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The Warren Alpert Medical School of Brown University Annual Research Forum

Warren Alpert Medical School of Brown University Annual Research Forum: Resident Project Winners

Anna Hardesty, MD[1], Arun Muthiah, MD[1], Charles Fox Sherrod, MD[1], Hyun Lee, MD[1], Suleiman Ilyas, MD[1], Vishnu Kadiyala, MD[1], Matthew Murphy, MD, MPH[2]

[1] Medicine, The Warren Alpert Medical School of Brown University,
[2] Medicine, The Warren Alpert Medical School of Brown University, Brown University School of Public Health

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ANNA HARDESTY: USE OF ANTI-SPIKE MONOCLONAL ANTIBODIES IN KIDNEY TRANSPLANT RECIPIENTS WITH COVID-19: EFFICACY, ETHNIC AND RACIAL DISPARITIES

Background: Organ transplant recipients may not mount an adequate immune response to COVID-19 infection, and therefore may benefit greatly from passive immunization with anti-spike monoclonal antibodies (mAb), which have been shown to decrease hospitalization rates in the general outpatient population. We evaluated the efficacy of mAb therapy in decreasing hospitalizations or emergency room (ER) visits among kidney transplant recipients (KTR) with COVID-19. Methods: We identified KTR with COVID-19 between 3/1/2020 and 4/30/2021. Patients were excluded if they had multiorgan transplant or hospital-acquired COVID-19. Data were analyzed by Cox regression with mAb administration as time-dependent variable, and the day of symptom onset as baseline. Results: We studied 95 KTR; 20 received mAb. Comorbidities and immunosuppression were balanced between the two groups. mAb administration was associated with a significant decrease in hospitalizations or ER visits (15 vs. 76%, P<0.001). This association remained significant after adjustment for confounders and by analyzing mAb administration as a time-dependent variable. No KTR who received mAb died or required mechanical ventilation. Black or Hispanic KTR were less likely to receive mAb and more likely to be admitted to the hospital or visit the ER. Conclusions: In our KTR population, mAb therapy for COVID-19 may have helped decrease hospitalizations and ER visits. Healthcare inequities, including access to investigational treatments, were exacerbated by the COVID-19 pandemic. Acknowledging the non-concurrent control group as a limitation, we found a strong signal for benefit from mAb treatment. Antiviral mAb are a promising therapeutic modality for immunosuppressed patients.

ARUN MUTHIAH: CHARACTERIZING ONLINE ENGAGEMENT AND ACADEMIC IMPACT OF ONCOLOGY RESEARCH DURING THE COVID-19 PANDEMIC

Background: There is increasing use of social media as a platform to discuss research and educate. An article's impact can be assessed through the Altmetric Attention score (AAS), which considers the volume of social media mentions (Twitter, Facebook, Wikipedia, policy, etc.), and the PlumX Impact score, which incorporates interactions on these platforms and citations. COVID-19 has encouraged novel literature in oncology, and these metrics may holistically evaluate the immediate impact of articles in addition to gradual accrual of citations. We explored the relationship between traditionally used bibliometrics (citations, impact factor) and new bibliometrics (AAS, PlumX) of the top 100 trending articles on cancer and COVID-19. Methods: The 100 articles with highest AAS featuring keywords "cancer" and "COVID-19" between March 1, 2019, and January 15, 2022, were identified via Altmetric explorer. AAS, journal, social media mentions, open access status and other characteristics were collected. Scopus database was utilized to identify PlumX scores and citation count. Analysis included Spearman correlation coefficients and ANOVA. Results: Of the 100 articles, 64% were original investigations, 18% editorials/perspectives, 6% guidelines/consensus articles and remaining article types <6% each. Original investigations comprised of 41% retrospec-

tive cohort, 33% cross-sectional, 20% prospective cohort, and remainder <4% each. Most articles were open access (91%), from cancer-focused journals (77%), and based in North America (36%); 25% were in Europe, 24% Multicontinental, and remainder <8% each. Most publications were in 2020 (56%) and 2021 (40%). AAS and PlumX did not correlate with number of citations or impact factor. Open access publications were associated with greater PlumX (p= 0.033) compared to closed access; this was not seen with AAS. ANOVA showed greater AAS in Australian articles (p= .004) and greater PlumX in North American articles (p= .04). Article type or publication year did not impact AAS and PlumX. Conclusions: In our analysis, Altmetrics and PlumX did not correlate to traditional bibliometrics (citation count, impact factor) in cancer and COVID-19 articles. This suggests that these tools may be complimentary rather than predictive of citations. However, this may change given likely insufficient time for citations to accrue for 2021 studies. There were more editorials/perspective articles compared to similar studies in other specialties, suggesting greater impact of such articles in oncology during COVID-19; this is perhaps due to reliance on expert opinion given paucity of data. Additionally, we noted that PlumX benefits from open access status. Overall, as the use of social media for research dissemination grows, researchers and journal editors may employ alternative metrics to better understand ways to increase the influence of oncology literature during the pandemic.

