DOI: 10.1002/jpen.70046

ABSTRACTS

Harry M. Vars Award Candidates Abstracts

Sunday, February 15, 2026
Premier Paper Session and Vars Award Competition

Harry M. Vars Award Candidate

2181400 - Volume-Based Feeding Critically Ill Children: A Feasibility Randomized Controlled Trial of Volume- Versus Rate-Based Enteral Nutrition

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Financial Support: This work was supported by the ASPEN Rhoads Research Foundation.

Background: Enteral nutrition (EN) has been associated with better clinical outcomes in critically ill children. However, frequent feed interruptions are common, resulting in underfeeding. Traditionally, tube feeds are provided using hourly rate-based feeding goals. Volume-based feeding allows nurses to adjust feed rates to compensate for interruptions. This study examined the feasibility of conducting a randomized controlled trial (RCT) to evaluate volume-based EN (VBEN) in the pediatric intensive care unit (PICU) by assessing participant recruitment, enrollment and consent rates, protocol adherence and secondary clinical outcomes in order to inform the design of a future study.

Methods: We conducted a parallel, partially blinded 1:1 randomized feasibility trial of children admitted to the Alberta Children's Hospital PICU from March to November 2024. Eligible children were 1 month to 18 years old, expected to remain in the PICU ≥ 48 hours, and require EN. Randomization was block-stratified by age and ventilator support. A deferred consent strategy was used to facilitate timely enrollment, randomization, and protocol initiation. After 24 hours of feed initiation and titration, participants received either the unit standard or intervention: Comparator (RBEN, unit standard): Nurses followed a fixed hourly feed rate with no adjustments for missed volumes. Intervention (VBEN): Nurses were provided a 24-hour target feed volume and instructed to adjust rates following interruptions, within a predefined maximum rate to avoid rapid infusions. Daily data was collected from enrollment to PICU discharge or 7 days of study protocol, whichever came first. Participants were analyzed according to the intention-to-treat principle.

Results: A total of 436 children were screened for eligibility. Of these, 120 (28%) met the initial inclusion criteria. After applying exclusion criteria, 61 children (51%) remained eligible and 60 (98%) were successfully enrolled and randomized. One child was enrolled but never started on EN. Among 178 study days, five protocol violations occurred (2.8%); two due to incorrect study orders entered in the electronic medical system and three due to feed rates administered outside the VBEN protocol parameters. Notably, feed rates were never run above the maximum infusion rate. One child with an undiagnosed metabolic disorder was removed from the study by the medical team to allow for closer titration of parenteral and enteral nutrition. Consent was declined by two participants (3.2%) prior to protocol initiation and by seven participants (11.5%) after study protocol had started, resulting in an overall consent rate of 85.0%. Baseline characteristics were similar between groups, except for more females in the VBEN group ($p = 0.01$) (Table 1). VBEN showed non-significantly higher energy and protein adequacy (Figure 2), a lower cumulative energy deficit (273 vs. 861 kcal, $p = 0.04$) (Table 1), and no increase in feed intolerance ($p = 0.46$) (Table 1) compared with RBEN. Secondary outcomes were underpowered to detect differences, and findings should be considered exploratory and hypothesis-generating.

Conclusion: This study demonstrates the feasibility of conducting a RCT of VBEN in a PICU. High enrollment (98%) and consent (85%) rates, potentially facilitated by a deferred consent strategy, support the acceptability of the trial design. Protocol adherence

was generally high, with few violations. The exclusion of one child with an undiagnosed metabolic disorder highlights the need to consider excluding children with known or suspected metabolic disorders in future trials. These findings support the feasibility of VBEN implementation in the PICU and provide key data to inform the design of a larger, adequately powered trial to evaluate clinical outcomes.

