5-2-2023

Prognostic value of echocardiographic parameters in congenital diaphragmatic hernia: a systematic review and meta-analysis.

Mohan Pammi

Yashaswini Kelagere

Sara Koh

Amy Sisson

Joseph Hagan

See next page for additional authors

Prognostic value of echocardiographic parameters in congenital diaphragmatic hernia: a systematic review and meta-analysis

Mohan Pammi ,[1] Yashaswini Kelagere,[2] Sara Koh,[3] Amy Sisson,[4] Joseph Hagan,[1] Joshua Kailin,[1] Caraciolo J Fernandes [1]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/archdischild-2022-325257).

[1]Department of Pediatrics, Baylor College of Medicine, Houston, Texas, USA
[2]Department of Pediatrics, Saint Peters Hospital, New Brunswick, New Jersey, USA
[3]Rice University, Houston, Texas, USA
[4]Texas Medical Center Library, Houston Academy of Medicine, Houston, Texas, USA

Correspondence to
Dr Mohan Pammi, Department of Pediatrics, Baylor College of Medicine, Houston, TX 77030, USA; mohanv@bcm.edu

Received 19 December 2022
Accepted 19 April 2023

To cite: Pammi M, Kelagere Y, Koh S, *et al*. *Arch Dis Child Fetal Neonatal Ed* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/archdischild-2022-325257

ABSTRACT

Background Prognostication of mortality and decision to offer extracorporeal membrane oxygenation (ECMO) treatment in infants with congenital diaphragmatic hernia (CDH) can inform clinical management.

Objective To summarise the prognostic value of echocardiography in infants with CDH.

Methods Electronic databases Ovid MEDLINE, Embase, Scopus, CINAHL, the Cochrane Library and conference proceedings up to July 2022 were searched. Studies evaluating the prognostic performance of echocardiographic parameters in newborn infants were included. Risk of bias and applicability were assessed using the Quality Assessment of Prognostic Studies tool. We used a random-effect model for meta-analysis to compute mean differences (MDs) for continuous outcomes and relative risk (RR) for binary outcomes with 95% CIs. Our primary outcome was mortality; secondary outcomes were need for ECMO, duration of ventilation, length of stay, and need for oxygen and/or inhaled nitric oxide.

Results Twenty-six studies were included that were of acceptable methodological quality. Increased diameters of the right and left pulmonary arteries at birth (mm), MD 0.95 (95% CI 0.45 and 1.46) and MD 0.79 (95% CI 0.58 to 0.99), respectively) were associated with survival. Left ventricular (LV) dysfunction, RR 2.40, (95% CI 1.98 to 2.91), right ventricular (RV) dysfunction, RR 1.83 (95% CI 1.29 to 2.60) and severe pulmonary hypertension (PH), RR 1.69, (95% CI 1.53 to 1.86) were associated with mortality. Left and RV dysfunctions, RR 3.30 (95% CI 2.19 to 4.98) and RR 2.16 (95% CI 1.85 to 2.52), respectively, significantly predicted decision to offer ECMO treatment. Limitations are lack of consensus on what parameter is optimal and standardisation of echo assessments.

Conclusions LV and RV dysfunctions, PH and pulmonary artery diameter are useful prognostic factors among patients with CDH.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Many antenatal and postnatal prognostic factors in congenital diaphragmatic hernia have been reported, but there is a lack of consensus on optimal echocardiographic parameter(s) and measure(s) and the timing at which they should be evaluated.

WHAT THIS STUDY ADDS

⇒ In this systematic review and meta-analysis, we found that dimensions of right and left pulmonary arteries at birth positively correlate with survival, and right ventricular dysfunction, left ventricular dysfunction and severe pulmonary hypertension negatively correlate with survival and the decision to offer extracorporeal membrane oxygenation (ECMO) treatment.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ We identified echocardiographic parameters useful in prognosticating survival and the decision to offer ECMO treatment in patients with congenital diaphragmatic hernia (CDH), which might direct consensus for prognostication in CDH.

INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a developmental defect of the diaphragm characterised by protrusion of abdominal contents into the thoracic cavity. The incidence of CDH is estimated to be between 1.7 and 5.7 per 10 000 live births.[1] An international, multicentre study estimated the mortality of CDH to be 37.7%, of which hospital-based registries reported more deaths among live births than population-based registries (45.1% vs 33.8%) despite the advancements of medical and surgical management of CDH. Clinical features and outcomes of patients with CDH depend primarily on the severity of lung hypoplasia and associated pulmonary vascular maldevelopment that leads to pulmonary hypertension (PH).[2] Myocardial dysfunction can occur in infants with CDH with or without PH, sometimes necessitating support with extracorporeal membrane oxygenation (ECMO).[3]

Predictors for significant clinical outcomes range from prenatal imaging estimates of lung size and liver position on ultrasonography and MRI (absolute and observed to expected lung-to-head ratios, total fetal lung volume and per cent liver herniation)[4 5] to postnatal estimates of lung function (pCO_2, oxygenation index) to severity scores like the Score for Neonatal Acute Physiology-II (SNAP-II) and Score for Neonatal Acute Physiology with perinaatl extension-11 (SNAPPE-II).[6] PH and cardiac dysfunction related to PH or other pathology have implications for management and prognosis.[2] Current guidelines recommend detailed

echocardiographic evaluations in newborns with CDH as early as 24 hours post birth.[7] The evidence for echocardiographic markers in prognostication has not been summarised to inform clinical practice. In this systematic review, we sought to determine the prognostic value of various echocardiographic markers for mortality and the decision to offer ECMO treatment in infants with CDH without other major congenital anomalies.

