Shokr *et al.*
Egyptian Pediatric Association Gazette (2023) 71:10
https://doi.org/10.1186/s43054-023-00157-y

Egyptian Pediatric Association Gazette

RESEARCH

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Echocardiography-directed management of hemodynamically unstable neonates in tertiary care hospitals

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Abstract

Background Hemodynamic instability and inadequate cardiac performance are common in critically ill children. The clinical assessment of hemodynamic status is reliant upon physical examination supported by clinical signs such as heart rate, blood pressure, capillary refill time, and measurement of urine output and serum lactate. Unfortunately, all of these parameters are surrogate markers of cardiovascular well-being, and they provide limited direct information regarding the adequacy of blood flow and tissue perfusion. A bedside point-of-care echocardiography can provide real-time hemodynamic information by assessing cardiac function, loading conditions (preload and afterload), and cardiac output, which makes it an ideal tool for monitoring hemodynamic assessment in neonates and children.

Methods A prospective cross-section study was carried out on all neonates admitted to the NICU of Cairo University Children's Hospital (CUCH) during the period from September 2017 through August 2018 in whom manifestations of hemodynamic instability were elected regardless of gestational age, weight, gender, or type of disease.

Results There is a positive correlation between EF, FS, LVOT, RVOT, LVTI, RVTI, MAPSE, and TAPSE with birth weight. There is a negative correlation between birth weight and either LVO or RVO. In neonates weighted > 1500 g, there is a significant correlation between decreases in longitudinal systolic function of the heart (TAPSE and MAPSE) and either hemodynamic instability or need for echo-directed management, but there is no significant correlation between both in neonates weighted ≤ 1500 g. There is a significant relationship between birth weight and survival "the more the births weight the better survival chance and between complete compliance with ECDM protocol and achieving normal hemodynamic state."

Conclusions Decreases in EF, FS, TAPSE, and MAPSE in low birth weight neonates' ≤ 1500 g are late signs of hemodynamic instability. TAPSE and MAPSE are the earliest parameters noticed to be decreased in hemodynamically unstable neonates > 1500 g even before EF and FS but return to normal values latterly. There is a significant relationship between complete compliance with ECDM protocol and achieving normal hemodynamics. Birth weight of ≤ 1500 g was an independent predictor of mortality regardless of the degree of compliance with the protocol.

Keywords Echocardiography, Hemodynamic assessment, Hemodynamically unstable neonates

Background

The newborn may experience a variety of hemodynamic problems with variable and complex pathophysiology, with limited clinical manifestations at times. This cardiovascular vulnerability stems from specific newborn characteristics such as incomplete myocardial development,

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the presence of fetal shunts, changes in systemic and pulmonary vascular resistance, and, more broadly, the complex hemodynamic changes that occur during the transition to extrauterine life [1].

Despite advances in neonatal intensive care technology, most newborn hemodynamic monitoring is still based on continuous heart rate, blood pressure (BP), acid–base status, urine output, or poorly validated clinical signs such as capillary refill time [2, 3].

While these measures provide important and useful information to clinicians, they are simply variables that are related to tissue perfusion, for which an adequate monitoring method has yet to be developed [4].

Poor perfusion can be caused by the persistence of fetal channels such as the ductus arteriosus, blood loss, immature myocardium, or ischemic damage after hypoxic injury, as well as a symptom of sepsis or underlying heart disease. Because it is not possible to treat all these conditions with the same approach, selecting a specific inotrope requires more information than just a blood pressure reading to target the therapy to the underlying problem. With the availability of bedside assessment tools such as echocardiography, it is clear that we must modify our approach and rely on more objective data before initiating treatment [5].

Echocardiography is one of the emerging technologies that can be used to measure cardiac output in critically ill newborn infants, particularly since the clinical estimation of cardiac output is quite inaccurate [6–8]. Furthermore, echocardiography can be used to assess the mechanisms of circulatory failure and the effectiveness of therapeutic interventions. Neonatologist-performed echocardiography (NPE) can inform clinicians about the possible underlying pathophysiology of the newborn's hemodynamic status and has the potential to improve neonatal intensive care [9–13].

This method is designed to improve clinical judgment, provide a better understanding of active physiological processes, and monitor treatment response. It has been demonstrated that combining clinical examination and bedside echocardiography improves clinical diagnosis and patient management [13].

Targeted neonatal echocardiography (TnECHO) is now used as a standard of care in many NICUs, even if evidence of its beneficial effect on patient outcomes is limited. However, a growing number of prospective studies are highlighting the potential benefits of TnECHO in identifying cardiovascular compromise and guiding neonatal cardiovascular care [14, 15].

Shock is a complex clinical syndrome characterized by the circulatory system's acute failure to maintain adequate tissue and organ perfusion. As a result, body tissues receive insufficient oxygen and nutrient substrates, and metabolic waste product removal is compromised. This causes cellular dysfunction, which can lead to cell death, organ failure, and death [16].

More than blood pressure, cardiac output, and blood flow influence oxygen delivery to tissue. Readings of systolic, diastolic, and mean arterial blood pressure which is usually considered abnormal may not be pathological. Similarly, hypotension is not synonymous with shock; rather, it is a feature that emerges in the later stages of shock [16].

