showed head shape improvements after corrective surgery during clinical evaluation. Linear temporal regression indicates a CSA index decrease of 0.43 ± 0.05 during the first year after surgery. We found no significant correlation between a patient's age at surgery and the patient's CSA index after surgery (Pearson's correlation coefficient 0.17, p = 0.20) or the patient's change in CSA index before and after surgery (Pearson's correlation coefficient 0.22, p = 0.11), suggesting that sagittal craniectomy is equally effective for all patients who are between 85 and 331 days old at the time of surgery. DISCUSSION/SIGNIFICANCE: Our new CSA index is a sex- and age-specific metric of head shape anomalies built upon the observed statistical distributions in the normative pediatric population. Our metric can objectively evaluate pre- and post-surgical head shapes and will allow the investigation of the reported variability in surgical outcomes among patients and procedures.

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Omics based analysis to identify novel markers of TMZ response in Glioblastoma Multiforme

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OBJECTIVES/GOALS: MGMT methylation status is used to predict the response to TMZ. However, a subpopulation of patients lacking MGMT methylation still respond to TMZ. We applied omics approaches and functional studies to a cohort of GBM patients to identify novel markers that may more accurately predict TMZ response. METHODS/STUDY POPULATION: We applied a combination of omics approaches and functional studies to a cohort of GBM patients to search for novel markers that would predict the response to TMZ treatment more accurately than traditional markers. Using a set of 47 primary and secondary GBM tumor samples, we employed comparative transcriptomics, whole exome sequencing, data independent acquisition (DIA) proteomics, and phosphoproteomics to look for DNA mutations and changes in gene expression and/or protein expression that correlated to response or non-response to TMZ. Subsequently, we performed functional studies and analyzed patient treatment data to validate our results. RESULTS/ANTICIPATED RESULTS: This study is in early stage, but we anticipate that our combination of methods may allow us to identify and validate at least one novel biomarker for TMZ response in patient GBM. For example, comparative transcriptomics or phosphoproteomics may identify a previously unrecognized gene or protein over/under-expression in a subset of patients. In this case we will validate findings using western blotting, IHC staining, and through siRNA of target gene/protein on patient derived GBM cells to examine if removal of this marker leads to TMZ sensitivity. We will further confirm prediction of marker correlation through comparison with matched patient treatment data. DISCUSSION/SIGNIFICANCE: The identification of improved biomarkers to predict response to TMZ treatment is a discovery that could rapidly become standard of care for GBM patients. It would ensure that all responders receive TMZ and avoid exposing nonresponders unnecessarily to TMZ and its potential side effects.

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Optimizing the Identification and Prediction of Statin Intolerance to Improve Statin Adherence Using Natural Language Processing and Machine Learning

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OBJECTIVES/GOALS: Aim1: To develop a natural language processing (NLP) algorithm to effectively identify statin associated muscle symptoms (SAMS) in patients'electronic health records (EHRs). Aim2: To develop a machine learning model based on clinical features within EHRs that predict the likelihood of SAMS occurrences. METHODS/STUDY POPULATION: A retrospective cohort of adult patients initiated on statins within the Minnesota Fairview Healthcare System EHRs from 2010 to 2020 will be analyzed. NLP-PIER (Patient Information Extraction for Research) platform will be used to search and identify patients who developed SAMS after statin initiation. Manual annotation of clinical notes will be completed to validate the accuracy of identified SAMS cases. Then, a selection of clinical features within the EHRs will be input as predictors for machine learning algorithms development. Select machine learning classifiers will be deployed to generate models for the prediction of SAMS and the best-performing model will be selected based on model performance. RESULTS/ANTICIPATED RESULTS: The expected outcomes include generation of a fine-tuned NLP algorithm that can rigorously identify SAMS occurrences within EHRs. Further, we anticipate having a practical risk model that accurately predicts patients'risks of developing SAMS when taking statins. DISCUSSION/SIGNIFICANCE: The positive and translational impact of our research will be to equip healthcare providers with such informatics tools to improve statin adherence, ultimately promoting patient optimal health and outcomes by maximizing the tolerance and thus realizing the therapeutic benefits of statins.

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Optimizing Urinary cell mRNA profiling of kidney allograft recipients: Development of a home processing protocol for noninvasive diagnosis of T cell mediated rejection and BK virus nephropathy

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OBJECTIVES/GOALS: Development of a user friendly home kit that enables kidney transplant recipients to process urine at home and post the lysate containing RNA to a Core Laboratory would simplify urinary cell mRNA profiling and facilitate longitudinal monitoring. We report our home processing protocol and investigation of its diagnostic performance characteristics. METHODS/STUDY POPULATION: We developed a home processing protocol (HPP) consisting of urine filtration and lysis of urinary cells, both