METHODS

We hypothesise that echocardiographic measures before or after birth will predict mortality and the decision to offer ECMO treatment in infants with CDH.

Objective

This study aims to determine the prognostic value of echocardiographic markers for mortality and decision to offer ECMO treatment in infants with CDH without other major congenital anomalies.

We conducted this systematic review and meta-analysis in accordance with the Preferred Reporting for Systematic Reviews and Meta-Analysis statement and guidelines for prognostic reviews.[8 9]

Literature search

We systematically searched in Ovid MEDLINE, Embase, Scopus, CINAHL and Cochrane Library up to July 2022, with the assistance of a librarian (AS) without language restrictions in the online supplemental efile 1.

Inclusion criteria

Types of studies

We included retrospective and prospective observational studies that assessed any prognostic indicators related to prenatal or postnatal echocardiogram.

Condition to be studied

This work studied CDH without any other major anomalies.

Participants

Participants in this study included neonates with CDH diagnosed either prenatally or postnatally. Cases with other associated major malformations and/or chromosomal abnormalities were excluded.

Outcomes

The primary outcome was mortality before discharge.

Secondary outcomes included mortality at 7 days, decision to offer ECMO treatment, duration of ventilation, length of stay, and need for oxygen and/or inhaled nitric oxide (iNO).

Study selection and data abstraction

Three authors (YK, SK and MP) independently reviewed the titles and abstracts of all original citations and determined the need for a full paper review based on eligibility criteria. A consensus meeting was held to discuss any citations where there are differences in determination among reviewers. A full paper review was then independently conducted by the same reviewers, and another consensus meeting was held to determine final inclusion. Study characteristics and outcome data were extracted independently by two authors (YK and JH) on predesigned spreadsheets and were compared for consistency after completion.

Risk of bias in individual studies

Risk of bias for all included studies was assessed independently by two reviewers (YK and CJF) using the Quality Assessment of Prognostic Studies (QUIPS) tool.[10] Elements in the tool can be classified as low, unclear or high risk of bias. If all elements are considered low risk of bias, the study overall will be at low risk of bias. If any single element was at high risk of bias, the study was at high risk of bias. Any elements rated unclear risk will put the study overall at unclear risk of bias.

Synthesis of results and statistical analysis

Each prenatal and postnatal echocardiographic prognostic indicator was assessed individually and reported descriptively. A meta-analysis of either our primary or any secondary outcomes was performed for indicators where two or more studies reported the same prognosticator. We report risk ratios (RRs) with 95% CIs for dichotomous variables, and mean differences (MDs) with 95% CIs for continuous variables from random-effect models for survivors versus non-survivors for echocardiographic parameters, with similar analyses performed for patients who did versus did not need ECMO. Heterogeneity was estimated using the I^2 statistic. If heterogeneity was high (≥75%), we had planned to explore possible causes by performing post hoc subgroup analyses when applicable and if data were available. We used the 'metaphor' package in R V.4.1.2 (The R Foundation for Statistical Computing, Vienna, Austria) and RevMan V.5.4 for meta-analysis (Review Manager V.5.4.1, The Cochrane Collaboration, 2020).

RESULTS

Our systematic literature search identified 4989 publications, and our selection process is detailed in online supplemental eFigure 1. A total of 28 publications met the eligibility criteria and were included in our final analysis (online supplemental eTable 1).[11–38]

Assessment of quality of included studies

The methodological assessment of the included studies using QUIPS[10] is summarised in online supplemental eTable 2. All but two studies reported in the abstract form only were assessed to be of low risk of bias for the elements of the QUIPS assessment.[19 28]

Meta-analyses of echocardiographic prognostic factors were possible for survival and decision to offer ECMO treatment in infants with CDH (figures 1 and 2). In prognosticating survival, summary estimates of continuous outcomes were right pulmonary artery (RPA) diameter at birth (mm) (MD 0.95 (95% CI 0.45 to 1.46), three studies, 86 participants); left pulmonary artery (LPA) diameter at birth (mm) (MD 0.79 (95% CI 0.58 to 0.99), three studies, 86 participants); left:right pulmonary artery ratio (L:R) (MD −0.03 (95% CI −0.19 to 0.12), two studies, 47 participants); heart rate (beats/min) (MD 0.44 (95% CI −13.21 to 14.10), two studies, 63 participants); systolic duration (ms) (MD −0.01 (95% CI −0.03 to 0.01), two studies, 49 participants); and diastolic duration (ms) (MD −0.00 (95% CI −0.07 to 0.07), two studies, 49 participants) (figure 1). Left ventricular (LV) and right ventricular (RV) dysfunctions were based on interpretation of combined qualitative and quantitative echocardiographic parameters by experienced operators.[11] Summary estimates for dichotomous outcomes are as follows: LV dysfunction (RR 2.37 (95% CI 1.98 to 2.85), three studies, 1870 participants); RV dysfunction (RR 1.70 (95% CI 1.25 to 2.32), three studies, 1863 participants); and severe PH defined as peak pulmonary artery pressure of >2nd/3rd systemic pressure[29 32]