The main types of neonatal shock and their causes are as follows [16]:

Hypovolemic shock is caused by acute blood or fluid and electrolyte loss.
Cardiogenic shock is caused by cardiomyopathy, myocardial ischemia, arrhythmias, and heart failure.
The distributive shock is caused by sepsis, vasodilation, myocardial depression, or endothelial injury.
An obstructive shock from tension pneumothorax or cardiac tamponade.
A dissociative shock from severe anemia or methemoglobinemia

As a result, treating all of the above requires more information than just a blood pressure reading, and thus, the selection of a specific inotrope requires more information than just a blood pressure reading to target the therapy to the underlying problem.

Aim of the work

The goal of the study was to estimate the outcome (mortality and morbidity) among hemodynamically unstable neonates, as well as the time to return to hemodynamic stability following the use of ECHO in the management of hemodynamically unstable neonates.

Methods

This prospective cross-sectional study was carried out on all neonates admitted to the NICU of Cairo University Children's Hospital (CUCH) during the period from September 2017 through August 2018 in whom manifestations of hemodynamic instability were detected regardless of gestational age, weight, gender, or type of disease.

Inclusion criteria

Neonates admitted to the NICU of Cairo University Children's Hospital require intervention due to hemodynamic instability, regardless of the type of delivery: cesarian or normal vaginal delivery.

Exclusion criteria

Neonates admitted to the NICU of Cairo University Children's Hospital with the following:

1. Significant intracardiac shunt (VSD)
2. Persistent pulmonary hypertension (PPHN)
3. Complex congenital heart disease
4. Cardiac arrhythmias
5. Genetic or skeletal abnormalities

Data collection plan

- The gestational age was determined according to the New Ballard score [17].
- The neonates were weighed immediately before admission and subdivided according to their birth weight into two groups either ≤ 1500 or > 1500 g.
- Full clinical examination for manifestation or signs of hemodynamic instability and daily thereafter until discharge.
- An echocardiographic assessment was ordered by a neonatologist if manifestations of hemodynamic instability or shock appeared.
- Transthoracic color Doppler echocardiography to exclude structural and/or functional abnormality and it was performed and interpreted by a pediatric cardiologist.
- The imaging planes were identified by transducer location (subxiphoid, apical, parasternal, suprasternal notch, and right parasternal). The segmental approach was used to describe all of the major cardiovascular structures in sequence. The evaluation includes wall thickness assessment and quantitation of function.

Neonates enrolled in the study were stratified by echocardiographic values into four subgroups as follows [18]:

a) Neonates with low left ventricular output (LVO) and impaired left ventricular contractility, 5 cases (2 ≤ 1500, 3 > 1500 g).
b) Neonates with low left ventricular output and hypovolemia (under-filled left ventricle), 3 cases (1 ≤ 1500, 2 > 1500 g).
c) Neonates with normal or high left ventricular output without PDA, 22 cases (13 ≤ 1500, 9 > 1500 g).
d) Neonates with normal or high left ventricular output and hemodynamically significant PDA, 22 cases (15 ≤ 1500, 7 > 1500 g).

The plan of management was tailored for each of the previously mentioned subgroups as follows:

1. Neonates with low LVO and impaired left ventricular contractility: dobutamine at a dose of 5–20 μg/kg/min was given, and if no improvement, volume expansion as a single intravenous infusion of 10–20 ml/kg of the crystalloid solution was given. If still no improvement, hydrocortisone at a dose of 1 mg/kg every 4 h was added. If improvement was not achieved, epinephrine was added at a dose of 0.05–2.6 μg/kg/min [18].
2. Neonates with LVO and hypovolemia (under-filled left ventricle): volume expansion as a single intravenous infusion of 10–20 ml/kg of the crystalloid solution was given. If still no improvement, it was repeated [18].
3. Neonates with normal or high LVO without PDA: dopamine at a dose of 5–20 μg/kg/min was given. If no improvement, hydrocortisone at a dose of 1 mg/kg every 4 h was added. If improvement was not achieved, epinephrine was added at a dose of 0.05–2.6 μg/kg/min [18].
4. Neonates with normal or high LVO and hemodynamically significant PDA: PDA was treated either medically or surgically [18].
5. During the current study period, all previously mentioned hemodynamically unstable neonate values were compared to values collected from the controlled group (200 hemodynamically stable neonates).
6. Neonates were monitored daily and subjected to repeated echocardiographic and clinical examinations to detect clinical and laboratory findings suggestive of hemodynamic instability or shock: temperature instability, irritability, cool peripheries, prolonged capillary refill, changes in skin color (mottling, cyanosis, and pallor), a weak pulse, hypotension, tachycardia or bradycardia, lethargy, an increase in serum lactate, elevated liver and renal function tests, and decreased urine output are among the clinical and laboratory findings [16].
7. Before participating in the current study, all neonates' parents provided written consent.

Statistical analysis Data were analyzed using IBM© SPSS© Statistics version 23 (IBM© Corp., Armonk, NY) and MedCalc© version 18.2.1 (MedCalc© Software bvba, Ostend, Belgium). Normally distributed numerical variables were presented as mean and SD, and inter-group differences were compared using the unpaired *t* test.