CHARLES SHERROD: REHOSPITALIZATION FOLLOWING INPATIENT CARDIOMEMS IMPLANTATION: INSIGHTS FROM THE NATIONWIDE READMISSIONS DATABASE

Background: All-cause and heart failure re-hospitalizations are reduced following implantation of the CardioMEMS pulmonary artery pressure monitor in ambulatory patients with NYHA Class III heart failure regardless of left ventricular ejection fraction or pathogenesis who are on optimal guideline-directed therapy and have been hospitalized during the prior year. Whether device implantation in the inpatient setting is also effective is unknown. Methods: Patients who underwent inpatient CardioMEMS implantation between 2016-2018 were identified in the National Readmissions Database. Those who were transferred to or from another hospital during their index hospitalization, whose length of stay (LOS) was < 2 days, whose primary diagnosis was not for circulatory system disease, or who died were excluded. Those who underwent CardioMEMS implantation were propensity matched 5:1 to a hospitalized usual care group on 38 patient- and hospital-related factors as well as on discharge month and number of preceding admissions that year. Outcomes included all-cause (primary) and heart failure readmission at 30, 60, 90 and 180 days, inpatient LOS and cost. Results: There were 530 CardioMEMS and 2,650 usual care patients in the matched cohort. Mean age was 68 years and 37% were women. All-cause, and heart failure readmission rates were similar in the CardioMEMS and usual care cohorts at all time points (Table). Median [IQR] LOS was 8 [5,13] vs 6 [3,10] days (p=0.42), and median [IQR] cost was $48372 [$35509, $67440] vs $16415 [$8396, $38534] (p < 0.001) in the CardioMEMS and usual care groups, respectively. Conclusions: Using a large US national claims dataset, we observed no difference in all-cause or heart failure readmission rates in the 6 months after index hospitalization, but significantly higher inpatient costs following inpatient CardioMEMS implantation than usual care.

HYUN LEE: ETOPOSIDE USE IN SECONDARY HEMATOPHAGOCYTIC LYMPHOHISTIOCYTOSIS DUE TO INFECTIOUS ETIOLOGIES.

Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a syndrome of immune hyperactivity caused by a wide variety of underlying genetic mutations and secondary triggers. Treatment of secondary HLH in adults varies by associated conditions. Whereas autoimmune-associated HLH is typically treated with steroids and treatment directed at the underlying autoimmune disorder, retrospective data has suggested benefits of adding etoposide for malignancy-associated HLH in adults. The utility of etoposide in infection associated HLH lacks data to point toward either direction, and the current practice guideline remains equivocal. Herein we describe our single center experience in treating infection associated HLH with and without etoposide. Methods: We identified patients who received HLH diagnosis between 1/1/2007 to 1/1/2017 using ICD-10 code of D76.1. Notable inclusion criteria included meeting 5 of 8 HLH-2004 diagnostic criteria and presence of severe infection at presentation. Notable exclusion criteria were age less than 18, active cancer, chemotherapy within 1 year, and active autoimmune disorder. From records review, we obtained data for baseline characteristics, treatment modality, and survival at 3 years. Fisher's exact tests were used to differentiate categorical variables (Gender and mortality). Student T-tests were used for continuous variables (Age, comorbidity index, ferritin level). Additionally, we calculated median time from hospital admission to etoposide initiation then compared the mortality between those who received etoposide before versus after this median time. P value less than 0.05 was considered statistically significantly different. Results: 57 patients were identified with ICD-10 code and 13 patients were eligible for the study after application of inclusion and exclusion criteria.

Median age was 55, 7 (54%) were male, and 6 (46%) patients received etoposide for HLH. All patients received steroids and one patient received bone marrow transplant after etoposide therapy. Two (15%) patients received tacrolimus in addition to etoposide. Most common infections were viral, including 5 CMV (38%), 2 HIV (15%), 1 parvovirus (8%), and 1 HSV1 (8%). Other causes included 2 anaplasmosis (15%), 1 mycoplasmosis (8%), 1 klebsiella bacteremia (8%), and 1 histoplasmosis in addition to HIV (8%). All but one patient was followed until year 3 or death. One patient lost to follow up was included up to year 2 mortality comparison but excluded for year 3. Between etoposide group and control group, age, gender, comorbidity index, and initial ferritin were not significantly different (P = 0.38, 0.62, 0.12, and 0.33 respectively). Mortality comparison at week 8 (50% vs 86%, P = 0.21), year 1 (50% vs 86%, P = 0.21), year 3 (20% vs 86%, P = 0.08) showed no statistical significance but showed a trend toward worse outcome with etoposide use. Median time between presentation and etoposide initiation was 16.5 days. Mortality analysis between patients who received etoposide before versus after day 16.5 showed no significant difference in survival (66% v. 33%, P = 0.5). Conclusions: We identified a trend toward higher mortality with etoposide use in adults with infection associated HLH. Further studies with larger sample size are required to confirm this observation. Our data does not suggest that timing of etoposide affects outcomes.

