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Cardiac dysfunction in congenital diaphragmatic hernia: Pathophysiology, clinical assessment, and management

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ABSTRACT

Cardiac dysfunction is an important consequence of pulmonary hypertension in congenital diaphragmatic hernia and a determinant of disease severity. Increased afterload leads to right ventricular dilatation and diastolic dysfunction. Septal displacement and dysfunction impair left ventricular function, which may also be compromised by fetal hypoplasia. Biventricular failure contributes to systemic hypotension and hypoperfusion. Early and regular echocardiographic assessment of cardiac function and pulmonary artery pressure can guide therapeutic decision-making, including choice and timing of pulmonary vasodilators, cardiotropes, ECMO, and surgery.

Introduction

Pulmonary hypertension due to abnormal pulmonary vascular development is an important determinant of disease severity in congenital diaphragmatic hernia (CDH).[1] Pulmonary hypertension (PH) has the following two major pathophysiological consequences: hypoxemic right-to-left shunting and impaired cardiac function.

Until recently cardiac function in CDH had been relatively poorly understood. However, newer functional echocardiographic (echo) techniques are helping to elucidate the nature, timing, and clinical significance.

In this article, we firstly review current understanding of ventricular dysfunction in CDH, including relationships with disease severity and outcome. In the second half of the article we discuss clinical techniques for assessing cardiac function, timing of these, and the use of cardiac function to guide therapeutic decision making.

Part 1: Pathophysiology of ventricular dysfunction in CDH

The right ventricle in CDH

The normal right ventricle (RV) is a thin-walled structure, crescenteric in cross section and triangular in longitudinal view. It contracts mainly by longitudinal shortening but also by circumferential shortening creating an inward "bellows" action of the RV free wall.[2] The cardiac cycle in the RV, as in the LV, consists of systolic rapid isovolumic contraction (IVC) and prolonged ejection (S) phases, followed in diastole by active early relaxation in diastole (E phase) and later diastolic filling due to atrial contraction (A phase).

Abnormal RV loading in CDH

In the normal infant pulmonary vascular resistance (PVR) falls rapidly in the first days after birth. In CDH the RV is exposed to chronically elevated PVR (afterload).[1,3] In the presence of a patent ductus arteriosus (PDA) with right-to-left shunting the RV is also volume loaded, with higher output than the LV. Abnormal loading conditions lead to structural and functional changes in the RV in CDH.

RV structural changes in CDH

The abnormal elevation in postnatal afterload (PVR) causes the compliant RV to dilate. The septum is flattened and displaced leftward compressing the LV.[4] RV hypertrophy follows creating a concentric, thicker-walled ventricle. Hypertrophy may be a maladaptive process; increased myocardial oxygen demand combined with a reduced coronary perfusion gradient creates a set-up for myocardial ischemia and dysfunction.[5]

In right-sided CDH (R-CDH), Dekoninck et al.[6] have additionally observed fetal RV hypoplasia. This may be a predisposing factor for postnatal RV dysfunction.

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Table 1
Frequency of myocardial dysfunction in the first 48 h of life in 33 infants with CDH.

n (%)	Diastolic dysfunction, *n* (%)	Systolic dysfunction, *n* (%)
RV dysfunction		
19 (58%)	19 (58%)	1 (0.3%)
Septal dysfunction		
8 (24%)	7 (21%)	4 (12%)
LV dysfunction		
19 (58%)	18 (54%)	10 (30%)

Abbreviations: RV, right ventricle; LV left ventricle.
Myocardial function was assessed using pulse wave tissue Doppler imaging (TDI) to measure myocardial velocities in the basal RV, LV, and septum. Myocardial dysfunction was defined as a myocardial velocity <2 SD below normal mean.

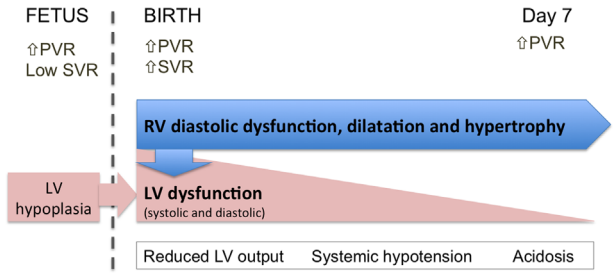

Fig. 1. Pathophysiology of early cardiac dysfunction in CDH. *Abbreviations*: PVR, pulmonary vascular resistance; SVR systemic vascular resistance; RV, right ventricle; LV, left ventricle.

