School-age Morphological And Neurodevelopmental Outcomes In Patients With Sagittal Craniosynos

Annahita R Fotouhi[1], Abdullah M Said[1], Gary B Skolnick[1], Mary M Cradock[2], Sybill D Naidoo[1] and Kamlesh B Patel[1]
[1]Washington University in St. Louis School of Medicine and [2]St. Louis Children's Hospital

OBJECTIVES/GOALS: Several studies compare perioperative parameters and postoperative morphology of open cranial vault remodeling (CVR) and endoscopic-assisted craniectomy (EAC) in the treatment of sagittal craniosynostosis. However, data on neurodevelopmental outcomes comparing these techniques is lacking. METHODS/STUDY POPULATION: Patients with repaired sagittal synostosis were enrolled from a single tertiary care center between five and fifteen years of age. Patients with any craniofacial syndrome (e.g., 22q11.2 deletion) or other medical conditions that could affect neurodevelopment were excluded. Neurodevelopment was measured using the Differential Ability Scale-II (DAS-II). The General Cognitive Ability (GCA) score was the primary outcome measure, describing overall intellectual ability. Secondary outcome measures were measurements of cephalic index (CI) from pre- and postoperative imaging studies. Family socioeconomic status (SES) was estimated using the Hollingshead index (total score, continuous). RESULTS/ANTICIPATED RESULTS: 26 patients [10 CVR (2 Female:8 Male), 16 EAC (6 F:10 M)] were studied. Mean age at repair was greater with CVR than EAC (15.5 Â± 8.5 months vs 3.5 Â± 1.3 months, respectively, p < 0.001). Mean age at DAS-II testing was 9.0 Â± 2.2 years. Patients GCA scores were within the average range relative to test norms (CVR 95.7 Â± 15.4 vs EAC 102.6 Â± 17.4). After adjusting for SES and preoperative CI, group differences in GCA were modest and statistically nonsignificant (p = 0.646). GCA scores were associated with SES (p = 0.054) but not preop CI (p = 0.479). Differences between CVR and EAC were not statistically significant for any of the imaging parameters (pre and postop CI, pre to postop change in CI, or age at postop imaging; 0.131 <= p <= 0.867). None of the independent variables were significantly associated with postop CI (0.140 <= p <= 0.689). DISCUSSION/SIGNIFICANCE: Interim analysis of the preliminary data suggests no association between surgical procedure and cognitive and morphological outcomes at school-age in patients with sagittal craniosynostosis who underwent CVR versus EAC. Collection of data continues, with the goal to enroll 50 participants in each group by 2022.

Identification of Symptom-Based Phenotypes in PASC Patients through Bipartite Network Analysis: Implications for Patient Triage and Precision Treatment Strategies

Suresh K. Bhavnani[1], Weibin Zhang[1], Sandra Hatch[1], Randall Urban[1] and Christopher Tignanelli[2]
[1]University of Texas Medical Branch and [2]University of Minnesota

OBJECTIVES/GOALS: Approximately 10% of COVID-19 patients experience multiple symptoms weeks and months after the acute phase of infection. Our goal was to use advanced machine learning methods to identify PASC phenotypes based on their symptom profiles, and their association with critical adverse outcomes, with the goal of designing future targeted interventions. METHODS/STUDY POPULATION: Data. All COVID-19 outpatients from 12 University of Minnesota hospitals and 60 clinics. Independent variables consisted of 20 CDC-defined PASC symptoms extracted from clinical notes using NLP. Covariates included demographics, and outcomes included New Psychological Diagnostic Evaluation, and Number of PASC Hospital Visits (>=5). Cases (n=3235) consisted of patients with at least one symptom, and controls (n=3034) consisted of patients with no symptoms. Method. (1) Used bipartite network analysis and modularity maximization to identify patient-symptom biclusters. (2) Used multivariable logistic regression (adjusted for demographics and corrected through Bonferroni) to measure the odds ratio of each patient bicluster to adverse outcomes, compared to controls, and to each of the other biclusters. RESULTS/ANTICIPATED RESULTS: The analysis identified 6 PASC phenotypes (http://www.skbhavnani.com/DIVA/Images/Fig-1-PASC-Network.jpg), which was statistically significant compared to 1000 random permutations of the data (PASC=.31, Random Median=.27, z=11, P<.01). Three of the clusters (Cluster-1, Cluster-4, and Cluster-5 encircled with ovals in Fig. 1) contained CNS-related symptoms, which had statistically significant risk for one or both of the adverse outcomes. For example, Cluster-1 with critical CNS symptoms (depression, insomnia, anxiety, brain-fog/difficulty-thinking), had a significantly higher OR compared to the controls for New Psychological Diagnostic Evaluation (OR=6.6, CI=4.9-9.1, P-corr<.001), in addition to having a significantly higher ORs for the same outcome compared to all the other clusters. DISCUSSION/SIGNIFICANCE: The results identified distinct PASC phenotypes based on symptom profiles, with three of them related to CNS symptoms, each of which had significantly higher risk for specific adverse outcomes compared to controls. We will test whether these phenotypes replicate in the N3C data, and explore their translation into triage and treatment strategies.