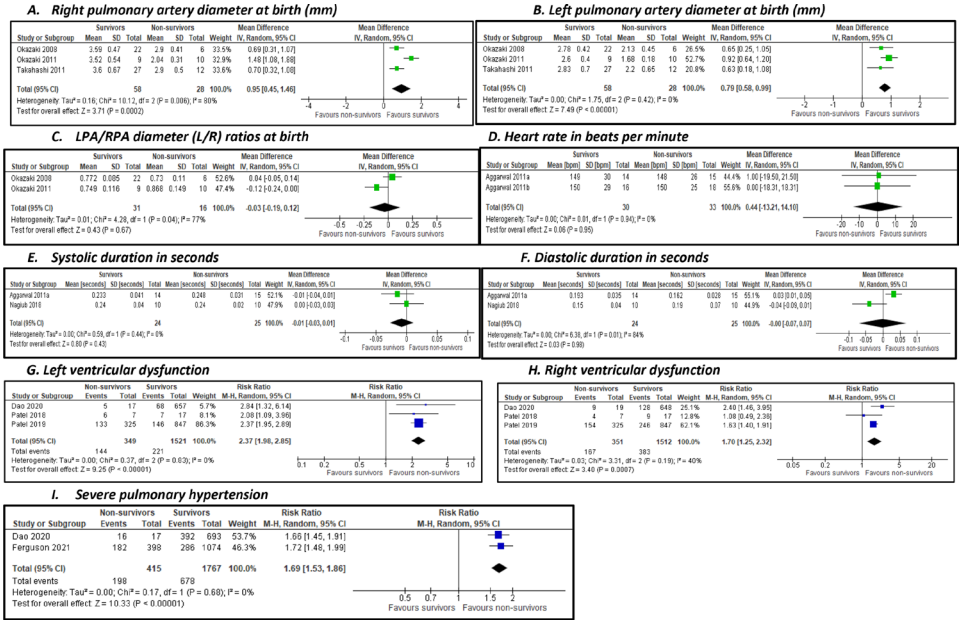

Figure 1 Comparison of prognostic factors in survivors versus non-survivors in prognosticating survival, summary estimates of continuous outcomes reported as MD with 95% CI were RPA at birth (mm) (A), LPA at birth (mm) (B), L:R (C), heart rate (beats/min) (D), systolic duration (s) (E) and diastolic duration (s) (F) for prognostic factors with dichotomous outcomes, expressed as RR with 95% CI, left ventricular dysfunction (G), right ventricular dysfunction (H) and severe pulmonary hypertension (I) showed significant differences in survival. The I^2 statistic for heterogeneity ranged from 0% to 84%. LPA, left pulmonary artery; L:R, left:right pulmonary artery ratio; MD, mean difference; RPA, right pulmonary artery; RR, relative risk, M-H - Mantel -Haenszel.

(RR 1.69 (95% CI 1.53 to 1.86), two studies, 2182 participants) showed significant differences in survival. In prognosticating the need for ECMO, LV dysfunction (RR 2.68 (95% CI 1.63 to 4.39), three studies, 1871 participants) and RV dysfunction (RR 2.00 (1.44 to 2.77), three studies, 1864 participants) were significant (figure 2).

Some echocardiographic parameters were reported by only one study or data were insufficient to perform a meta-analysis (table 1). Findings from single studies comparing echocardiographic parameters between survivors and non-survivors of infants with CDH are summarised in table 2. Data from single studies showed that the RV systolic duration to diastolic

