Ho J, Kane M, Haji M, et al. Warren Alpert Medical School of Brown University Annual Research Forum: Resident Project Winners. *Brown Hospital Medicine*. 2023;2(3). doi:10.56305/001c.77583

The Warren Alpert Medical School of Brown University Annual Research Forum

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

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Keywords: research, academic, research projects, Brown university, academia, Warren alpert medical school

https://doi.org/10.56305/001c.77583

Journal of Brown Hospital Medicine

Vol. 2, Issue 3, 2023

JONATHAN HO: HELICOBACTER PYLORI ANTIBIOTIC RESISTANCE IN THE UNITED STATES BETWEEN 2011-2021: A SYSTEMATIC REVIEW AND META-ANALYSIS

Introduction: Antimicrobial resistance among Helicobacter pylori (H. pylori) strains has been rising globally, leading to declining eradication rates. We performed a systematic review and meta-analysis of the resistance patterns of H. pylori strains in the United States between 2011 and 2021. Methods: Ovid MEDLINE, Embase, CINAHL, and Cochrane CENTRAL databases were searched for manuscripts and conference abstracts published between 2011 and 2021 reporting H. pylori antibiotic resistance. A mixed effects model estimated pooled rates of resistance to clarithromycin, amoxicillin, metronidazole, tetracycline, rifabutin, levofloxacin, or a combination of these, with 95% confidence intervals (CI). Results: A total of 19 studies, including 2660 samples, met inclusion criteria. The pooled rate of resistance to metronidazole was 42.1% [95% CI 27.3%-58.6%], levofloxacin 37.6% [95% CI 26.3%-50.4%], clarithromycin 31.5% [95% CI 23.6%-40.6%], amoxicillin 2.6% [95% CI 1.4%-5.0%], tetracycline 0.87% [95% CI 0.2%-3.8%], rifabutin 0.17% [95% CI 0.00%-10.9%], and dual clarithromycin and metronidazole 11.7% [95% CI 0.1%-94.0%]. Considerable data heterogeneity was evident for pooled resistance prevalence rates (I2 >50%), with the exception of rifabutin resistance. Conclusion: Metronidazole, levofloxacin, and clarithromycin resistance rates each exceed 30%; thus, choosing an empiric antibiotic regimen without knowledge of the likely pattern of antibiotic resistance is not appropriate. Resistance to tetracycline, rifabutin, and amoxicillin remains low. Given the scarcity of available data with considerable heterogeneity among studies, continued surveillance, ideally with a more systematic approach to data collection, is an increasingly important goal in H. pylori management.

MICA KANE: HOME BLOOD PRESSURE MONITORING: PATIENT AND PCP RESIDENT EXPERIENCES AND PERSPECTIVES

Background: Several studies have demonstrated that compared to elevated blood pressures measured in clinic, elevated home blood pressure readings confer a greater risk of future cardiovascular events and are more predictive of renal disease progression and mortality. Furthermore, home blood pressure monitoring improves treatment adherence and blood pressure control compared to in-office measurement alone. Many patients with hypertension at the CPC lack access to a reliable home blood pressure cuff, leaving residents with sporadic clinic readings to guide management. Methods: Home blood pressure cuffs were provided to twenty-five CPC patients with hypertension. Each patient was educated on how to use their home cuff and about healthy lifestyle interventions. Patients were asked to measure and record their blood pressure twice daily. Home blood pressure measurements were collected once each month over a three-month period, recorded in the EMR, and routed to the PCP resident to make appropriate medication changes and lifestyle recommendations. Patients completed pre-and post-surveys, and PCP residents also completed surveys at baseline. Results: The twenty-five patient participants were on average 59.1 (SD 12.8) years old, 28% were women, and 48% spoke a primary language other than English. After measuring their home blood pressure for three months, 62% of patients indicated that they had a better understanding of how their daily routines including exercise and diet affect their blood pressure, and 69% of patients felt they had more control over keeping their blood pressure at a healthy level. 23% of patients indicated that they took their blood pressure medications more frequently as prescribed after measuring their blood pressure at home. Analysis of patients' reported home blood pressures revealed that there was a significant decrease in mean reported home systolic BP from one to three months (mean difference -8.5 mmHg (95% CI -13.9, -3.0), p<0.01)). Analysis of resident survey data (n = 12) showed that 75% of PCP residents felt that their patients' home blood pressure readings are fairly to completely representative of their actual day-to-day blood pressure. 67% of residents felt