Skewed numerical data were presented as median and interquartile range, and between-group differences were compared using the Mann–Whitney test. Nominal variables were presented as numbers and percentages and differences were compared using Fisher's exact test. Multivariable binary logistic regression analysis was used to determine the relation between mortality and compliance with echo-directed management protocol as adjusted for birth weight. Cox proportional hazard regression analysis was used to determine the effect of compliance with echo-directed management protocol on patient survival with adjustment for the effect of birth weight as a confounding factor. Two-sided p values < 0.05 were considered statistically significant.

Results

The current study included 252 neonates of both sexes (200 as a control group and 52 as cases) in the NICU of Cairo University Children's Hospital (CUCH) from September 2017 to August 2018.

We attempted to reduce inter-observer and intra-observer variability in data collection by collecting all of our echocardiographic values by the same operator, the same echo machine SonoSite M-Turbo Ultrasound System with transducer P10x/8-4 MHz (6ft/1.8 m), and at the same anatomical site in the same echocardiographic views to be more accurate in our study.

There were no available birth weight-specific references for echocardiographic values in Egyptian neonates. As a result, we created a birth weight-specific reference for (EF, FS, LVO, LOVT, LVTI, MAPSE, RVO, RVOT, RVTI, and TAPSE) in our study based on echocardiographic values collected from the control group (200 hemodynamically stable neonates) during the current study period.

Control group ($n = 200$)

Distribution of birth weight-specific reference interval

The distribution of centiles of EF (%) (ejection fraction), FS (%) (fractional shortening), LVO (ml/kg/min) (left ventricular output), LVOT (cm^2) (left ventricular outflow tract diameter), LVTI (left flow tract velocity time integral), MAPSE (mitral annular plane systolic excursion), RVO (right ventricular output), RVOT (cm^2) (right ventricular outflow tract diameter), RVTI (right flow tract velocity time integral), and TAPSE (tricuspid annular plane systolic excursion) in control group according to birth weight (Supplementary Tables 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 and Figs. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10).

Case group vs. control group

As shown in Table 1, there was a statistically significant difference at baseline in GA (gestational age), BW (birth weight), HR (heart rate), LVOT (left ventricular outflow tract diameter), LVO (left ventricular output), RVOT (right ventricular outflow tract diameter), RVTI (right flow tract velocity time integral), RVO (right ventricular

Table 1 Comparison of echocardiography-directed management (ECDM) and control groups at baseline

Variable	ECDM ($n = 52$)		Control ($n = 200$)		Difference	95% CI	*P* value*
	Mean	SD	Mean	SD			
GA (week)	31.40	3.08	37.52	2.12	6.12	5.40 to 6.84	**< 0.0001**
BW (kg)	1.47	0.52	2.71	0.69	1.24	1.04 to 1.44	**< 0.0001**
HR (bpm)	144.06	18.75	133.19	14.93	− 10.87	− 15.71 to − 6.03	**< 0.0001**
LVOT (cm^2)	0.35	0.05	0.39	0.05	0.05	0.03 to 0.06	**< 0.0001**
LVTI	11.48	3.04	11.31	1.48	− 0.17	− 0.76 to 0.41	0.559
LVO (ml/kg/min)	422.76	155.26	227.97	50.52	− 194.79	− 220.42 to − 169.17	**< 0.0001**
RVOT (cm^2)	0.36	0.06	0.39	0.05	0.03	0.02 to 0.05	**< 0.0001**
RVTI	11.18	3.23	12.18	1.59	0.99	0.37 to 1.62	**0.002**
RVO (ml/kg/min)	426.28	162.12	245.77	56.21	− 180.51	− 207.81 to − 153.22	**< 0.0001**
FS (%)	33.71	4.56	33.87	3.23	0.15	− 0.95 to 1.25	0.784
EF (%)	66.22	7.07	66.05	4.41	− 0.18	− 1.75 to 1.40	0.827
TAPSE (cm)	0.69	0.14	0.89	0.12	0.21	0.17 to 0.25	**< 0.0001**
MAPSE (cm)	0.45	0.08	0.56	0.06	0.11	0.09 to 0.13	**< 0.0001**

GA gestational age, *BW* birth weight, *HR* heart rate, *LVOT* left ventricular outflow tract diameter, *LVTI* left flow tract velocity time integral, *LVO* left ventricular output, *RVOT* right ventricular outflow tract diameter, *RVTI* right flow tract velocity time integral, *RVO* right ventricular output, *FS* fractional shortening, *EF* ejection fraction, *TAPSE* tricuspid annular plane systolic excursion, *MAPSE* mitral annular plane systolic excursion

Data are the mean and standard deviation (SD)

95% CI = 95% confidence interval

* Unpaired *t* test

The significance in (*GA*, *BW*, *HR*, *LVOT*, *LVO*, *RVOT*, *RVTI*, *RVO*, *TAPSE*, *MAPSE*)and it's *P*-value

output), TAPSE (tricuspid annular plane systolic excursion), MAPSE (mitral annular plane systolic excursion) (*P* value = < 0.0001, < 0.0001, < 0.0001, < 0.0001, < 0.0001, < 0.0001, 0.002, < 0.0001, < 0.0001, and < 0.0001, respectively).

