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In vitro hemodynamic investigation of the embryonic aortic arch at late gestation

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Abstract

This study focuses on the dynamic flow through the fetal aortic arch driven by the concurrent action of right and left ventricles. We created a parametric pulsatile computational fluid dynamics (CFD) model of the fetal aortic junction with physiologic vessel geometries. To gain a better biophysical understanding, an *in vitro* experimental fetal flow loop for flow visualization was constructed for identical CFD conditions. CFD and *in vitro* experimental results were comparable. Swirling flow during the acceleration phase of the cardiac cycle and unidirectional flow following mid-deceleration phase were observed in pulmonary arteries (PA), head-neck vessels, and descending aorta. Right-to-left (oxygenated) blood flowed through the ductus arteriosus (DA) posterior relative to the antegrade left ventricular outflow tract (LVOT) stream and resembled jet flow. LVOT and right ventricular outflow tract flow mixing had not completed until ~3.5 descending aorta diameters downstream of the DA insertion into the aortic arch. Normal arch model flow patterns were then compared to flow patterns of four common congenital heart malformations that include aortic arch anomalies. Weak oscillatory reversing flow through the DA junction was observed only for the Tetralogy of Fallot configuration. PA and hypoplastic left heart syndrome configurations demonstrated complex, abnormal flow patterns in the PAs and head-neck vessels. Aortic coarctation resulted in large-scale recirculating flow in the aortic arch proximal to the DA. Intravascular flow patterns spatially correlated with abnormal vascular structures consistent with the paradigm that abnormal intravascular flow patterns associated with congenital heart disease influence vascular growth and function.

Keywords: Cardiac development; Hemodynamics; CFD; Cardiovascular fluid dynamics; Congenital heart defects; Fetal circulation; Embryonic aortic arch

1. Introduction

The fetal aortic arch is formed by the great vessels of the human arterial circulation and functions as a conduit for multiple flow streams during fetal life. The fetal aortic arch has two inlets represented by the right and left ventricular outflow tracks (RVOT and LVOT), and distributes oxygenated blood from the placenta and deoxygenated blood from the fetus via two outlets represented by the ascending aorta and pulmonary arteries to the head-neck vessels and the descending aorta (DAo) (Brezinka, 2001; Long, 1990; Sadler, 2006). The fetal aortic arch is in constant transformation in order to optimally match the hemodynamic requirements of the growing embryo (Keller et al., 2007). The higher oxygen saturated blood from the placenta is diluted with deoxygenated blood through a series of mixing events, while maintaining preferential flow of higher saturated blood to the developing brain (Blackburn, 2006; Stock and Vacanti, 2001; Szwast and Rychik,

Abbreviations: CFD, computational fluid dynamics; CHD, congenital heart disease; DA, ductus arteriosus; DAo, descending aorta; HLHS, hypoplastic left heart syndrome; LVOT, left ventricular outflow tract; PA, pulmonary artery; PAT, pulmonary atresia; RVOT, right ventricular outflow tract; TOF, Tetralogy of Fallot..

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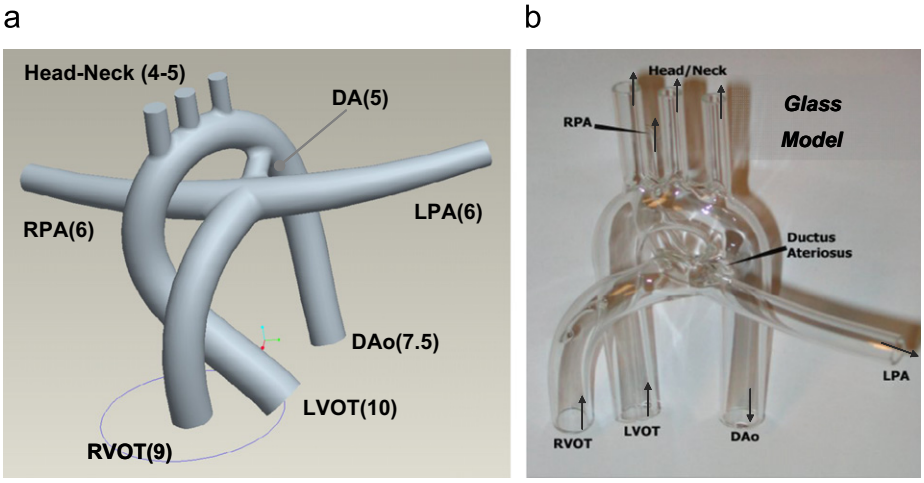

