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Scientific Poster Abstracts

Justin Muste, MD
Research
PGY3 - Cleveland Clinic Cole Eye Institute

Inpatient Topical Glaucoma Medication Discrepancies: A Retrospective Cohort Study of Frequency and Risk Factors for Inaccurate Reconciliation

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Background:
Discrepancies between prescribed outpatient and inpatient medications are known to occur. These errors have not been characterized in topical glaucoma medications.

Objectives:
To describe the frequency of topical glaucoma medication discrepancies and to determine if factors such as number of glaucoma medications, demographic factors, and admitting service confer greater odds of a medication discrepancy.

Methods:
This is a retrospective cohort study of a random sample of adult patients with primary open angle glaucoma on at least one topical glaucoma medication admitted to any Cleveland Clinic facility between January 1, 2012 to January 1, 2023. All patients were required to have a at least one visit to a Cole Eye Institute ophthalmologist within 12 months prior to admission. Chart review was done to collect demographics, hospital site, discrepant medications, provider degree, admitting service, and pharmacy consultation. Inpatient reconciliation at admission, transfer, and discharge was compared against the outpatient ophthalmic record for discrepant prescriptions. Logistic and ordinal regression was used to appreciate factors associated with odds of error.

Results:
After screening 1,756 charts, 970 encounters were analyzed. Discrepancies were noted in 278 of 970 (28.6%) encounters. Patient demographics, hospital site, provider type, admitting service, and pharmacy consultation did not alter the odds of error. The rate of discrepancies was highest in patients on three medications (41.2%) followed by one medication (29.3%) and then two medications (26.8%) ($P<0.001$). On regression analysis, there was no correlation between the number of glaucoma medications and frequency of discrepancies. Medication discrepancy in previous hospitalization increased odds of discrepancy in subsequent admission (OR 5.1, 95% CI [3.2-8.4], $P<0.001$). A discrepancy on admission significantly increased error rates at transfer and discharge ($P<0.001$).

Significance:
Glaucoma medications are often associated preventable discrepancies that may propagate through an admission and from prior admissions. Future studies are needed to better understand, and ideally, prevent, the factors associated with these errors.

Alexander Arch, BA
Research
MS3 - University of Toledo

Whole-exome Sequencing Identifies Rare Variants and Genes Associated with Glaucoma

Glaucoma is the leading cause of irreversible blindness worldwide, with primary open-angle glaucoma (POAG) being the most common form of this condition. To date, genome-wide association studies have identified over 100 loci associated with POAG, predominantly utilizing common variants. The contribution of rare variants has remained largely unexplored. This study undertook a large-scale exome-wide association study to delve deeper into the genetic basis of glaucoma.

We examined exome sequencing data from 453,023 individuals (comprising 15,606 cases and 437,417 controls) from the UK Biobank, a prospective cohort study of approximately 500,000 participants living in the United Kingdom. Our focus was on rare variants with a minor allele frequency of less than 0.01. Using REGENIE and SAGE, we performed single variant and gene-based analyses on these variants, adjusting for age, sex, and the first 10 principal components of genetic ancestry. To replicate our results, we utilized the FinnGen dataset, encompassing data from around 200,000 Finnish subjects.

Our investigation confirmed previously identified rare variants associated with glaucoma, such as rs28939688 (p.Glu50Lys) in OPTN ($P = 3.21 \times 10\text{-}8$) and rs74315329 (p.Gln368Stop) in MYOC ($P = 1.01 \times 10\text{-}37$). Additionally, we discovered novel genes implicated in glaucoma through gene-based analysis, including MLH3 ($P = 1.37 \times 10\text{-}8$), PRR22 ($P = 1.84 \times 10\text{-}8$), PTBP1 ($P = 2.87 \times 10\text{-}8$), and MIR4745 ($P = 2.88 \times 10\text{-}8$). These significant associations were further corroborated using the FinnGen dataset. The findings of our study underscore the critical role of rare variants in identifying new genes and elucidating disease associations. Such discoveries are pivotal for refining clinical treatment strategies and improving prognostic precision for glaucoma.

