Percentage of viable tumor Versus radiation treatment effect in surgical specimens is not associated with outcomes in recurrent glioblastoma

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OBJECTIVES/SPECIFIC AIMS: In patients with recurrent glioblastoma (GBM) who undergo a second surgery following standard chemoradiotherapy, histopathologic examination of the resected tissue often reveals a combination of viable tumor and treatment-related inflammatory changes. However, it remains unclear whether the degree of viable tumor Versus “treatment effect” in these specimens impacts prognosis. We sought to determine whether the percentage of viable tumor Versus “treatment effect” in recurrent GBM surgical samples, as assessed by a trained neuropathologist and quantified on a continuous scale, is associated with overall survival.

METHODS/STUDY POPULATION: We reviewed the records of 47 patients with histopathologically confirmed GBM who underwent surgical resection as the first therapeutic modality for suspected radiographic progression during standard radiation therapy and temozolomide. The percentage of viable tumor Versus “treatment effect” in each specimen was estimated by one neuropathologist who was blinded to patient outcomes.

RESULTS/ANTICIPATED RESULTS: After adjusting for other known prognostic factors in a multivariate Cox proportional hazards model, there was no association between the degree of viable tumor and overall survival (HR 0.83; 95% CI 0.20–3.4; p = 0.20). DISCUSSION/SIGNIFICANCE OF IMPACT: These results suggest that, in patients who undergo resection for recurrent GBM following standard first-line chemoradiotherapy, histopathologic quantification of the degree of viable tumor Versus “treatment effect” present in the surgical specimen has limited prognostic influence and clinical utility.

2016

Plasma microRNA markers of upper limb recovery following human stroke

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OBJECTIVES/SPECIFIC AIMS: MicroRNAs are small, non-coding RNAs that control gene expression by inhibiting protein translation. Preclinical studies in rodent stroke models suggest that changes in microRNA expression contribute to neural repair mechanisms. To our knowledge, no one has previously assessed microRNA changes during the recovery phase of human stroke. Our goal was to determine whether patients with significant upper limb recovery following stroke have alteration of neural repair-related microRNA expression when compared to those with poor recovery. METHODS/STUDY POPULATION: Plasma was collected at 19 days post-stroke from 27 participants with mild-moderate upper extremity impairment enrolled in the Critical Periods After Stroke Study. MicroRNA expression was assessed using TaqMan microRNA assays (Thermo Fisher Scientific). Good recovery was defined as ≥ 6 point change in the Action Research Arm Test (ARAT) score from baseline to 6 months. Bioinformatics analysis compared the plasma microRNA expression profiles of participants with good Versus poor recovery. Candidate biomarkers were verified after correcting for multiple comparisons using a false discovery rate <0.05. RESULTS/ANTICIPATED RESULTS: Eleven microRNAs had significantly altered expression in the good (n = 22) Versus poor (n = 5) recovery groups, with 2 showing increased expression—mir-371-3p and mir-520g, and 9 showing decreased expression—mir-449b, mir-519b, miR-581, mir-616, mir-892b, mir-941, mir-1179, mir-1292, and mir-1293. Three of these could be implicated in neural repair mechanisms. Elevated mir-371-3p levels increase the likelihood that pluripotent stem cells will differentiate into neural progenitors. Mir-892b decreases levels of amyloid precursor protein, which has been implicated as a regulator of synapse formation. Finally mir-941, the only known human-specific microRNA, downregulates the CSF1 protein which is involved in neurotransmitter release. DISCUSSION/SIGNIFICANCE OF IMPACT: This preliminary study suggests that circulating microRNAs in the plasma may help serve as biomarkers of neural repair and aid in understanding human neural repair mechanisms. If validated in larger studies with appropriate controls, these markers could aid in timing rehabilitation therapy or designing recovery-based therapeutics.