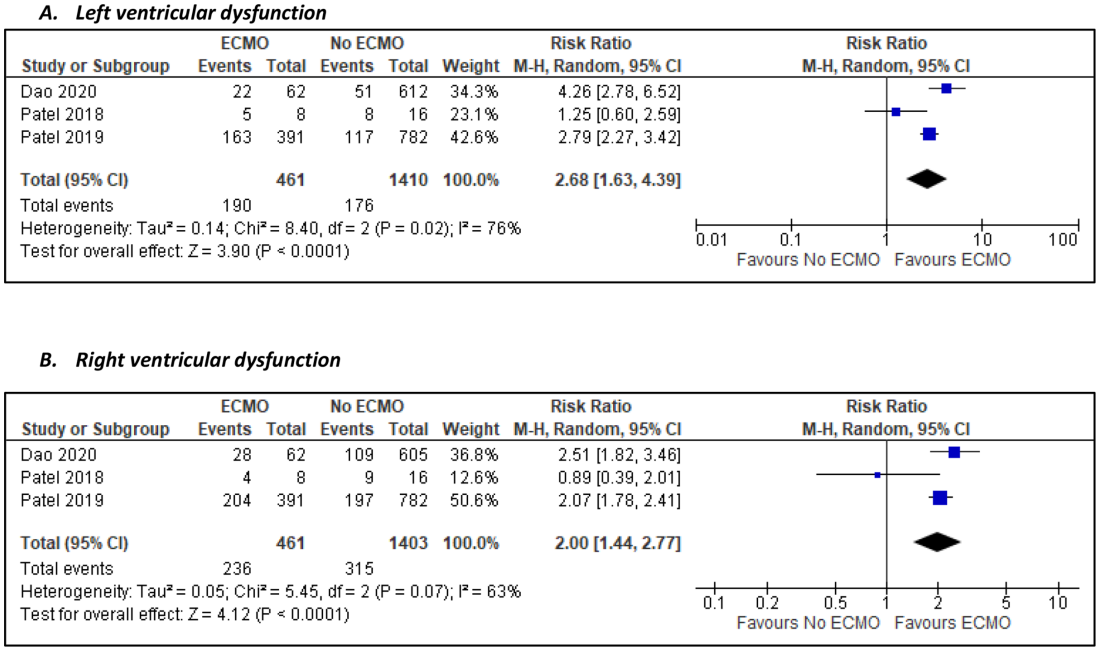

Figure 2 Comparison of prognostic factors for the decision to offer ECMO treatment In prognosticating the need for ECMO, expressed as RR with 95% CI. Left ventricular dysfunction (A) and right ventricular dysfunction (B) were significant. The I^2 statistic for heterogeneity ranged from 10% to 68%. ECMO, extracorporeal membrane oxygenation, M-H - Mantel -Haenszel.

Table 1 Echocardiographic prognostic factors not included in the meta-analysis

Echo parameters	Sample size	Mortality	Decision to offer ECMO treatment	Mortality or decision to offer ECMO treatment	Duration on oxygen or iNO use	Duration of ventilation	Length of stay
LPA diameter[12]	21				CC (−0.69) p=0.009	CC (−0.68) p=0.007	CC (−0.77) p=0.002
RVE′d1−d2[20]	20				CC (−0.84) p=0.0001		CC (−0.75) p=0.002
$PSR_{preoperative}$[20]	20					CC (0.76) p=0.02	CC (0.75) p=0.03
Fetal mitral valve z-score[24]	52		OR=0.43 (95% CI 0.18 to 1.01), p=0.05		iNO use only OR=0.39 (95% CI 0.15 to 1.05), p=0.06		
Fetal aortic valve z-score[24]	52				iNO use only OR=0.32 (95% CI 0.12 to 0.89), p=0.03		
Severity of tricuspid regurgitation ≥mild[31]	95	30-day mortality OR=4.5 (95% CI 1 to 20), p=0.05					
Biventricular dysfunction at early echo[11]	1173	HR=1.59 (95% CI 1.11 to 2.27), p=0.011	OR=5.88 (SE=1.31), p<0.001				
Pulmonary artery capacitance[27]	20	RR=25.8 (95% CI 3.1 to 215.8), p=0.003					
TPV:RVET ≤0.29 vs TPV:RVET >0.29[26]	40			RR=5.88 (95% CI 1.52 to 22.76)			
PDA/RLVTI ≥0.6 vs PDA/RLVTI <0.6[35]	56			OR=33.75 (95% CI 2.04 to 557.64)			
PAAT:ET ≤0.290 vs >0.290[36]	87		RR=4.3, p<0.001				
PAAT:ET ≤0.256 vs >0.256[36]	87	RR=6.0, p<0.001					
List of echo parameters[38]	44		Significantly higher for ECMO patients ► Tricuspid annular plane systolic excursion ► Eccentricity index. ► RV peak global longitudinal systolic. ► RV peak global longitudinal strain rate. ► Left ventricular peak global longitudinal systolic. Significantly lower for ECMO patients Ejection fraction.Fractional area change of right ventricle. Acceleration time to RV ejection time of right ventricular outflow tract. Velocity time integral of RV outflow tract. RV longitudinal size. RV early diastolic strain rate				

CC, correlation coefficient; ECMO, extracorporeal membrane oxygenation; iNO, inhaled nitric oxide; LPA, left pulmonary artery; PAAT:ET, index of the pulmonary artery acceleration time to the right ventricular ejection time; PDA/RLVTI, patent ductus arteriosus flow velocity time integral from right to left; $PSR_{preoperative}$, preoperative pulmonary:systemic peak pressure ratio; RR, relative risk; RV, right ventricular; RVE′d1–2, right ventricular early-diastolic myocardial velocity averaged on days 1 and 2 of life; TPV:RVET, time to peak velocity:right ventricular ejection time ratio.