equally-to-more confident making clinical management decisions based on home blood pressure readings alone vs. in-office readings alone. All residents indicated that they felt more comfortable titrating a patient's anti-hypertensive medication regimen when they have home blood pressure readings available to supplement in-office readings. Conclusions: After measuring their blood pressure at home and having these measurements interpreted by their PCP resident, many of our patients at the CPC reported a better understanding of how their lifestyle affects their blood pressure and better perceived control over their blood pressure. Additionally, resident PCPs unanimously feel more comfortable adjusting their patients' treatment regimens when provided with home blood pressure readings.

MOHAMMED HAJI: OUTCOMES OF ADVANCED HEART FAILURE THERAPY AMONG PATIENTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS: A SYSTEMATIC REVIEW AND META-ANALYSISOUTCOMES OF ADVANCED HEART FAILURE THERAPY AMONG PATIENTS LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Introduction: As the prevalence of heart failure (HF) among patients living with human immunodeficiency virus (PLWH) rises, naturally, more PLWH will need to be considered for advanced HF therapies such as heart transplantation (HT) and left ventricular assist devices (LVAD). This study aims to synthesize the limited data on HT and LVAD outcomes among PLWH compared to controls without human immunodeficiency virus (HIV). Methods: We systematically searched multiple databases to identify studies of PLWH who received HT and LVAD. We extracted relevant data on patient characteristics and outcomes. Clinical outcomes, including mortality rates and hazard ratios (HRs), were pooled across studies by type of advanced HF treatment using random-effects meta-analysis. We used meta-regression to compare event rates between PLWH and controls, and account for age differences. Results: This review found 9 studies (5 HT, 3 LVAD, and 1 Study with both) that identified 210 and 169 PLWH, and 274,450 and 49,590 patients without HIV who received HT and LVAD, respectively. The PLWH receiving HT and LVAD were 4 and 2 years younger respectively than comparable control groups. PLWH and controls who received HT and LVAD were predominantly male. Due to limitations from registries, most studies did not report data on the status of HIV-specific traits. The pooled average 1- year mortality for PLWH after HT (6.4% [95% CI, 1.5-13.6]) was lower than that for controls (13.4% [11.1-15.8], p-value = p=0.009); the difference was no longer significant after accounting for age in meta-regression (p=0.16). The 1-year morality for PLWH after LVAD (22.6% [16.3-29.5]) was comparable to that for controls (18.9% [16.0-22.0], p=0.35). The 5-year mortality after HT for PLWH (20.1% [13.5-27.6]) was comparable to that of controls (24.7% [22.2-27.3, p = 0.15). Among studies reporting relative risk estimates, there was no significant difference in mortality between PLWH and controls for HT (HR, 95% CI: 0.8, 0.5-1.3) or LVAD recipients (1.4, 0.9-2.1), without significant heterogeneity across the studies. Conclusion: Synthesis of limited extant data on PLWH who received advanced HF treatment suggests that these patients have comparable 1-year and 5-year mortality with HIV-negative controls. Overall, the findings support the idea that HIV status is not a strong predictor of HT or LVAD outcomes and should not be a contraindication to advanced HF therapies.