Table 1. Baseline characteristics and secondary outcomes

Variable Name	Full cohort (51)	VBEN (25)	RBEN (26)	p-value
Baseline Characteristics				
Age adjusted for prematurity (years) Median (IQR)	1.9 (0.4-9.6)	1.5 (0.2-8.4)	3.3 (0.7-9.8)	0.48
Sex (female) (n) %	23 (45)	16 (64)	7 (27)	0.01
PRISM III score Median (IQR)	4 (1-8)	3.5 (0-7.5)	4 (1-8)	0.56
Admitting diagnosis n (%)				
Cardiovascular	5 (10)	2 (8)	3 (12)	0.54
Respiratory	27 (53)	12 (48)	15 (58)	
Trauma	1 (2)	1 (4)	0 (0)	
GI/Hepatic	1 (2)	0 (0)	1 (4)	
Neurological	7 (14)	4 (16)	3 (12)	
Infectious disease	5 (10)	4 (16)	1 (4)	
Hem/Oncology	2 (4)	0 (0)	2 (8)	
Other	3 (6)	2 (8)	1 (4)	
Invasive ventilation at time of randomization n (%)	39 (76)	20 (80)	19 (73)	0.74
Secondary Outcomes[a]				
28-day Vent Free Days Median (IQR)	22 (12-26)	24 (21-27)	22 (8-24)	0.10
PICU length of stay (days) Median (IQR)	6 (4-10)	4 (3-8)	7 (4-13)	0.17
Hospital length of stay (days) Median (IQR)	12 (7-22)	11 (7-16)	17 (8 -26)	0.09
Overall Mortality n (%)	3 (6)	1 (4)	2 (8)	1.00
60-day Hospital readmission n (%)	14 (27)	5 (20)	9 (35)	0.35
Percentage of study days where feed intolerance occurred n (%)	7 (4)	4 (5)	3 (3)	0.46
Cumulative total energy deficit (kcal)[b] Mean (SD)	580 (976)	273 (491)	861 (1212)	0.04

This feasibility study was underpowered to detect differences in secondary outcomes; all estimates should be considered exploratory and hypothesis-generating. Cumulative total energy deficit includes energy intake from enteral nutrition, parenteral nutrition and other intra-venous sources such as dextrose and propofol. Abbreviations: VBEN = volume-based enteral nutrition; RBEN = rate-based enteral nutrition; IQR = interquartile range; SD = standard deviation; kcal = kilocalories. P-values were estimated using Wilcoxon signed rank test, Fisher's exact test or student t-test, as appropriate.

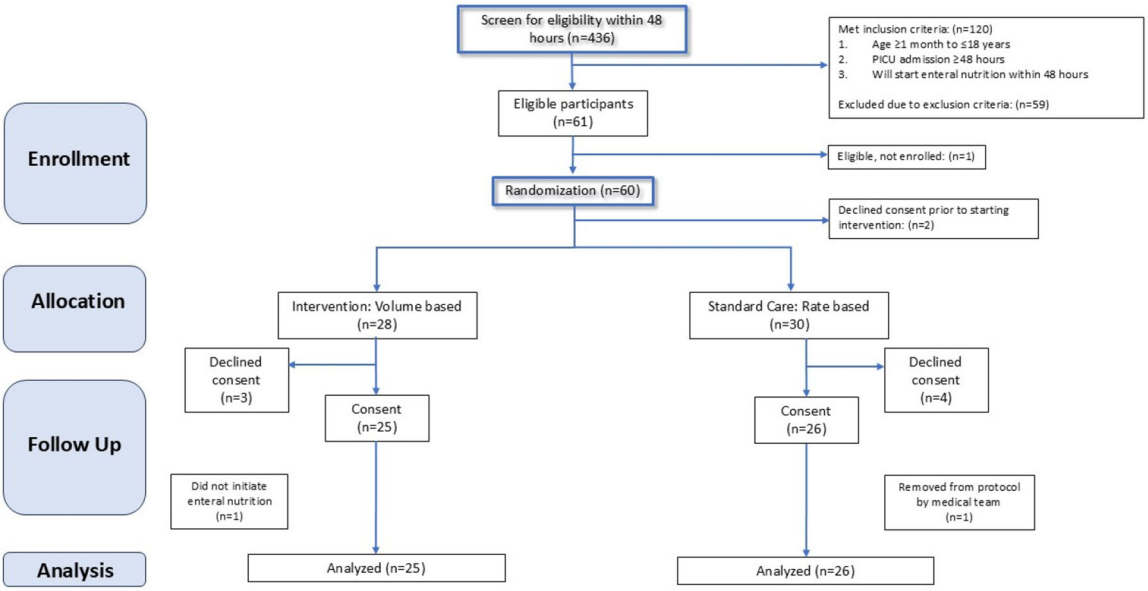

Figure 1. Volume-based enteral nutrition feasibility randomized control trial CONSORT flow diagram