Fig. 1. Fetal aortic arch junction. The parametric solid computer aided design model in (a) with the normal vessel dimensions, given in parenthesis in millimeters. The glass replica of this model is shown in (b) which is used in flow visualization experiments. This idealized model has physiological vessel dimensions and flow rates for human fetus at late gestation (DA: ductus arteriosus, LVOT: left ventricular outflow tract, RVOT: right ventricular outflow tract, DAo: descending aorta, LPA: left pulmonary artery, RPA: right pulmonary artery). Vessel diameters (LVOT, RVOT, DA, PA, DAo) in mm used for congenital morphologies are as follows: HLHS (1.5, 12, 6, 10–7, 7.5), TOF (12, 5, 5, 8–5, 7.5) and PAT (0, 12, 5, 9–6, 7.5), respectively. Corresponding morphologies span a hypoplastic LVOT (HLHS) to a hypoplastic RVOT (PAT) (see also Fig. 7a).

2005). The fetal circulation (Allan et al., 2000; Huhta, 2001; Kiserud, 2005; Phoon, 2001) functions in a *fail-safe mode* where brain perfusion is "spared" in the setting of reduced antegrade aortic arch flow due to the presence of a parallel circulation with the capacity for retrograde perfusion via the ductus arteriosus (DA) (Fig. 1a). While the DA usually involutes spontaneously during the first week of life, a persistent DA is a common post-natal cardiovascular problem and may be essential for survival in the setting of some forms of congenital heart disease (CHD) (Frydrychowicz et al., 2007; Schneider and Moore, 2006). Patency of the DA can be maintained pharmacologically to support systemic and/or pulmonary blood flow in the setting of complex, cyanotic CHD where hypoplasia of the LVOT reduces antegrade aortic arch flow or hypoplasia of the RVOT reduces antegrade PA flow.

Cardiovascular solid mechanics and hemodynamic studies of cardiac development have predominantly focused on *early embryonic stages and ventricular flows* (Gleason et al., 2004; Nerurkar et al., 2006; Ramasubramanian et al., 2006). In 1928, Harvard University anatomist Bremer sketched the 3D spiral flow streams in fetal chick hearts at several developmental stages and highlighted the association between form and flow (Bremer, 1928). Systematic *in vivo* flow visualization confirmed these observations where CHDs reproducibly created via altered venous flow patterns (Hogers et al., 1995). Engineering fluid dynamic analysis tools have only recently supported the quantification of these observations. Pioneering fluid mechanics experiments performed by Gharib and co-workers (Forouhar et al., 2006; Hove et al., 2003) used high-frame rate confocal particle image velocimetry systems on zebrafish embryos and by Vennemann et al. (2006) used conventional microscopic particle image velocimetry techniques in chick embryos. Limited data is available using complementary computational fluid dynamics (CFD) analysis in the developing human heart. DeGroff et al. (2003) used postmortem micro-dissected human fetal ventricles at the pre- and post-looping stages (Pentecost et al., 2001) and Loots et al. (2003) used a simplified tubular heart model to perform CFD simulations. More recently, analysis of fluid-structure interactions in the outflow-tract (Rugonyi et al., 2007), active embryonic heart analytical models (Taber et al., 2007), and mechanical loading of the atrioventricular cardiac cushions (Butcher et al., 2007) in chick embryo have been presented. To our knowledge the hemodynamics of fetal aortic arch during mid-to-late gestation period has not been investigated in spite of its clear significance to perinatal/neonatal arch structure and function (Friedman and Fahey, 1993; Maeno et al., 1999) and the clinical management of patients with CHD (Cohen, 2001; Hoffman and Kaplan, 2002). Likewise, excellent previous studies have investigated the dynamics of the embryonic circulation through lumped parameter models (Pennati et al., 2003; Pennati and Fumero, 2000; Peskin, 1981; Yoshigi and Keller, 1997; Yoshigi et al., 2000); the main focus of the current study is to identify the large scale 3D flow structures and baseline governing flow physics using experimental flow visualization and CFD models for the normal fetal aortic arch and for great vessel flow patterns in the setting of selected major CHDs.

Hemodynamics of the normal adult-scale aorta is a classical topic of cardiovascular fluid dynamics (Caro et al., 1978; Fung, 1984; McDonald, 1974) and has been extensively studied (Jin et al., 2003; Leuprecht et al., 2003; Mori and Yamaguchi, 2002; Morris et al., 2005; Nakamura et al., 2006; Shahcheraghi et al., 2002; Suo, 2005; Wood et al., 2001). A detailed literature survey is provided in our recent work, where an *in vitro*/*in vivo*