Correlating Pulmonary Hypertension by Echocardiogram with Mortality in Premature Infants

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BACKGROUND

- Pulmonary hypertension is difficult to diagnose and treat in premature infants.
- Cardiac catheterization is the gold standard but is challenging to perform in small, sick, premature infants.
- Data are lacking on the utility of echocardiography for diagnosing pulmonary hypertension and predicting outcomes in these challenging patients.
- We investigated the relationship between pulmonary hypertension diagnosed by echocardiogram and mortality in premature infants.

METHODS

- Echocardiograms from infants born ≤ 28 weeks gestation at two sites were independently read by 3 masked pediatric cardiologists.
- Diagnostic criteria for the presence and severity of pulmonary hypertension were a priori defined (Table 1).
- Demographic characteristics were compared among patients with and without pulmonary hypertension.
- Multivariable logistic regression adjusted for gestational age and gender was used to evaluate the association between pulmonary hypertension and mortality prior to discharge.
- Survival time by group was illustrated with Kaplan-Meier survival curves and compared by Wilcoxon test.

RESULTS

- 483 echocardiograms were reviewed from 49 infants.
- Pulmonary hypertension was diagnosed in 15 (30.6%) infants: 7 classified as moderate and 8 as severe.
- Demographic characteristics including gestational age, birth weight, sex, race, outborn status, C-section rate, APGAR score, antenatal steroid administration, surfactant therapy, and treatment site were similar between groups.
- Odds ratio of mortality prior to hospital discharge adjusted for gestational age and gender was higher in patients with pulmonary hypertension compared to those without (OR=5.56 95% CI 1.05-29.43, p-value 0.044).

RESULTS

Table 1: Pulmonary hypertension composite score of echocardiographic measures

Subjective quantification of RV pressures	Absolute criteria		Supportive criteria	
	Septal geometry in systole	Shunting	RV function	RV / RA size
Normal (< 1/3 systemic)	Septum round Eccentricity index ≤ 1.0	L to R	Normal	Normal
Mildly elevated (1/3-2/3 systemic)	Septal geometry mildly distorted, Eccentricity index 1.01-1.20	L to R	Normal	Mildly dilated
Moderately elevated (≥ 2/3 systemic)	Septum moderately distorted but not flat, Eccentricity index 1.21-1.4	L to R	Mildly depressed	Moderately dilated
Severely elevated (≥ systemic)	Septum flat or bowing into left ventricle, Eccentricity index > 1.4	R to L	≥Moderately depressed	Severely dilated

The presence of pulmonary hypertension was defined by tricuspid regurgitation jet velocity > 3.0 m/s, an estimated right ventricular systolic pressure / systolic blood pressure ratio ≥ 0.67, or by a composite score of quantitative and qualitative echocardiographic features.
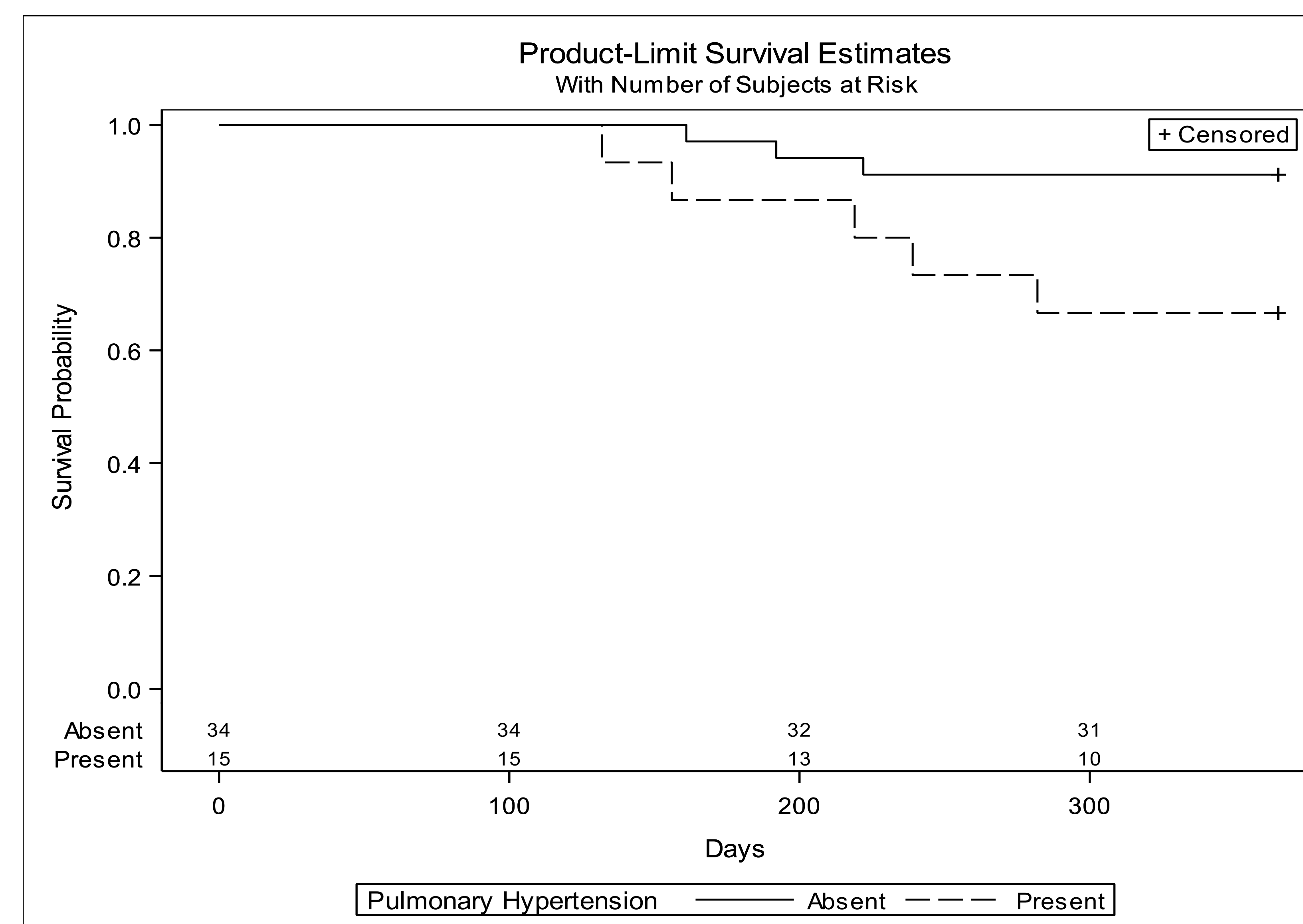

