

Fetal Ventricular-arterial Coupling: Development, Physiology, and Ultrasonographic Advances

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Abstract: Ventricular-arterial coupling (VAC) is a key determinant of cardiovascular function, reflecting the interaction between cardiac pump performance and arterial load, and plays a crucial role during fetal development. The fetal cardiovascular system undergoes a continuous process from cardiac tube formation and chamber septation to vascular remodeling, providing the structural and functional basis for postnatal circulatory adaptation. Physiologically, VAC represents a dynamic balance between myocardial contractility, ventricular compliance, arterial resistance, and elasticity, ensuring hemodynamic stability and adequate oxygen delivery in utero. During the transition from fetal to neonatal circulation, the closure of placental circulation and the opening of pulmonary circulation induce profound hemodynamic changes, leading to remodeling of VAC with important implications for long-term cardiovascular health. Recent advances in echocardiography and Doppler techniques have enabled comprehensive evaluation of fetal VAC by integrating cardiac functional indices with hemodynamic parameters, facilitating early detection of abnormalities and potential risks. Emerging modalities, including speckle-tracking echocardiography, three-dimensional imaging, and artificial intelligence-assisted analysis, are expected to allow more precise and reproducible quantification of fetal VAC, thereby supporting risk stratification, optimized surveillance, and individualized prenatal management. Thus, research on fetal VAC not only deepens our understanding of cardiovascular developmental and adaptive mechanisms but also provides a clinically relevant framework for ultrasound-based assessment and decision-making in fetal medicine.

Key words: Fetus; Ventricular-arterial coupling; Cardiovascular development; Echocardiography

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Ventricular-arterial coupling (VAC) the dynamic interaction between cardiac performance and the arterial system-serves as a key determinant of cardiovascular function [1]. Previous studies have demonstrated that VAC is not only a critical parameter for evaluating cardiovascular efficiency and energy uti-

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lization but also represents a central mechanism underlying the development and progression of various cardiovascular diseases (CVD). VAC encompasses multiple dimensions, ranging from the structural formation of the cardiovascular system during embryogenesis to its functional regulation under physiological conditions, and to pathological alterations during disease processes [2]. The transition from the fetal to the neonatal stage is recognized as a crucial period characterized by profound physiological, anatomical, and biochemical changes within the cardiovascular system [3]. Echocardiography has become an essential tool for visualizing fetal cardiac structures during both early and late gestation, facilitating the confirmation of normal morphology, the detection of congenital anomalies, and the assessment of cardiac function [4].

The echocardiographic single-beat method proposed by Chen et al. [5] is a validated noninvasive gold standard for assessing VAC (Ea/Ees). This approach estimates end-systolic elastance (Ees) using single-beat echocardiographic parameters combined with blood pressure measurements, including stroke volume (SV), left ventricular ejection fraction (LVEF), the ratio of pre-ejection period to ejection time (tNd), systolic blood pressure (SBP), and diastolic blood pressure (DBP). Good agreement between noninvasive and catheter-derived pressure-volume loop measurements has confirmed the accuracy and reliability of this method. With ongoing technological advances, this method has become a first-line noninvasive approach for evaluating VAC in CVD assessment and risk stratification [6].

This review aims to provide a comprehensive summary of current advances in the understanding of VAC during embryonic development and physiological regulation, and to highlight the applications of ultrasound techniques in its evaluation, thereby offering insights for future research and clinical practice in this field.

Development of the Fetal Cardiovascular System

The critical role of the placenta in VAC

The cardiovascular system is among the earliest to develop and function in the fetus. Cardiac morphogenesis begins in the early third week of gestation, when progenitor cells derived from the neural crest initiate heart formation, and the primitive heart tube starts to contract by the end of the third week [7]. Cardiac looping occurs soon after, while the vascular system begins to develop during the fourth week, followed by the formation of septa and semilunar valves around the tenth week of gestation [8]. At this stage, the placenta becomes an

integral component of fetal circulation, providing a system with low systemic vascular resistance (SVR). The placenta serves as both the primary source of oxygen and nutrients for the fetus and as a finely tuned dynamic interface between the maternal and fetal circulations [9]. Oxygenated blood from the placenta is delivered to the fetus via the umbilical vein, which channels through the ductus venosus (DV) into the fetal heart. Most of this blood bypasses the right heart through the foramen ovale (FO), entering the left atrium and subsequently the left ventricle.