As shown in Table 2, in the cohort of patients with birth weight ≤ 1500 g (subgroup A) at baseline, there was a statistically significant difference between the echocardiography-directed management and control group in GA (gestational age), BW (birth weight), HR (heart rate), LVOT (left ventricular outflow tract diameter), LVO (left ventricular output), RVOT (right ventricular outflow tract diameter), RVO (right ventricular output), and FS (%) (fractional shortening) (*P* value = < 0.0001, < 0.0001, 0.094, 0.007, < 0.0001, 0.005, 0.0001, 0.038, respectively).

As shown in Table 3, in the cohort of patients with birth weight > 1500 g at baseline, there was a statistically significant difference in GA (gestational age), BW (birth weight), HR (heart rate), LVOT (left ventricular outflow tract diameter), LVTI (left flow tract velocity time integral), LVO (left ventricular output), RVO (right ventricular output), TAPSE (tricuspid annular plane systolic excursion), MAPSE (mitral annular plane systolic excursion) (*P* value = < 0.0001, < 0.0001, 0.003, 0.024, 0.038, < 0.0001, < 0.0001, < 0.0001, and < 0.0001, respectively).

As shown in Table 4, there was a statistically significant difference in HR (heart rate), LVOT (left ventricular outflow tract diameter), LVO (left ventricular output), RVOT (right ventricular outflow tract diameter), and RVO (right ventricular output) between the echocardiography-directed management group after treatment and the control group in the cohort of patients with birth weight ≤ 1500 g (*P* value = 0.015, 0.023, 0.0001, 0.010, and 0.0001, respectively).

As shown in Table 5, in the cohort of patients with birth weights greater than 1500 g, there was a statistically significant difference in HR (heart rate), LVO (left ventricular output), FS (%) (fractional shortening), EF (%) (ejection fraction), TAPSE (tricuspid annular plane systolic excursion), and MAPSE (mitral annular plane systolic excursion) after treatment (*P* value = 0.0001, < 0.0001, < 0.0001, 0.014, 0.006, 0.0001, and 0.0008, respectively) (Figs. 1, 2 and 3).

As shown in Table 6, after adjustment for the confounding effect of the other covariate, neither birth weight (hazard ratio = 1.270, 95% CI = 0.666 to 2.421, *P* value = 0.469) nor compliance with the protocol (hazard ratio = 0.726, 95% CI = 0.392 to 1.347, *P* value = 0.310) was an independent predictor for survival time Fig. 4.

Discussion

During the study period, 252 neonates were enrolled, 52 of whom had hemodynamic instability with a mean gestational age of 31.40 ± 3.08 weeks and a mean birth

Table 2 Comparison of echocardiography-directed management (ECDM) and control groups in the cohort of patients with birth weight ≤ 1500 g at baseline

Variable	BW ≤ 1500 g				Difference	95% CI	*P* value*
	ECDM (*n* = 31)		Control (*n* = 15)				
	Mean	SD	Mean	SD			
GA (week)	29.39	1.69	32.93	2.58	3.55	2.27 to 4.82	**< 0.0001**
BW (kg)	1.10	0.17	1.37	0.11	0.27	0.17 to 0.36	**< 0.0001**
HR (bpm)	144.52	21.03	133.27	20.66	− 11.25	− 24.51 to 2.01	**0.094**
LVOT (cm^2)	0.32	0.04	0.28	0.04	− 0.04	− 0.06 to − 0.01	**0.007**
LVTI	10.92	2.28	10.06	1.15	− 0.86	− 2.13 to 0.40	0.177
LVO (ml/kg/min)	474.09	152.10	277.26	63.96	− 196.83	− 279.82 to − 113.84	**< 0.0001**
RVOT (cm^2)	0.33	0.05	0.28	0.05	− 0.05	− 0.08 to − 0.02	**0.005**
RVTI	10.77	2.44	10.99	1.27	0.22	− 1.1453 to 1.58	0.751
RVO (ml/kg/min)	479.37	154.13	303.08	74.62	− 176.29	− 261.45 to − 91.12	**0.0001**
FS (%)	34.37	3.75	31.97	3.03	− 2.41	− 4.67 to − 0.14	**0.038**
EF (%)	67.52	5.84	64.00	4.77	− 3.52	− 7.05 to 0.02	0.051
TAPSE (cm)	0.64	0.08	0.65	0.08	0.01	− 0.04 to 0.07	0.664
MAPSE (cm)	0.42	0.06	0.43	0.06	0.01	− 0.03 to 0.05	0.586

GA gestational age, *BW* birth weight, *HR* heart rate, *LVOT* left ventricular outflow tract diameter, *LVTI* left flow tract velocity time integral, *LVO* left ventricular output, *RVOT* right ventricular outflow tract diameter, *RVTI* right flow tract velocity time integral, *RVO* right ventricular output, *FS* fractional shortening, *EF* ejection fraction, *TAPSE* tricuspid annular plane systolic excursion, *MAPSE* mitral annular plane systolic excursion

Data are mean and standard deviation (SD)

95% CI = 95% confidence interval

* Unpaired *t* test

The significance in (*GA*, *BW*, *HR*, *LVOT*, *LVO*, *RVOT*, *RVO*, *FS*) and it's *P*-value

