response" significance variants. RESULTS/ANTICIPATED RESULTS: Among the 89CYP2D6 alleles with ClinVar "drug response" significance classification, 7 of 11 (64%) were more frequent (≥ 0.10) in the East Asian ancestry subgroup compared to the overall population. Among 6,262 CYP2D6 alleles with "undefined" significance classification, 60 showed elevated frequencies (≥ 0.10) in at least one subgroup: Middle Eastern (31/60; 52%), African (22/60; 37%), East Asian (21/60; 35%), and South Asian (4/60; 7%) ancestries. Of these 60 alleles, 16 (27%) map to 41–76, star allele haplotypes that contain at least one sub-allele with "definitive" allele evidence level in PharmVar. DISCUSSION/SIGNIFICANCE OF IMPACT: Our findings highlight the differential distribution and potential pharmacological relevance of CYP2D6 alleles across ancestral subgroups. These insights support potential reclassification of certain "undefined" alleles and highlight the importance of inclusive pharmacogenomic research.

389

Fronto-parietal white matter integrity and neurometabolic profiles in medication-naïve first-episode psychosis

James Bryant[1], Tobias Goodwin-Allcock[1], Ravi Tripathi[1], Adrienne C. Lahti[2] and Nina V. Kraguljac[1]
[1]The Ohio State University and [2]University of Alabama at Birmingham

OBJECTIVES/GOALS: In psychosis spectrum disorders, diffusion tensor imaging studies consistently report reduced fractional anisotropy in the superior longitudinal fasciculus, a major tract linking frontal and parietal cortices, yet the neurochemical underpinnings of these microstructural abnormalities remain poorly understood. METHODS/STUDY POPULATION: We collected diffusion MRI scans and single-voxel PRESS magnetic resonance spectroscopy scans both in parietal and frontal white matter in 48 medication naïve patients and 39 healthy controls. Fractional anisotropy within the superior longitudinal fasciculus was quantified in using TORTOISE and compared with frontal and parietal neurometabolic profiles processed with LC model and partial volume corrected. RESULTS/ANTICIPATED RESULTS: Myoinositol and TNAA were significantly different between patients and controls in both frontal and parietal white matter. Fractional anisotropy of the superior longitudinal fasciculus was significantly different between patients and controls. Both myoinositol and TNAA were associated with superior longitudinal fasciculus fractional anisotropy when modeled independently, but when jointly modeled only TNAA was significantly associated with fractional anisotropy in the parietal white matter while only myoinositol was significant in the frontal white matter. Both parietal and frontal white matter had a significantly greater association between myoinositol and fractional anisotropy than controls. DISCUSSION/SIGNIFICANCE OF IMPACT: Disruptions in neuronal integrity and glial dysfunction likely contribute to decreased fractional anisotropy in frontoparietal white matter in first-episode psychosis spectrum disorders. These disturbances are not related to medication effects.

390

Assessment of nutritional status and associated postoperative outcomes in total joint replacement patients

Shiloah Kviatkovsky, J. Ryan Hill, Benjamin M. Stronach, Jeffrey B. Stambough, Simon C. Mears, C. Lowry Barnes, ustin M. Rabinowitz, Noah D. Bogart, Reagan E. Dodd, London J. Parsons, Carsten R. Johnson, Dylan J. White, Landon B. Sandage and Jayden A. Goff
University of Arkansas for Medical Sciences

OBJECTIVES/GOALS: Nutrition status is an overlooked, modifiable driver of total joint arthroplasty (TJA) recovery that can reduce complication rates. Therefore, we will profile preoperative nutrition status in TJA patients using integrated clinical measures, identify metrics that predict postoperative complications, and validate their clinical utility. METHODS/STUDY POPULATION: We will enroll 800 elective hip (THA), knee (TKA), and shoulder (TSA) arthroplasty patients. Assessments will include blood biomarkers (albumin, lymphocytes, vitamin D/A, zinc, HbA1c, lipids), bioelectrical impedance (BIA) for body composition metrics (phase angle, body fat%, skeletal muscle index: SMI, visceral adipose area: VFA), and handgrip strength (muscle quality index: MQI). Biomarkers will inform on deficiencies, immunity, and metabolic health, reflecting surgical readiness. We will compute Onodera's Prognostic Nutritional Index (OPNI), SMI, and MQI and will evaluate infections, hospitalizations, revisions, and prolonged stay via records and encounters at 3 months and 1 year postop. Analyses will link nutrition metrics to complications to identify the strongest, actionable predictors. RESULTS/ANTICIPATED RESULTS: Among the first 100 arthroplasty participants assessed (THA: 43%, TKA: 49%, TSA: 8%), 56% were male (age 66.3±10.4 yrs). Mean lymphocytes was 1.9±0.6×109/L (normal: 1.0-4.8×109/L). Zinc averaged 59.9±11.6 μg/dL (normal: 60-120 μg/dL) with 47% deficient (50.9±6.6 μg/dL) versus 53% in normal range (66.8±5.0 μg/dL). Average vitamin D was 36.3 ng/mL (sufficient: >30 ng/mL), with 42% of patients low (20.8±5.6 ng/mL) versus 48% sufficient (47.8±15.1 ng/mL). Body composition measures: BMI 30.2 ±5.9 kg/m2 (2% underweight, 18% normal, 27% overweight, 27% obese 1, 14% obese 2, 6% obese 3); body fat 35.1±9.4%, VFA 155.8±55.3 cm2 (healthy: <100 cm2), SMI 7.9±1.5 kg/m2, phase angle 5.0±0.8°; and MQI 1.4±0.4. Comorbidities: T2DM 18%, HTN 67%, hypercholesterolemia 28%, CVD 37%; and 8% used GLP-1 medications. DISCUSSION/SIGNIFICANCE OF IMPACT: These early data show high zinc and vitamin D deficiency (47% and 42%, respectively), obesity (47% class I–III), and substantial comorbidities, underscoring the need for standardized nutrition screening in orthopedics. These findings justify targeted preop interventions and support an NIH R01 focused on reducing complications.

https://doi.org/10.1017/cts.2026.10551 Published online by Cambridge University Press