The developmental timeline of the placenta closely parallels that of the fetal cardiovascular system. Recent studies have revealed a strong association between placental dysfunction and congenital heart disease (CHD), suggesting shared molecular signaling pathways that govern the development of both organs [10,11]. This has led to the proposal of the “placenta-heart axis” concept, which posits that placental abnormalities can directly influence cardiac morphogenesis and hemodynamic adaptation. Placental abnormalities are more frequently observed in pregnancies complicated by fetal CHD. Several subtypes, including tetralogy of Fallot and other conotruncal defects, have been associated with reduced placental weight and impaired placental vascular development [12,13]. These findings underscore the placenta’s pivotal role not only as a metabolic and respiratory organ but also as a key regulator of VAC during fetal life.

Structural development and functional differentiation of the heart

Cardiac development is a multistage, dynamic, and genetically regulated process. During gastrulation, the bilaminar embryonic disc transforms into a trilaminar structure consisting of ectoderm, mesoderm, and endoderm. The heart arises from mesodermal precursor cells migrating from the primitive streak to the anterolateral embryonic disc [14–16]. Cardiac progenitors subsequently differentiate into distinct lineages: the endocardium and myocardium from the mesoderm, the epicardium and coronary vasculature from the proepicardial organ, and neural crest cells contributing to valve formation, outflow tract septation, and parasympathetic innervation [15]. These coordinated developmental events establish the structural foundation for efficient fetal circulation and postnatal cardiac adaptation [17].

1) Early cardiac formation (Day 8–18): Occurring before body folding, early cardiogenesis begins with the specification of the cardiac crescent during gastrulation and concludes with the formation of two endocardial tubes, which later fuse and become enveloped by myocardial lineage cells. At this stage, the primitive

myocardial structure supports the initiation of cardiac contractility, although VAC remains immature due to limited myocardial organization and low arterial load.

2) Morphogenetic stage (Week 4-8): This stage is initiated by the development of a linear heart tube derived from the first heart field, and concludes with the incorporation of second heart field give rise to the primordial four-chambered heart. Progressive chamber formation and elongation of the outflow tract increase stroke volume and ventricular pressure generation, representing early steps toward functional coordination between ventricular performance and the developing arterial system.

3) Septation and remodeling (around day 30): During mid-embryonic development, the cardiac primordium undergoes rapid growth, chamber septation, and valve formation, while the atria and ventricles acquire their morphological identities. These structural refinements contributing to the gradual maturation of ventricular-arterial interaction.

4) Maturation and tissue differentiation (Week 16-38): In the fetal stage, myocardial histological maturation, valvular differentiation (including chordae tendineae and papillary muscles), and the development of the coronary vasculature and conduction system occur.

Cardiac functional differentiation is an adaptive process. Contractility initiates early and rapidly increases before reaching stability. This maturation is supported by the formation and alignment of sarcomeres, the evolution of electrophysiological properties, and the influence of mechanical forces that together shape cardiac morphology and promote functional refinement [18]. Importantly, this process of myocyte alignment and maturation is thought to be the primary driver for the observed increase in ventricular elastance (Ees) throughout the second and third trimesters, thereby playing a central role in the functional maturation of VAC.

The fetal circulation is characterized by right ventricular (RV) dominance, with RV output significantly exceeding that of the left ventricle (LV) throughout gestation [19]. The median right-to-left cardiac output ratio is approximately 1.42 and remains relatively stable across gestational ages, with RV output accounting for about 59% and LV output for approximately 41% of the total biventricular cardiac output. When indexed to fetal weight, the median combined cardiac output is approximately $425 \text{ mL} \cdot \text{min}^{-1} \cdot \text{kg}^{-1}$. The placenta receives more than 40% of the combined ventricular output, serving as a major low-resistance vascular bed within the fetal circulation [3]. After birth, pulmonary blood flow increases dramatically with lung expansion, while clamping of the umbilical vein eliminates the placental low-resistance circuit [20]. Consequently, the LV assumes

responsibility for systemic circulation, and the associated increases in afterload and pulmonary venous return lead to elevated left atrial and ventricular pressures, resulting in a transition from right- to left-dominant circulation.