RV dysfunction in CDH

Initial studies of RV function in CDH demonstrated impaired global function using the myocardial performance index (MPI), a time-based composite measure of function.[7]

Subsequent investigations revealed that RV dysfunction in CDH is predominantly diastolic in nature. Aggarwal et al.[8] observed increased systolic: diastolic ratio (SDR) in infants with CDH due to diastolic shortening. Using the technique of pulse wave tissue Doppler imaging (TDI) to assess regional myocardial velocities in both systole and diastole we have similarly observed a significant reduction in early RV diastolic function.[9]

Of note, RV dysfunction in CDH does not demonstrate a linear correlation with PAP.[10] RV function cannot, therefore, be predicted from PAP and in the clinical setting should be assessed directly.

Timing and frequency of RV dysfunction in CDH

RV diastolic dysfunction is not present in the fetus but presents early as afterload increases in transition from placental to postnatal circulations.[11,12] Early RV dysfunction is common; in a cohort recently studied by ourselves 58% of infants had impaired RV function in the first 48 h of life (Table 1, previously unpublished data).

RV diastolic dysfunction appears to improve by 72–96 h of age but may deteriorate again after surgery.[12] This may have important implications for timing of surgery, as discussed later.

Thereafter, RV function tends to improve with PAP, but may deteriorate if there is an exacerbation of PH for example at the time of weaning cardiorespiratory support or sedation, or during sepsis.

The longer-term natural history of RV dysfunction in CDH remains unclear, though Egan et al.[13] have observed impaired RV diastolic function in children 5 years after surgical repair.

Clinical significance of RV dysfunction

Severity of early RV diastolic dysfunction in the first 48 h of life is predictive of mortality and correlates with length of stay and duration of respiratory support.[4,8,12] Pulmonary artery pressure (PAP) in the first 48 h does not correlate with the same outcomes. This suggests that in CDH, as in other chronic pulmonary hypertensive diseases, RV dysfunction rather than PAP is a key mediator of disease severity and not simply a side effect of increased PVR.[14]

RV dilatation, hypertrophy, and dysfunction lead to increased metabolic demand, while also impacting LV performance, as discussed below. Biventricular failure contributes a clinical picture of systemic hypoperfusion, acidosis, and organ dysfunction, which may threaten survival (Figure 1).

The left ventricle in CDH

The normal left ventricle is elliptical in short axis and narrows from base to apex, giving a cone-like appearance. It is thicker-walled than the RV reflecting the higher operating pressures. During contraction the LV undergoes longitudinal and circumferential shortening, radial thickening, and a twisting action.[15]

RV and LV interdependence in PH disease

LV and RV function are inseparably related due to their shared pericardial space, myocardial fibers, and interventricular septum. In pulmonary hypertensive disease RV dilatation leads to septal displacement and dysfunction resulting in secondary impairment of LV function and output.[16]

LV hypoplasia in left-sided CDH

LV hypoplasia, particularly in left sided (L-CDH) may also be an important contributor to LV dysfunction in CDH. LV hypoplasia has been observed in post-mortem and fetal echocardiographic studies and correlates with fetal lung volume.[17,18] Proposed mechanisms are mechanical compression and reduced fetal LV filling, due to reduced pulmonary blood flow and altered ductus venosus flow.[19] In the fetus LV function is preserved despite relative hypoplasia.[11,20] However, at birth hypoplasia may predispose to postnatal dysfunction.

LV dysfunction in CDH

The triad of fetal LV hypoplasia, compression by the dilated RV and dysfunctional septum, and acute increases in LV preload and afterload at birth, may create a “perfect storm” for LV dysfunction in CDH (Figure 1).

Sernich et al. have observed global LV dysfunction, using LV MPI, in the first 48 h of life in CDH. This was recently confirmed by Tanaka et al.,[21] who also demonstrated the presence of both LV systolic and diastolic dysfunction on the first day of life.

We similarly observed significant impairment in LV function in the first 48 h of life in a recent cohort of 33 infants with CDH (Table 1). In all, 58% had LV dysfunction, predominantly diastolic, 16% had LV dysfunction alone, and 42% had combined RV and LV dysfunction.

This early LV dysfunction may be transient; function improved within 72 h in the cohorts studied by ourselves (Figure 2) and Tanaka et al.[21]

Clinical significance of LV dysfunction and hypoplasia

LV dysfunction and reduced pulmonary blood flow lead to reduced LV output and systemic hypotension in CDH. In our experience early LV dysfunction may be severe enough to threaten survival.