SULEIMAN ILYAS: EVALUATION OF A DEEP LEARNING ALGORITHM AND PHONOCARDIOGRAPHY FOR DETECTING ELEVATED PULMONARY ARTERY SYSTOLIC PRESSURE

Background: Pulmonary hypertension (PH) is common, frequently associated with cardiopulmonary diseases and associated with poor outcomes. However, PH continues to go undiagnosed because of non-specific clinical symptoms, and need for echocardiography or right heart catheterization. Use of artificial intelligence machine learning (AI/ML) tools that run on digitally enhanced stethoscopes could be a cost effective, easy, and quick way to screen for PH. We evaluated a previously developed AI/ML tool to detect elevated pulmonary artery systolic pressure (PASP), using phonocardiograms (PCGs) recorded from digital stethoscopes. Methods: Digital stethoscope recordings were taken from patients undergoing cardiac echocardiography at 6 thoracic auscultation points using the Eko DUO digital stethoscope at the Providence VA Medical Center. Corresponding echocardiogram-calculated PASP was used as a ground truth for training a binary classifier AI/ML PH algorithm to identify PASP above 40mmHg where the output of the algorithm is the probability of having PH. Per-recording and per-patient algorithm performance was evaluated across the probability output from the algorithm and compared. Results: One hundred ninety-nine (199) patients were enrolled. Seventy (70) patients were excluded due to no corresponding PASP measurement and/or poor heart sound recordings. The remaining 129 patients had a total of 478 matched recordings. Across different recording positions, pulmonic and clavicle positions showed increased performance (AUC of 0.821 and 0.831 respectively), however, confidence intervals for all the recording positions are overlapping. Incorporating patient age, gender and BMI into the model did not improve performance. Conclusions: An AI/ML tool using PCG recorded using a digital stethoscope has the ability to detect PH and can be a low-cost, rapid, and minimally invasive screen for elevated PASP in a point-of-care setting. Further refining of the algorithm using per-patient analyses and multiple sites of auscultation is likely to improve the performance.

VISHNU KADIYALA: BLEEDING RISK SCORES PREDICT IN-HOSPITAL PCI OUTCOMES

Background: Bleeding events result in morbidity and mortality in patients undergoing percutaneous coronary intervention (PCI). There is limited data on PRECISE-DAPT and ARC-HBR scores' ability to predict in-hospital outcomes in PCI patients. Methods: Consecutive patients undergoing PCI at tertiary centers from January 2016 to March 2018 were identified and bleeding risk scores were calculated. The primary endpoint was NCDR-defined in-hospital bleeding stratified by low vs. high predicted bleeding risk. Major and net adverse cardiovascular events were also examined. Discriminatory ability of risk models was determined using receiver operating characteristic curves. Results: Among 3659 patients studied, 3.3% (n=121) suffered in-hospital major bleeding. Patients characterized as high bleeding risk by either score had higher bleeding rates compared to those with low-risk scores (ARC-HBR 5.4% vs 3.3%, p<0.001; PRECISE-DAPT 5.8% vs 2.4%, p<0.001); as well as higher MACE and NACE. The risk scores showed moderate and similar predictive ability (ARC-HBR high risk AUC 0.62, PRECISE-DAPT ≥25 AUC 0.61, p=0.49) with no incremental benefit to adding the scores (AUC 0.60). Subgroup analysis revealed that women had higher bleeding rates than men (5.53% vs 2.39%, p< 0.001), however predictive ability of the scores were similar in women and men. Conclusions: In a large retrospective study of consecutive PCI patient, the PRECISE-DAPT and the ARC-HBR scores showed ability to predict in-hospital major bleeding and adverse outcomes in both women and men.

Corresponding Author

Matthew Murphy MD, MPH
Assistant Professor of Medicine, Warren Alpert School of Medicine
Rhode Island Hospital
593 Eddy Street, Plain Street Building, First Floor
Providence, RI 02903
Phone Number: 401- 606-2249
Fax Number: 401-444-5040
Email: matthew.murphy@lifespan.org

Conflicts of Interest

The authors have no conflicts of interest to declare.