Communication about Genetic Testing to Adult Women with a Higher Risk of Cancer in the United States: A Cross-sectional Analysis of the Health Information National Trends Survey (2017-2020)

Camille Pottinger[1]
[1]Johns Hopkins University School of Medicine, Morgan State University School of Community Health and Policy

OBJECTIVES/GOALS: The aim of this study is to examine the prevalence of communication sources about genetic testing among adult women with a higher risk of cancer in the U.S. and identify factors associated with these communication sources by analyzing the Health Information National Trends Survey (HINTS; 2017-2020) data, a large, nationally representative sample. METHODS/STUDY POPULATION: HINTS aims to gain knowledge about the use of and access to cancer information by the public. Used data was collected between 2017 and 2020 from a sample of adult participants who self-reported as female, aged 18+, having no personal cancer diagnosis, and having a family history of cancer. The primary outcome measure is source of communication about genetic testing. Some categories are the media, family members, or a healthcare professional. Analytical approaches include the Pearsons Chi-squared test and poisson regression model to estimate prevalence ratios

and examine the association between sociodemographic characteristics and sources of communication, adjusting for clinical and health belief factors as covariates. RESULTS/ANTICIPATED RESULTS: This study is in progress. It is anticipated that the most overall prevalent method of communication about genetic testing will be via the media. In multivariate models, it is anticipated that women who are younger, Black, have a lower education, have lower income, and no health insurance are more likely to receive communication about genetic testing from a source other than a health professional or not at all. After adjusting for clinical and health belief factors such as co-morbid conditions, having a primary care physician, and general knowledge about genetic testing, there may be some association between the above mentioned sociodemographic factors and receiving communication about genetic testing via a healthcare professional. DISCUSSION/SIGNIFICANCE: Reporting on the association between sociodemographic factors and sources of communication can aid in an intervention design to better promote genetic testing. This can be most beneficial among vulnerable groups like Black women to better understand their own genetic risk of cancer and to make informed decisions about their health.

369

The impact of asymmetric lung injury on gas and pressures distribution in a mechanical ventilation model with implementation of compartmentalized inspiratory hold*

Glen Meyerowitz[1] and Igor Barjaktarevic[1]
[1]UCLA

OBJECTIVES/GOALS: Asymmetries in lung pathophysiology can result in a maldistribution of gas between regions of the lungs which may generate dangerous pressures that are not observable by clinicians. Our study aims to demonstrate and quantify this through use of high-fidelity simulators to represent a range of commonly encountered clinical pathologies. METHODS/STUDY POPULATION: A benchtop study was performed with two high-fidelity breathing simulators, each representing one lung. This system allows for real-time monitoring of pressure and lung dynamics in a two-lung asymmetric injury model. One simulator was set to a fixed compliance and a resistance. A second simulator had a range of compliance and resistance values. Data were collected for 15 different test cases across a distribution of asymmetries. Each test case is run for 30 cycles. At the end of each ventilatory cycle, a short expiratory hold is performed, allowing pressure in the lung simulator, tubing, and ventilator circuit to equilibrate between cycles. RESULTS/ANTICIPATED RESULTS: Maldistribution of tidal volume was demonstrated when the compliance ratio between lung models (CL1/CL2) was 0.2 and the resistance ratio (RL1/RL2) was 10 with 23.9% (99% CI: 23.9-24.0%) of the gas volume distributed to lung 1 (103 mL L1 vs 327 mL in L2). Additionally, the injured lung when compared with the normal lung experienced higher peak pressures (12.8 cm H_2O vs. 6.9 cm H_2O, L1 and L2 respectively) and higher compartmentalized plateau pressures (11.5 cm H_2O vs. 6.8 cm H_2O, L1 and L2 respectively). DISCUSSION/SIGNIFICANCE: We demonstrate significant maldistribution of volume and pressures between two lungs in an asymmetric injury model. This study suggests significant impact of asymmetry in current lung-protective mechanical ventilation strategies and calls for better understanding of case-specific pathophysiologic changes affecting each of the two lungs.

