ESPR Top Science Webinar II

Wednesday, September 23 12:00-1:00 PM EDT

Moderators
Elizabeth Yen, MD – Floating Hospital for Children at Tufts Medical Center

EDT	Abstract	Title	Presenting Author
12:00 PM		Welcome and Introductions	
12:05-12:15 PM	3385989	Resuscitation with an Intact Cord Enhances Pulmonary Vasodilation and Ventilation but Reduces Systemic Oxygen Toxicity and Oxygen Load in a Preterm Ovine Model.	Dr. Praveen Chandrasekharan, University at Buffalo
12:15-12:25 PM	3382580	Phytosterols in Lipid Emulsions Downregulate Expression of 78-kD Glucose-Regulated Protein (GRP78) in Neonatal Rat Lung.	Dr. Naureen Memon, Goryeb Children's Hospital, Atlantic Health System
12:25-12:35 PM	3375141	Banff Inflammatory Indices May Be Superior to the NIH Scoring in Predicting CKD Progression in Lupus Nephritis.	Dr. Minh Dien Duong Children's Hospital at Montefiore
12:35-12:45 PM	3379463	Novel Biomarkers in Autosomal Recessive Polycystic Kidney Disease (ARPKD).	Lindsay Fleischer, Cooper Medical School of Rowan University
12:45-1:00 PM	3385821	Optimal Depth of Chest Compressions Targeting Gas Exchange in Neonatal Cardiac Arrest.	Dr. Vikash Agrawal, University at Buffalo
1:00 PM		Wrap Up	

CONTROL ID: 3385989

TITLE: Resuscitation with an intact cord enhances pulmonary vasodilation and ventilation but reduces systemic oxygen toxicity and oxygen load in a preterm ovine model

DIGITAL OBJECT IDENTIFIER (DOI):

ABSTRACT STATUS: Sessioned

PRESENTER: Praveen Chandrasekharan

AUTHORS/INSTITUTIONS: P. Chandrasekharan, S. Gugino, C. Koenigsknecht, J. Helman, L. Nielsen, M. Rawat, J. Nair, V. Agrawal, Pediatrics, University at Buffalo, Buffalo, New York, UNITED STATES|D. Sankaran, S. Lakshminrusimha, Pediatrics, UC Davis, Sacramento, California, UNITED STATES|

CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal/Infant Resuscitation

ABSTRACT BODY:

Background: Resuscitation with an intact cord in depressed term infants has shown to improve saturation (SpO_2) and Apgar scores (NEPCORD III trial). Initiating resuscitation with 21% oxygen (O_2) has been associated with increased death from respiratory failure in extremely preterm infants (Oei et al Pediatrics 2017). We hypothesized that resuscitation with 30-60% O_2 with an intact cord would promote pulmonary vasodilation, enhance gas exchange but would reduce oxygen load (O_2L) and systemic oxygen toxicity due to continued contribution from umbilical venous flow to left ventricular preload.

Objective: To study the effect of delayed cord clamping with ventilation (DCCV) and early cord clamping with ventilation (ECCV) on O_2 exposure, gas exchange and hemodynamics in an asphyxiated preterm ovine model with RDS.

Design/Methods: Preterm lambs (127-128d) were randomly assigned to DCCV or ECCV. Asphyxia was induced by cord occlusion until the heart rate (HR) was <90 bpm. In DCCV, positive pressure ventilation (PPV) was initiated with an intact cord for 5 min, followed by clamping. In ECCV, the cord was clamped once target HR<90 bpm was achieved and PPV was initiated. Oxygen load per breath was calculated as [$VT*FiO_2$]/kg, where VT is tidal volume and the total O_2L calculated as the summation of breaths for 5 min.

Results: Fifteen asphyxiated preterm lambs were randomized to DCCV (N=7) or ECCV (N=8) (fig 1). The FiO_2 (0.4 (IQR 0.3-0.4) vs. 0.6 (IQR 0.4-0.8), $p<0.01$) and O_2L (520 (IQR 414-530) vs. 775 (IQR 623-868), $p<0.01$) in the DCCV group were significantly lower than ECCV to maintain target SpO_2 (fig 2). Arterial PaO_2 and $PaCO_2$ were significantly lower (fig 3) and systolic pulmonary blood flow was higher with DCCV (fig 4).

Conclusion(s): In an asphyxiated preterm lambs, resuscitation with an intact cord decreased FiO_2 required to achieve NRP recommended target SpO_2. Ventilation was significantly better in DCCV suggesting an active contribution of the placenta for gas exchange. Lower arterial oxygenation and O_2L in the DCCV group along with higher pulmonary blood flow suggests that resuscitation with an intact cord may minimize oxidative injury while facilitating pulmonary vascular transition in asphyxiated preterm infants with RDS.

(no table selected)

IMAGE CAPTION:

Table 1 – Characteristics of preterm ovine model		
Characteristics	**DCCV (N=7)**	**ECCV (N=8)**
Gestational age (days)	128±0.84	127±0.52
Female (N)	3	4
Birth weight (kg)	3.3±0.70	3.3±0.63
Born by multiplicity (N)	Twin – 4	Twin – 6
Heart rate at asphyxia (bpm)	86±10	88±8
Mean blood pressure at asphyxia (mmHg)	34±10	36±8
pH before resuscitation	7.0±0.08	7.04±0.08
$PaCO_2$ before resuscitation (mmHg)	101±23	90±25
PaO_2 before resuscitation (mmHg)	15±11	14±6
Data presented as numbers or as average and standard deviation.		