Table 2 Echocardiographic prognostic factors comparing survivors versus non-survivors in CDH

Echo parameter	Studies (n)	Participants (n)	Summary estimates, mean (SD), P value
SD:DD (RV systolic to diastolic duration)	1[17]	56	1.23 (0.28) vs 1.55 (0.17), p=0.002
LV cardiac index	1[18]	34	4.4 (1.5) vs 2.9 (1.4), p=0.01
Eccentricity index (systole)	1[18]	34	0.71 (0.15) vs 0.58 (0.13), p=0.05
LV MPI	1[18]	34	0.47 (0.14) vs 0.62 (0.16), p=0.005
RV MPI	1[18]	34	0.43 (0.17) vs 0.66 (0.25), p=0.005
RVE'*	1[20]	16	4.4 (1.8) vs 5.8 (1.0) vs 3.0 (1.4), p=0.001
PSR (pulmonary:systemic peak pressure ratio)–preoperative*	1[20]	16	0.69 (0.24) vs 0.5 (0.2) vs 0.9 (0.1), p=0.03
Mean RVE', week 1*	1[20]	16	5.2 (2.5) vs 6.6 (2.1) vs 4.1 (2.2), p<0.0001
Mean RVE', week 2*	1[20]	16	4.0 (3.0) vs 7.0 (2.6) vs 3.6 (2.8), p=0.013
Severity of pulmonary hypertension†	1[22]	140	0.87 (0.81 to 0.94) vs 0.83 (0.75 to 0.91) vs 0.8 (0.72 to 0.88), (p<0.001)
Aortic valve z-score	1[24]	52	−0.44 (1.04), p<0.01
Mitral valve z-score	1[24]	52	0.10 (1.43), p=0.66
LV short-axis dimension z-score	1[24]	52	−0.89 (1.59), p<0.01
Mean LV end-diastolic diameter (mm)	1[25]	62	15.00 (1.19) vs 10.75 (0.42), p<0.001
sPAPecho (mm Hg)	1[25]	62	41.8 (15.0) vs 70.50 (7.20), p<0.001
dPAPecho (mm Hg)	1[25]	62	12.94 (2.48) vs 19.07 (1.52), p<0.001
Tricuspid regurgitation (m/s)	1[25]	62	2.91 (0.52) vs 4.00 (0.22), p<0.001
Pulmonary regurgitation (m/s)	1[25]	62	1.25 (0.22) vs 1.75 (1.17), p<0.001
RV velocity time integral (mL)	1[27]	20	12.3 (3.2) vs 9 (3.1), p=0.02
Pulmonary artery capacitance in ($mL^3 \times mm\ Hg^{-1}$)	1[27]	20	0.3 (0.2) vs 0.18 (0.07), p=0.002

*All survivors vs Duration of respiratory support (DRS) <21 days vs DRS ≥21 days.
†Values reported are Area under receiver operating characteristic curve (AUROC) (SD) and compared between three groups (death vs death or prolonged intubation (>28 days) vs death or prolonged respiratory support >56 days).
dPAPecho, diastolic pulmonary artery pressure on conventional echocardiography; LV, left ventricular; MPI, Myocardial Perfusion Index; RV, right ventricular; RVE', right ventricular early-diastolic myocardial velocity; SD:DD, systolic duration to diastolic duration ratio; sPAPecho, Systolic pulmonary artery pressure on conventional echocardiography.

duration ratio (SD:DD),[17] LV cardiac output index, diastolic and systolic eccentricity index, and LV and RV myocardial performance index[18] predict the decision to offer ECMO treatment and mortality. In other studies, severity of PH at 2 weeks of life correlated with mortality[22]; mean left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD) were significantly higher in survivors[25]; and RV outflow tract velocity time integral velocity time integral (RVOT-VTI) of >10.5 mL and pulmonary artery capacitance (PAC) of >0.24 $mL^3 \times mm\ Hg$ predicted survival.[27] The timing of assessment may be of importance in prognostication; in 18 of the included studies, echo was performed in the first 7 days of age, of which most (17 studies) were in the first 48 hours of age. Four studies reported fetal echocardiographic parameters with or without postnatal echocardiograms, and in six studies, the timing of echo was unclear. Structural dimensions, such as LPA and RPA diameters, are more predictive at birth,[13 15 16] while functional parameters like assessment of PH[22] and ventricular function may vary, depending on many factors, such as gestational age, severity of CDH and anatomical and physiological changes pre-repair and post repair of the CDH. Lusk *et al* evaluated a retrospective cohort of 140 infants with CDH (84% left-sided) and >1 echo and found that severity of PH at 2 weeks of life correlated with mortality (area under the curve (AUC)=0.87, 95% CI 0.81 to 0.94, p<0.001) and adverse respiratory outcome, including prolonged intubation/home oxygen (AUC=0.80–0.83, 95% CI 0.72 to 0.91, p<0.001).[22] In their evaluating left-sided heart structures in 52 patients with CDH, Kailin *et al* found association with increased mortality and iNO use.[24] Of the early (<24 hours of life) comparison of echocardiographic measurements in 35 patients with CDH and 27 healthy newborns, mean LVEDD and LVESD were found to be significantly lower and tricuspid regurgitation (TR) was significantly higher in the CDH group than in controls and between survivors and non-survivors (p<0.001 for both, respectively).[25] An LVEDD of <11 mm (95% CI 88 to 100) and TR of >3.5 m/s (95% CI 73 to 98) were associated with poor prognosis. In their study of 20 infants with CDH, Nagiub *et al* found an RVOT VTI of >10.5 mL and PAC of >0.24 $mL^3 \times mm\ Hg$ were useful in differentiating survivors from non-survivors.[27] Of these, in a study of 29 infants with CDH with 27 controls, the RV SD:DD was evaluated and proposed as a simple prognostic marker of survival and/or decision to offer ECMO treatment; at a cut-off of 1.3, SD:DD had a sensitivity of 92.8% (95% CI 64% to 99%) and a specificity of 61.5% (95% CI 32% to 85%).[17] In another study of a total of 34 consecutive infants with CDH (70% left-sided) with 35 controls, the same investigators evaluated and found LV cardiac output index, diastolic and systolic eccentricity index and LV and RV myocardial performance index were all significantly associated with decision to offer ECMO treatment and death.[18] Altit *et al* compared patients with CDH who needed ECMO (n=15) with those who did not (n=29) and reported decreased LV and RV functions and output and higher RV eccentricity index in those who required ECMO.[38]