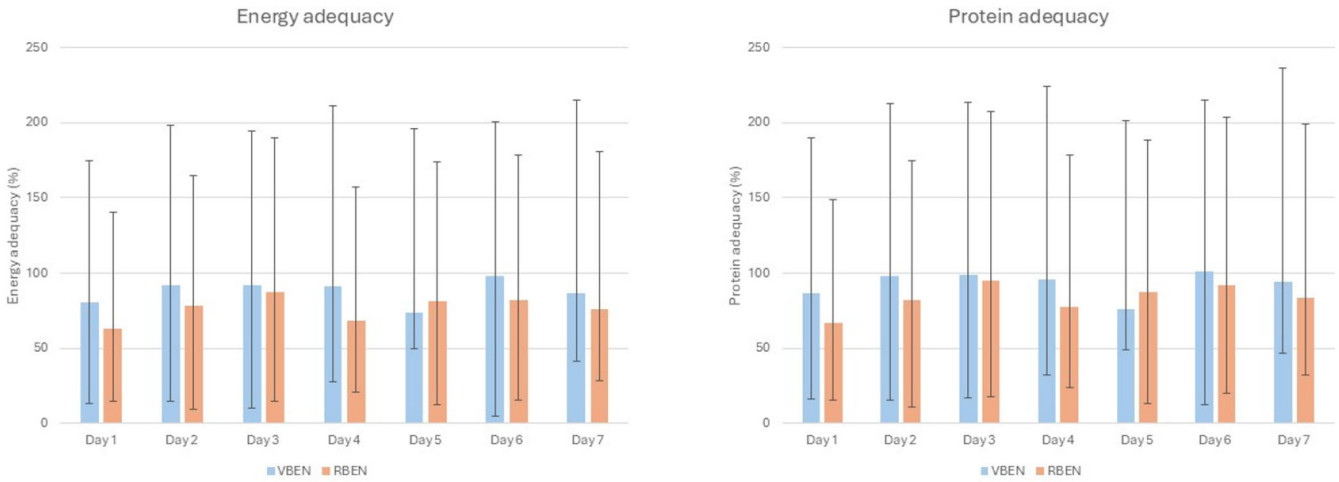

Figure 2. Average enteral energy and protein adequacy per study day

VBEN = volume-based enteral nutrition; RBEN = rate-based enteral nutrition. Enteral energy and protein adequacy are presented as the mean daily delivered enteral energy and protein intake compared to prescribed amounts for study days 1 to 7. Error bars represent 95% confidence intervals, overlapping confidence intervals represent non-significant differences.

Harry M. Vars Award Candidate

2207139 - Differential Metabolomic Profiles Between Human Milk Versus Infant Formula-Fed Piglets in Relation to Neurodevelopment

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Financial Support: ASPEN Rhoads Research Foundation Grant, NIH 1R56HD113572-01, University of Idaho Office of Research and Economic Development Internal Grant.

Background: Human milk (HM) feeding in infancy is associated with higher IQ and school performance in school age children, and HM is the recommended feeding for the first six months by the American Academy of Pediatrics. However, there is no solid research on the mechanisms

affecting neurodevelopment in response to different feedings and their metabolic processes. We hypothesized that HM-fed piglets will result in upregulation of metabolites beneficial to neurodevelopment compared to infant formula (IF)-fed piglets.

Methods: Twelve two-day old piglets were obtained and split into two feeding groups: HM (n = 6) and IF (n = 6) feedings for 28 days. The piglets' digesta (reflecting local intestinal metabolites; jejunum, ileum, and colon) and urine (reflecting systemic metabolites) were collected at necropsy. The samples underwent metabolomic sequencing and the metabolites were analyzed using a publicly available software. Metabolites were first visualized using Principal Component Analysis and heat maps. The differences between the two groups were then compared using T-tests and visualized with volcano plots that showed up- and down-regulations comparing groups. Pathway analyses were performed to identify metabolites within specific metabolic processes. Metabolites that differed between the groups were determined within the metabolic pathways.

Results: In the digesta samples, no metabolites were significantly different in the jejunum, 15 in ileum (4 upregulated in HM; 11 downregulated in HM), and one in colon (upregulated in HM) compared with IF. In the urine samples, five metabolites were significantly different between the groups (3 up, 2 down in HM). Pathway analyses showed that two metabolites in two pathways were significantly different between groups in digesta samples, and two metabolites in three pathways were significantly different between groups in urine samples. Specifically, HM had downregulation of Lysine degradation and upregulation of Galactose metabolism in digesta. Upregulation in HM group of valine, leucine, and isoleucine biosynthesis and metabolism, and a downregulation in HM of Fatty acid biosynthesis were seen in the urine.