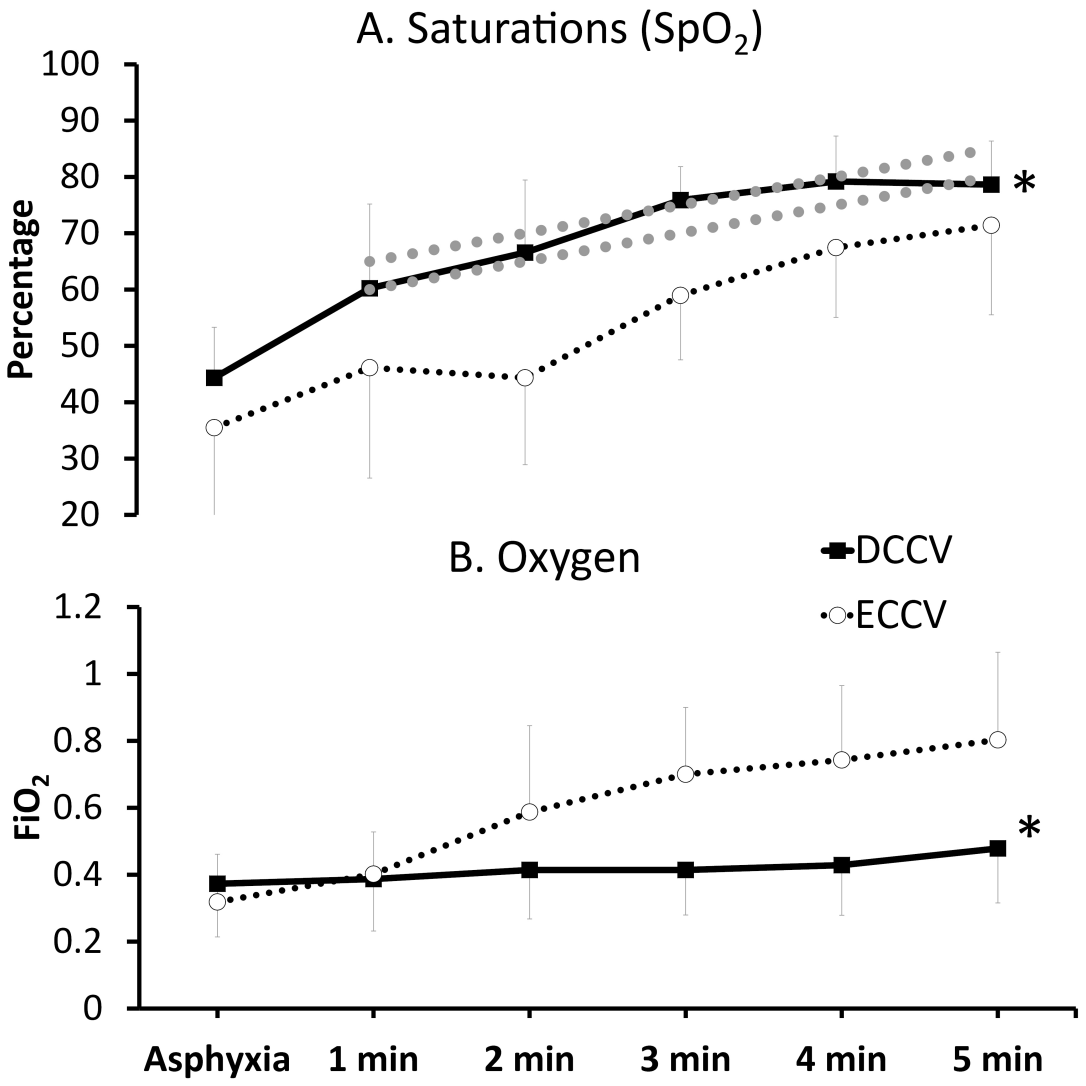


Figure 2: Saturations (SpO_2) and fraction of inspired oxygen (FiO_2) are shown during the first 5 min between DCCV and ECCV. * $p<0.05$ statistical significance by ANOVA. The grey interrupted line represents NRP recommended SpO_2 ranges.

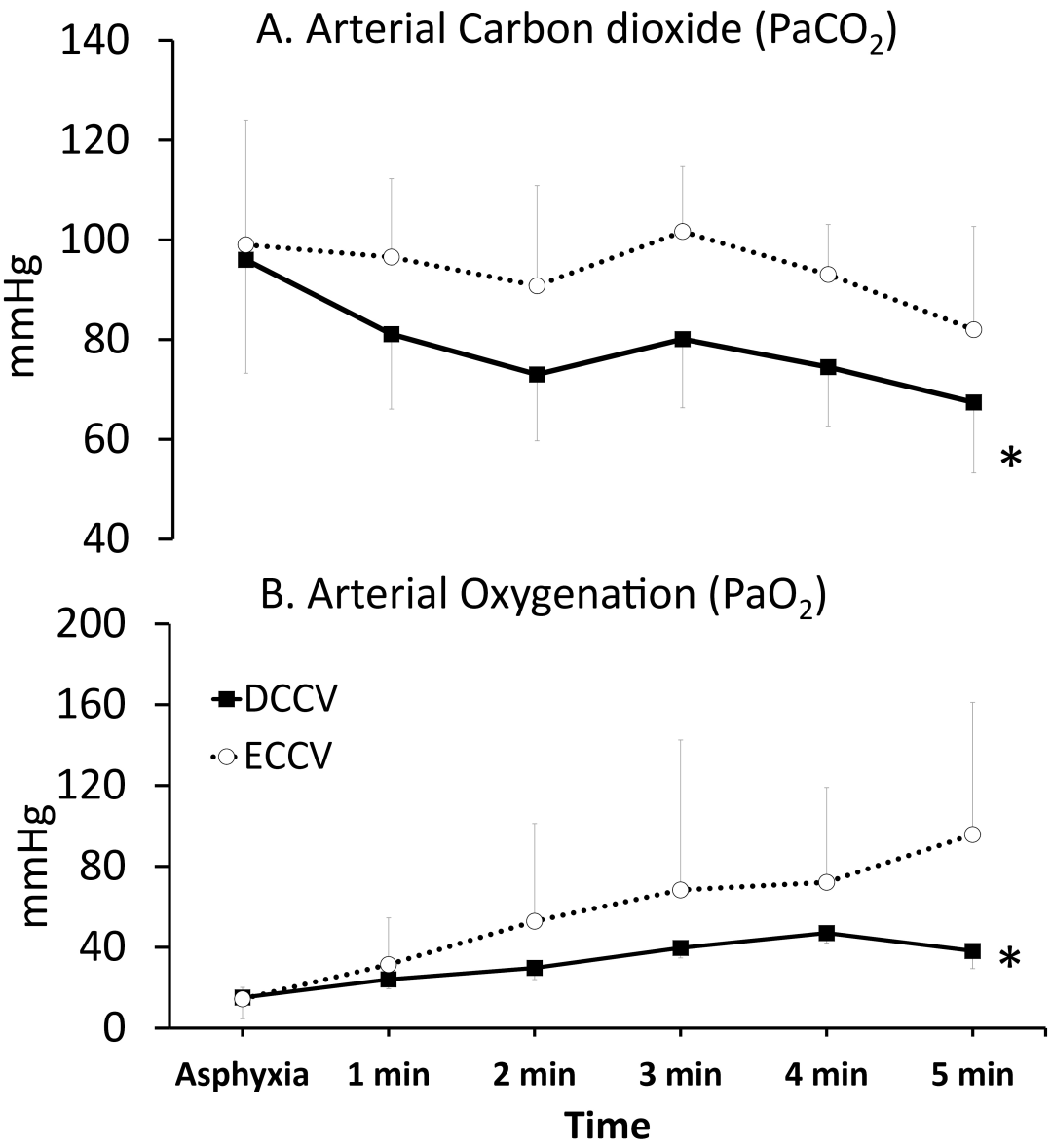


Figure 3: Gas exchange – Arterial carbon dioxide ($PaCO_2$) and arterial Oxygenation (PaO_2) are shown during the first 5 min between DCCV and ECCV. * $p<0.05$ statistical significance by ANOVA.

