

# Role of Echocardiography in Initiating and Predicting The Length of Inhaled Nitric Oxide Therapy in Near and Full Term Newborns with PPHN

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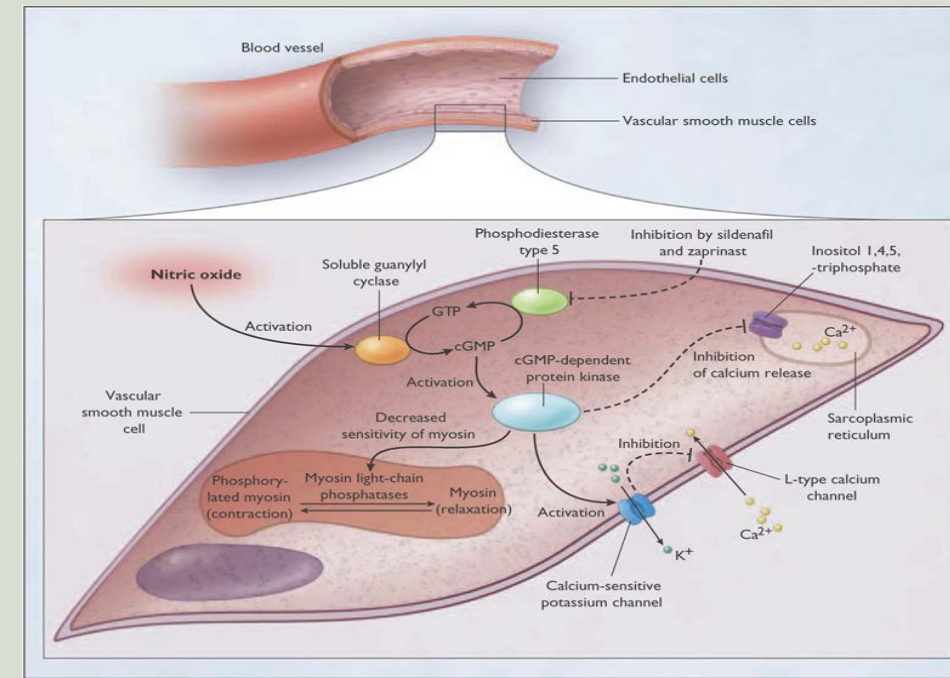
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## Background

- Persistent pulmonary hypertension of the newborn (PPHN) is a condition of acute respiratory failure in newborns. It is characterized by systemic hypoxemia (in the absence of cyanotic congenital heart disease) due to:
  - \*Increased pulmonary vascular resistance
  - \*Intra-pulmonary shunting
  - \*Extra-pulmonary shunting: PDA, atrial septum
- Inhaled nitric oxide (iNO) improves oxygenation, and reduces the need for ECMO in PPHN.
- It activates guanylate cyclase, which increases cyclic-GMP levels, consequently causing vascular smooth muscle relaxation.
- The echocardiogram estimates pulmonary arterial pressures, cardiac function/anomalies, and direction of the shunt across the patent ductus and the atrial septum.