Conclusion: This study showed differential metabolomic differences between HM and IF-fed piglets that may have relevance in neurodevelopment. Previous studies have shown that histidine, lysine, and threonine can reduce mTOR activity, important in brain development. Our data showed downregulation in lysine degradation in HM-fed digesta samples. This could be related to protein concentrations in HM (an average of 0.8–1.0 g per 100 mL) vs. the IF used (2.1 grams per 100 mL). In studies on classic galactosemia, impaired galactose metabolism can negatively impact brain function and development. Our data showed significant upregulation of galactose metabolism in HM digesta samples, which may also be a potential mechanism for increased neurodevelopment. Studies also show that leucine activates the mTOR pathway, and our urine data showed a significant upregulation in valine, leucine, and isoleucine biosynthesis and metabolism in HM group which could positively impact neural network development and brain function. Overall, we found select differences in metabolomic profiles of HM- vs. IF-fed piglets that may have neurodevelopmental impact, warranting further investigation.

Harry M. Vars Award Candidate

2207147 - Neuroactive Microbial Metabolites Remain Dysregulated in Alcohol-Associated End-Stage Liver Disease Patients Following Liver Transplantation

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Financial Support: None Reported.

Background: Chronic alcohol misuse can cause multi-system organ dysfunction and alcohol-related liver disease (ALD), which may advance to end-stage liver failure, ultimately necessitating liver transplantation. Neuropsychiatric disorders such as depression, sleep disorders, and anxiety are common among patients after receiving a liver transplant. It has been hypothesized that neuropsychiatric sequelae following liver transplantation may be correlated with changes to the gut microbiome. Glutamate, GABA, dopamine, and serotonin are primary neurotransmitters that both alcohol use and the gut microbiome can directly influence. Such a connection suggests that microbial imbalances resulting from alcohol consumption may disrupt neurotransmission. We hypothesize that the metabolomic signatures of neuroactive metabolites in patients with ALD awaiting liver transplantation are distinct from those of healthy control subjects and are correlated with changes to the gut microbiota.

Methods: A secondary data analysis was conducted on data from a larger, single-center, non-randomized, prospective pilot study involving patients awaiting liver transplantation to examine metabolomic and microbial changes before and after the transplant. Urine samples were collected 24 hours prior to liver transplantation, and again at 3 and 6 months post-operation. These urine samples were adjusted for urine osmolality, and untargeted metabolomic analysis was performed using UPLC-MS/MS. Fecal samples were also collected at the same time points and analyzed for fecal microbiota composition through 16S rRNA sequencing. Welch's paired t-tests were used to determine statistical significance of urinary metabolites. Spearman's correlations were conducted to identify relationships between urinary metabolites and microbial genera.

Results: Analysis of the urinary metabolome between ALD and healthy control patients before liver transplant revealed significant changes in over 80 neuroactive metabolites. We found that, among these pre-transplant metabolites, pathways related to dopamine and serotonin production remained dysregulated six months after liver transplantation. Urinary levels of vanillacetate, a precursor to serotonin and dopamine, were significantly higher in ALD patients before transplantation compared to healthy controls ($p = 0.0003$), and these levels stayed elevated at both the 3-month ($p = 0.0094$) and 6-month ($p = 0.0468$) timepoints. Interestingly, compared to healthy controls, levels of microbially derived neuroactive metabolites, including indole-3-carboxylate ($p < 0.001$), 4-hydroxyphenylalanine ($p < 0.001$), and kynurenine ($p = 0.0339$) were significantly altered in ALD patients prior to liver transplant and did not recover within 6 months following the procedure. Permutation tests of 16S rRNA sequencing data revealed that core microbial genera differed significantly between cohorts, with a notable increase in the abundance of Bacteroides and Escherichia in the ALD cohort. When Spearman's correlations were performed between urinary metabolites and microbial genera, significant correlations were found between Escherichia and 4-hydroxyphenylalanine ($p = 0.0155$). Bacteroides were significantly correlated with indole-3-carboxylate ($p = 0.0327$, indole lactate($p = 0.048$), and 5-hydroxyindoleacetate $P = 0.0378$).