NIRAV HARIBHAKTI: GENOMIC ANALYSIS OF CLEAR CELL CARCINOMAS

Introduction: Clear cell carcinomas (CCC) are rare histologies outside of the kidney and are typically less sensitive to standard treatments. Genomic alterations in chromatin remodeling pathways involving ARID1A or the intracellular PI3K-mTOR signaling pathway are found in both renal and ovarian CCC. It is unclear whether CCCs originating from different anatomic sites share a common genomic landscape. This CARIS Precision Oncology Alliance project sought to determine whether CCC of different organs shared similar genomic signatures and to identify potential pathways that could be targeted in a tumor-agnostic clinical trial. Methods: CCCs (N=861) from multiple primary tumor sites, including kidney (30.5%), ovary (39%), endometrium (23.9%), other gynecologic sites (e.g., cervix, fallopian tube, 3.3%), and miscellaneous (non-kidney or gynecologic sites, 3.3%) were analyzed at the Caris Life Sciences Laboratory (Phoenix, AZ). Using hierarchical clustering (HC) and principal component analysis (PCA), the samples were compared across 648 total genes from five metabolic gene sets consisting of angiogenesis, glycolysis, hypoxia, oxidative phosphorylation, and fatty acid metabolism. Gene Set Enrichment Analysis (GSEA) was further conducted on the samples across fifty hallmark gene sets representing specific biologic processes and expression. Samples were also analyzed for individual genomic alterations and immune oncology associated biomarkers. PD-L1 (SP142) expression was evaluated by immunohistochemistry (positive threshold: 2+ stain intensity and ? 5% tumor cells). Results: HC and PCA demonstrated that renal CCC formed distinct clusters compared to non-renal CCC. Tumors from gynecologic sites could not be separated into distinct clusters. GSEA showed that the hypoxia gene set was significantly upregulated in the renal but not in non-renal CCCs. Mutations involving TP53, ARID1A, PIK3CA were found to be the most altered genes in endometrial (62%, 26%, 31%), ovarian (13%, 55%, 48%), other gynecological sites (33%, 38%, 44%), and non-gynecologic CCC (13%, 17%, 12%) respectively. PD-L1 expression, high tumor mutational burden (?10 mutations/Mb), and deficient mismatch repair/microsatellite instability rates across sites were: kidney (11%, 2%, 2%), endometrium (13%, 12%, 7%), ovary (9%, 4%, 3%), other gynecological sites (31%, 11%, 11%), and miscellaneous sites (11%, 19%, 4%). Conclusion: Initial metabolic gene expression clustering analysis shows

that CCCs do not separate by organ of origin beyond renal versus extra-renal. TP53, ARID1A, and PIK3CA were the most frequently altered genes in non-renal CCC. Out of fifty hallmark gene sets, only two were statistically significantly different among gynecological CCCs. This similarity between gynecological CCC can be leveraged by targeting pathways such as PI3K-AKT-mTOR, DNA repair, and MYC targets in a site agnostic manner. Furthermore, high PD-L1 expression is found in other gynecological sites.

THOMAS FRITZ SIEGERT: GLOBAL HEALTH FELLOWSHIP LEADERS' PERSPECTIVES ON GLOBAL HEALTH CORE CONTENT AND FELLOWSHIP ACCREDITATION