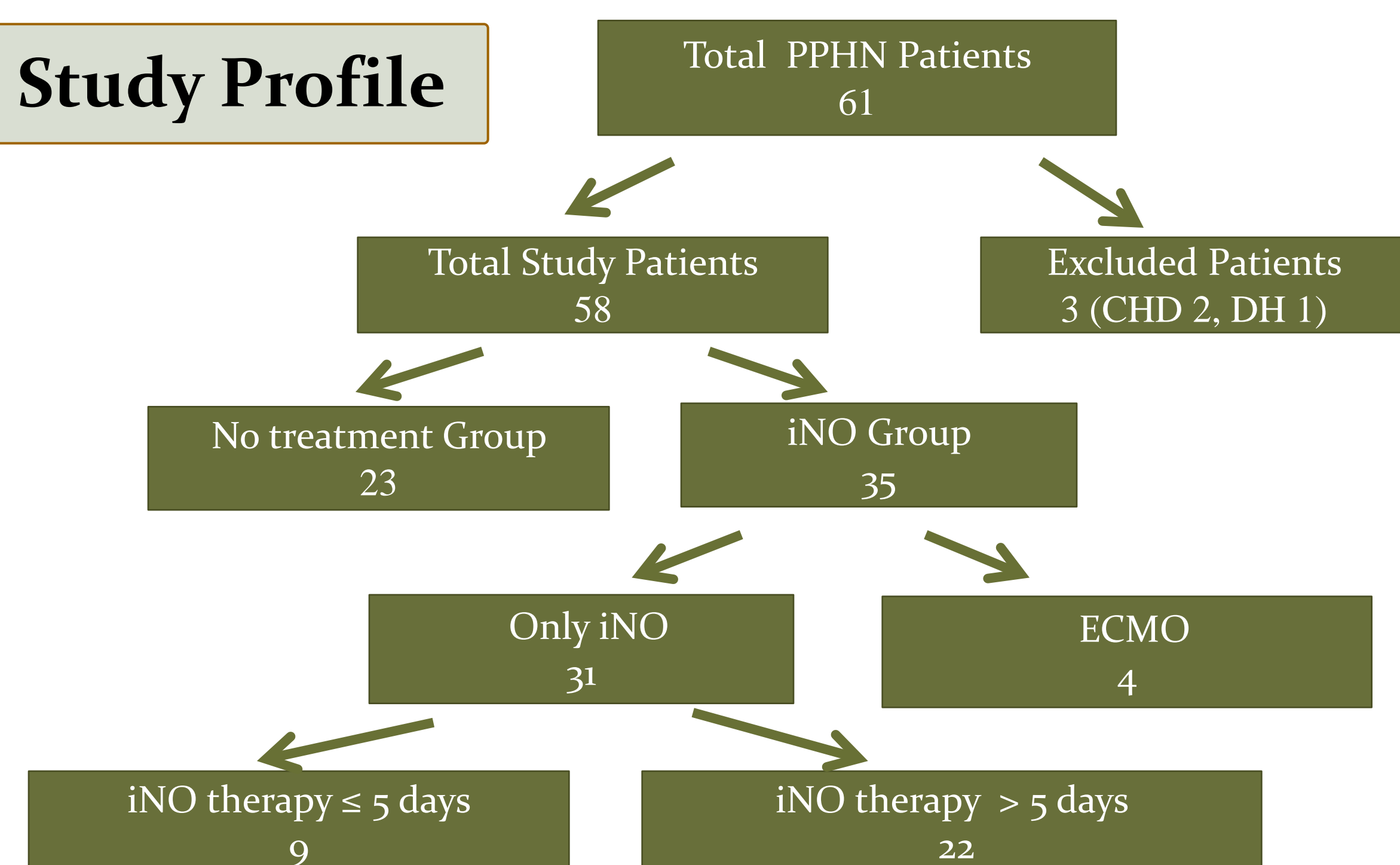
## Objective

The goal of this study is to identify the role of echocardiography in initiating and predicting the duration of iNO therapy in near and full term newborns with PPHN.

## Design/Methods

- It is a retrospective study over a 7-year period: Jan 2005 – May 2012 (in Sparrow Hospital Regional Neonatal Intensive Care unit (RNICU)).
- PPHN Criteria:**
  - Newborns with hypoxic respiratory failure who needed mechanical ventilator.
  - Echocardiographic finding of Bidirectional or R-L shunt at PDA or atrial defect.
- Eligibility Criteria:**
  - Newborns  $\geq 35$  weeks gestational age (GA).
  - Diagnosis of PPHN requiring mechanical ventilation.
  - Echocardiogram during the first week of life.
- Exclusion criteria:**
  - Newborns with diaphragmatic hernia or CHD.
- RNICU Protocol for Initiation of iNO:**
  - Post ductal PaO<sub>2</sub> < 70 mmHg in FiO<sub>2</sub> of 100%.
  - Oxygenation index (OI) > 15 & Alveolar-arterial gradient (AaDO<sub>2</sub>) > 500 measured twice at least 15 minutes apart.
  - Echocardiogram before iNO initiation to exclude CHD.
- ECMO is considered when OI is > 40 or AaDO<sub>2</sub> > 610.
- A cardiologist, blinded to the clinical data, interpreted the echocardiograms.
- Patients were divided into: **iNO group** and **No treatment group**.
- The iNO group** were further divided according to the duration of iNO treatment into  **$\geq 5$  days** and  **$\leq 5$  days**.