Conclusion: Taken together, our data suggest that urinary levels of neuroactive metabolites may be correlated with gut dysbiosis during alcohol-associated end-stage liver disease both pre- and post-liver transplantation. Our data highlight the chronic disruptions to the gut milieu that occur with chronic alcohol consumption and highlight the importance of further research into the mechanisms by which the gut-brain axis may modulate neurotransmission during ALD.

Harry M. Vars Award Candidate

2208142 - Western Diet Induces Progression of Metastatic Colorectal Cancer in Mice

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Financial Support: ASPEN Rhoads Research Foundation.

Background: Dietary prehabilitation is associated with improved disease-free survival after primary colorectal cancer (CRC) resections. The mechanisms underlying this observation remain unclear, but are thought to be related to the direct effects of the gut microbiota on systemic immune function. We hypothesized that prehabilitation will impact local antitumor immunity and progression of metastatic CRC in a mouse model.

Methods: We utilized a validated model of CRC peritoneal metastases in balb/c mice with syngeneic CT26 CRC cells. Four mice per group received four preoperative weeks of dietary treatment with: 1) standard chow; 2) a high fat, zero fiber western-style diet (western); or 3) switched from western diet to chow a week prior to surgery (prehabilitation). Three weeks after surgery, blinded examiners measured extent of disease using the peritoneal carcinomatosis index (PCI). An immunofluorescence panel was used to quantify intratumoral immune microenvironment. 16 s rRNA sequencing of expelled stool was used to characterize the fecal micriobiome.

Results: Substantial gut dysbiosis, as measured by alpha diversity (Figure 1) and pathogenic overgrowth (mean relative abundance of specific pathogens) of the fecal microbiome, was induced by surgery in the western diet group. This effect was statistically significant and partially rescued in the prehabilitation group. All mice in the chow and prehabilitation groups survived to endpoint. One mouse in the western-fed group died of intraabdominal sepsis. Preoperative weight gain was higher in the western group (Fig. 2 A 7.88 ± 0.39 g western vs 5.83 ± 0.38 g chow, $p < 0.01$, One-way ANOVA). We observed no difference in PCI between the western and prehabilitation groups ($p = 0.96$, one-way ANOVA). However, PCI was significantly lower in the chow group (Fig. 2B, 10.25 ± 0.95) when compared to both the western (17.00 ± 2.31, $p = 0.02$) and prehabilitation groups (16.50 ± 0.65, $p = 0.02$, One-way ANOVA). Tumors from the chow group demonstrated significantly more CD4+cells/mm than the western but not the prehabilitation group (Fig. 2 C, $p < 0.05$, One-way ANOVA). Tumors from the prehabilitation group had significantly more CD8+cells/mm than the western but not the chow group ($p < 0.05$, One-way ANOVA). No intergroup differences were observed in macrophage infiltrate.

Conclusion: Mice fed a western diet demonstrated substantial gut dysbiosis after surgery that was partially rescued by dietary prehabilitation. Chow-fed mice demonstrated decreased peritoneal tumor bulk compared to western-fed mice. Dietary prehabilitation rescued the local immune infiltrate, but not tumor progression as measured in our model. This may be due to the effects of the gut micriobiota on the systemic function of the immune system, or the gut-immune axis. These findings may underlie the observation of decreased recurrence rates after prehabilitation for CRC surgery in humans.

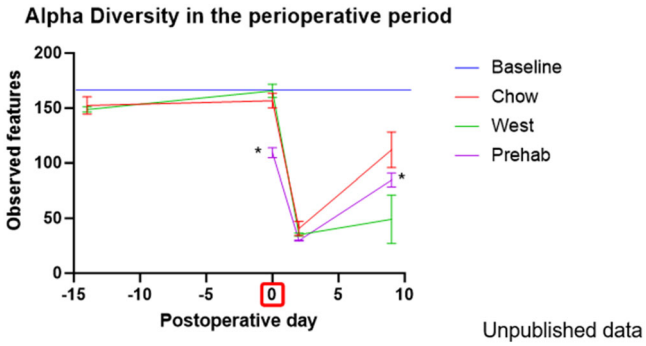

Figure 1.