Development of the arterial tree

Cardiovascular development begins around day 18-19 of embryogenesis. Two endocardial tubes form bilaterally, fuse ventral to the foregut in a cranio-caudal direction, and create the primitive heart tube. From the aortic sac, six pairs of pharyngeal (aortic) arches connect to the dorsal aortae between weeks 4-6; the first, second, and fifth pairs regress. The third arches form the common and external carotid arteries; the fourth form the aortic arch (left) and proximal right subclavian artery (right); the sixth form the proximal pulmonary arteries, with the left distal segment becoming the ductus arteriosus [7]. The proximal pulmonary artery develops from the arterial trunk, whilst the distal pulmonary artery, the aorta, and the proximal right pulmonary artery develop from the ventral sixth aortic arch artery. The distal right pulmonary artery and left pulmonary artery originate from the postbranchial artery, which itself develops from the lung bud and surrounding mesoderm. The ductus arteriosus arises from the distal left sixth aortic arch artery [21]. This asymmetric remodeling establishes the definitive arterial tree, ensuring proper systemic-pulmonary flow distribution in fetal and postnatal life.

This complex remodeling process establishes the unique parallel circulatory pathways and the high-compliance, low-resistance placental circuit, which are the principal determinants of the low effective arterial elastance (Ea) characteristic of the fetal circulation.

Fetal-specific characteristics of ventricular-arterial coupling

In fetal life, VAC is uniquely adapted to a parallel circulation characterized by high pulmonary vascular resistance and placental gas exchange [1,22,23]. Deoxygenated blood returns to the heart via the superior and inferior venae cavae and enters the right atrium (RA), from which it is ejected by the right ventricle (RV) into the pulmonary artery. Because pulmonary vascular resistance is markedly elevated, only a small fraction of right ventricular output perfuses the lungs, whereas the majority bypasses the pulmonary circulation through the ductus arteriosus, enters the systemic circulation, and returns to the placenta via the umbilical arteries (Fig. 1) [8].

Within this configuration, the RV operates against a high-impedance pulmonary-ductal-systemic arterial system and contributes the majority of the combined car-

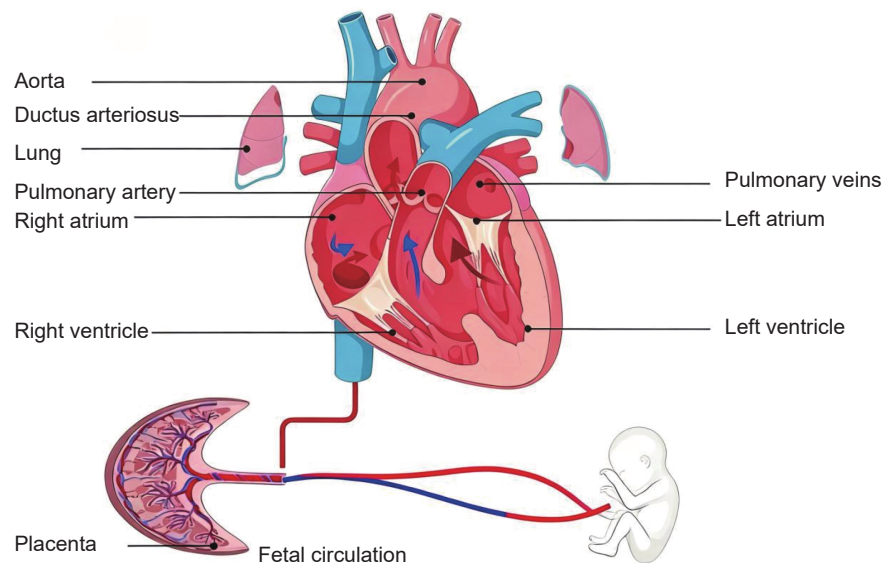


Figure 1 Fetal cardiac circulation. Deoxygenated blood returns via the superior and inferior venae cavae to the right atrium and is ejected by the right ventricle (RV) into the pulmonary artery. Owing to high pulmonary vascular resistance, most RV output bypasses the lungs through the ductus arteriosus, enters the systemic circulation, and returns to the placenta via the umbilical arteries.