Table 3 Comparison of echocardiography-directed management (ECDM) and control groups in the cohort of patients with birth weight > 1500 g at baseline

Variable	BW > 1500 g				Difference	95% CI	*P* value*
	ECDM (*n* = 21)		Control (*n* = 185)				
	Mean	SD	Mean	SD			
GA (week)	34.38	2.06	37.89	1.58	3.51	2.77 to 4.25	**< 0.0001**
BW (kg)	2.01	0.38	2.82	0.59	0.81	0.55 to 1.07	**< 0.0001**
HR (bpm)	143.38	15.25	133.18	14.44	− 10.20	− 16.80 to − 3.61	**0.003**
LVOT (cm^2)	0.39	0.04	0.40	0.03	0.02	0.002 to 0.03	**0.024**
LVTI	12.29	3.79	11.41	1.46	− 0.88	− 1.70 to − 0.05	**0.038**
LVO (ml/kg/min)	349.44	130.85	223.97	47.28	− 125.47	− 153.06 to − 97.87	**< 0.0001**
RVOT (cm^2)	0.40	0.05	0.40	0.03	0.00	− 0.02 to 0.02	0.998
RVTI	11.77	4.09	12.27	1.57	0.50	− 0.39 to 1.40	0.269
RVO (ml/kg/min)	356.45	151.55	241.12	52.00	− 115.08	− 146.98 to − 83.19	**< 0.0001**
FS (%)	32.80	5.46	34.02	3.20	1.22	− 0.36 to 2.80	0.130
EF (%)	64.43	8.30	66.21	4.36	1.78	− 0.44 to 4.001	0.115
TAPSE (cm)	0.76	0.18	0.91	0.10	0.16	0.11 to 0.21	**< 0.0001**
MAPSE (cm)	0.48	0.08	0.57	0.05	0.08	0.06 to 0.11	**< 0.0001**

GA gestational age, *BW* birth weight, *HR* heart rate, *LVOT* left ventricular outflow tract diameter, *LVTI* left flow tract velocity time integral, *LVO* left ventricular output, *RVOT* right ventricular outflow tract diameter, *RVTI* right flow tract velocity time integral, *RVO* right ventricular output, *FS* fractional shortening, *EF* ejection fraction, *TAPSE* tricuspid annular plane systolic excursion, *MAPSE* mitral annular plane systolic excursion

Data are mean and standard deviation (SD)

95% CI = 95% confidence interval

* Unpaired *t* test

The significance in (*GA*, *BW*, *HR*, *LVOT*, *LVTI*, *LVO*, *RVO*, *TAPSE*, *MAPSE*) and it's *P*-value

Table 4 Comparison of the echocardiography-directed management (ECDM) group after treatment and the control group in the cohort of patients with birth weight ≤ 1500 g

Variable	BW ≤ 1500 g				Difference	95% CI	*P* value*
	ECDM (*n* = 19)		Control (*n* = 15)				
	Mean	SD	Mean	SD			
HR (bpm)	150.68	18.81	133.27	20.66	− 17.42	− 31.24 to − 3.60	**0.015**
LVOT (cm^2)	0.32	0.04	0.28	0.04	− 0.04	− 0.07 to − 0.01	**0.023**
LVTI	10.51	2.11	10.06	1.15	− 0.46	− 1.69 to 0.78	0.458
LVO (ml/kg/min)	468.45	157.72	277.26	63.96	− 191.19	− 279.93 to − 102.45	**0.0001**
RVOT (cm^2)	0.33	0.05	0.28	0.05	− 0.05	− 0.08 to − 0.01	**0.010**
RVTI	11.18	2.19	10.99	1.27	− 0.19	− 1.49 to 1.11	0.770
RVO (ml/kg/min)	513.21	172.05	303.08	74.62	− 210.13	− 307.8 to − 112.50	**0.0001**
FS (%)	33.71	3.66	31.97	3.03	− 1.74	− 4.13 to 0.65	0.148
EF (%)	66.58	5.24	64.00	4.77	− 2.58	− 6.12 to 0.97	0.148
TAPSE (cm)	0.66	0.08	0.65	0.08	− 0.01	− 0.07 to 0.05	0.718
MAPSE (cm)	0.43	0.05	0.43	0.06	0.001	− 0.04 to 0.04	0.970

HR heart rate, *LVOT* left ventricular outflow tract diameter, *LVTI* left flow tract velocity time integral, *LVO* left ventricular output, *RVOT* right ventricular outflow tract diameter, *RVTI* right flow tract velocity time integral, *RVO* right ventricular output, *FS* fractional shortening, *EF* ejection fraction, *TAPSE* tricuspid annular plane systolic excursion, *MAPSE* mitral annular plane systolic excursion

Data are mean and standard deviation (SD)

95% CI = 95% confidence interval

* Unpaired *t* test

The significance in (*HR*, *LVOT*, *LVO*, *RVOT*, *RVO*) and it's *P*-value

Table 5 Comparison of the echocardiography-directed management (ECDM) group after treatment and the control group in the cohort of patients with birth weight > 1500 g