## Study Profile



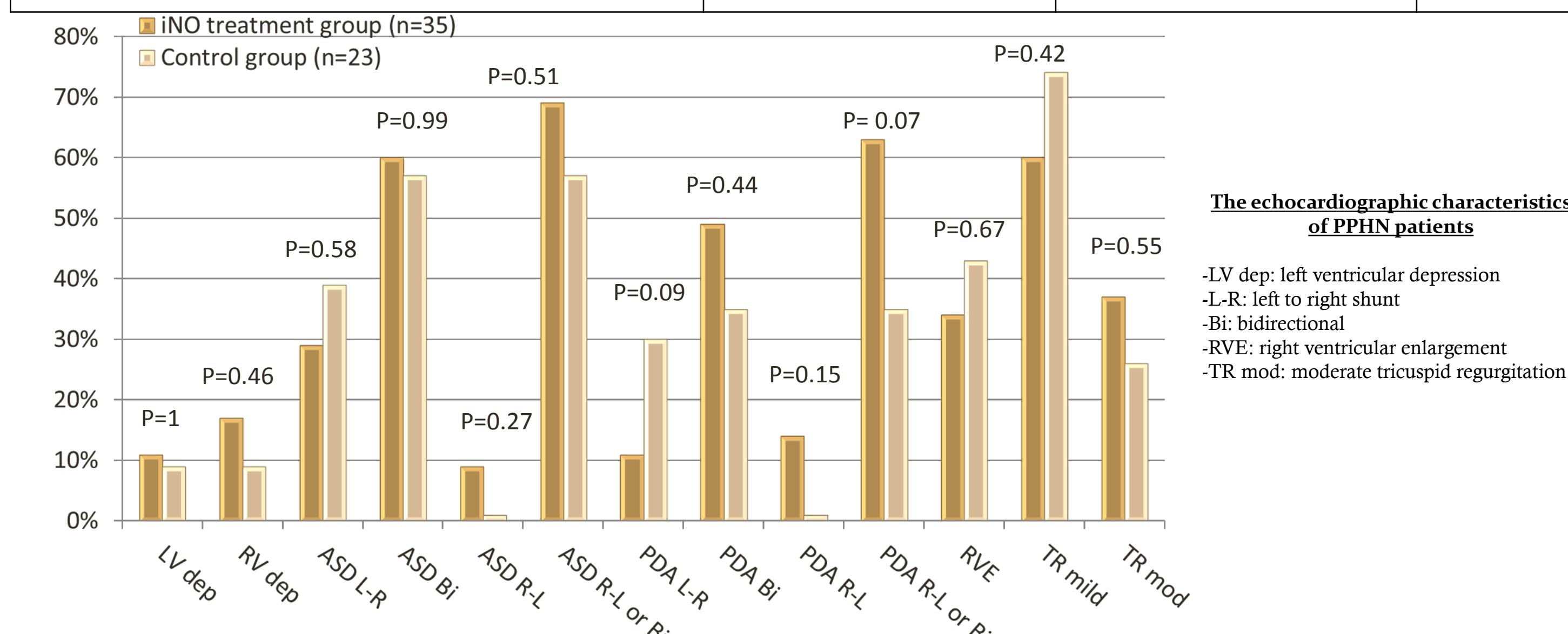
## Results

### Respiratory and cardiovascular support of the infants with PPHN

Characteristics	iNO group (n=35)	No treatment group (n=23)	p value
High Frequency Ventilation	26/35 (74%)	4/23 (17%)	<0.001
Ventilation Days (median 25%-75%)	11(7-14)	5 (4-7)	<0.001
OI (median 25%-75%)	25 (17-42)	10 (7-13)	<0.001
A-a gradient (median 25%-75%)	597(578-610)	532 (473-557)	<0.001
Pressors	33/35 (94%)	16/23 (70%)	0.022

### The echocardiographic characteristics of PPHN patients

Characteristics	iNO group (n=35)	No treatment group (n=23)	p value
TR PG mmHg (mean $\pm$ 1 SD)	50 $\pm$ 15 (18/35)	40 $\pm$ 9 (9/23)	0.07
Systolic BP on the day of echo (mean)	63 $\pm$ 8	57 $\pm$ 7	0.022