diac output. In contrast, the LV is preferentially coupled to the cerebral and upper-body circulation via the aortic arch, receiving relatively well-oxygenated blood through foramen ovale streaming³. This asymmetric ventricular loading and output distribution reflects a developmental pattern of VAC optimized for efficient energy transfer, stable hemodynamics, and preferential cerebral perfusion during fetal life.

Transition of VAC to the neonatal period

After birth, the opening of the pulmonary circulation and the termination of the placental circulation cause profound changes in preload and afterload, leading to the remodeling of VAC [24]. This transition represents one of the most complex phases of cardiovascular adaptation and is critical for neonatal circulatory stability.

With the first breaths, PVR falls sharply, resulting in a marked increase in pulmonary blood flow [25]. Consequently, RV afterload decreases, while LV preload rises due to increased pulmonary venous return. At the same time, interruption of the placental circulation eliminates the low-resistance vascular bed, elevating SVR and LV afterload [3,26].

Following birth, the ductus arteriosus, ductus venosus, and foramen ovale close sequentially [27]. This redistribution of preload and afterload triggers a rapid adjustment in VAC, requiring the neonatal heart to adapt swiftly to new hemodynamic conditions. The LV progressively assumes dominance as the systemic pump, with increasing wall thickness and contractility to match the higher afterload. Conversely, RV pressure declines, transitioning to a low-pressure pulmonary circuit [28]. The rebalanced VAC, when well matched, ensures sta-

ble cardiac output and adequate oxygen delivery, supporting the successful adaptation from fetal to neonatal life.

Application of Echocardiography in Fetal and Neonatal VAC

Echocardiography is a noninvasive and convenient imaging modality that has become the primary tool for real-time evaluation of fetal cardiac structure and function. It enables comprehensive assessment of cardiac morphology and hemodynamics, and plays a crucial role in the prenatal detection of CHD [29]. Fetal echocardiographic examination-when clinically indicated-is recommended between 18 and 22 weeks of estimated gestational age (EGA) [30]. This period provides optimal visualization for assessing cardiac anatomy, chambers symmetry, and outflow tract development, supporting both structural diagnosis and functional evaluation in the context of fetal-neonatal VAC.

Two-dimensional echocardiographic assessment of cardiac structure

Two-dimensional (2D) echocardiography is the primary tool for fetal cardiac evaluation, serving both screening and functional assessment. Standard screening views include the four-chamber view, left and right ventricular outflow tracts, and the three-vessel-trachea view, which allow initial assessment of cardiac anatomy, chamber proportions, and outflow tract connections. For functional assessment, 2D imaging is combined with M-mode and Doppler techniques to quantify ventricular systolic and diastolic function, including interventricu-

lar septal motion, ejection time, and blood flow velocity [31]. Comprehensive fetal echocardiography is typically performed between 18 and 22 weeks of gestation, when all four chambers and major outflow tracts are clearly visualized (Fig. 2) [30,32,33].

The examination begins with determination of fetal position. From the transverse abdominal view, the stomach, abdominal aorta, and inferior vena cava are identified, followed by cranial advancement of the transducer to obtain the four-chamber view. The cardiac apex should be leftward, occupying approximately 30% of the thoracic cross-section, with the interventricular septum oriented at $45^\circ \pm 20^\circ$ to the anteroposterior axis. Further cranial angulation reveals the outflow tracts and the three-vessel–trachea view, enabling systematic assessment of chamber symmetry and great vessel alignment and providing a basis for functional and hemodynamic evaluation [33–36].

