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Patient-specific biomechanical model of hypoplastic left heart to predict post-operative cardio-circulatory behaviour

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ABSTRACT

Hypoplastic left heart syndrome is a complex congenital heart disease characterised by the underdevelopment of the left ventricle normally treated with a three-stage surgical repair. In this study, a multiscale closed-loop cardio-circulatory model is created to reproduce the pre-operative condition of a patient suffering from such pathology and virtual surgery is performed. Firstly, cardio-circulatory parameters are estimated using a fully closed-loop cardio-circulatory lumped parameter model. Secondly, a 3D standalone FEA model is build up to obtain active and passive ventricular characteristics and unloaded reference state. Lastly, the 3D model of the single ventricle is coupled to the lumped parameter model of the circulation obtaining a multiscale closed-loop pre-operative model. Lacking any information on the fibre orientation, two cases were simulated: (i) fibre distributed as in the physiological right ventricle and (ii) fibre as in the physiological left ventricle. Once the pre-operative condition is satisfactorily simulated for the two cases, virtual surgery is performed. The post-operative results in the two cases highlighted similar hemodynamic behaviour but different local mechanics. This finding suggests that the knowledge of the patient-specific fibre arrangement is important to correctly estimate the single ventricle's working condition and consequently can be valuable to support clinical decision.

1. Introduction

The improvements in the diagnostic techniques, together with the progress in computational analyses, create new possibilities for the understanding of pathological conditions and their treatments. Indeed, the use of computational models built up from patient-specific information enables performing virtual surgery, predicting the post-operative behaviour and evaluating the treatment outcomes. In this context, an interesting application of computational approach is the surgical planning in patients affected by congenital heart disease such as the hypoplastic left (or right) heart syndrome (HLHS or HRHS) [1,2]. HLHS is more common than HRHS with a reported incidence of HLHS ranging from 0.16 to 0.36 per 1000 live births with a male predominance [3]. This severe and rare cardiac defect consists in the underdevelopment of one ventricular chamber and requires for surgical intervention within the first week of life to prevent the patient death. If not treated it would be responsible for 25–40% of neonatal cardiac deaths and fatal in 95% of cases within few weeks from birth [4]. The elective surgical treatment for such a pathological condition is the Fontan procedure [5,6]. This technique is a three-stage surgical repair which goal is to restore a physiological-like condition obtaining separated pulmonary and systemic circulations. Each surgical stage is characterised by changes in the circulatory layout. In the final configuration, the venous return passively flows into the lungs whereas the functional single-ventricle (SV) pumps blood in to the systemic district [7,8]. Stage 1 (or Norwood procedure) consists in the insertion of a conduit between a systemic and a pulmonary artery (systemic-to-pulmonary) to provide adequate pulmonary perfusion as the right heart is absent. Stage 2 (bidirectional cavopulmonary anastomosis or Glenn procedure) involves the ligation of this shunt and the redirection of the upper portion of the systemic venous return to the lungs bypassing the SV, thus helping to relieve ventricular volume overload and resulting in the upper body (UB) systemic circulation being in series with the pulmonary circulation. Stage 3 (total cavopulmonary connection or Fontan operation) redirects also the lower part of the venous return to the pulmonary arteries. Over the last decades, the

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survival rates after the surgical stages have improved. Retrospective analysis reported a survival rates between 74% and 93% [9–12] after stage 1 palliation. The mortality for stage 2 is low with a 1-year survival higher than 95% [13,14]. Hospital mortality after stage 3 for HLHS is excellent, with a survival rate of 95% in short-term [15–18], of 77–95% at 5 years and 72–91% at 10 years [15,17,19].

Despite major improvements in the life expectation, these patients may be subjected to postoperative complications. Significant morbidity characterises the stage 1 postoperative period, including both cardiac and non-cardiac etiologies. Inter stage (i.e., the time between hospital discharge after stage 1 and before stage 2) deaths showed rates of 2–16% [20–24]. These deaths are associated with the presence of residual or progressive anatomic lesions (e.g., stenosis of the shunt or conduit, aortic arch, and/or pulmonary arteries, insufficiency of the tricuspid valve) [25,26]. The complications after stage II are lower than after stage 1 and they concerns the superior vena cava syndrome, severe tricuspid valve insufficiency, arrhythmias, phrenic nerve injury, and embolic complications. After stage 3, complications leading to significant morbidity in adults include arrhythmias [27,28], thromboembolism, heart failure, exercise intolerance [29], Fontan circulation or pulmonary vein obstruction, hepatic dysfunction, and aortic root and valve abnormalities in those with repaired HLHS [30]. For a comprehensive description of the postoperative complication, the reader is referred to Feinstein et al. [31].