Variable	BW > 1500 g				Difference	95% CI	*P* value*
	Cases post-treatment ($n=14$)		Controls ($n=185$)				
	Mean	SD	Mean	SD			
HR (bpm)	149.00	18.56	133.18	14.44	− 15.82	− 23.89 to − 7.76	**0.0001**
LVOT (cm^2)	0.39	0.04	0.40	0.03	0.02	− 0.002 to 0.04	0.086
LVTI	12.00	2.63	11.41	1.46	− 0.59	− 1.44 to 0.27	0.177
LVO (ml/kg/min)	338.90	93.31	223.97	47.28	− 114.92	− 143.13 to − 86.72	**< 0.0001**
RVOT (cm^2)	0.40	0.05	0.40	0.03	0.00	− 0.02 to 0.023	0.702
RVTI	11.87	2.64	12.27	1.57	0.40	− 0.51 to 1.31	0.382
RVO (ml/kg/min)	345.72	96.60	241.12	52.00	− 104.79	− 135.42 to − 74.15	**< 0.0001**
FS (%)	36.16	1.87	34.02	3.20	− 2.14	− 3.86 to − 0.43	**0.014**
EF (%)	69.50	2.38	66.21	4.36	− 3.29	− 5.62 to − 0.96	**0.006**
TAPSE (cm)	0.79	0.13	0.91	0.10	0.12	0.06 to 0.18	**0.0001**
MAPSE (cm)	0.52	0.07	0.57	0.05	0.05	0.02 to 0.07	**0.0008**

HR heart rate, *LVOT* left ventricular outflow tract diameter, *LVTI* left flow tract velocity time integral, *LVO* left ventricular output, *RVOT* right ventricular outflow tract diameter, *RVTI* right flow tract velocity time integral, *RVO* right ventricular output, *FS* fractional shortening, *EF* ejection fraction, *TAPSE* tricuspid annular plane systolic excursion, *MAPSE* mitral annular plane systolic excursion

Data are mean and standard deviation (SD)

95% CI = 95% confidence interval

* Unpaired *t* test

The significance in (*HR*, *LVO*, *RVO*, *FS*, *EF*, *TAPSE*, *MAPSE*) and it's *P*-value

weight of 1.47 ± 0.52 kg, and 200 who were healthy with a mean gestational age of 37.52 ± 2.12 weeks and a mean birth weight of 2.71 ± 0.69 kg.

Low GA, low birth weight, high heart rate, high RVO, and high LVO were all significantly associated with the development of hemodynamic instability and the need for echo-guided management, according to our findings. In neonates weighing more than 1500 g, there was a significant correlation between decreases in longitudinal systolic function of the heart (TAPSE and MAPSE) and hemodynamic instability and the need for echo-directed management, but not in neonates weighing less than 1500 g.

Similar to the current study, Noori et al. found that maintaining hemodynamic homeostasis is especially difficult in very preterm neonates during the complex process of transition to extrauterine life [1].

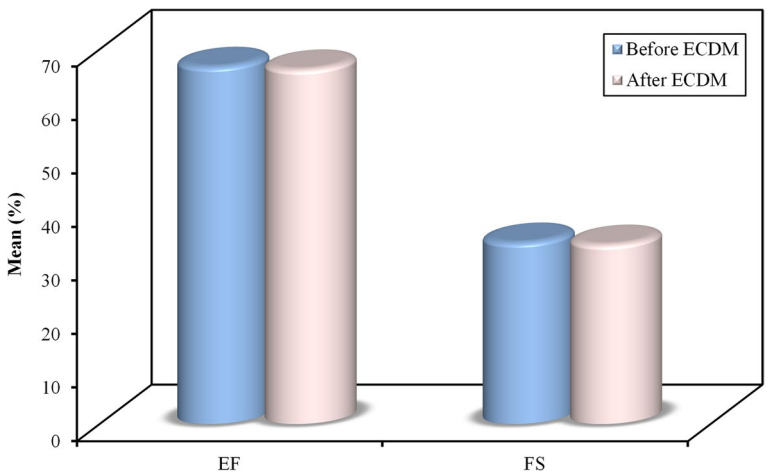

Fig. 1 Compression between the mean of EF and FS before and after ECDM in patients with birth weight ≤ 1500 g

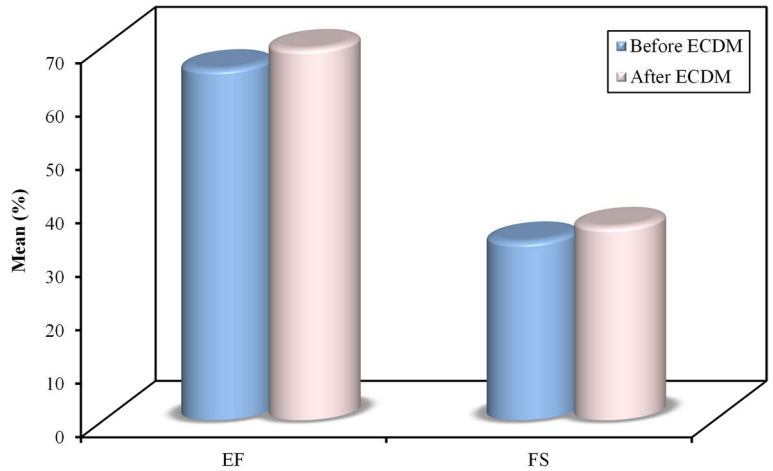

Fig. 2 Compression between the mean of EF and FS before and after ECDM in patients with birth weight > 1500 g