Jessica Lee, BS Research
MS2 - Northeast Ohio Medical University/Bascom Palmer Eye Institute

Mechanosensitive Channel Distribution in Crushed (Control) and Axon Regenerating Optic Nerves

Purpose:
Regenerating retinal ganglion cell (RGC) axons within the optic nerve is crucial, offering the potential to recover lost vision resulting from conditions such as glaucoma. Mechanical forces determine the movement of regenerating RGC axons, facilitating their navigation to intended targets within the brain. Mechanosensitive (MS) ion channels detect mechanical forces within cell membranes and play a potential role in transducing these stimuli. We investigated the expression of 12 different MS channels (PKD2, PIEZO1, PIEZO2, ASIC2, alpha ENaC, TRPC2, TRPC3, TRPC5, TRPA1, TRPV4, TMC1, TRPM2) in crushed and axon regenerating optic nerves of the mouse to determine whether they are associated with regenerating axons.

Methods:
Two groups of C57BL/6J mice (n=6) were studied: the first group underwent pharmacologically induced axon regeneration via AAV-mediated ciliary neurotrophic factor (CNTF) followed by optic nerve crush (ONC), and the second (control) group underwent ONC without treatment. Prior to euthanasia, both groups received fluorophore-conjugated CTB intravitreal injections. Optic nerves were extracted, prepared for immunohistochemistry (IHC), and imaged using a confocal light microscope. Fluorescence data was analyzed using a densitometric scan and ImageJ software to calculate the mean and standard deviation of MS channel expression levels. The means of both groups were compared using a student's t-test, and IHC data was compared with Gene Expression Omnibus (GEO) transcriptomic datasets.

Results:
Image analysis using ImageJ subjected to a t-test suggested significant differences ($p \leq .05$) between crushed and axon regenerating optic nerves in certain channels. Of the 12 MS channels evaluated, 5 yielded similar expression levels between crushed and regenerating optic nerves. Of the other 7, TRPC3, TRPC5, TMC1, and PIEZO2 demonstrated upregulation in regenerated optic nerves, whereas TRPM2, ASIC1, and ASIC2 demonstrated downregulation. Transcriptomic dataset analysis was consistent with these results with a positive fold change in TRPC3, TRPC5, and TMC1 and a negative fold change in TRPM2 and ASIC1.

Conclusion:
Our findings suggest that MS channels are differentially present in crushed versus axon regenerating optic nerves. Future experiments will explore whether specific channel levels are associated with the looping or misdirection of axons, guiding strategies for directing regenerating axons toward correct brain regions.

James Rogers, BS
Research
MS1 - Wright State University Boonshoft School of Medicine

Outcomes for Intermittent Exotropia Using Three Common Surgical Approaches

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Introduction:
Several surgical approaches are used for treating intermittent exotropia (IXT). The procedure used largely depends on surgeon preference. This study compares a single surgeon's surgical outcomes using bilateral lateral rectus recession (BLR), unilateral lateral rectus recession and medial rectus resection (RR), and unilateral lateral rectus recession and medial rectus plication (RP).

Methods:
A retrospective review of all surgeries for basic IXT between 2015 and 2023 was performed. Only patients with initial correction using BLR, RR, or RP were included. Exclusion criteria included age >18-years, vertical deviation, any non-refractive ocular diagnoses, prior ocular surgery, and inadequate follow-up.

Results:
There were 460 patients identified; 131 met inclusion criteria with 54 in the BLR group, 41 in the RR group, and 28 in the RP group. The average pre-operative distance alignment (and standard error) for the BLR, RR, and RP groups were 25.07 (7.35), 22.44 (5.95), and 23.84 (6.42) prism diopters (PD), respectively. At 1-year the post-operative distance alignment for BLR, RR, and RP groups were 8.72 (7.89), 7.46 (6.31), and 12.83 (6.82) PD respectively ($p = 0.03$). A sub-analysis found a significant difference between the BLR and RP ($p = 0.02$) and RR and RP ($p = 0.02$) groups. There was no difference between the BLR and RR groups ($p = 0.57$).

Conclusion:
This study of three surgical approaches for IXT found RP had a significantly larger angle of exodeviation compared to BLR and RR at 1-year of follow up. Both BLR and RR were equally effective approaches for treating IXT.

James Dai, BS
Research
MS1 - Wright State University Boonshoft School of Medicine

In Vitro Formation of Cataract as a Model for Age-Related Cataract

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Age-related cataract affects 22% of individuals over the age of 75 years and data suggest that delaying progression rate by 10 years would decrease cataract surgery by 50%. When rodent lenses are incubated in culture medium, they lose their transparency after 24-48 hours because protein aggregation changes the index of refraction resulting in light scattering and opacity. We hypothesized that finding ways to prevent or delay this process through manipulation of the culture medium would provide important clues toward cataract prevention and present a solid foundation for drug testing model on specific mutated mice lens for cataract treatment.