Application of flow-related techniques

The cardiovascular system operates through complex hemodynamic processes involving vascular branching, flow dynamics, and blood viscosity. Thus, a complete cardiac evaluation requires not only 2D echocardiography but also color, power, and pulsed Doppler imaging to obtain key parameters such as flow velocity, pattern, and wall shear stress [37]. In fetal echocardiography, Doppler ultrasound is used to assess blood flow across the atrioventricular and semilunar valves, FO, aortic arch, and ductus arteriosus, identifying waveform patterns and potential abnormalities under physiological conditions [38,39].

Slowflow Heart Quantification (SlowflowHD) is a novel power Doppler imaging technique that visualizes slow peripheral blood flow in fetal microvessels, enabling early assessment of cardiovascular morphology and potential detection of CHD during pregnancy

[40,41]. However, this technique does not provide information on flow direction or velocity. In a study by Hata et al. [40], transvaginal SlowflowHD imaging in early pregnancy clearly depicted key cardiac structures, including the four-chamber view, ventricular outflow tracts, aortic arch, and pulmonary veins, thereby facilitating early embryonic and fetal cardiac evaluation.

Assessment of cardiac function

Cardiac function can be evaluated through morphological indices-including ventricular and atrial diameters, chamber areas, and myocardial wall thickness-as well as by assessing systolic and diastolic performance [42,43].

In addition, Fetal Heart Quantification (Fetal HQ), based on speckle-tracking imaging combined with advanced image analysis, provides a noninvasive and integrated assessment of fetal cardiac morphology and function [44,45]. This technique enables the measurement of parameters such as left ventricular ejection fraction (LVEF), fractional area change (FAC), fractional shortening (FS), and global longitudinal strain (GLS) [46], offering quantitative evaluation of fetal myocardial contractility (Table 1).

Tissue doppler imaging (TDI)

TDI applies the Doppler principle to measuring myocardial motion velocities throughout the cardiac cycle, providing quantitative assessment of systolic and diastolic function, which is distinct from conventional Doppler techniques that evaluate blood flow velocity [47]. Studies have demonstrated that TDI is more sensitive than traditional Doppler methods-such as atrioventricular inflow or Tei index-for detecting fetal systolic and diastolic dysfunction. Clinically, TDI has been used to identify fetal growth restriction (FGR) and cardiac dysfunction in fetuses of diabetic mothers, allowing early detection of impaired myocardial performance before the appearance of structural abnormalities [48,49].

Two-dimensional speckle tracking echocardiography

Two-dimensional speckle tracking echocardiography (2D-STE) tracks natural acoustic markers within the myocardium to quantify multidirectional myocardial strain and strain rate, including longitudinal, circumferential, and radial components.

Although 2D-STE does not directly measure VAC, it provides important insights into myocardial mechanics. In particular, global longitudinal strain (GLS), a key metric derived from 2D-STE, is increasingly used as a practical, angle-independent surrogate for myocardial contractility, thereby providing a window into the ven-

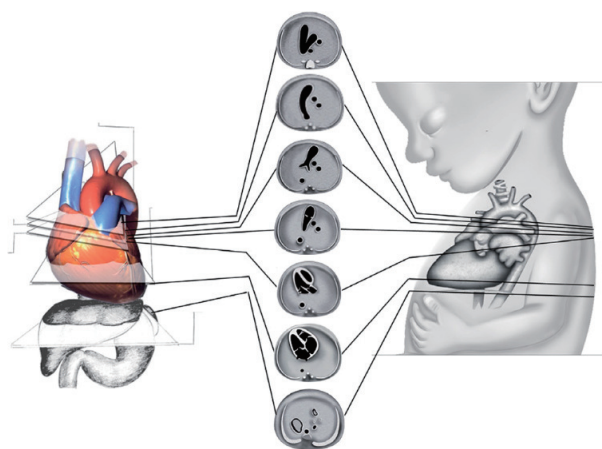


Figure 2 Anatomical structures examined in the four cardiac chambers and outflow tracts of the fetal heart [32].

Table 1 Fetal cardiac function assessment indicators.