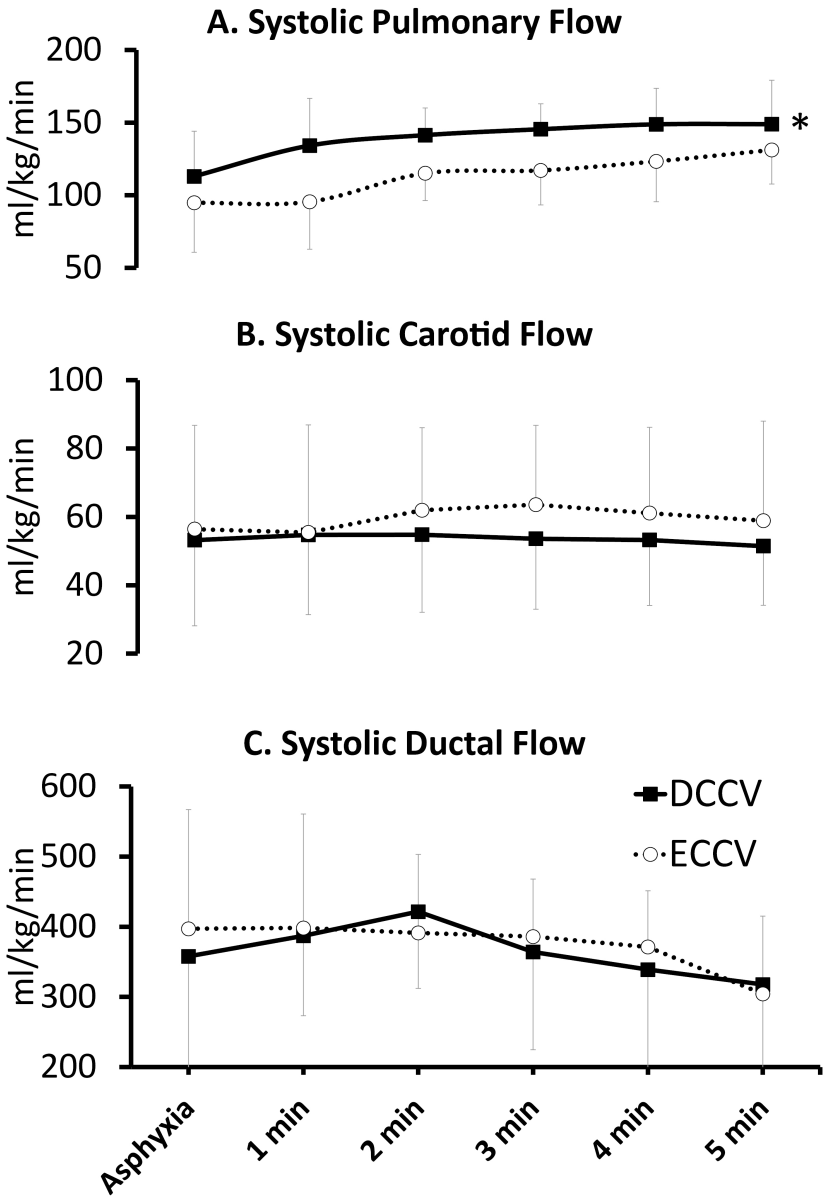


Figure 4: Hemodynamics – Pulmonary, Carotid and Ductal flow are shown during the first 5 min between DCCV and ECCV. * $p<0.05$ statistical significance by ANOVA. A positive ductal value indicated right to left ductal shunting.

CONTROL ID: 3382580

TITLE: Phytosterols in Lipid Emulsions Downregulate Expression of 78-kD Glucose-Regulated Protein (GRP78) in Neonatal Rat Lung

DIGITAL OBJECT IDENTIFIER (DOI):

ABSTRACT STATUS: Sessioned

PRESENTER: Naureen Memon

AUTHORS/INSTITUTIONS: N. Memon, C. Stryker, Goryeb Children's Hospital, Atlantic Health System, Morristown, New Jersey, UNITED STATES|C. Lee, A. Herdt, E. Eckman, MidAtlantic Neonatology Associates, Cedar Knolls, New Jersey, UNITED STATES|

CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal Pulmonology

ABSTRACT BODY:

Background: The lipid component of parenteral nutrition (PN) is derived from soybean oil and contains toxic plant cholesterols, known as phytosterols (PS). Cellular studies have shown that plasma PS levels 2-fold higher than normal activate intrinsic cell death; newborns receiving short-term PN can have PS levels up to 5-fold higher than normal. Animal studies have also confirmed that the neonatal lung is particularly vulnerable to PS accumulation. The physiological impact of PS accumulation in developing lungs has not been studied.

Objective: To study the RNA expression of major regulators of mitochondrial and endoplasmic reticulum (ER)-stress mediated apoptotic pathways in rat pup lungs after short-term exposure to PS.

Design/Methods: β-sitosterol, campesterol, and stigmasterol were dissolved in β-cyclodextrin (vehicle) to create a solution with a PS profile comparable to 20% Intralipid. Sprague-Dawley rat pups (n=5) received intraperitoneal injections of PS solution, every other day, from P0-P14; a dosing regimen that approximates 2 g/kg/d Intralipid. Saline (n=4) and vehicle (n=5) exposed pups served as controls. Plasma and lung PS concentrations were quantified by LC-MS/MS. Total RNA was isolated from lung tissue and 8 transcripts (Fig 2) were measured using QuantiGene Plex assays. Data were normalized to the SDHA gene and differences in relative gene expression between the groups were determined using Kruskal-Wallis nonparametric analysis and Mann-Whitney t-test, when appropriate. Statistical significance was set at $p < 0.05$.

Results: Plasma PS concentrations were significantly elevated in pups receiving PS solution vs. vehicle (22.2 ± 0.7 vs. 13.8 ± 0.4 µg/mL, p=0.02) and comparable to PS levels found in preterm infants; the lung PS concentration was nearly doubled in treated pups (172.6 ± 1.1 vs. 96.7 ± 3.2 µg/mL) (Fig 1). Transcripts regulating mitochondrial mediated apoptosis were not different between the groups. However, RNA expression of the 78-kD glucose-regulated protein (GRP78) was significantly downregulated in PS exposed lungs ($p < 0.05$) (Fig 2).