2016

Pre-treatment sleep disturbance as a risk factor for radiation therapy induced pain in 676 women with breast cancer


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OBJECTIVES/SPECIFIC AIMS: The purpose of the present secondary data analysis was to examine the effect of moderate-severe disturbed sleep before the start of radiation therapy (RT) on subsequent RT-induced pain. METHODS/STUDY POPULATION: Analyses were performed on 676 RT-naive breast cancer patients who received definitive, whole breast radiation therapy (n = 676, subject to the Cambridge Core terms of use, available at https://www.cambridge.org/core/terms).
cancer patients (mean age 58, 100% female) scheduled to receive RT from a previously completed nationwide, multicenter, phase II randomized controlled trial examining the efficacy of an oral calcium channel blocker on radiation dermatitis severity. The trial was conducted at 21 community oncology practices throughout the US affiliated with the University of Rochester Cancer Center NCI’s Community Oncology Research Program (URCC NCORP) Research Base. Sleep disturbance was assessed using a single item question from the modified MD Anderson Symptom Inventory (SI) on a 0–10 scale, with higher scores indicating greater sleep disturbance. Total subjective pain as well as the subdomains of pain (sensory, affective, and perceived) were assessed by the short-form McGill Pain Questionnaire. Pain at treatment site (pain-Tx) was also assessed using a single item question from the SI. These assessments were included for pre-RT (baseline) and post-RT. For the present analyses, patients were dichotomized into 2 groups: those who had moderate-severe disturbed sleep at baseline (score ≥ 4 on the SI; n = 101) versus those who had mild or no disturbed sleep (control group; score = 0–3 on the SI; n = 575). RESULTS/APRONTICIPATED RESULTS: Prior to the start of RT, breast cancer patients with moderate-severe disturbed sleep at baseline were younger, less likely to have had lumpectomy or partial mastectomy while more likely to have had total mastectomy and chemotherapy, more likely to be on sleep, anti-anxiety/depression, and prescription pain medications, and more likely to suffer from depression or anxiety disorder than the control group (all p’s < 0.002). Spearman rank correlations showed that changes in sleep disturbance from baseline to post-RT were significantly correlated with concurrent changes in total pain (r = 0.38; p < 0.001), sensory pain (r = 0.35; p < 0.001), affective pain (r = 0.21; p < 0.001), perceived pain intensity (r = 0.37; p < 0.001), and pain-Tx (r = 0.35; p < 0.001). In total, 92% of patients with moderate-severe disturbed sleep at baseline reported post-RT total pain compared with 79% of patients in the control group (p = 0.006). Generalized linear estimating equations, after controlling for baseline pain and other covariates (baseline fatigue and distress, age, sleep medications, anti-anxiety/depression medications, prescription pain medications, and depression or anxiety disorder), showed that patients with moderate-severe disturbed sleep at baseline had significantly higher mean values of post-RT total pain (by 39%; p = 0.033), post-RT sensory pain (by 41%; p = 0.046), and post-RT affective pain (by 55%; p = 0.035) than the control group. Perceived pain intensity (p = 0.066) and pain-Tx (p = 0.086) at post-RT were not significantly different between the 2 groups. DISCUSSION/SIGNIFICANCE OF IMPACT: These findings suggest that moderate-severe disturbed sleep prior to RT is an important predictor for worsening of pain at post-RT in breast cancer patients. There could be several plausible reasons for this. Sleep disturbance, such as sleep loss and sleep continuity disturbance, could result in impaired sleep related recovery and repair of tissue damage associated with cancer and its treatment; thus, resulting in the amplification of pain. Sleep disturbance may also reduce pain tolerance threshold through increased sensitization of the central nervous system. In addition, pain and sleep disturbance may share common neuroimmunological pathways. Sleep disturbance may modulate inflammation, which in turn may contribute to increased pain. Further research is needed to confirm these findings and whether interventions targeting sleep disturbance in early phase could be potential alternate approaches to reduce pain after RT. OBJECTIVES/SPECIFIC AIMS: To investigate the prognostic value of left ventricular mitral annular longitudinal displacement (LD) measured with color tissue Doppler imaging (TDI) in patients with acute coronary syndrome.