Index	Main point
Cardiothoracic ratio	From a 4-chamber (4C) view, Cardiomegaly if > 0.35 ; Severe if > 0.50 [82]
Global longitudinal strain (GLS)	$-21.5 \pm 2.0\%$ at 28-32 weeks [52]
Cardiac output (CO)	$CO = SV \times \text{heart rate}$; Median combined CO: 425 mL/min/kg; Right/left CO: 1.4 [38]
Ejection fraction (EF)	Reference values $> 50\text{-}60\%$ [83]
Fractional shortening (FS)	$(EDVD - ESVD)/EDVD$; Reference values $> 28\%$ [82,84]
Tei index or Myocardial performance index (MPI)	$(ICT + IRT)/ET$; 0.39-0.55 at 11- 41 weeks [85]

GLS, global longitudinal strain; SV, stroke volume; EDVD, end-diastolic ventricular dimension; ESVD, end-systolic ventricular dimension; MPI, myocardial performance index; ICT, isovolumetric contraction time; IRT, isovolumetric relaxation time; ET, ejection time.

tricular elastance (Ees) component of the VAC equation. This technique enables a comprehensive evaluation of myocardial deformation with reduced angle dependence and lower susceptibility to fetal or maternal motion, and has demonstrated excellent feasibility and reproducibility in fetal cardiac assessment [50-52].

Fetal 2D-STE has been applied as a research tool in various clinical conditions such as CHD, twin-to-twin transfusion syndrome (TTTS), FGR, and maternal diabetes. In a prospective longitudinal study of 124 normal pregnancies, van Oostrum et al. [52] reported that LVGLS, LVGLSR, RVGLS, and RVGLSR values increased with advancing gestational age (18-41 weeks), indicating a progressive reduction in myocardial shortening. Throughout gestation, RVGLS remained significantly higher than LVGLS, reflecting physiological right ventricular dominance in fetal circulation.

Three- and four-dimensional echocardiography

Three-dimensional echocardiography (3DE) provides dynamic, volumetric visualization of the fetal heart, allowing reconstruction of detailed cardiac anatomy through computer-based image processing [53]. It offers more intuitive assessment of cardiac morphology and is currently the recommended echocardiographic technique for measuring Left ventricular volumes and LVEF [54]. Transthoracic 3DE has been extensively validated against cardiac magnetic resonance (CMR), showing superior accuracy and reproducibility over conventional 2D methods for LV volume and LVEF measurement [55,56]. Compared with CMR, transthoracic 3DE tends to slightly underestimate end-diastolic and end-systolic volumes, primarily due to its limited spatial resolution [55,57].

The spatio-temporal image correlation (4D STIC) system enables real-time acquisition and offline three-dimensional reconstruction of the fetal cardiac cycle [58]. It allows evaluation of any region of interest at any time point within the cardiac cycle. 4D STIC has been proposed for ventricular volume measurement, providing more accurate estimation of stroke volume (SV), cardiac output (CO), and LVEF. Offline analysis can

also assess annular displacement of the mitral and tricuspid valves. However, this technique requires considerable operator experience and a long learning curve [59].

Other Ultrasound Assessment Methods

Hemodynamic assessment of the placenta and umbilical arteries

Adequate placental perfusion is essential for normal fetal cardiac development, while CHD may in turn impair placental function. In cases of cardiovascular obstruction or absence of key fetal channels-such as premature ductus arteriosus closure-the resulting increased right ventricular load can lead to fetal hydrops and veno-placental congestion, causing placental insufficiency and thrombus formation, which may further exacerbate CHD [60]. Monitoring umbilical artery hemodynamics provides valuable insight into placental function. During normal pregnancy, placental vascular resistance progressively decreases, leading to higher end-diastolic flow velocity and reduced resistance index (RI), pulsatility index (PI), and systolic/diastolic (S/D) ratio. In late gestation, the S/D ratio decline slows and stabilizes. In placental insufficiency, vascular resistance in the placenta and umbilical arteries increases, manifesting as elevated PI, RI, and S/D ratios or abnormal Doppler waveforms, such as absent or reversed end-diastolic flow, indicating compromised uteroplacental circulation.

Application of artificial intelligence in prenatal diagnosis of fetal cardiac abnormalities

Artificial intelligence (AI) technologies, including machine learning, deep learning, and neural networks, have demonstrated strong capabilities in medical image analysis, data integration, and decision support [60]. While current AI applications in prenatal cardiology have primarily focused on image acquisition and view recognition, emerging developments suggest that AI has substantial potential to advance quantitative functional assessment, particularly in the evaluation of VAC [61].