DISCUSSION

To our knowledge, this is the first systematic review of echocardiographic prognostic factors predicting survival and decision to offer ECMO treatment in infants with CDH as per recommended guidelines.[8] Of the 28 included studies, all but two studies had a low risk of bias.[10] Two studies were assessed to

have moderate to high risk of bias as they were only reported in abstract format, and we were unable to ascertain the details of the reports. Overall, we detected low risk of bias of the included studies using the QUIPS tool. Left-sided CDH is often associated with LV hypoplasia and a combination of RV dysfunction, and LV hypoplasia with pulmonary venous hypertension result in severe PH.[39] LV hypoplasia, severe PH and myocardial dysfunction lead to severe hypoxia, decision to offer ECMO treatment and death.[39]

Meta-analysis was feasible for only five echocardiographic parameters, namely, RPA at birth (mm), LPA at birth (mm), L:R, heart rate (beats/min), systolic duration (seconds) and diastolic duration (seconds). Of these parameters, only the size of the LPA and RPA at birth predicted survival in infants with CDH. We postulate that the size of the pulmonary arteries may correlate with the size of the lung (inversely to pulmonary hypoplasia) and may have implications for prognostication as well as support for fetal intervention, which may ultimately improve fetal lung and pulmonary artery growth.[5] Heart rate and systolic and diastolic durations, which likely represent physiological changes following adaptation to extrauterine life, may rapidly change secondary by postnatal environmental factors. Heart rate and systolic and diastolic durations may not correlate with the size of the lung or the degree of pulmonary hypoplasia and, hence, were not significant in our meta-analysis. Systolic:diastolic ratio may be a better predictor of survival or decision to offer ECMO treatment, but there were insufficient data for meta-analysis.

We included small single-centre cohort studies (n=25, mean sample size 48) and large registry analyses (three studies, sample size mean of 1134). Registry-based studies may answer research questions with more precision than single studies. Registry studies reported broad functional classification (ventricular dysfunction and PH) that are relevant clinically for monitoring and appropriate interventions.[11 32 33] Single studies that could not be included in the meta-analysis report association of RV and LV ventricular dimensions, ventricular output, ventricular dysfunction, myocardial performance, or strain and PH associated with mortality and decision to offer ECMO treatment. Structural dimensions, such as LPA and RPA diameters, are more predictive at birth and may not change with the timing of the echocardiogram, but functional parameters, for example, PH or ventricular dysfunction, may be timing-dependent, which may affect our comparisons between studies. Few studies reported on the correlation between postnatal or fetal echo parameters and conventional markers for CDH severity, for example, size of the defect, degree of liver herniation or expected lung volume measurements (online supplemental eTable 1).

Clinical applicability of our results

We found that the size of the pulmonary arteries, presence of ventricular dysfunction and severe PH were important in prognosticating survival and the decision to offer ECMO treatment. However, many echocardiographic parameters were evaluated at various time points (fetal to evaluation in the first few days of life) by different studies, which point to the knowledge or consensus gap in regarding echo prognostication. Timely and early echocardiograms for parameters including ventricular dysfunction or PH may inform use of medications such as inotropes or iNO or other pulmonary vasodilators.[11 26] Performing an echocardiogram in critically ill newborn infants is not without challenges, as performing the echo may cause and/or increase their haemodynamic instability, and this review outlines the importance of some echo parameters form priorities for future research.

Strengths and limitations of the review

The strengths of the review include following recommended guidelines for performing and reporting prognostic studies (according to standard guidelines).[8] We comprehensively searched for eligible articles with the help of a librarian and derived the most efficient search strategy after many iterations. Two authors selected studies for inclusion, extracted data independently and agreed on conflicts. The methodological quality of the prognostic studies was assessed by the recommended QUIPS tool.[10] Limitations include limited data for meta-analysis and exclusion of some studies because of incomplete reporting. We planned to but could not explore heterogeneity by subgroup or sensitivity analyses due to insufficient data.