Introduction: Global health (GH) has evolved over time and is now an area of practice in nearly all clinical specialties. With this growth has been an increased interest in GH fellowships from US medical trainees. Despite this growth and increased popularity, there is no required core content, core competencies, or widespread accreditation for US GH fellowships across specialties. We conducted a nationwide survey study to better understand US GH fellowship leaders' perspectives on core content and accreditation. Methods: A cross-sectional survey study was designed in RedCAP by research team members with expertise in GH across multiple specialties. The survey related to 1) existence and importance of core content in GH, 2) potential benefits of fellowship accreditation, 3) potential barriers to accreditation, and 4) demographics and fellowship program characteristics. The target population was current US-based GH fellowship leadership, and was sent to 129 program contacts. Statistical analysis was conducted using SPSS and thematic analysis was conducted for open-ended survey questions. Results: Ultimately, 123 viable survey invitations were sent with 45 responding to the survey (37% response rate). 84% of respondents identified as GH fellowship program directors. Respondents represented GH fellowships in emergency medicine (50%), pediatrics (22%), family medicine (16%), internal medicine (11%), internal medicine-pediatrics (2%), and obstetrics and gynecology (2%). Eighty-nine percent of respondents indicated there was core content in GH that is important for GH fellows to learn regardless of specialty and 55% of respondents signaled that core content was "very important" or "extremely important." Only 30% indicating accreditation of any kind would be "very" or "extremely beneficial." A majority of respondents (52%) "disagreed" or "strongly disagreed" that there was a need for accreditation specifically through the American College of Graduate Medical Education. Thematic analysis of written comments identified three themes regarding the potential positive impact of accreditation: 1) promotion of standardization, 2) formal recognition of trainees, 3) certification of graduates is desirable. Four themes related to potential negative impacts were identified: 1) increased restrictions, 2) increased burdens, 3) lack of impact of accreditation, and 4) concerns about potential accreditors. Conclusion: A significant majority of respondents indicated that core content in GH both exists across specialties and should be learned by GH fellows. However, there was less consensus around how important this core content is, possibly due to concerns about potential negative impacts of the accreditation needed to define and regulate core content. There was also significantly less consensus around the need for accreditation. Respondents overall indicated stronger perceptions around the potential negative impacts of accreditation than they did the potential positive impacts. Next steps include understanding perceptions around GH core content and accreditation amongst other key stakeholders including colleagues from the Global South and low-and-middle-income-countries and GH trainees.

TIFFANY HO: INCREASED CORONARY ARTERY CALCIFICATION IN VETERANS WITH MOOD DISORDERS

Introduction: Mood disorders such as depression, anxiety, and posttraumatic stress disorder are implicated in cardiovascular disease risk. While the exact pathway of chronic stress on cardiovascular disease is unknown, it is hypothesized that chronic activation of the sympathetic nervous system creates responses within the circulatory system such as the release of oxygen, hormones, and cytokines across tissues which correspond to increased heart rate and vasodilation. Over time, repeat exposure to stressors results in physiological and neurological changes in the amygdala which further cause dysregulation and remodeling of the stress response system, further leading to poor cardiovascular health and mental health. There is an increasing body of evidence showing that the presence of mood disorders have been associated with atherosclerosis in coronary heart disease. Coronary artery calcification (CAC) is a predictive of total atherosclerotic burden, risk of cardiovascular disease, and all-cause mortality. We assessed the prevalence of mood disorders such as major depressive disorder (MDD), posttraumatic stress disorder (PTSD), and schizophrenia with the coronary artery calcification score. Methods: This was a retrospective single-center study of U.S. Veterans who underwent lung cancer screening computed tomography between 10/1/2013 and 7/31/2014 at the Providence Veterans Association Medical Center. A diagnosis of MDD, PTSD, and schizophrenia was obtained from the EMR. Patients with lung cancer or established atherosclerosis were excluded. The main outcome was CAC score derived from lung cancer screening tomography. The Welch two-sample t-tests were used and further multivariate adjustment on ASCVD, BMI, and GFR were performed. Results: Out of a total of 1,560 patients: 502 out of 614 total individuals with MDD had a diagnosis of MDD before their CT scan, 329 out of 425 total individuals with PTSD had a diagnosis of PTSD before their CT scan, 37 out of 46 total individuals with schizoaffective disorder or schizophrenia had a diagnosis of such before their CT scan. Using the Welch t-test, the mean difference in CAC score was 350.105 ($p=0.0748$) in individuals with and without MDD; 243.695 ($p=0.04598$) in individuals with and without

PTSD; 465.019 (p=0.06641) in individuals with and without schizophrenia or schizoaffective disorder. Multivariate analyses are ongoing. Conclusion: Veterans with a diagnosis of MDD, PTSD, and schizoaffective disorder are associated with increased CAC score. This is consistent with the hypothesis that chronic stress is associated to greater cardiovascular risk.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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Submitted: May 24, 2023 EDT, Accepted: May 30, 2023 EDT