Doppler imaging in patients with acute coronary syndrome
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OBJECTIVES/SPECIFIC AIMS: To investigate the prognostic value of left ventricular mitral annular longitudinal displacement (LD) measured with color tissue Doppler imaging (TDI) in a large population suffering from acute coronary syndrome (ACS). METHODS/STUDY POPULATION: In total, 501 ACS patients underwent an echocardiography within 9 days after a percutaneous coronary intervention. Regional LD was obtained from the 6 mitral annular regions with TDI and GLD was calculated as an average. RESULTS/APRONTICIPATED RESULTS: During a median follow-up time of 4.4 years 46 ACS patients suffered CVD. Mean value of GLD in the population was 8.78 ± 2.4. GLD and LD obtained from the inferior wall remained significantly important predictors after multivariate adjustment for clinical parameters, GLD (HR: 1.43, 95% CI: 1.12–1.82, p = 0.014, per 1mm decrease), inferior LD (HR: 1.38, 95% CI: 1.14–1.66, p = 0.001). Furthermore, inferior wall LD was the primary source of prognostic information in GLD since only inferior LD remained significant when both measures were included in the same model. GLD (HR: 0.95, 95% CI: 0.64–1.40, p = 0.781); inferior LD (HR: 1.60, 95% CI: 1.15–2.22, p = 0.005). Of all walls, only inferior wall LD remained as an independent predictor after multivariate adjustment. DISCUSSION/SIGNIFICANCE OF IMPACT: GLD provides independent prognostic information in ACS patients over and beyond all conventional echocardiographic measures. Regional inferior LD was the primary source of prognostic information gained from GLD. GLD proved to be a better predictor of cardiovascular events than conventional echocardiographic measures. This could lead to better risk stratification in the clinical setting and open up for earlier intervention in high-risk individuals.

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Prophylactic broad-spectrum antibiotics for childhood malnutrition
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OBJECTIVES/SPECIFIC AIMS: A course of oral broad-spectrum antibiotics frequently has a positive effect on morbidity and mortality in severe acute malnutrition (SAM), but the actual mechanism for this effect is unknown. This mechanism is especially important to find and quantify because of the possibility that using antibiotics prophylactically may accelerate the danger from antibiotic resistant infections. This study aims to answer (1) how antibiotic therapy improves the nutritional recovery and (2) how much it affects the prevalence of resistance genes in the microbiome. METHODS/STUDY POPULATION: Stool samples were collected from children with SAM between 6 and 60 weeks of age who received either one week of amoxicillin or placebo (n = 164). The children were followed for 12 weeks with longitudinal sampling, and a subset were followed out to 2 years. All samples were frozen at ~80°C and prepared for metagenome shotgun sequencing via the Illumina Nextera platform. RESULTS/APRONTICIPATED RESULTS: Antibiotic treatment at the start of the nutritional program is associated with significant improvements in weight gain, mid-upper-arm circumference, and graduation from the treatment program. It is also associated with qualitative decreases in early-life fermenter Lactobacillus and known enteropathogen Campylobacter. Two years after the use of amoxicillin, the Shannon diversity index is significantly higher than that of malnourished children (effect size 0.507, 95% CI: 0.204–0.630, p = 0.0007), while children who received placebo are not distinguishable from malnourished children by the same metric (effect size 0.147, 95% CI: −0.311, 0.630, p = 0.5878). Sustained antibiotic resistance gene enrichment within the microbiota did not occur, as the enrichment effects disappears by week 4 of follow-up. DISCUSSION/SIGNIFICANCE OF IMPACT: The use of amoxicillin to treat uncomplicated SAM has therapeutic benefits visible by anthropometry and by content of the gut microbiota. The main concern with the use of prophylactic antibiotics for this purpose is the effect on antibiotic resistance gene enrichment in the children’s microbiota. This concern was not supported here. The benefit/cost ratio for the use of prophylactic antibiotics for individuals in this cohort is positive when weighing effects on anthropometry, microbiome, and antibiotic resistance. The results of this study impact the treatment of millions of children each year at nutritional therapy clinics around the world.

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Racial/ethnic variation in the relationship between metabolic syndrome components and cardiovascular disease and the role of uric acid among population with metabolic syndrome
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OBJECTIVES/SPECIFIC AIMS: To examine the racial/ethnic variation in the relation between metabolic syndrome (MetS) components and cardiovascular disease (CVD) as well as examine the role of uric acid as a predictor of CVD among population with MetS. METHODS/STUDY POPULATION: We analyzed National Health and Nutrition Examination Surveys data (1999–2010) for adults aged >20 years with MetS. Using the ATP III clinical criteria for diagnosing MetS,