13 culture conditions each comprising 4-6 adult C57BL6 mice lenses were tested whereby variations in glucose, pyruvate, fructose, antioxidant, osmolality (sorbitol), crowding agent (polyethylene glycol) were varied. The extent of opacification, the type of opacity (nuclear vs cortical) and the lens diameter were determined as of function of incubation time.

Results show that compared to the baseline conditions (Medium TC199), basic nutrition materials that lenses need for survival and antioxidants that prevents oxidative stress in lens show no improvement in preventing lens opacification. Next, we mimic the lens environment in the eye and test hyperosmolarity. PEG 1000 stood out among the rest by successfully preventing cataract formation in all of its lens. We also notice the lens size difference between PEG 1000 condition and the rest. PEG 1000 successfully prevents the lens from swelling and keep lens volume low. Thus, from our result, we tested the another set of biopolymers which could prevent massive intake of medium to the lens that we saw in previous conditions. We saw that Lymphoprep successfully kept lens clear until day 4 (96 hours), which was a major improvement compared to the rest of the conditions that we tested. In conclusion, this project would be novel in approach as the first to develop a system of drug testing lens model for cataract by keep mice lenses clear and transparent for 7-14 days, while we were still on the process of reaching 7-14 days of clarity in lens, we already tested out some strong potential conditions that improved lens transparency in vitro incubations such as PEG 1000 & Lymphoprep. We would further test on the possible conditions for optimizing lens culture medium for in vitro lens transparency. Specifically, we plan to focus on mimicking lens environment in eye to pertain lens homeostasis.

Jonathan Regenold, BS
Research
MS2 - University of Cincinnati College of Medicine

Midzonal Iris Pigment Epithelial Cysts: Surprising Findings Revealed by UBM

Purpose:
We conducted a case series study of the clinical characteristics of midzonal iris pigment epithelial (IPE) cysts, particularly their shapes and sizes and associated lesions revealed by ultrasound biomicroscopy (UBM).

Methods:
Charts of patients with midzonal IPE cysts encountered by one or more of the authors were reviewed retrospectively. Pertinent demographic information and clinical data about these patients and their cysts were abstracted.

Results:
69 patients with at least one midzonal IPE cyst in at least one eye were identified. At initial diagnosis, patients ranged in age from 14.8 to 89.5 years (median: 66.0 years, mean: 64.3 years). 38 patients (55.1%) were female. 74 eyes (39 right, 35 left) in this series contained one or more clinically identified midzonal IPE cysts. The cysts involved the right eye alone in 34 patients (49.3%), the left eye alone in 30 patients (43.5%), and both eyes in 5 patients (7.2%). The midzonal IPE cysts were located most often inferotemporally (51.4%) and second most often temporally (23.0%). UBM imaging had been performed on 44 of the 74 affected eyes. The median largest basal diameter of the midzonal IPE cysts evaluated by UBM was 4.5 mm (extremes: 1.5 to 13 mm), and the median depth of these cysts was 1.5 mm (extremes: 0.6 to 6 mm). All 5 UBM-evaluated eyes that appeared by slit lamp biomicroscopy to have two or more distinct midzonal IPE cysts were shown by UBM to have a single sausage or kidney-bean shaped partial ring cyst with radial folds between the lobules and not separate multiple cysts. UBM imaging also identified peripheral IPE cysts in 32 of 44 evaluated eyes (72.7%).

Conclusions:
Our case series confirmed reported findings regarding age at diagnosis and most common locations of midzonal IPE cysts. However, our UBM images revealed that most multifocal IPE cysts identified by slit lamp biomicroscopy are partial ring cysts with radial folds in the cyst wall between lobules and not true independent multiple cysts and that clinically unsuspected peripheral IPE cysts are frequently associated with midzonal IPE cysts.

Jonathan Shirian, BA
Research
MS2 - Case Western Reserve University School of Medicine

Associations of Androgen Exposure, PCOS, and Transmasculine Individuals with Central Serous Chorioretinopathy: A Cross-Sectional Study

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Purpose:
The prevalence of central serous chorioretinopathy (CSCR) among transmasculine and androgen-exposed individuals remains largely unexplored. This cross-sectional study, conducted utilizing a national database, aims to determine the prevalence of CSCR in cohorts with exogenous androgen exposure, female-to-male transgender individuals, and those diagnosed with polycystic ovary syndrome (PCOS).

