aorta (see, for example, Condemi et al\(^5\)) have demonstrated that data acquisition of PC-MRI flow and cuff pressure is much standardized, but yet suboptimal approaches for tuning the boundary conditions are used. This strengthens the applicability of our method even in other retrospective studies.

As expected, results show that the use of patient-specific data under the optimization strategy works much better than the use of literature data. Furthermore, we found that modifying flow waves a priori to satisfy the conservation of mass, which is one of the modelling assumptions, leads to much better results than using the raw data, even though the mathematical model does not require it.

Mixed results were found regarding the pressure field when raw data, as extracted from PC-MRI, were used. In two patients, the pressure waves appear to be close to the prescribed one used to build the lumped model. In the other case, its shape resulted significantly different and not only “up to a constant.” We attribute this difference to the significant mismatch between the data and the modelling assumptions. The impact on the pressure is not clearly understood at present, and it will be studied in detail in subsequent works.

5.1 | Limitations

Results should be interpreted in the context of some limitations related to both data acquisition and modelling assumptions.

Aortic wall was assumed rigid for the sake of lowering the computational time in all simulations, whereas FSI would give a better appraisal of the velocity field.\(^14\) However, the constrained optimization method used for tuning the 3WK parameters relies on patient’s measurements retrieved from clinical data and is thus not affected by this simplifying assumption.
Regarding the simulation results, the main indicator of vessel damage (ie, TAWSS) has demonstrated to be immune to this simplification.55

Differences between the four boundary conditions schemes have only been discussed qualitatively, whereas a quantitative comparison with real hemodynamics should be performed to validate our method. We did not carried out such an analysis because of the lack of volumetric flow data (ie, 4D PC-MRI) and the technical challenge of comparing point-wise velocity data from different imaging sources such as CT and PC-MRI (ie, image registration and interpolation from one domain to the other). To overcome this limitation, future studies will require 4D PC-MRI flow to be acquired prospectively and the surface segmentation to be based on MRI imaging.

In these three patients, the same pressure wave was used for the parameter tuning process. Even though it has been scaled to accommodate some individual characteristics such as the age and the duration of the heartbeat, a patient-specific measurement (yet relying in a noninvasive approach) would further improve the parameter estimation.

6 | CONCLUSIONS

In the context of the iCardioCloud project aimed at systematically performing CFD simulations in diseased thoracic aortas, we faced the challenge of assimilating an important quantity of measured data such as PC-MRI flow measurements at the inlet and all the outlets of the domain, as well as the cuff pressure. At a first analysis, retrieved flow data did not satisfy one of our modelling assumptions, which is the conservation of mass.

For this reason, we used a 3D/0D multiscale modelling (ie, 3D incompressible NSE with rigid wall and 3WK). Additionally, we used a nonlinear least-square approach to evaluate the Windkessel parameters (also known as beat-to-beat parameter estimation). To the best of our knowledge, this is the first time that the 3D/0D multidomain approach has been coupled with a beat-to-beat method. The rationale behind this idea is filtering the measurement errors by assessing all the parameters at once in a least-square sense. Furthermore, the method allows for assimilating the cuff pressure measurement.

We first found that the pressure wave reconstructed using the Windkessel parameters found by multivariable optimization, fit much better the target data than the individual calibration of the lumped model components. Second, while the method allows for using directly raw data (thus mismatching the modelling assumptions), the results show that it is preferable to modify the data a priori.

Finally, this surrogate method for data assimilation and boundary condition enforcement has the advantage to be extremely cheap with respect to alternative robust methods such as via a Kalman filter approach. This study also stresses, again, the importance of clinical and patient-specific data for running computational hemodynamics studies.

ACKNOWLEDGMENTS

We would like to thank Dr Francesco Secchi and Dr Santi Trimarchi from IRCCS Policlinico San Donato for providing imaging data and clinical support. Simulations were performed under the XSEDE project Computational Hemodynamics from Proof of Concept to Clinical Trials TG-ASC160069. We acknowledge the CINECA and the Regione Lombardia award under the LISA initiative 2016-2018, for the availability of high performance computing resources and support. iCardioCloud project was supported by Fondazione Cariplo, under the grant 2013-1779. R.M.R. wishes to thank the staff of the Department of Mathematics and Computer Science at Emory University for the kind hospitality during the Spring Semester 2017. A.V. acknowledges the support of the US National Science Foundation, Project NSF DMS 1620406.

CONFLICT OF INTEREST

The authors declare no potential conflict of interests.

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**How to cite this article:** Romarowski RM, Lefieux A, Morganti S, Veneziani A, Auricchio F. Patient-specific CFD modelling in the thoracic aorta with PC-MRI–based boundary conditions: A least-square three-element Windkessel approach. *Int J Numer Meth Biomed Engng.* 2018;e3134. [https://doi.org/10.1002/cnm.3134](https://doi.org/10.1002/cnm.3134)