https://doi.org/10.1017/cts.2023.370

performed at home by the kidney transplant recipients (KTR) themselves, followed by isolation of total RNA from the lysate and mRNA enrichment using a silica-membrane-based cartridge, both performed at the Core Laboratory. Using the HPP, total RNA was isolated from kidney allograft biopsy-matched urines and absolute copy numbers of CD3ÎµmRNA, CXCL10 mRNA, and 18S rRNA, components of the Clinical Trials in Organ Transplantation 04 (CTOT-04) three-gene TCMR diagnostic signature, and urinary cell BKV VP1 mRNA copy number, were measured using customized RT-qPCR assays. RESULTS/ANTICIPATED RESULTS: CTOT-04 three-gene TCMR diagnostic signature scores in urine processed using HPP discriminated KTR with TCMR (12 TCMR biopsies from 11 KTR) from KTR with no TCMR/BKVN (29 No TCMR/No BKVN biopsies from 29 KTR) (P=0.0005, Mann-Whitney test), and AUROC was 0.84 (95% CI, 0.69 to 0.98). TCMR was diagnosed with sensitivity of 67% (95% CI, 35 to 89) at a specificity of 86% (95% CI, 67 to 95) using the CTOT-04 validated cutpoint of -1.213 (P=0.0016,Fisher exact test). BKV VP1 mRNA copy number in urine processed with HPP discriminated KTR with BKVN (n=7) from KTR with no TCMR/BKVN (n=29) and AUROC was 1.0 (95% CI, 1.00 to 1.00). BKVN was diagnosed with a sensitivity of 86% (95% CI, 42 to 99) at specificity of 100% (95% CI, 85 to 100) with the previously validated cutpoint of 6.5x10^8 BKV VP1 mRNA copies/µg of RNA (P DISCUSSION/SIGNIFICANCE: Urine processed using the HPP predicted TCMR and BKVN in KTR. The HPP represents not only a significant advance towards portability of urinary cell mRNA profiling but also should improve patient management by minimizing visits for urine collection.

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Oxygenated Peritoneal Perfluorodecalin Improves Response to Normobaric Hypoxic Exposure in Swine

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OBJECTIVES/GOALS: Patients suffering from respiratory failure have few options to support oxygenation and carbon dioxide removal aside from mechanical ventilation. Our objective was to test a novel extrapulmonary mechanism of gas exchange via peritoneal oxygenated perfluorocarbon (PFC) in a large animal model. METHODS/STUDY POPULATION: Using two 50 kg swine, hypoxia was modeled with subatmospheric oxygen and hypercarbia induced with acute hypoventilation. Through a midline laparotomy, cannulas were placed into the peritoneal space to allow for PFC infusion and circulation. After abdominal closure, these cannulas were connected to a device capable of draining, oxygenating, and infusing PFC. One animal was subjected to acute hypoxia (12% FiO2) and another animal to acute hypoventilation (4 breaths per minute). Primary outcomes were times for SpO2 to reach 75 mmHg, respectively. Trials were performed without PFC and with PFC dwelling or circulating through the peritoneal space, during which abdominal and bladder pressures were monitored and maintained under 20 mmHg by regulation of the PFC volume contained in the animal. RESULTS/ANTICIPATED RESULTS: In the animal subjected to acute hypoxia (12% FiO2), survival time improved from 5:55 to 20:00 (min:sec) after 2.5 liters of oxygenated PFC was instilled in the peritoneal space. Oxygen percent saturation of PFC before and after dwelling in the peritoneal space was measured at 100% before and 70% after dwelling in the animal during this hypoxic period corresponding with a gas transfer of 300 mL of oxygen over the 20-minute trial (i.e., 15 mL/min). Continual PFC circulation did not further extend the survival time during hypoxic conditions over PFC dwelling in the abdomen. In the animal that was acutely hypoventilated, there were no detectable differences in the rate of CO2 accumulation as measured by EtCO2 or direct blood pCO2 measurements with PFC dwelling or circulating through the peritoneal space. DISCUSSION/SIGNIFICANCE: Oxygenated PFC dwelling in the peritoneal space increased the duration of systemic arterial blood saturation remaining greater than 50% during normobaric hypoxic (12% FiO2) conditions but did not appreciably clear blood carbon dioxide during hypoventilation. Future experiments will focus on maximizing the rate of systemic oxygen uptake.

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Paired associative stimulation: a tool for assessing sensorimotor neural signaling and lower limb function post-stroke[+]

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OBJECTIVES/GOALS: A stroke can impair neural communication between sensory and motor pathways thus compromising walking function. Paired associative stimulation (PAS) is a useful assay of sensorimotor integration (SMI) with limited use post-stroke. The objective of this study will be to determine lower extremity PAS effectiveness and reliability post-stroke. METHODS/STUDY POPULATION: This study will use a pre-post, cross-sectional design. Ten healthy controls and 10 individuals with chronic stroke (>6 months) will be recruited. PAS protocols will be individualized to account for between-subject variability in sensorimotor signaling by first measuring cortical sensory signaling using electroencephalography. Post-stroke participants will then receive PAS targeting the paretic tibialis anterior muscle; healthy controls will receive PAS targeting the non-dominant TA. Changes in cortically derived muscle responses will be characterized by absolute motor-evoked potential amplitude (MEPAmp) change, elicited by transcranial magnetic stimulation, over two sessions separated by >24 hours. Clinical measures of sensorimotor function and walking ability will also be performed. RESULTS/ANTICIPATED RESULTS: By individualizing PAS protocols, we expect to see significant increases in MEPAmp pre to post PAS, determined using paired t-tests. We also anticipate reliable PAS-induced increases in MEPAmp, which will be assessed using two reliability statistics: intraclass correlation coefficient and coefficients of variation of method error. Lastly, the increases in MEPAmp will be correlated with measures of sensorimotor function and walking ability, anticipating that greater increases in MEPAmp will be related to better walking ability and sensorimotor functioning. Correlations will be assessed via a Pearson's correlation. A preset alpha = 0.05 will be used to determine significant findings. DISCUSSION/SIGNIFICANCE: The importance of this study is that establishing individualized PAS protocols could potentially provide a reliable and clinically relevant measure of SMI. Understanding post-stroke lower extremity SMI is necessary for furthering targeted and personalized interventions to combat walking deficits.

[+]Kirstin-Friederike Heise has been added as an author. An addendum detailing this change has also been published (doi:10.1017/cts.2023.563).

https://doi.org/10.1017/cts.2023.370