Conclusion(s): To our knowledge, this is the first study looking at the deleterious effects of PS in neonatal lungs. GRP78, the master regulator of ER stress and unfolded protein response, is significantly downregulated in PS exposed lungs. GRP78 is essential for lung development and decreased expression may increase susceptibility to ER stress and apoptosis, thereby contributing to the pathogenesis of bronchopulmonary dysplasia (BPD).

(no table selected)

IMAGE CAPTION: Plasma and Lung Phytosterol Concentrations in Neonatal Rats RNA Expression of Regulators of Mitochondrial and ER-stress Mediated Apoptotic Pathways in Neonatal Rat Lungs Exposed to Phytosterols

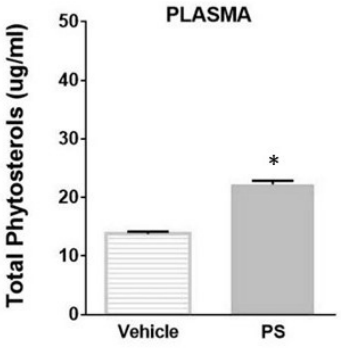


Fig 01(A). Plasma PS concentrations in rat pups after 2-week exposure to vehicle (control) or PS solution. (n = 5 rats/group, *p < 0.05)

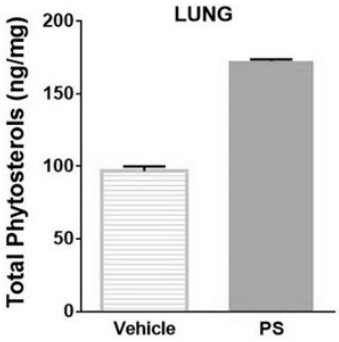


Fig 01(B). Lung PS concentrations in rat pups after 2-week exposure to vehicle (control) or PS solution. (n = 2 rats/group)

Plasma and Lung Phytosterol Concentrations in Neonatal Rats

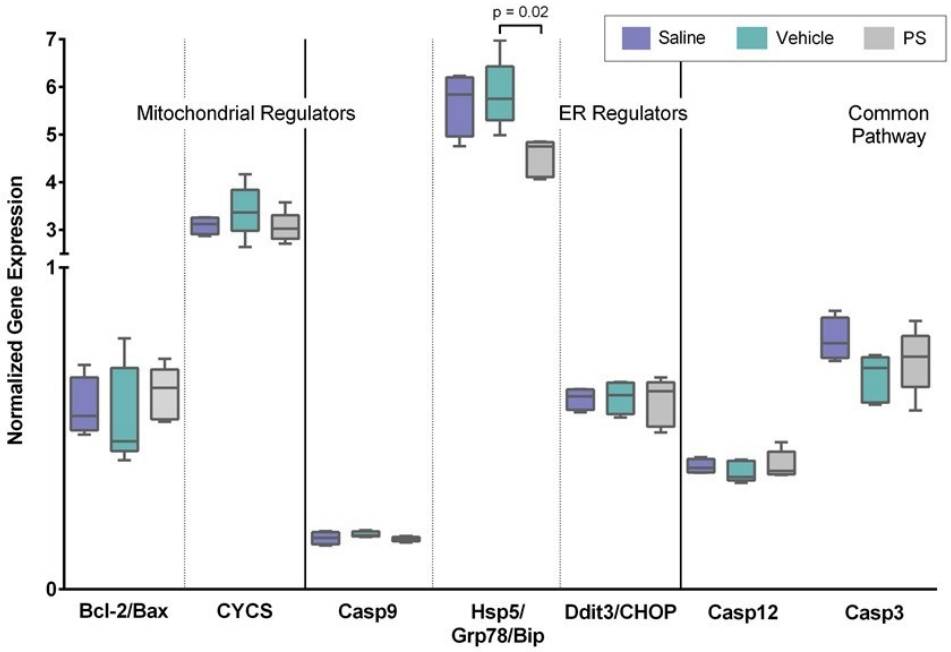


Figure 02. RNA Expression of Regulators of Mitochondrial and ER-stress Mediated Apoptotic Pathways in Neonatal Rat Lungs Exposed to Phytosterols. *B-cell lymphoma 2 (Bcl-2), Bcl-2-associated X protein (Bax), Binding immunoglobulin protein (Bip), Caspase 3 (Casp3), Caspase 9 (Casp9), Caspase 12 (Casp12), Cytochrome c (CYCS), C/EBP Homologous Protein (CHOP), DNA damage inducible transcript 3 (Ddit3), 78-kDa glucose-regulated protein (GRP78) (Grp78), Heat shock 70 kDa protein 5 (HSPA5).*

RNA Expression of Regulators of Mitochondrial and ER-stress Mediated Apoptotic Pathways in Neonatal Rat Lungs Exposed to Phytosterols

CONTROL ID: 3375141

TITLE: Banff Inflammatory Indices May Be Superior to the NIH Scoring in Predicting CKD Progression in Lupus Nephritis

DIGITAL OBJECT IDENTIFIER (DOI):

ABSTRACT STATUS: Sessioned

PRESENTER: Minh Dien Duong

AUTHORS/INSTITUTIONS: M. Duong, B. Goilav, Pediatric Nephrology, Children's Hospital at Montefiore, Bronx, New York, UNITED STATES|D. Schwartz, Surgical Pathology, Montefiore Medical Center, Bronx, New York, UNITED STATES|S. Wang, A. Broder, Rheumatology, Montefiore Medical Center, Bronx, New York, UNITED STATES|

CURRENT CATEGORY: Nephrology

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: Chronic kidney disease/end stage renal disease (CKD/ESRD) from lupus nephritis (LN) is a major cause of morbidity and mortality. Advanced tubulo-interstitial disease (TID) in LN is a better predicor of renal outcome than glomerular lesions. However, the current NIH classification is heavily weighted towards glomerular lesions and only provides a semi-qualitative assessment of TID. In contrast, the Banff classification of renal allograft pathology provides 6 reproducible scores for TID (inflammation, fibrosis and atrophy). Therefore, Banff scoring may better predict CKD/ESRD in LN than the NIH classification

Objective: We compared Banff grading vs. NIH scoring as predictors of CKD progression at 5 years, defined as a decline in estimated glomerular filtration rate (eGFR) of ≥30%, a strong risk factor for ESRD and mortality

Design/Methods: We included lupus patients with LN class III, IV, V on the index biopsy between Jan 1, 2005 and Dec 31, 2018. H&E and PAS-stained slides were reviewed and scored by an experienced pathologist. Six TID Banff scores (0/1 vs. 2/3), NIH activity/chronicity (AI/CI); and NIH interstitial fibrosis/tubular atrophy (IF/TA), tubulo-interstitial inflammation (TII) scores (none/mild vs. moderate/severe) were evaluated as predictors of CKD progression using survival analyses

