Age-Related Dysregulation of Hypoxia Signaling Limits Skeletal Muscle Regeneration in Aging

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INTRODUCTION: The ability of skeletal muscle to regenerate declines significantly with aging. In this study, we explored the role of the hypoxia pathway and aryl hydrocarbon receptor translocator (ARNT) in age-related deterioration in regenerative response after injury.

METHODS: Young (2-3 months old) and old (23-25 months old) mice were compared in their hypoxia-related gene expression. A mouse model of inducible skeletal muscle-specific ARNT knockout was created (ARNT mKO) to study the effect of suppressing the hypoxia inducible factor (HIF)-induced hypoxia-related gene expression. Injured skeletal muscle and muscle stem cells were harvested from young, old, ARNT wild type (WT) and ARNT mKO mice with or without treatment with ML228, a hypoxia pathway activator, for histologic as well as biochemical analysis.

RESULTS: The expression of ARNT, a critical component of the hypoxia signaling pathway, was less abundant in skeletal muscle of old mice. This loss of ARNT was associated with decreased levels of Notch1 intracellular domain (N1ICD) and impaired regenerative response to injury, as compared with young (2-3 months old) mice. Knockdown of ARNT in a primary muscle cell line impaired differentiation in vitro. Skeletal muscle-specific ARNT deletion in young mice resulted in decreased levels of whole muscle N1ICD and limited muscle regeneration. Administration of a systemic hypoxia pathway activator (ML228) rescued skeletal muscle regeneration in both old and ARNT-deleted mice.

CONCLUSION: The loss of ARNT in the skeletal muscle contributes to diminished myogenic potential in aging, and activation of hypoxia signaling holds promise for rescuing regenerative activity in aged muscle.

Anticoagulants and Progression of Injury after Subdural Hematoma: Doomsday Clock or No Big Deal?

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INTRODUCTION: The purpose of this study was to determine if pre-injury anticoagulant (AC) use increased progression of hemorrhage after subdural hematoma (SDH) in elderly trauma patients.

METHODS: We reviewed patients >65 years of age, admitted with SDH from 2017 to 2018. Data collected included demographics, mechanism of injury (MOI), Injury Severity Score (ISS), use of direct oral anticoagulant (DOACs), warfarin (VKAs), antiplatelet therapy (APT), international normalized ratio, Glasgow Coma Scale, admission vital signs, hospital length of stay (LOS), surgical ICU LOS, functional status (FIM) at discharge, discharge disposition, and in-hospital mortality. Our primary outcome was injury progression identified by new or worsening hemorrhage on follow-up head CT. Comparisons were made between those using DOACs, VKAs, APT, or no agent.

RESULTS: A total of 213 patients were included: 23% had progression of injury, 18% had pre-injury AC usage, 49% had APT usage, and INR was 2.8 $\pm$ 1.8. Fall was the most common MOI. Although 82% of patients with AC or APT had progression, mortality was 2% and not different from those without progression. Logistic regression revealed patients on DOACs had significantly ($p < 0.05$) more progression of injury on subsequent CT scans compared with those on VKAs or APT. There was no difference between the groups with respect to the remaining collected metrics. Survivors were more likely to be discharged to a short-term nursing facility after hospitalization.

CONCLUSION: In AC patients, only pre-injury DOAC use was a risk factor for progression of injury after SDH. Despite progression, pre-injury DOAC, VKAs, or APT use did not increase mortality in elderly patients with SDH.

Artificial Intelligence Facilitates Performance Review and Characterization of Prehospital Emergency Medical Services Treatment

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INTRODUCTION: A total of 20% of US trauma death is preventable due to quality gaps. A prehospital study is needed. Manual review of prehospital data is time consuming and cost-prohibitive. Natural language processing (NLP) technology provides a solution to identify treatment appropriateness efficiently. The purpose of this study was to use an NLP pipeline to characterize prehospital treatment.

METHODS: Emergency medical services (EMS) data were obtained for 22,529 patients after motor vehicle collision (MVC). A validated NLP pipeline was used to characterize treatment indications and procedures for all patients. For NLP validation, manual review of 243 records was performed by 2 trauma surgeons. NLP results were compared with manual review.