CONCLUSIONS

Implications for practice

Our review highlights the prognostic value of structural (RPA and LPA diameter at birth) and functional echocardiographic markers (severity of PH, RV and LV dysfunction). Our review highlights the lack of consensus on which echocardiographic parameters to evaluate and when to evaluate for reliable prognostication.

Implications for research

Well-designed prospective studies are needed that may use the existing registries and study groups of infants with CDH. Research and consensus should focus on the optimal echocardiographic parameters and timing of evaluation for accurate prognostication.

Twitter Mohan Pammi @mohan_pammi

Contributors MP and CJF: guarantors, conceptualised and designed the study. YK and SK: designed the data collection instruments, collected the data, initial analyses. AS: search strategy, data collection. JH: substantial contributions to the analyses and interpretation of the data. JK: data interpretation.

Funding MP was funded by the following extramural source: National Institutes of Health (R03HD098482 and R21HD091718).

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement All data relevant to the study are included in the article or uploaded as supplementary information.

ORCID iDs
Mohan Pammi http://orcid.org/0000-0002-5571-6239
Caraciolo J Fernandes http://orcid.org/0000-0001-5744-3409

REFERENCES

1 Balayla J, Abenhaim HA. Incidence, predictors and outcomes of congenital diaphragmatic hernia: a population-based study of 32 million births in the United States. *J Matern Fetal Neonatal Med* 2014;27:1438–44.
2 Harting MT. Congenital diaphragmatic hernia-associated pulmonary hypertension. *Seminars in Pediatric Surgery* 2017;26:147–53.
3 Grover TR, Rintoul NE, Hedrick HL. Extracorporeal membrane oxygenation in infants with congenital diaphragmatic hernia. *Semin Perinatol* 2018;42:96–103.