Future AI-driven approaches could move beyond

plane identification toward automated, beat-to-beat segmentation of ventricular volumes from fetal echocardiographic datasets, as well as intelligent analysis of Doppler flow velocity envelopes. Such developments would enable rapid, reproducible, and operator-independent estimation of stroke volume, ventricular pressure surrogates, and arterial load [62]. By integrating these parameters, AI could facilitate automated calculation of key VAC components, including ventricular end-systolic elastance (Ees) and effective arterial elastance (Ea), which currently require labor-intensive post-processing and expert interpretation. In this context, AI-based workflows may significantly improve the feasibility and scalability of VAC assessment in both research and clinical settings, paving the way for more standardized evaluation of fetal cardiovascular function.

Clinical Applications

Fetal growth restriction (FGR)

The principal pathophysiological feature of FGR is placental insufficiency accompanied by maternal cardiovascular maladaptation, leading to a chronic state of increased vascular resistance and increased cardiac load within the fetal circulation [63]. In response to this altered hemodynamic environment, FGR fetuses undergo adaptive structural and functional cardiovascular remodeling. Recent studies have demonstrated that these in utero cardiovascular alterations may persist after birth, extending into infancy, childhood, and even adolescence [64–66], consistent with epidemiological and experimental evidence linking low birth weight to an increased lifetime risk of CVD and mortality [67] (Fig. 3).

Although direct quantification of VAC parameters in FGR remains limited, chronic placental insufficiency and persistently elevated vascular resistance are consistently observed in this condition, resulting in a decline in maternal cardiac output, increased arterial load (Ea), and a relatively inadequate compensatory increase in ventricular contractility (Ees) [68].

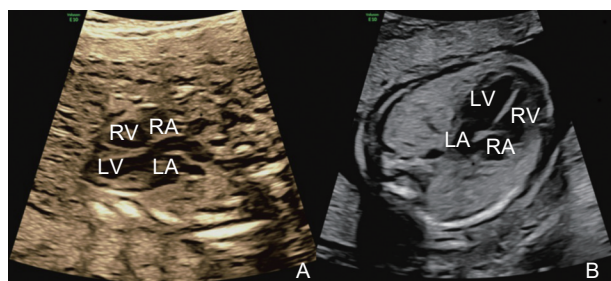


Figure 3 Ultrasound images of the fetal heart. (A) is the normal fetal heart, (B) is the fetal heart in a case of Fetal Growth Restriction (FGR). RA, right atrium; RV, right ventricle; LV, left ventricle; LA, left atrium.

Fetal congenital heart disease

CHD, particularly complex malformations such as hypoplastic left heart syndrome (HLHS) and transposition of the great arteries (TGA), is characterized by a profound mismatch between ventricular pumping capacity and arterial load, resulting in impaired hemodynamic adaptation and altered VAC.

Marinari et al. [69] reported that children following cardiac surgery frequently exhibited elevated VAC values ($Ea/Ees > 1$), indicative of ventricular-arterial decoupling. Patients with higher VAC demonstrated significantly reduced end-systolic elastance (Ees), whereas arterial elastance (Ea) did not differ significantly, suggesting that impaired coupling was primarily driven by reduced ventricular contractile efficiency. Moreover, VAC was inversely correlated with pre-ejection period, total ejection time, and LVEF, underscoring the association between abnormal VAC and diminished ventricular performance.

HLHS refers to abnormal development of the left-sided cardiac structures, resulting in obstruction to blood flow from the left ventricular outflow tract [70]. In classical HLHS, the aortic valve is atretic, with either atresia or severe hypoplasia of the mitral valve. Consequently, the RV is exposed to severe volume and pressure overload, as it must generate systemic pressures while accommodating increased preload. This abnormal loading condition leads to maladaptive VAC, likely reflecting adaptation to acutely altered RV loading in response to increased cardiac output demands and pulmonary artery flow [71].