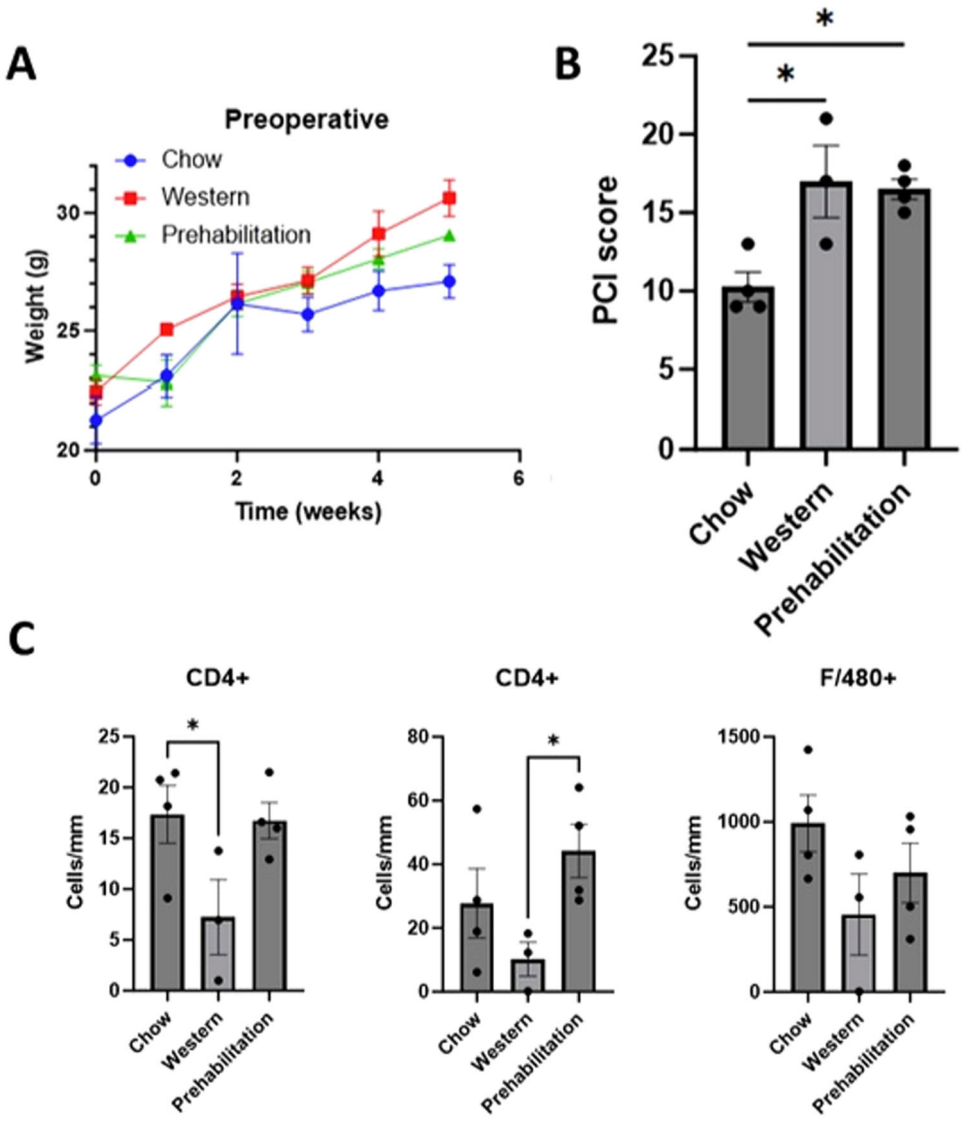

Figure 2.

Harry M. Vars Award Candidate

2207088 - Barrier Dysfunction in Intestinal Failure is Driven by Nutrient Deprivation and Wnt Signaling Suppression

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[1]Noorda COM, St. Louis, Missouri; [2]Saint Louis University School of Medicine, St. Louis, Missouri

Financial Support: None Reported.

Background: Short bowel syndrome (SBS) is a devastating condition. While Total parenteral nutrition (TPN) in SBS can provide the necessary nutritional support, side effects of severe gut atrophy limit its full utility. Since a large portion of intracellular ß-catenin is associated with e-cadherin, we hypothesized that the loss of e-cadherin results in an altering of the e-cadherin/ß-catenin complex as well a severe redistribution of intracellular ß-catenin driving alterations in intercellular signaling.

Methods: Using our novel ambulatory model (US Patent: US 63/136,165), 12 piglets were randomly allocated to enteral nutrition (EN; n = 4), TPN only (n = 4), or TPN + SBS (n = 4) for 14 days. Gut tissues were assessed through histology, qPCR, and western immunoblotting. Statistical analysis was performed using 'Graph Pad Prism 10.1.2 and referenced against historical controls. All tests were 2-tailed using a significance level of 0.05.