4 Ruano R, da Silva MM, Salustiano EMA, *et al*. Percutaneous laser ablation under ultrasound guidance for fetal hyperechogenic microcystic lung lesions with hydrops: a single center cohort and a literature review. *Prenat Diagn* 2012;32:1127–32.
5 Akinkuotu AC, Cruz SM, Abbas PI, *et al*. Risk-Stratification of severity for infants with CDH: prenatal versus postnatal predictors of outcome. *Journal of Pediatric Surgery* 2016;51:44–8.
6 Coleman AJ, Brozanski B, Mahmood B, *et al*. First 24-h SNAP-II score and highest PaCO2 predict the need for ECMO in congenital diaphragmatic hernia. *J Pediatr Surg* 2013;48:2214–8.
7 Snoek KG, Reiss IKM, Greenough A, *et al*. Standardized postnatal management of infants with congenital diaphragmatic hernia in Europe: the CDH Euro Consortium consensus-2015 update. *Neonatology* 2016;110:66–74.
8 Riley RD, Moons KGM, Snell KIE, *et al*. A guide to systematic review and meta-analysis of prognostic factor studies. *BMJ* 2019:k4597.
9 Moher D, Liberati A, Tetzlaff J, *et al*. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009;339:b2535.
10 Hayden JA, van der Windt DA, Cartwright JL, *et al*. Assessing bias in studies of prognostic factors. *Ann Intern Med* 2013;158:280–6.
11 Patel N, Lally PA, Kipfmueller F, *et al*. Ventricular dysfunction is a critical determinant of mortality in congenital diaphragmatic hernia. *Am J Respir Crit Care Med* 2019;200:1522–30.
12 Sokol J, Shimizu N, Bohn D, *et al*. Fetal pulmonary artery diameter measurements as a predictor of morbidity in antenatally diagnosed congenital diaphragmatic hernia: a prospective study. *Am J Obstet Gynecol* 2006;195:470–7.
13 Okazaki T, Okawada M, Shiyanagi S, *et al*. Significance of pulmonary artery size and blood flow as a predictor of outcome in congenital diaphragmatic hernia. *Pediatr Surg Int* 2008;24:1369–73.
14 Al-Hathlol K, Elmahdy H, Nawaz S, *et al*. Perioperative course of pulmonary hypertension in infants with congenital diaphragmatic hernia: impact on outcome following successful repair. *J Pediatr Surg* 2011;46:625–9.
15 Okazaki T, Nakazawa N, Ogasawara Y, *et al*. Increase in fetal pulmonary artery diameters during late gestation is a predictor of outcome in congenital diaphragmatic hernia with liver herniation. *J Pediatr Surg* 2011;46:2254–9.
16 Takahashi T, Koga H, Tanaka T, *et al*. Pulmonary artery size has prognostic value in low birth weight infants with congenital diaphragmatic hernia. *Pediatr Surg Int* 2011;27:847–50.
17 Aggarwal S, Stockman PT, Klein MD, *et al*. The right ventricular systolic to diastolic duration ratio: a simple prognostic marker in congenital diaphragmatic hernia? *Acta Paediatr* 2011;100:1315–8.
18 Aggarwal S, Stockmann P, Klein MD, *et al*. Echocardiographic measures of ventricular function and pulmonary artery size: prognostic markers of congenital diaphragmatic hernia? *J Perinatol* 2011;31:561–6.
19 Madueme PC, Lim FY, Michelfelder E. The modified mcgoon index is no longer a strong predictor of survival in newborns with congenital diaphragmatic hernia. *J Am Soc Echocardiogr* 2014;27:B92.
20 Moenkemeyer F, Patel N. Right ventricular diastolic function measured by tissue Doppler imaging predicts early outcome in congenital diaphragmatic hernia. *Pediatr Crit Care Med* 2014;15:49–55.
21 Steurer MA, Moon-Grady AJ, Fineman JR, *et al*. B-Type natriuretic peptide: prognostic marker in congenital diaphragmatic hernia. *Pediatr Res* 2014;76:549–54.
22 Lusk LA, Wai KC, Moon-Grady AJ, *et al*. Persistence of pulmonary hypertension by echocardiography predicts short-term outcomes in congenital diaphragmatic hernia. *The Journal of Pediatrics* 2015;166:251–256.
23 Aggarwal S, Natarajan G. Echocardiographic measures of pulmonary vascular compliance: novel prognostic markers for congenital diaphragmatic hernia? *J Am Soc Echocardiogr* 2017;30:B11.
24 Kailin JA, Dhillon GS, Maskatia SA, *et al*. Fetal left-sided cardiac structural dimensions in left-sided congenital diaphragmatic hernia-association with severity and impact on postnatal outcomes. *Prenat Diagn* 2017;37:502–9.
25 Karpuz D, Giray D, Celik Y, *et al*. Prognostic markers in congenital diaphragmatic hernia: left ventricular diameter and pulmonary hypertension. *Pediatr Int* 2018;60:122–6.
26 Kipfmueller F, Heindel K, Schroeder L, *et al*. Early postnatal echocardiographic assessment of pulmonary blood flow in newborns with congenital diaphragmatic hernia. *J Perinat Med* 2018;46:735–43.
27 Nagiub M, Klein J, Gullquist S. Echocardiography derived pulmonary artery capacitance and right ventricular outflow velocity time integral on first day of life can predict survival in congenital diaphragmatic hernia. *Progress in Pediatric Cardiology* 2018;48:107–10.
28 Otaño J, Josefkowicz M, Salas G, *et al*. Evolution predictors in congenital diaphragmatic hernia on the first day of life. *Pediatr Res* 2018;84:468–9.
29 Chaudhary J, Shivprasad B, Lakshmi V, *et al*. Analysis of prognostic factors in congenital diaphragmatic hernia in neonates. *J Indian Assoc Pediatr Surg* 2019;24:176–9.
30 Gaffar S, Ellini AR, Ahmad I, *et al*. Left ventricular cardiac output is a reliable predictor of extracorporeal life support in neonates with congenital diaphragmatic hernia. *J Perinatol* 2019;39:648–53.
31 Oh C, Youn JK, Han J-W, *et al*. Predicting survival of congenital diaphragmatic hernia on the first day of life. *World J Surg* 2019;43:282–90.
32 Dao DT, Patel N, Harting MT, *et al*. Early left ventricular dysfunction and severe pulmonary hypertension predict adverse outcomes in "low-risk" congenital diaphragmatic hernia. *Pediatr Crit Care Med* 2020;21:637–46.
33 Ferguson DM, Gupta VS, Lally PA, *et al*. Early, postnatal pulmonary hypertension severity predicts inpatient outcomes in congenital diaphragmatic hernia. *Neonatology* 2021;118:147–54.
34 Massolo AC, Romiti A, Viggiano M, *et al*. Fetal cardiac dimensions in congenital diaphragmatic hernia: relationship with gestational age and postnatal outcomes. *J Perinatol* 2021;41:1651–9.
35 Aggarwal S, Shanti C, Agarwal P, *et al*. Echocardiographic measures of ventricular-vascular interactions in congenital diaphragmatic hernia. *Early Hum Dev* 2022;165:105534.
36 Kipfmueller F, Akkas S, Pugnaloni F, *et al*. Echocardiographic assessment of pulmonary hypertension in neonates with congenital diaphragmatic hernia using pulmonary artery flow characteristics. *J Clin Med* 2022;11:3038.
37 Patel N, Massolo AC, Paria A, *et al*. Early postnatal ventricular dysfunction is associated with disease severity in patients with congenital diaphragmatic hernia. *J Pediatr* 2018;203:400–7.
38 Altit G, Bhombal S, Van Meurs K, *et al*. Ventricular performance is associated with need for extracorporeal membrane oxygenation in newborns with congenital diaphragmatic hernia. *J Pediatr* 2017;191:28–34.
39 Chandrasekharan PK, Rawat M, Madappa R, *et al*. Congenital diaphragmatic hernia-a review. *Matern Health Neonatol Perinatol* 2017;3:6.