Results: Of the 125 patients, 46 had CKD progression and 20 subsequently developed ESRD. There were no differences between progressors and non-progressors in terms of baseline demographic, clinical or lupus-specific characteristics (Table 1). The Banff ti score (total inflammation) was associated with CKD progression in bivariate analyses and in time-dependent analyses. However, the NIH TII score and the corresponding Banff i score were not predictive (Table 2, Fig 1). The overall NIH AI and CI were not predictive of CKD progression. Moderate-to-severe NIH IF/TA was associated with CKD progression as was the Banff ci (interstitial fibrosis) score (Table 2, Fig 2). Banff scores for atrophy were not predictive. Importantly, in a subset of 92 patients with preserved or only mildly impaired renal function at the time of biopsy (eGFR≥60ml/min/1.73m^2), only the Banff ti score (but not the i score or the NIH TII or IF/TA) was predictive of CKD progression (Fig 1)

Conclusion(s): Banff inflammation scores may be superior predictors of CKD/ESRD progression at 5 years, compared to the currently used NIH classification. Detection of inflammation by Banff scores may allow earlier interventions to prevent ESRD

(no table selected)

IMAGE CAPTION: Table 1: Baseline demographic, clinical and renal histology data in patients who did and did not progress to CKD within 5 years Table 2: NIH and Banff scores in patients who did and did not progress to CKD within 5 years
 Figure 1: Association of NIH and Banff inflammation scores with ESRD progression
 Figure 2: Association of NIH and Banff fibrosis scores with ESRD progression

Table 1: Baseline demographic, clinical and renal histology data in patients who did and did not progress to CKD within 5 years

	Progressors[1] (n=46)	**Non-progressors** (n=79)	p value
Demographic			
Female, n (%)	36 (78)	69 (87)	0.182
Age (years) at renal biopsy, median (IQR)	26 (20-41)	29 (21-43)	0.525
Age at renal biopsy < 18 years, n (%)	7 (15)	13 (16)	0.855
Race, n (%)			0.817
White	4 (9)	4 (5)	
Black	18 (39)	35 (44)	
Asian	1 (2)	1 (1)	
Other/unknown	23 (50)	39 (50)	
Ethnicity, n (%)			0.726
Hispanic	19 (41)	32 (41)	
Non-Hispanic	21 (46)	40 (51)	
Unknown	6 (13)	7 (8)	
Clinical data			
Diabetes, n (%)	5 (11)	3 (4)	0.119
Hypertension, n (%)	33 (72)	55 (70)	0.802
Baseline eGFR ml/min/1.73m^2 median (IQR)	96.05 (56.6-117.8)	88.9 (47-117)	0.509
C3 (mg/dL), median (IQR)	71 (52-88)	67.5 (43-94)	0.58
C4 (mg/dL), median (IQR)	12.65 (9-23)	12 (7-20)	0.476
Anti-ds DNA titer (IU), median (IQR)	108.7 (36.6-194.9)	151.3 (39.2-200)	0.57
Total SLEDAI score, median (IQR)	11 (8-16)	12 (8-16)	0.47
Renal SLEDAI score, median (IQR)	8 (4-12)	8 (4-12)	0.96
LN class, n (%)			0.152
Proliferative GN[2] (class III, IV)	18 (39)	30 (38)	
Non-proliferative GN (class V)	9 (20)	27 (34)	
Mixed GN (class V and III or IV)	19 (41)	22 (28)	

[1] Progressors were defined as LN patients with an estimated glomerular filtration rate (eGFR) decline of ≥30% at 5 years post index biopsy. [2] GN: glomerulonephritis

Table 1: Baseline demographic, clinical and renal histology data in patients who did and did not progress to CKD within 5 years

Table 2: NIH and Banff scores in patients who did and did not progress to CKD within 5 years

NIH scores	**Progressors** (n=46)	**Non-progressors** (n=79)	p value
Overall NIH AI, median (IQR)	1 (0-4)	1 (0-3)	0.609
NIH AI cut-off ≥ 11, n (%)	1 (2)	3 (3.8)	0.619
Overall NIH CI, median (IQR)	3 (0-5)	2 (0-3)	0.33
NIH CI cut-off ≥ 3, n (%)	24 (52)	28 (35.44)	0.067
NIH TII score, n (%)			0.053
None-to-mild NIH TII	39 (84.78)	75 (94.94)	
Moderate-to-severe NIH TII	7 (15.22)	4 (5.06)	
NIH IF/TA score, n (%)			0.049
None-to-mild NIH IF/TA	30 (65.22)	64 (81.01)	
Moderate-to-severe NIH IF/TA	16 (34.78)	15 (18.99)	
TID Banff scores	**Progressors** (n=46), n (%)	**Non-progressors** (n= 79), n (%)	p value
Tubulitis (t score)	0	0	
Interstitial inflammation (i score) 2/3 (vs. 0/1)	3 (6.52)	5 (6.33)	0.966
Total inflammation (ti score) 2/3 (vs. 0/1)	16 (34.78)	12 (15.19)	0.011
Tubular atrophy (ct score) 2/3 (vs. 0/1)	16 (34.78)	16 (20.25)	0.073
Interstitial fibrosis (ci score) 2/3 (vs. 0/1)	17 (36.96)	15 (18.99)	0.026
Inflammation in area of interstitial fibrosis and/or tubular atrophy (i-IFTA score) 2/3 (vs. 0/1)	(n= 26)* 18 (69)	(n=51)* 25 (49)	0.091

* Total number of biopsies is smaller, due to inability to apply score to biopsies without areas of fibrosis and tubular atrophy.