Figure 1. Kaplan-Meier Survival Curve comparing patients with and without pulmonary hypertension. From a total of 49 patients, 15 (30.6%) were diagnosed with pulmonary hypertension on echocardiogram. For those patients with pulmonary hypertension, 10 (66.7%) survived to hospital discharge or one year of age, while 31 (91.2%) without pulmonary hypertension survived to hospital discharge or one year of age. Wilcoxon p = 0.032.

Table 2: Pulmonary hypertension by severity

Characteristic	None/Mild (N=34)	Moderate (N=7)	Severe (N=8)
Gestational Age (weeks)	24.0 (22.0, 28.0)	25.0 (23.0, 26.0)	25.0 (23.0, 27.0)
Birth weight (grams)	670.5 (420.0, 910.0)	720.0 (477.0, 915.0)	570.0 (440.0, 882.0)
Female	18/34 (52.9%)	4/7 (57.1%)	6/8 (75.0%)
Race			
Asian	1/34 (2.9%)	0/7 (0.0%)	0/8 (0.0%)
Black/African American	18/34 (52.9%)	4/7 (57.1%)	5/8 (62.5%)
Other	3/34 (8.8%)	2/7 (28.6%)	0/8 (0.0%)
White/Caucasian	12/34 (35.3%)	1/7 (14.3%)	3/8 (37.5%)
Hispanic/Latino	2/34 (5.9%)	1/7 (14.3%)	0/8 (0.0%)
Outborn	6/34 (17.6%)	1/7 (14.3%)	2/8 (25.0%)
Caesarian Section	20/34 (58.8%)	4/7 (57.1%)	7/8 (87.5%)
5 Minute APGAR	6.0 (1.0, 9.0)	5.0 (3.0, 7.0)	5.5 (3.0, 9.0)
Received Antenatal Steroids	27/34 (79.4%)	5/7 (71.4%)	7/8 (87.5%)
Received Surfactant Therapy	33/34 (97.1%)	6/7 (85.7%)	8/8 (100.0%)
Site			
UNC	19/34 (55.9%)	5/7 (71.4%)	3/8 (37.5%)
Duke	15/34 (44.1%)	2/7 (28.6%)	5/8 (62.5%)
Survival to Hospital Discharge*	31 (91.2%)	7 (100%)	3 (37.5%)

Values presented are counts(%) for categorical variables or median(min, max) for continuous variables. *Wilcoxon p = 0.0002.

CONCLUSIONS

- Echocardiography-diagnosed pulmonary hypertension using a priori defined criteria is associated with an increased risk of death prior to hospital discharge.
- Infants with severe pulmonary hypertension by echocardiogram have significantly reduced survival to hospital discharge.
- Further work defining and staging pulmonary hypertension in infants using prospectively acquired research echocardiograms is warranted.