RESULTS: Of the 22,529 patients, 936 (4.2%) had an indication for an airway intervention (AI), and 242 (1.1%) received an AI. A total of 170 (0.8%) had an indication for an intraosseous access (IO), and 110 (0.5%) received an IO; 237 (1.1%) patients had an indication for a crystalloid bolus (CB), and 319 (1.4%) received

a CB. Of these, 157 (0.7%) patients had an indication for chest compression system (CCS), and 53 (0.2%) received CCS. Fifty-five (0.2%) had an indication for needle decompression (ND), and 21 (0.1%) received an ND. Patients treated by paramedics (vs Emergency Medical Services) trended toward receiving more indicated airway procedures (odds ratio 2.02, 95% CI 0.92 - 4.46, p = 0.08).

CONCLUSION: This is one of the earliest studies using AI in the prehospital trauma setting. Use of NLP pipelines for data extraction has potential to optimize prehospital systems and, ultimately, to improve outcomes for patients.

Association Between Sociodemographic Factors and Long-Term Pressure Ulcer Development in Spinal Cord Injury Patients

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INTRODUCTION: Development of a pressure ulcer (PU) is a highly debilitating and costly complication associated with spinal cord injury (SCI). We investigated whether an association exists between sociodemographic variables and PU development beyond initial hospitalization within the SCI population.

METHODS: We identified patients over 18 years of age who suffered a traumatic SCI and were admitted to Froedtert Hospital between January 1, 2002 and December 31, 2018. Sociodemographic factors including sex, marital status, age, median household income (MHI) of patient ZIP code, and ethnicity were collected. SPSS was used to conduct descriptive statistics and bivariate logistic regression analyses.

RESULTS: A total of 448 patients met inclusion criteria (79% male, 59% white, 34% African American, 6% Hispanic, mean age 44 ± 18 years, 32% unmarried, mean MHI by ZIP code $56,075 ± $20,743). Significantly more male patients (40% vs 22%, $p < 0.001$) and unmarried patients (41% vs 28%, $p < 0.01$) developed PUs. There was a trend toward lower MHI of ZIP code and PU development, but it did not reach statistical significance (odds ratio [OR] 1.00, p = 0.077). Predictors of PU development included male sex (OR 2.38, $p < 0.01$) and unmarried status (OR 1.83, $p < 0.01$), while age (OR 1.006, p = 0.348) and ethnicity (OR 0.879 , p = 0.101) were not predictive. PU incidence was greater in unmarried men than in all other patients (44.3% vs 27%).

CONCLUSION: Sex and marital status are predictive of long-term PU development in the SCI population, with unmarried men at highest risk. Further investigation into PU development and markers of socioeconomic status is warranted.

Association Between Socioeconomic Status and Outcomes Post-Burn Injury

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INTRODUCTION: Socioeconomic factors have been identified as risk factors in trauma, but this impact has not been explored among the burn injury population. This study sought to identify risk factors affecting long-term patient-reported outcomes in burn injury patients.

METHODS: A retrospective review of the 2015 to 2019 Burn Model System national database was performed. All surviving patients ≥18 years of age afflicted with a burn injury were identified and divided into 2 groups: low income (<$25,000) and moderate/high income (≥$25,000). Parametric and nonparametric tests were used as appropriate. Multivariable regression analysis was performed to examine the association of various socioeconomic factors at 6-months post-injury.

RESULTS: In total, 322 patients were identified with 225 (69.9%) men and 97 (30.1%) women, with median age at time of injury of 47 years (interquartile range [32, 58]). Of these, 156 (48.4%) patients were classified as low-income and 166 (51.6%) were in the moderate/high income group. Individuals from the low-income group were found to have higher anxiety scores (p = 0.018) and a trend toward a higher likelihood for post-traumatic stress disorder (PTSD) at 6-month follow-up. Additionally, there was no significant difference in pain scores between groups (p = 0.327), but there was a higher likelihood for the moderate/high income group to receive more prescription pain medications at 6 months (odds ratio 1.29, 95% CI 1.05-1.58).

CONCLUSION: Evaluation of burn injury should include consideration for outcomes like anxiety, PTSD, and chronic pain. Health care practitioners should consider pain alternatives for burn injury patients to further limit unnecessary narcotics, which may also aid in control of anxiety and PTSD.

Beyond Morbidity and Mortality: Patient-Reported Outcomes in Trauma

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INTRODUCTION: The 2016 Zero Preventable Deaths report highlighted the need for comprehensive injury data to include long-term outcomes such as societal and workforce re-entry. Currently, postinjury quality of life is poorly understood. We