In TGA, parallel rather than serial circulatory circuits create a distinct, lesion-specific VAC mismatch. This condition is characterized by ventriculo-arterial discordance, with the aorta arising from the morphologic right ventricle and the pulmonary artery from the morphologic left ventricle [72], resulting in a unique VAC state for both ventricles: the RV pumps against systemic vascular resistance, while the LV ejects into the low-resistance pulmonary circulation. Pasqualin et al. [73] demonstrated that impaired VAC independently predicted a composite outcome of death, cardiac arrest, and heart failure hospitalizations (hazard ratio [HR], 2.09; 95% confidence interval [CI], 1.12–3.92), highlighting the potential of VAC as a tool for risk stratification in this complex population.

Tetralogy of fallot

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart defect, accounting for 5%–10% of all CHD. Its core anomalies comprise pulmonary artery stenosis, ventricular septal defect, overriding aorta, and right ventricular hypertrophy [74]. Echocardiography is

a non-invasive examination that can be performed at the patient's bedside, enabling precise assessment of the anatomical structure and severity of right ventricular outflow tract stenosis, the location and number of ventricular septal defects, associated anomalies, aortic arch morphology, and coronary artery variations. The primary limitation of transoesophageal echocardiography in patients with tetralogy of Fallot lies in its difficulty in visualising the distal pulmonary artery [75,76]. Tetralogy of Fallot (TOF) causes significantly elevated right ventricular afterload (Ea) due to pulmonary artery stenosis and hypoplasia. Compensatory right ventricular hypertrophy occurs alongside persistently increasing pressure load, while concomitant left-to-right shunting and reduced pulmonary circulation result in functional mismatch between the right ventricle and pulmonary artery [77]. Postoperatively, patients frequently retain ventricular - elevated ventricular-vascular coupling ratio (VVCR). This coupling dysfunction correlates with worsening cardiac function classification, compromising overall cardiovascular perfusion efficiency and long-term prognosis [78].

Impact of hypertensive disorders of pregnancy on fetal VAC

Hypertensive disorders of pregnancy (HDP)-including preeclampsia-can lead to placental hypoperfusion and increased peripheral vascular resistance, thereby imposing additional hemodynamic load on the fetal heart. Youssef et al. [79] observed signs of fetal cardiac remodeling and dysfunction in pregnancies complicated by preeclampsia, independent of the presence of FGR. Hendem et al. [80] compared fetal cardiac function between preeclamptic and control groups, exploring correlations with proteinuria severity. Their results showed that preeclampsia alters both systolic and diastolic cardiac function, with TDI enabling earlier and more sensitive detection of subclinical dysfunction. Fetuses from cases with severe proteinuria (> 3 g/24 h) exhibited more pronounced biventricular diastolic impairment. Furthermore, Yuan et al. [81] demonstrated significant maternal cardiac and carotid arterial remodeling, as well as LV-carotid coupling alterations in preeclamptic women, some of which persisted postpartum. These findings suggest that maternal cardiovascular adaptation plays a key role in preeclampsia. However, direct evidence regarding fetal VAC alterations remains limited, warranting larger studies in fetal populations to validate these associations.

Conclusion

Early identification of fetal cardiovascular structural

and functional abnormalities during pregnancy is of great clinical importance. Timely diagnosis and intervention can significantly improve fetal survival and perinatal outcomes. Looking ahead, the continuous advancement of multidisciplinary collaboration, deeper exploration of the molecular mechanisms underlying VAC, and ongoing optimization of ultrasound-based evaluation techniques-combined with large-scale, multicenter clinical studies-will provide stronger evidence-based support for the diagnosis and management of fetal cardiovascular diseases. These efforts are expected to contribute to long-term cardiovascular health and improved prognosis in affected populations.

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Author's Contributions

ZJL and LJ conceived and designed the study; XTJ drafted the manuscript; LWF and PPH revised the manuscript; RY and JM acquired and interpreted the data for the work; NW and TYW participated in data, image quality supervision. LY and WHR performed the format review and quality adjustment. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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Data Availability

Not applicable.

Declarations

Conflict of interest

The authors have no conflict of interest to declare.

Consent for publication

Not applicable.

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