Table 2: NIH and Banff scores in patients who did and did not progress to CKD within 5 years

Figure 1: Association of NIH and Banff inflammation scores with ESRD progression

Figure 1A. NIH TII score in complete cohort (n=125)

Unadjusted HR: 2.14 [0.95 - 4.79]

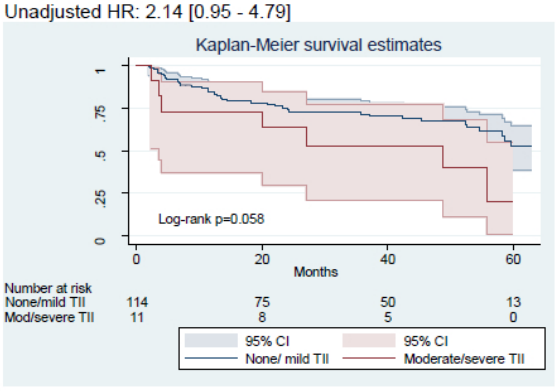


Figure 1B. Banff ti score in complete cohort (n=125)

Unadjusted HR: 2.96 [1.6 - 5.48]

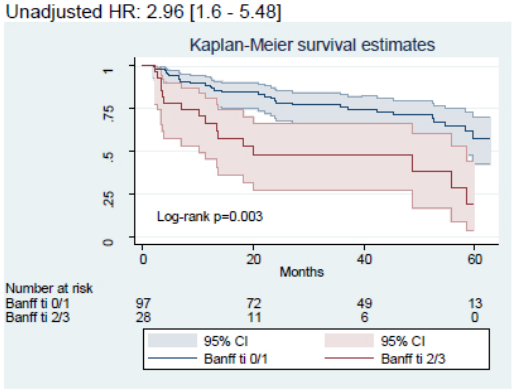


Figure 1C. NIH TII score in sub-cohort with baseline eGFR ≥60ml/min/1.73m^2 (n=92)

Unadjusted HR: 1.65 [0.39 - 6.91]

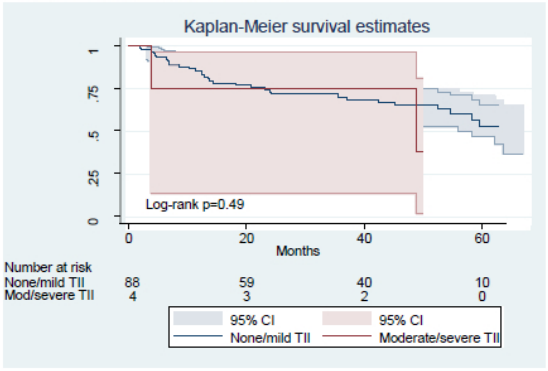


Figure 1D. Banff ti score in sub-cohort with baseline eGFR≥60ml/min/1.73m^2 (n=92)

Unadjusted HR: 3.82 [1.61 - 9.06]

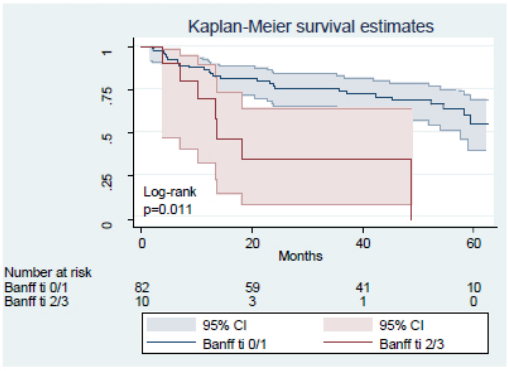


Figure 1: Association of NIH and Banff inflammation scores with ESRD progression

Figure 2: Association of NIH and Banff fibrosis scores with ESRD progression

Figure 2A. NIH IF/TA score in complete cohort (n=125)

Unadjusted HR: 2.12 [1.16 - 3.91]

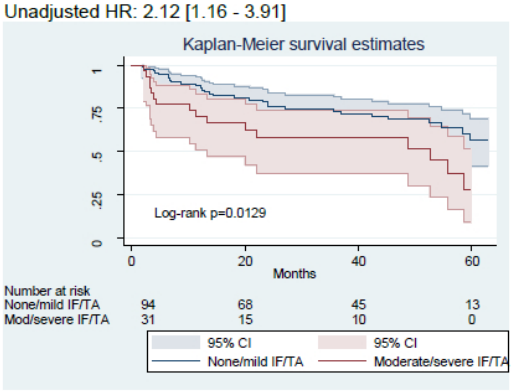


Figure 2B. Banff ci score in complete cohort (n=125)

Unadjusted HR: 2.27 [1.25 - 4.15]

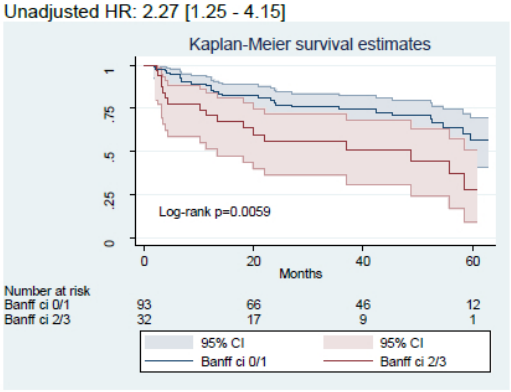


Figure 2C. NIH IF/TA score in sub-cohort with eGFR≥60ml/min/1.73m^2 (n=92)

Unadjusted HR: 1.76 [0.67 - 4.58]

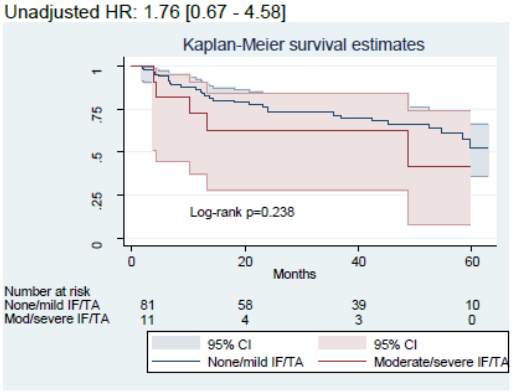


Figure 2D. Banff ci score in sub-cohort with eGFR≥60ml/min/1.73m^2 (n=92)

Unadjusted HR: 2.81 [1.2 - 6.56]

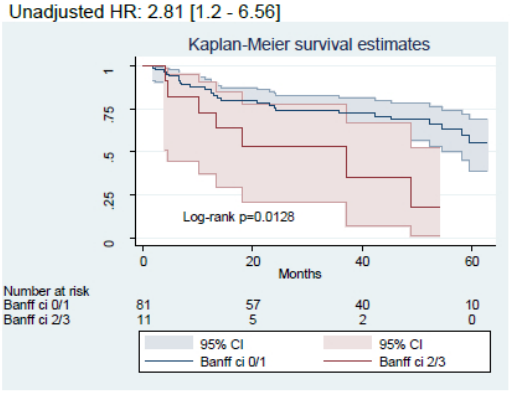


Figure 2: Association of NIH and Banff fibrosis scores with ESRD progression

CONTROL ID: 3379463

TITLE: Novel Biomarkers in Autosomal Recessive Polycystic Kidney Disease (ARPKD)

DIGITAL OBJECT IDENTIFIER (DOI):

ABSTRACT STATUS: Sessioned

PRESENTER: Lindsay Fleischer

AUTHORS/INSTITUTIONS: L. Fleischer, Cooper Medical School of Rowan University, Camden, New Jersey, UNITED STATES|L. Ballester, M. Dutt, K. Howarth, E. Hartung, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, UNITED STATES|

CURRENT CATEGORY: Nephrology

CURRENT SUBCATEGORY: None

ABSTRACT BODY:

Background: The clinical phenotype of ARPKD includes fibrocystic kidney disease, liver fibrosis, and portal hypertension of varying severities. Recent preclinical data suggest that serum Galectin-3 (Gal-3) and Intestinal Fatty Acid Binding Protein (I-FABP) levels are associated with kidney fibrosis and portal hypertension, respectively, and may potentially serve as biomarkers for kidney and liver disease severity in ARPKD.