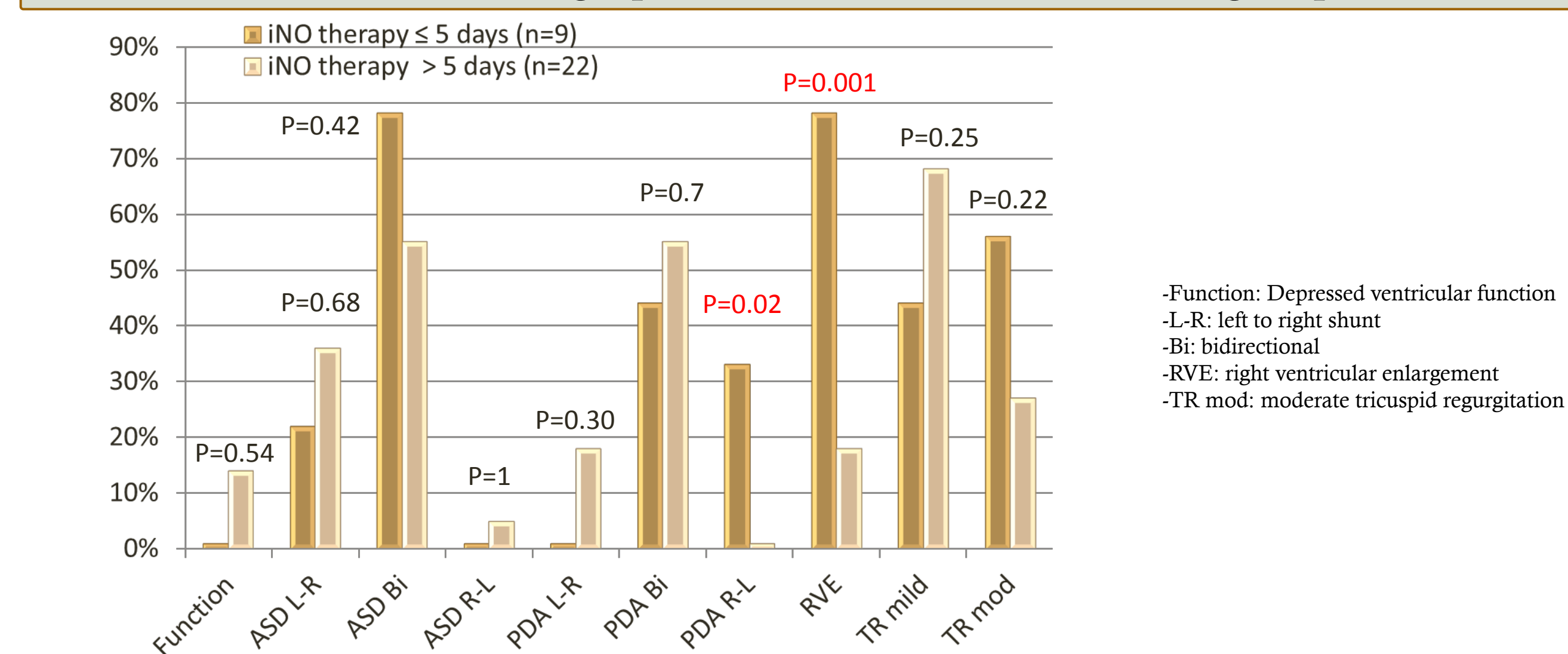
### Univariate analysis of the echocardiographic characteristics of PPHN patients

Characteristics	Odds Ratio	95% Confidence Interval	p value
R-L or Bidirectional shunt at PDA	3.63	1.17-11.22	0.025

### Echo day and iNO start day in the iNO group

	iNO $\leq 5$ days (n=9)	iNO > 5 days (n=22)	p value
Echo day (median 5%-95%)	2 (1-3)	2 (1-3)	0.89
iNO start day (mean)	2 $\pm$ 1	2 $\pm$ 1	0.62

### The clinical and echocardiographic characteristics of the iNO group



## Summary of the Results :

- Statistically **significant** echocardiographic findings in predicting the need for iNO: Presence of either right to left or Bidirectional shunting at the PDA.
- Statistically **non-significant** echocardiographic findings in predicting the need for iNO: PDA shunting: L-R shunt. ASD shunting: L-R, Bidirectional, R-L. Right ventricular enlargement. Depressed ventricular function.
- Statistically **significant** echo findings in predicting shorter duration of iNO treatment: Right to left shunting at the PDA. Right ventricular enlargement.
- Statistically **non-significant** echo findings in predicting shorter duration of iNO treatment: PDA shunting: L-R shunt, Bidirectional. ASD shunting: L-R, Bidirectional, R-L. Depressed ventricular function.