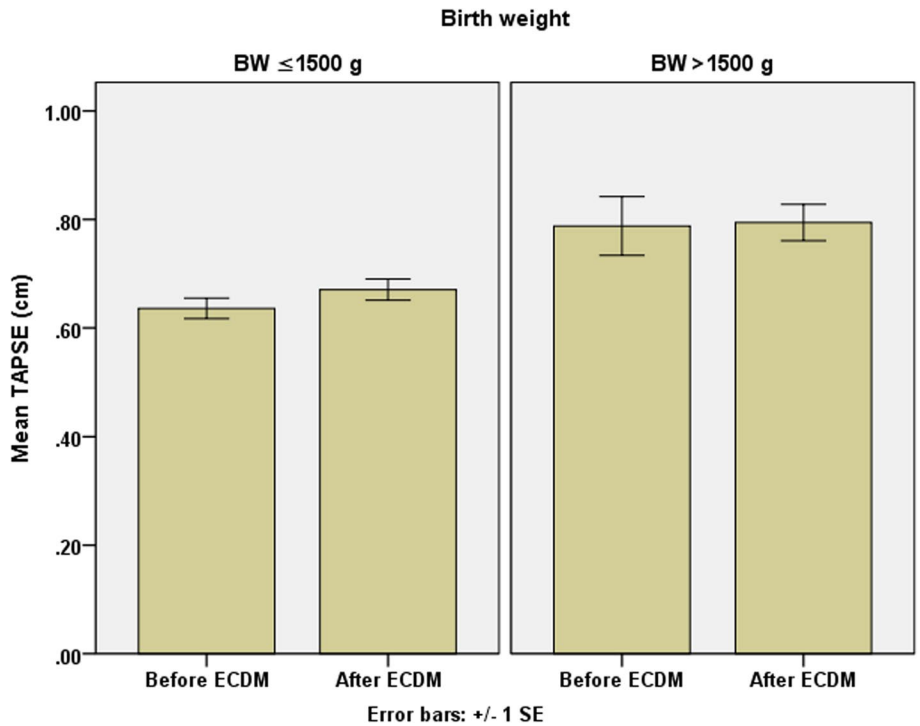

Fig. 3 Mean TAPSE before and after ECDM in patients with birth weight ≤ 1500 g or > 1500 g. Error bars represent the standard error of the mean (SE)

Despite the presence of signs of hemodynamic instability in newborns weighing less than 1500 g, baseline measurements of EF, FS, TAPSE, and MAPSE were similar to those in the control group (before treatment). This led us to believe it was a compensatory mechanism or a late sign. After treatment, these parameters remain unchanged. This gave us an idea of why this group did not respond well to inotropic support.

Similar to our study, Teitel et al. [19] and Geisinger et al. [20] reported that studies on neonatal lambs revealed that markers of myocardial performance are high at baseline [19]. This indicates that the neonatal myocardium is less contractile and operating at or near its physiological capacity. As a result, the ability to respond to additional

Table 6 Cox proportional hazard regression analysis for the relationship between survival time and compliance with echocardiography-directed management protocol as adjusted for birth weight

Covariate	*b*	SE	Wald	*P* value	Hazard ratio	95% CI
Birth weight ≤ 1500 g[a]	0.239	0.329	0.525	0.469	1.270	0.666 to 2.421
Complete compliance with ECDM[b]	−0.320	0.315	1.031	0.310	0.726	0.392 to 1.347

ECDM echocardiography-directed management, *b* regression coefficient, *SE* standard error, *95% CI* 95% confidence interval