Objective: To determine whether 1) serum Gal-3 level is associated with the severity of ARPKD-related kidney disease; and 2) serum I-FABP level is associated with the severity of ARPKD-related liver disease.

Design/Methods: Prospective, cross-sectional study of 21 participants with clinical diagnosis of ARPKD and presence of native kidneys (for Gal-3 analyses) and/or native livers (for I-FABP analyses). Serum Gal-3 and I-FABP levels were analyzed using enzyme linked immunosorbent assay. Kidney disease severity was determined by estimated glomerular filtration rate (eGFR) calculated using the 2012 Creatinine-Cystatin C based CKiD equation. Liver disease severity was characterized using ultrasound ARFI elastography [average shear wave speed (SWS) of the right and left lobes of the liver], spleen length index (actual spleen length/90th percentile for height), and platelet count. All variables were operationalized to a normalized z-score based on mean and standard deviation (SD). Multivariate linear regression was performed to examine the association between serum Gal-3 and eGFR (adjusted for liver disease severity variables) and between I-FABP and liver disease severity variables (adjusted for eGFR). Normality and regression diagnostic tests were conducted, and from them, sensitivity analyses were conducted to determine the impact of potentially violated assumptions.

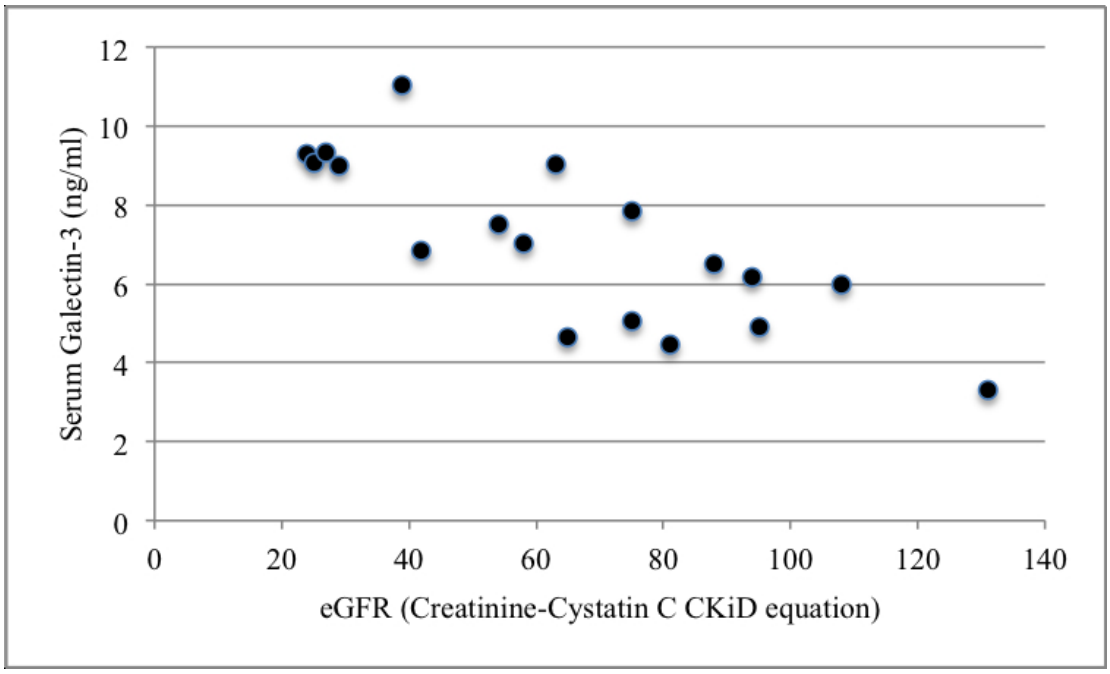
Results: Clinical and demographic characteristics are shown in Table 1. There was a significant negative association between serum Gal-3 level and eGFR (Fig1), specifically 1 SD lower eGFR was associated with 0.7945 SD higher Gal-3 level (95% CI -1.116, -0.473; $p<0.001$). When adjusted for markers of hepatic disease severity, the association remained significant. There was no significant association between serum I-FABP level and any liver disease severity variables in either unadjusted or adjusted models.

Conclusion(s): Serum Gal-3 level was found to be associated with the severity of kidney disease, suggesting its value as a possible novel biomarker in ARPKD. Serum I-FABP level did not appear to be associated with the severity of ARPKD-related liver disease.

(no table selected)

IMAGE CAPTION:

	Gal 3	I-FABP
Number of participants	18	21
Age*	6.0 [0.8, 13.2]	6.1 [2.3,13.2]
Male sex**	13 (72%)	14 (67%)
eGFR (mL/min/1.73m^2)*	64 [39,88]	65 [42,81]
Platelet Count (x10^3/uL)*	271 [144, 322]	269 [144, 315]
Spleen Length Index*	0.94 [0.86,1.40]	1.10 [0.89, 1.40]
*median [IQR] **N (%)		


Serum Galectin-3 (ng/ml)
12
10
8
6
4
2
0
0
20
40
60
80
100
120
140
eGFR (Creatinine-Cystatin C CKiD equation)

CONTROL ID: 3385821

TITLE: Optimal Depth of Chest Compressions Targeting Gas Exchange in Neonatal Cardiac Arrest

DIGITAL OBJECT IDENTIFIER (DOI):

ABSTRACT STATUS: Sessioned

PRESENTER: Vikash Agrawal

AUTHORS/INSTITUTIONS: V. Agrawal, S. Gugino, C. Koenigsknecht, J. Helman, M. Rawat, J. Nair, B. Mathew, S. Berkelhamer, P.J. Rivera-Hernandez, S. Mani, P. Chandrasekharan, Pediatrics, University at Buffalo, Buffalo, New York, UNITED STATES|D. Sankaran, S. Lakshminrusimha, Pediatrics, University of California Davis, Davis, California, UNITED STATES|

CURRENT CATEGORY: Neonatology

CURRENT SUBCATEGORY: Neonatal/Infant Resuscitation

ABSTRACT BODY:

Background: The goal of chest compressions (CC) during neonatal resuscitation is to increase perfusion to vital organs such as the heart, brain and lungs. With effective positive pressure ventilation (PPV) and CC, there is an improvement in gas exchange and perfusion to vital organs leading to the return of spontaneous circulation (ROSC). Noninvasive monitoring of gas exchange by measuring exhaled carbon dioxide ($ETCO_2$) may serve as a real-time feedback to provide effective PPV and CC. The relationship between the depth of CC, $ETCO_2$ and flow to vital organs is not known in perinatal asphyxia.