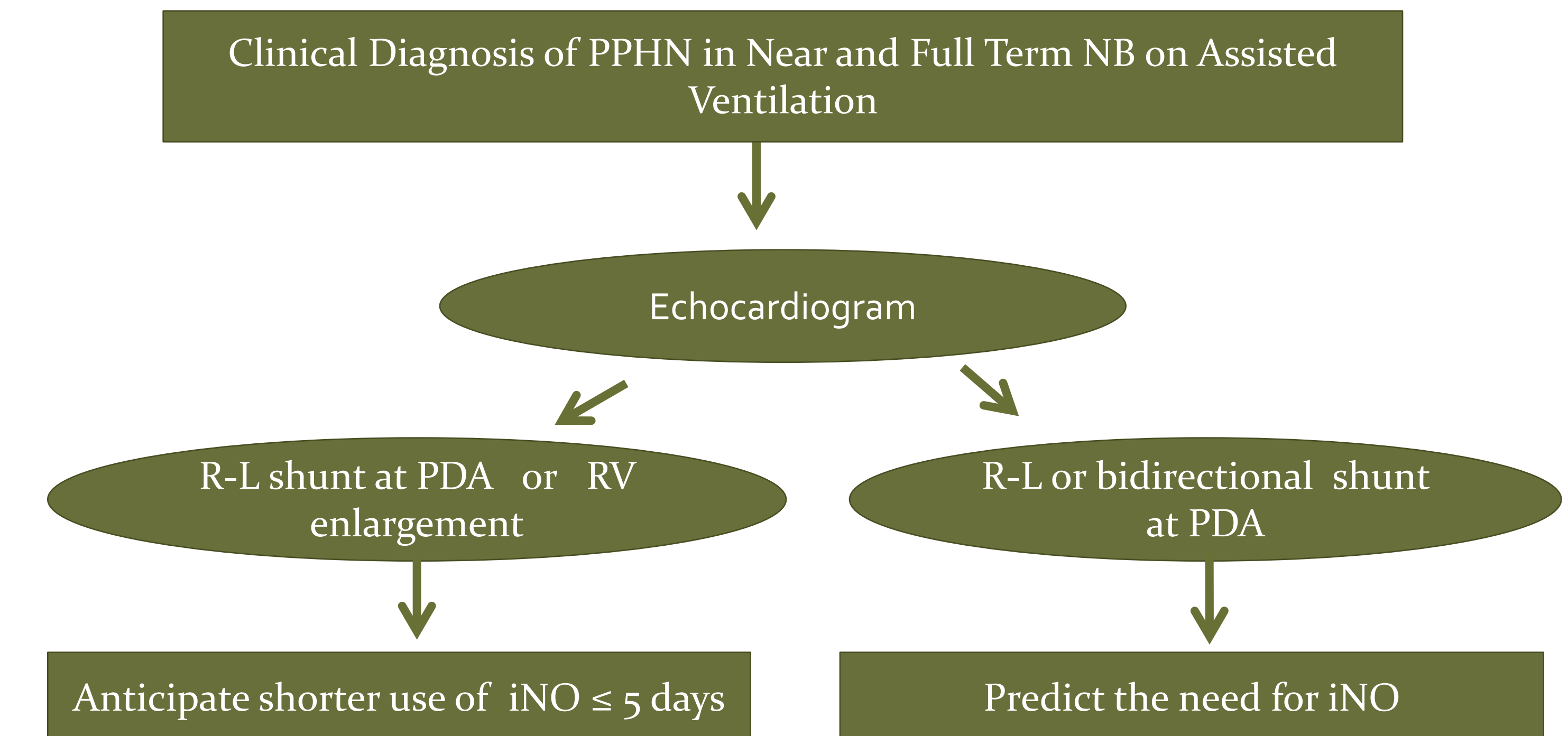
## Conclusion :

- In near and full term newborns with PPHN: Presence of either R-L or Bidirectional shunt at the PDA predicted the need for iNO.
- The presence of R-L shunt at PDA or right ventricular enlargement may help anticipate shorter duration of iNO therapy.

## Discussion:

Finding	Explanation
R-L or Bidirectional shunting at the PDA predicted the need for iNO	R-L and bidirectional ductal shunt are associated with higher pulmonary artery pressure.
R-L shunt at PDA predicted shorter duration of iNO therapy $\leq 5$ days	Prompter response to iNO by reversing of the extrapulmonary shunting.
Atrial Shunt Direction did not predict the need for iNO or the duration of treatment	Atrial flow is susceptible to many confounding factors that can transiently affect the systemic and pulmonary vascular resistance.
Right ventricular enlargement did not predict the need for iNO. It predicted shorter duration of iNO therapy $\leq 5$ days	iNO acutely decreases right ventricular size.

## Practical Application



## Acknowledgements

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