[a] Referenced to birth weight > 1500 g

[b] Referenced to partial or no compliance

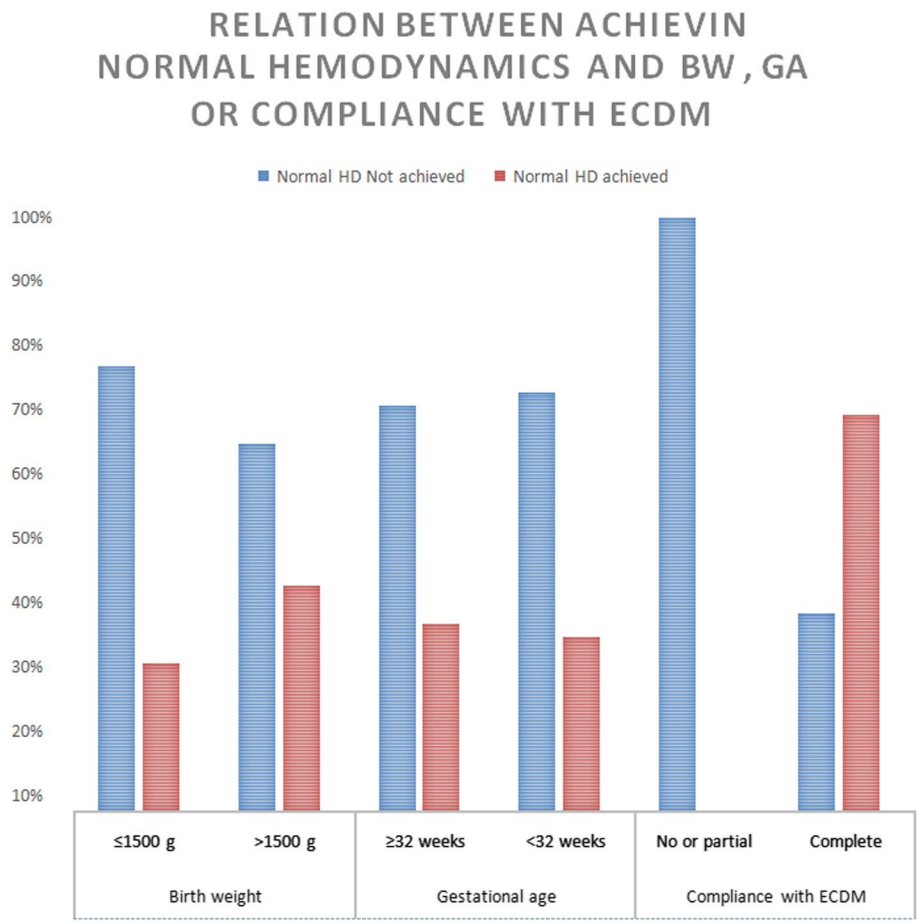

Fig. 4 Relation between the achievement of normal hemodynamics and birth weight, gestational age, or compliance with echocardiography-directed management protocol in the study group. BW birth weight, GA gestational age, ECDM echocardiography-directed management, HD hemodynamics

stress imposed by metabolic demands (for example, infection, changing loading conditions) or inotropes may be limited [20].

When compared to the control group, the appearance of manifestations of hemodynamic instability in neonates weighing more than 1500 g was associated with a decrease in EF, FS, TAPSE, and MAPSE at baseline. After treatment, TAPSE and MAPSE remained below normal in the control group, but EF and FS increased to more normal levels. As a result, we believe TAPSE and MAPSE are indicators of late improvement.

In our study, there was a significant relationship between birth weight and survival: "the greater the birth weight, the better the chance of survival" *P* value = 0.004.

Similar to our findings, Basso et al. [21], McIntire et al. [22], Jeschke et al. [23], Hussain & Tarar [24], and

D'Sa et al. [25] found that low birth weight preterm neonates were more likely to die than term neonates [21–25].

Despite having fewer deaths than the group with no or partial compliance, no significant relationship was found between survival and GA or ECDM protocol compliance. This could be due to the number of cases having decreased.

There was a significant relationship in our study between following the ECDM protocol completely and achieving a normal hemodynamic state (*P* value 0.0001). A normal hemodynamic state was not achieved in any of the cases of no or partial compliance.

Conclusion

1. Decreases in EF, FS, TAPSE, and MAPSE in low birth weight neonates ≤ 1500 g are late signs of hemodynamic instability.
2. TAPSE and MAPSE are the early parameters decreased in hemodynamically unstable neonates > 1500 g even before EF, and FS but return to normal latterly.
3. There is a significant relationship between complete compliance with ECDM protocol and achieving normal hemodynamics.
4. Birth weight ≤ 1500 g was an independent predictor of mortality regardless of the degree of compliance with the protocol.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s43054-023-00157-y.

Additional file 1: Control group(*n*=200):Distribution of birth weight-specific reference interval. **Table S1.** Birthweight-specific reference intervals for the EF(%). **Table S2.** Birthweight-specific reference intervals for the FS(%). **Table S3.** Birthweight-specific reference intervals for the LVO. **Table S4.** Birth weightspecific reference intervals for the LVOT*. **Table S5.** Birthweight-specific reference intervals for the LVTI. **Table S6.** Birthweight-specific reference intervals for MAPSE*. **Table S7.** Birthweight-specific reference intervals for the RVO. **Table S8.** Birthweight-specific reference intervals for the RVOT*. **Table S9.** Birthweight-specific reference intervals for the RVTI. **Table S10.** Birthweight-specific reference intervals for TAPSE. **Figure S1.** Birth weight-specificreference intervals for the EF. **Figure S2.** Birth weight-specificreference intervals for the FS. **Figure S3.** Birth weight-specificreference intervals for the LVO. **Figure S4.** Birth weight-specificreference intervals for the LVOT. **Figure S5.** Birth weight-specificreference intervals for the LVTI. **Figure S6.** Birth weight-specificreference intervals for MAPSE. **Figure S7.** Birth weight-specificreference intervals for the RVO. **Figure S8.** Birth weight-specificreference intervals for the RVOT. **Figure S9.** Birth weight-specificreference intervals for the RVTI. **Figure S10.** Birth weight-specificreference intervals for TAPSE.

Acknowledgements
We would like to thank the patients for participating in this research.

Authors' contributions
AS: software and writing the original draft. RT: supervision and conceptualization. HA: conceptualization and methodology. RE and SA: methodology and resources. The author(s) read and approved the final manuscript.

Funding
None.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
No. of approval: I-051016, Committee Name: Cairo University Faculty of Medicine, Research Ethics, Mobile: 01003657120, E-Mail: kasralainirec@gmail.com.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Received: 23 August 2022 Accepted: 25 January 2023
Published online: 06 March 2023

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