Results: There was a significant reduction in E-cadherin levels in both TPN ($p < .001$) and SBS ($p < .001$) vs EN, mimicking reductions in ß-Catenin levels in TPN ($p < .001$) and SBS ($p < .001$). To evaluate the extent of epithelial barrier impairment tight junction (TJ) proteins were included (Occludin and Claudin-4). Gene expression was notably decreased in TJ proteins for both TPN and SBS. To evaluate gut growth, we measured linear gut mass (LGM), calculated as the weight of the bowel per centimeter. There was severe gut atrophy in both TPN and SBS. Mean proximal gut LGM (g/cm) was EN 0.21, TPN, 0.12 and TPN-SBS 0.11. Distal gut LGM (g/cm) was EN 0.34, TPN 0.14 and TPN-SBS 0.13. There was also a significant reduction in the villus/crypt ratio in TPN 1.67 ($p < 0.001$), SBS 1.51 ($p = 0.007$) vs EN 2.13. Alterations in transcriptional activity were measured along the downstream targets, SAM Pointed Domain Containing ETS Transcription Factor (SPDEF) as well as Lymphoid enhancer-binding factor 1 (LEF1) with decreased expression in both TPN and SBS.

Conclusion: TPN results in a significant change in the small intestines by not only impacting the E-cadherin/ß-catenin complex but also altering the gut barrier. The implications of this loss are seen in the lack of transcriptional activity as well as decreased epithelial cell proliferation and contribute to the inflammatory responses noted with this lifesaving approach.