The application of computational approaches for a systematic analysis of such pathology can be a valuable tool to estimate and possibly improve the surgical outcome through virtual planning. Several models have been proposed in the literature to study the effect of surgeries on single ventricle patients (for example see [32–34]). Nowadays, the best approach is to use multiscale models in a closed-loop fashion to accurately evaluate the fluid dynamic in the surgical site, described using 3D patient-specific geometries [35–41]. Nevertheless, since the ventricle is the centre of the congenital disease, we consider crucial the modelling of the 3D structure of the SV to obtain information on the myocardium local mechanics (i.e., stress and strain) as indicators of the heart performance. The importance of a 3D modelling approach to investigate the SV behaviour is also corroborated by recent computational literature studies on HLHS cases accounting for the 3D SV [42–44]. However, these studies applied standalone ventricle models and, consequently, cannot be exploited for a surgical planning. Indeed, significant changes occur in the working conditions of the ventricle (both pre and afterload) across surgical stages and this could affect the ventricle response and adaptation as well as the effectiveness of the treatment. Commonly, stage 1 procedure is performed in neonate, stage 2 between 3 and 9 months of life and stage 3 approximately at 3–4 years of age [45]. The surgical timing can be optimised according to patient-specific heart wellbeing and vascular development. The assessment of post-operative condition via computational model could provide the surgeon important information thus helping in customising the timing of surgery or tailoring possible pharmacological treatment to improve patient's conditions.

To this end, our group recently developed the first multiscale patient-specific closed-loop model accounting for a 3-D structural description of the single ventricle [46] applied to a patient suffering from HRHS. Before performing virtual surgery, it is mandatory to accurately set-up the pre-operative patient-specific model based on the acquired clinical data. For the ventricular model, the specific anatomy is measured and the myocardium mechanical properties may be properly tuned to have a good match of the clinical intraventricular volumes and pressures. However, the fibre architecture has to be assumed, since in vivo measurements are not available in the clinical routine. While for HRHS, where the working ventricle is a left ventricle (LV), it is reasonable to assume a fibre orientation as the physiological LV [46], in case of HLHS patients, the choice of fibre orientation is not straightforward. Indeed, a rearrangement of the SV fibre orientation could be present being the single ventricle originally a right ventricle (RV) now subjected to systemic conditions (i.e. typical pressure of a LV). The assumption of the fibre organisation is important since it is expected to affect both local ventricular mechanics and global ventricular behaviour [47,48]. In the present work, we consider a multiscale closed-loop cardio-circulatory model of HLHS applied to perform stage 2 virtual surgery. Lacking any information on the fibre orientation, two possible cases were here investigated: (i) we adopted the fibre architecture according to physiological adult RV [49]; (ii) we simulated the case of fibre organisation as in the physiological adult LV [50].

2. Materials and methods

2.1. Clinical pre-operative data

The patient included in this study suffered from HLHS. The clinical data were collected at the University of Michigan Medical School, Division of Pediatric Cardiology (Ann Arbor, MI, USA) with Institutional Review Board approval, and informed consent was provided by the subject's parents. The patient (age $=4$ months; body surface area, BSA $=0.28\,m^2$) presented severe hypoplastic heart syndrome, unsuitable for a two-ventricle circulation and underwent surgical placement of a right modified Blalock–Taussig shunt in the first days of life. Catheterisation-derived pressure tracings, magnetic resonance (MR) flow tracings, MR derived reconstruction of the SV and echocardiographic Doppler velocity tracings were obtained prior to the stage 2 procedure. The SV anatomy was obtained starting from patient-specific MRI. Images were acquired at end diastole (ED), as defined by the peak of the R-wave.

2.2. Multiscale approach

The methodology used to develop the patient-specific multiscale closed-loop cardio-circulatory model was described by Meoli et al. [46] and Krishnamurthy et al. [51] and is briefly summarised below (Fig. 1). Two main phases can be distinguished: the development and set up of the pre-operative (stage 1) model and the virtual surgery (stage 2). The former involves three models: (i) a fully lumped parameters (LP) closed-loop cardio-circulatory model to obtain the cardio-circulatory parameters through an identification process based on clinical data; (ii) a standalone 3D finite element analysis (FEA) SV model consisting of a geometrical model and used to assess the myocardial active and passive parameters and (iii) the pre-operative multiscale closed-loop cardio-circulatory model which couples the 3D FEA SV to the LP model of the circulation.

2.3. Fully LP closed-loop cardio-circulatory model

A pure LP model of the cardiovascular system was implemented for the pre-operative condition (stage 1) to fully identify the circulatory parameters and to obtain information on the SV to be used subsequently. The model consists of four main blocks representing the single heart (i.e., the single atrium (SA) and the SV), the systemic UB and lower body (LB) circulations and the lungs.

Both the SA and the SV model consisted of a time-varying nonlinear elastance which behaviour directly accounts for the myocardial passive and active properties and a term representing the viscous behaviour. Concerning the heart passive behaviour, a classical exponential function was adopted for pressure-volume relationship. A sinusoidal activation function was applied to

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