370

Developing a Digitally Integrated Endotracheal Tube for Neonates to Improve Safety and Respiratory Function

Thomas Nienaber[1], Sarah Perez[1], Krista Stephenson[1], Joseph Sanford[2], Adria Abella[3], Morten Jensen[4] and Kevin Sexton[5]
[1]University of Arkansas for Medical Sciences, [2]UAMS Anesthesia/Clinical Informatics, UAMS Institute for Digital Health and Innovation., [3]UAMS Institute for Digital Health and Innovation, [4]University of Arkansas Bioengineering and [5]UAMS Surgery/Informatics, Institute for Digital Health and Innovation

OBJECTIVES/GOALS: Neonatal endotracheal tubes (ETTs) are usually uncuffed to avoid subglottic stenosis and other complications, but cuffed ETTs allow better ventilation. Our goal was to detect and control pressure in the cuff below the limit of occluding venous flow to minimize the risk of subglottic stenosis. METHODS/STUDY POPULATION: We designed a pressure sensor to fit on a 2.5 ETT for prototype testing in 8 age adult female rabbits. Eight uncuffed age- and sex- matched rabbits served as control. Study duration was 2 hours during which pressure in the cuff was limited by novel sensor (intervention) or auscultation (control). Anesthesia was maintained with sevoflurane. Ventilation was provided mechanically. Subsequently the tracheae were removed, sectioned crosswise, and compared histologically for mucosal damage. RESULTS/ANTICIPATED RESULTS: Preliminary data demonstrated an almost 30% greater amount of intact mucosa in the intervention group. The sensor also provided data on heart rate and respiratory rate, although this signal was not optimal. After filing an invention disclosure and provisional patent, we are refining our device to include multiple compartments for local control of cuff pressure and applying for a STTR Phase I/II application. DISCUSSION/SIGNIFICANCE: Ventilation in neonates with uncuffed ETTs can be suboptimal due to leak around the tube, but cuffed ETTs pose the threat of subglottic stenosis and other complications. We have designed a prototype cuffed ETT with a sensor to maintain low cuff pressure while preventing leaks and largely avoiding damage to the tracheal mucosa.

371

Decreased Contraction Rate, Altered Calcium Transients, and Increased Proliferation seen in Patient-specific iPSC-CMs Modeling Ebsteins Anomaly and Left Ventricular Noncompaction

Sai Suma Samudrala[1], Melissa Anfinson[1], Matthew Cavanaugh[2], Min-Su Kim[1], Peter Lamberton[2], Jackson Radandt[2], Ryan Brown[1], Huan Ling Liang[1], Karl Stamm[1], Afzal Zeeshan[1], Jennifer Strande[1], Michele Frommelt[3], John W. Lough[1], Robert Fitts[2], Michael E. Mitchell[1,3], Aoy Tomita-Mitchell[1]
[1]Medical College of Wisconsin, [2]Marquette University and [3]Childrens Wisconsin

OBJECTIVES/GOALS: In a familial case where 10 of 17 members inherited EA/LVNC in an autosomal dominant pattern, we discovered a novel, damaging missense variant in the gene KLHL26 that segregates with disease and comprises an altered electrostatic surface profile, likely decoupling the CUL3-interactome. We hypothesize that this KLHL26 variant is etiologic of EA/LVNC. METHODS/