The Prognostic Significance of Androgen Receptor Expression in Malignant Gliomas

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Methods: We performed a retrospective cohort study, identifying patients with gout using the VHA administrative data from 1/1999-9/2015 based on the presence of ≥2 ICD-9 codes for gout (274.X). Patients were followed from the index date until death or censoring. Potential predictors of mortality were defined using data prior to the index date. Multivariable Cox regression models were constructed to identify independent predictors of all-cause mortality.

Results: We identified 559,253 gout patients in the VHA during the study period. Over 4,250,477 patient-years of follow-up, there were 246,291 deaths. Multivariable adjusted associations with all-cause mortality are shown in Table 1. Risk factors associated with increased mortality risk included male sex, older age, Black non-Hispanic race, comorbidities, diuretic, opioid, ULT, colchicine, and steroid use. Factors associated with a lower risk of all-cause mortality included white Hispanic, black Hispanic, and Asian races, elevated BMI, comorbid HTN, and NSAID use.

Conclusion: We have preliminarily identified multiple risk factors for mortality in veterans with gout with the strongest risk factors being comorbid CVD, diabetes, lung disease, and cancer, as well as the use of steroids and opioids. Mechanisms underpinning associations between select medication use and survival will require additional study accounting for the effects of comorbid CKD is this CKD or CVD and measures of gout severity. ∎

Table 1.
Patient characteristics associated with all-cause mortality in veterans with gout.

Characteristic	Adjusted HR (95% CI)*
Demographics	
Age, Years	1.06 (1.06, 1.06)
Male (vs. Female) Sex	1.07 (1.02, 1.12)
Race and Ethnicity	
White Hispanic	0.81 (0.78, 0.83)
White Non-Hispanic	Referent
Black Hispanic	0.78 (0.69, 0.89)
Black Non-Hispanic	1.06 (1.04, 1.07)
Asian	0.62 (0.59, 0.66)
Other	1.07 (1.04, 1.09)
Missing	1.95 (1.93, 1.97)
Service Connected Condition	0.84 (0.83, 0.85)
Urban Residence (vs. Rural)	1.02 (1.02, 1.03)
VHA Enrollment Duration, Years	0.95 (0.95, 0.95)
Health Factors & Comorbidities	
Body Mass Index	
<20 kg/m2	0.97 (0.93, 1.02)
20 to <25 kg/m2	Referent
25 to <30 kg/m2	0.74 (0.73, 0.75)
≥30 kg/m2	0.68 (0.67, 0.69)
Comorbidities	
Myocardial infarction or atherosclerosis, %	1.11 (1.09, 1.13)
Other cardiovascular disease, %	1.46 (1.45, 1.47)
Stroke, %	1.17 (1.15, 1.19)
Hypertension, %	0.90 (0.89, 0.91)
Lung disease, %	1.59 (1.57, 1.61)
Depression, %	1.15 (1.14, 1.17)
Diabetes mellitus, %	1.34 (1.32, 1.35)
Ulcer or stomach problem, %	1.06 (1.04, 1.08)
Cancer, %	1.23 (1.21, 1.24)
Diuretic Use	1.37 (1.36, 1.39)
Gout Disease Characteristics and Medication Use	
ULT Use (Allopurinol, Febuxostat, Probenecid, Pegloticase)	1.04 (1.03, 1.05)
NSAID Use	0.87 (0.86, 0.88)
Steroid Use	1.15 (1.13, 1.16)
Colchicine Use	1.08 (1.07, 1.09)
Opioid Use	1.17 (1.16, 1.19)
≥1 Serum Urate Test During Prior Year	0.99 (0.98, 1.00)

*All variables included in multivariable model are shown in the table
Abbreviations: VHA, Veterans Health Administration; ULT, urate lowering therapy

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Mentor: Chi Zhang

Program: Radiation Oncology

Type: Original Research

Background: Androgen receptor (AR) overexpression has been identified in malignant gliomas, suggesting that AR plays an important role in tumor carcinogenesis. However, the prognostic significance of AR overexpression remains largely to be explored.

Methods: AR gene expression at the levels of mRNA, protein expression, and clinical data were obtained from the Cancer Genome Atlas (TCGA) and Chinese Glioma Genome Atlas (CGGA) databases. AR expression levels were compared across gliomas of different histopathologic and molecular subtypes. Lastly, Kaplan-Meier survival analyses in patients with different AR expression levels were investigated for the potential prognostic values of AR.