Objective: We hypothesized that using depth of CC correlates with coronary, carotid, and pulmonary blood flow and gas exchange, as evidenced by $ETCO_2$ in an ovine model of perinatal cardiac arrest.

Design/Methods: Near-term lambs were asphyxiated by umbilical cord occlusion until cardiac arrest. The diameter of the chest was measured using Vernier calipers. Resuscitation was initiated as per neonatal resuscitation program recommendations. During CC, the depth, peak blood flows, pressures, and $ETCO_2$ were recorded. A rate of 30PPV:90CC per minute was targeted. Resuscitation was continued until ROSC or until 20 min. We analyzed each CC for based on depth (<25%, 25-33%, 34-50 %, 51-75% & >75% of chest wall diameter), blood flows, blood pressures and $ETCO_2$.

Results: From seventeen lambs, we analyzed a total of 11,375 CC events. Table 1 shows the baseline flows and characteristics before resuscitation. Chest compression between 33-50% chest diameter resulted in the highest $ETCO_2$, peak carotid flow and systolic BP (table 2). Higher depth of CC > ½ chest diameter did not result in increased flow to vital organs or gas exchange. We then analyzed CC based on $ETCO_2$ achieved (table 3). There was no difference in tidal volume, respiratory and CC rates based on the $ETCO_2$ level. The carotid, pulmonary, ductal flows and blood pressures were highest when $ETCO_2$ was ≥11 mmHg. However, coronary flows were lower with $ETCO_2$ ≥11 mmHg (table 3).

Conclusion(s): Gas exchange ($ETCO_2$) during resuscitation reflects perfusion to the lung. High $ETCO_2$ correlates with high pulmonary blood flow. Excessive depth of CC and targeting higher $ETCO_2$ during resuscitation may compromise coronary flow by the direct squeezing of myocardial vessels and enhancing ductal shunt. These findings support the current NRP recommendation to target 1/3 chest diameter during CC. Clinical trials are needed to validate these findings.

(no table selected)

IMAGE CAPTION: Table 1

Table 1 – Characteristics of complete cardiac arrest ovine model	
Characteristics	**(n=17)**
Gestational age (days)	141 ± 1
Female (N)	8
Birth Weight (kg)	4.0 ± 1.2
Chest Diameter (mm)	56 ± 12
Born by Multiplicity (N)	11
Rate of ROSC (%)	76%
Time to ROSC (mins)	9 ± 4
Baseline flows & pressures before asphyxia	
Peak Carotid flow (ml/kg/min)	59±30
Peak Pulmonary flow (ml/kg/min)	80±10
Peak Ductal flow (ml/kg/min)	357±112
Peak Coronary flow (ml/kg/min)	8±5
Systolic Blood pressure (mmHg)	40±9
Diastolic Blood Pressure (mmHg)	27±8
Before Resuscitation	
pH	6.80 ± 0.05
$PaCO_2$ (mmHg)	129 ± 31
PaO_2 (mmHg)	16 ± 8
Lactate (mmol/L)	10 ± 4

Table 1

Table 2: Parameters based on depth of compressions

Depth of CC	$ETCO_2$ (mmHg)	Peak Carotid ml/kg/min	Peak Pulmonary ml/kg/min	Peak Ductal ml/kg/min	Peak Coronary ml/kg/min	SBP mmHg	DBP mmHg	Mean BP mmHg
<25% N-469	6.9±4.5	14.5±7.8	21.3±15.5	54.9±67.3	2.6±3.4	22.0±14.2	9.5±7.2	13.1±7.1
25-32% N-1034	9.1±7.0	17.0±10.7	13.1±10.4	41.0±65.5	3.5±3.6	23.2±13.4	10.7±4.4	15.5±5.0
33-50% N-4824*	11.7±6.9*	22.3±12.6*	14.9±16.1	60.3±77.3	3.0±3.1	26.3±10.5*	10.8±4.5	14.9±5.6
51-75% N 3573	9.9±5.9	11.6±10.3	15.0±11.3	40.8±26.4	3.1±3.0	21.7±7.8	9.5±4.6	13.0±3.9
>75% N-1475	8.9±5.5	14.9±6.1	16.1±13.7	35.9±21.9	3.3±3.8	26.8±6.1	11.2±3.8	15.4±3.0

*$p<0.001$ denotes significance by ANOVA between the groups. BP – blood pressure, $ETCO_2$ – end-tidal carbon dioxide. Note chest compressions of 1/4 , 1/3 , 1/2 , 3/4 are represented as 25, 33, 50, 75%.

Table 3: End-tidal carbon dioxide targeted chest compressions (CC) & changes in blood flows & pressures

$ETCO_2$ (mmHg)	No of CCs (N total – 11375)	Expired Tidal Volume (per kg)	RR per min	CC rate per min	Peak Carotid Flow (ml/kg/min)	Peak Pulmonary Flow (ml/kg/min)	Peak Ductal Flow (ml/kg/min)	Peak Coronary Flow (ml/kg/min)	Systolic Blood Pressure (mmHg)	Diastolic Blood pressure (mmHg)
≤ 5 # mmHg	3254 (29%)	7.8±0.5	32±5	96±12	15.0±8.4	13.2±8.5	32.3±30.7	3.5±3.4	22.2±8.5	10.4±4.1
6-10 # mmHg	3106 (27%)	8.0±0.4	30±6	95±12	13.9±10.3	12.3±8.8	33.7±35.7	3.3±3.2	23.1±7.6	10.1±4.1
≥11* mmHg	5015 (44%)	7.6±0.9	32±6	92±16	20.5±13.6	18.2±18.2	69.4±76.1	2.6±3.1	25.8±12.2	10.7±5.2

* $p<0.05$ by ANOVA – the flows (other than coronary flow) & pressures were higher between ≥11 mmHg and the rest of the groups. # The coronary flows were higher in 6-10 &≤ 5 mmHg. Tidal volume, RR - respiratory rates, CC rates were not different.