Methods:
A U.S. collaborative network of electronic health records of 94 million patients was examined for this study (TriNetX, Cambridge, MA). Patients receiving exogenous androgens, transmasculine individuals, and patients with PCOS were identified. Identification of transmasculine individuals was completed through previously published coding methodologies and involved combinations of the following cohorts: gender identity disorder (GID), sex-discordant hormone therapy, and female-to-male (FTM) surgery. Patients with an outcome of CSCR and no prior steroid prescriptions, anxiety disorders, or fluticasone use were included. Prevalence odds ratios (OR) with 95% confidence intervals (CI) were calculated.

Results:
19,371 patients with CSCR were identified. Patients receiving androgen therapy exhibited significantly increased odds of CSCR (OR: 6.44, 95% CI: 5.42-7.66), as did those with PCOS (OR: 1.80, 95% CI: 1.21-2.67). While an overall significant association with transmasculine individuals was not established, sub-analysis revealed increased prevalence odds in the sex-discordant hormone therapy (OR: 5.19, 95% CI: 3.01-8.95) and FTM surgery cohorts (OR: 6.93, 95% CI: 3.83-12.53). The GID cohort did not exhibit a significant relationship with CSCR (OR: 1.10, 95% CI: 0.52-2.30).

Conclusion:
This is the largest study to uniquely examine associations between transgender and PCOS patients and CSCR, demonstrating that exogenous androgen exposure and PCOS are likely associated with higher odds of CSCR. Additionally, specific transmasculine cohorts showed increased prevalence odds, indicating potential correlations between androgens and CSCR risk. Further studies are warranted to elucidate the underlying mechanisms and roles of androgens in CSCR pathogenesis. Disclosures: This project was supported by the Clinical and Translational Science Collaborative (CTSC) of Cleveland which is funded by the National Institutes of Health (NIH), National Center for Advancing Translational Science (NCATS), Clinical and Translational Science Award (CTSA) grant, UL1TR002548. We would like to thank Dr. David Kaelber and MetroHealth for TriNetX access.

Kevin Allan, MD, PhD
Research
PGY1 - Cleveland Clinic Cole Eye Institute

Demographics and Postoperative Outcomes between Anterior Chamber and Scleral Fixated IOL Procedures

Purpose:
Millions of patients receive cataract surgery every year and complications, such as lens dislocation, necessitate replacement of the intra-ocular lens (IOL) in an alternative anatomic site. However, the process of patient selection and outcomes between alternative site procedures remains an active area of investigation.

Methods:
A chart review of adult patients who underwent an anterior chamber (ACIOL) or scleral fixated (SFIOL) intraocular lens procedure at Cole Eye Institute between 2013 and 2022 with at least two months follow-up. Combined glaucoma, retina, or cornea surgery cases and patients without IOL calculations were excluded. Demographic and postoperative outcomes including uncorrected visual acuity (UCVA), best-corrected visual acuity (BCVA), and complications were collected at three months postop and final visit. Postoperative success was defined as visual acuity (VA) greater than or equal to 20/40 and a stabilization or improvement of VA from baseline. Fisher's exact test compared categorical variables while two-way ANOVA compared postoperative UCVA and BCVA over time.

Results:
Of the 354 eyes included in this study, 48.5% received an ACIOL. The ACIOL group was older (71.1 versus 67.8 years old, $p=0.033$) otherwise demographics were not different from the SFIOL group. Surgical indication was most commonly IOL dislocation for both ACIOL (67.4%) and SFIOL (63.7%) placement. SFIOL surgery took 23% longer than ACIOL ($p<0.0001$). Baseline UCVA and BCVA were not significantly different ($p=0.88$) and both procedures significantly improved UCVA and BCVA after three months ($p<0.0001$) and at the final visit ($p <0.0001$). Significantly fewer ACIOL cases were considered UCVA postoperative successes (32%) compared to SFIOL (57%) at the final visit ($p = 0.02$). This could be partially explained by worsening of UCVA in patients with an ACIOL between three months postop and their final visit (0.62 versus 0.8 logMAR, $p = 0.06$). There was no significant difference in BCVA postoperative success ($p=0.75$) nor number of complications ($p=0.76$) between these procedures at the final visit.

Conclusion:
There were minimal clinically relevant differences in demographics, complications, and visual acuity outcomes at both short- and long-term follow-up visits between patients receiving an ACIOL compared to SFIOL.