Results: Compared to normal brain tissue, malignant gliomas showed significantly

higher AR mRNA expression (p < .01). Furthermore, AR mRNA expression was more prominent in higher grade disease, regardless of histopathologic and molecular subtypes (p < 0.01). Similarly, at the protein level, AR protein was more abundant in GBM than in lower grade gliomas (LGG) (grade II and III) (p <0.0001). This was corroborated by a linear association between AR mRNA and protein expression (r = 0.65, p < 0.001). Finally, in LGG, both high AR gene and protein expression were associated with significantly worse overall survival. Five-year overall survival for patients with LGG with high AR

gene expression and low AR gene expression were 59.1% and 73.3% respectively (p < 0.0001). Gender did not appear to be associated with either AR gene expression or prognosis.

Conclusions: AR gene overexpression is frequent in malignant gliomas and correlates with increased protein expression. Higher AR expression levels are associated with higher grade disease and histopathologic features predicting poorer prognosis. Furthermore, high gene expression in LGG is correlated with poor prognosis but not within GBM, indicating saturated expression/functions of AR in GBM. It will be important to evaluate AR gene and protein status to properly interpret future clinical trials using AR inhibitors. ∎

The Effect and Utility of Emergency Medicine Residency Orientation

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Type: Original Research

Background: Most matriculating emergency medicine (EM) postgraduate year-ones (PGY-1s) receive a form of orientation to acclimate them to residency. With varying medical school education and clinical experiences, the orientation month is used to provide equal preparation for all PGY-1s. Educational best practices have yet to be identified for a universal curriculum despite the longstanding history of residency orientation. The objectives of this study were to determine the benefits of EM residency orientation and identify areas of improvement for future curriculum development.

Methods: In July 2020, 12 PGY-1s underwent their EM orientation month, which included lectures, self-study, procedure skills labs, and simulation. Pre- and post-orientation surveys were administered and assessed for perceived comfort with common EM skills, preferred instructional methods, and the effect orientation had on their medical knowledge. For quantitative analysis, a 100-question EM board style exam was given at the beginning and end of the month. Data were summarized with descriptive statistics. Analysis was done using Spearman correlation coefficients, the Wilcoxon signed-rank test, and the Mann-Whitney test. A P-value < 0.05 was considered statistically significant.

Results: The pre- and post-survey and exam completion was 100% (12 of 12 PGY-1s). There was a statistically significant difference (p < 0.0005) in the perceived benefit of the orientation month. Pharmacology (91.7%) and EMR documentation (66.7%) were identified as the largest knowledge gaps prior to residency. Skills labs (91.7%) and simulation (58.3%) were identified as the most effective instructional methods. There was a statistically significant (p < 0.05) improvement in perceived comfort performing ultrasounds, sutures, splints, central venous catheters (CVC), lumbar punctures (LP), intubations, donning of personal protective equipment (PPE), and interpretation of electrocardiograms (EKG) and computed tomography (CT).

Conclusion: The use of a residency orientation for EM PGY-1s improved the perceived comfort for beginning residency. Interactive instructional methods (skills labs and simulation) were perceived as more effective in learning, compared to lecture-based instruction. ∎

Patterns of Opiate Prescription Practices in Isolated Operative Ankle Fractures: Creating Guidelines

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Program: Orthopedic Surgery

Type: Original Research

Background: Opioid use is associated with significant morbidity and safer alternatives to pain control exist. The purpose of this study was to quantify our opioid prescribing practices for isolated, operative ankle fractures and to formulate guidelines for safe and effective opioid stewardship.

Methods: The baseline average quantity of opioids prescribed (as Morphine Milligram Equivalents) at discharge and in the 90 days after surgery for adults with operatively treated, isolated ankle fractures were determined and prescribing guidelines were implemented. Opioid use was correlated to patient demographics, comorbidities, fracture characteristics, and patient reported pain control in each group.

Results: The baseline and test groups had 37 (24 female, 13 male) and 34 (21 female, 13 male) patients, respectively. There was no significant difference in age (49.7 vs. 47.2 years), comorbidities, or open fractures (1 vs 3). The mean MME prescribed was 444.86 (stdev = 314.9, range = 0 – 1425), versus 361.5 (stdev 232.9, range = 112.5 – 1025). This 18.8% reduction was not statistically significant (p = 0.32). There was no difference in pain scores at the first or second postoperative visits (2.64 vs 2.84 and 1.56 vs 1.81). There was no correlation between patient demographics, comorbidities, or fracture characteristics and MME prescribed or pain scores. Patients with higher pain scores at the first visit had more MME prescribed (p = 0.02 and 0.03).

Conclusion: Postoperative opioid use in isolated, operative ankle fractures in adult patients was reduced without a significant difference in patient reported pain control, but the decrease was not statistically significant. ∎