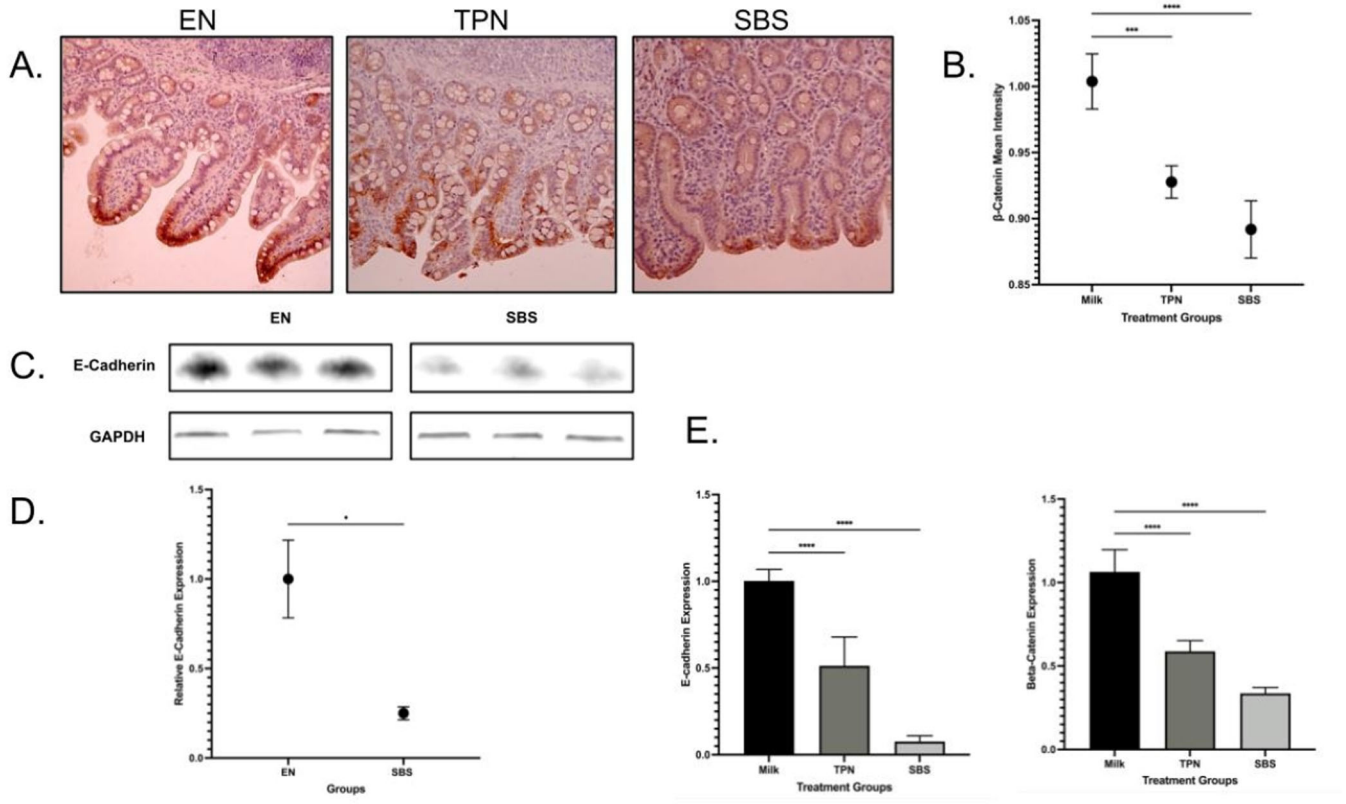

Figure 1.

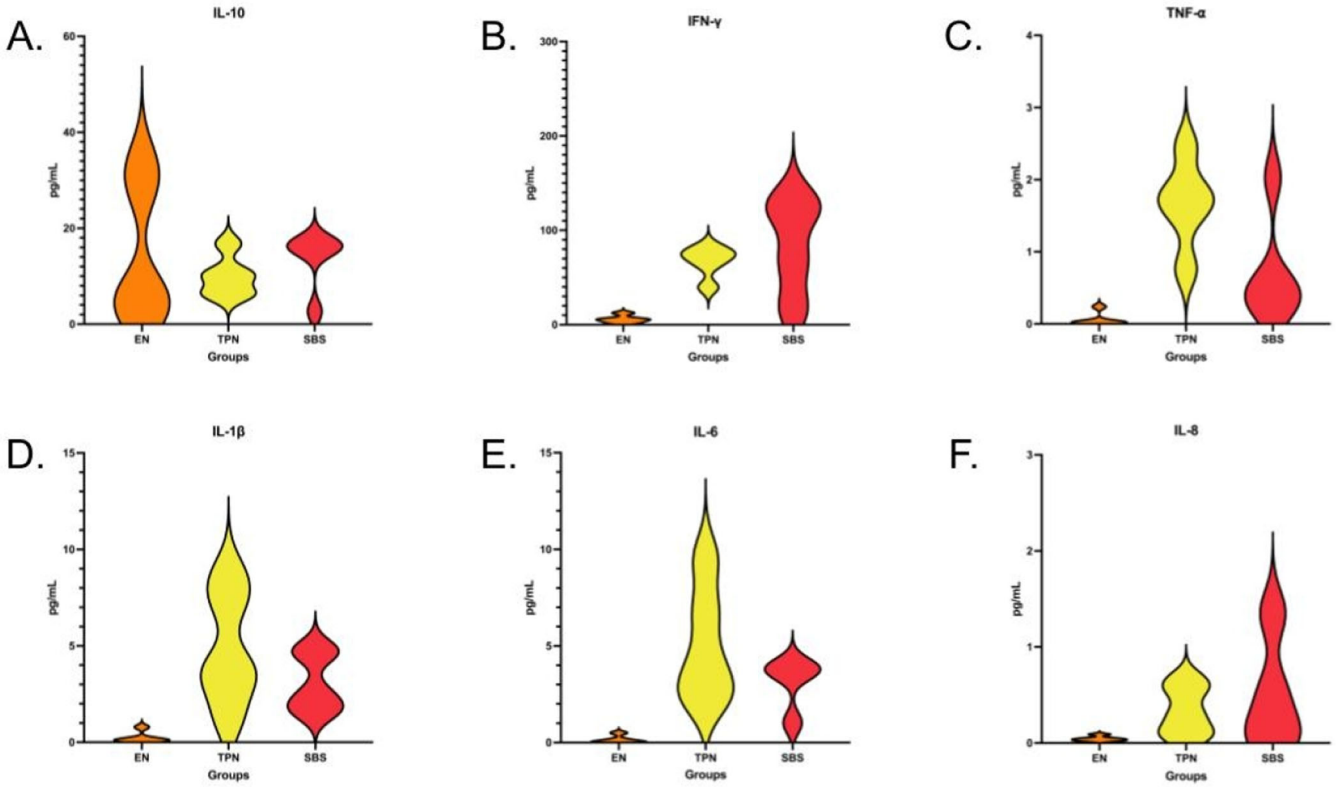

Figure 2.