DNA-Based Epigenetic Age is a Better Predictor of Complication than Chronological Age and Frailty

Rohit Bhan[1], Quanté Armonld Singleton[1], Yu Zhang[1], Christopher Ames, Michael Patrick Kelly, Bo A Zhang[2], Brian J Neuman[1]
[1]Washington University in St. Louis, [2]Washington University In St. Louis

INTRODUCTION:

The prevalence of symptomatic ASD is increasing with an aging population, with surgical complication rates of 37%-71%. Prior studies propose increased CA and frailty as risk factors for complications, but this may be due to differences in EA, suggestive of a patient's underlying biological reserve in response to stress. DNA methylation assays have emerged as the gold-standard for determining EA. We investigated the relationship between EA and complications within 6 weeks after ASD surgery.

METHODS:

ASD patients provided blood samples on the day of surgery. DNA methylation of PBMCs was analyzed using IlluminaEpic v2.0. EA was calculated using the Horvath biological clock (DNAmAge) algorithm. Edmonton Frailty Index (EFI) was collected at the pre-operative visit. EFI, EA, and CA were assessed as risk factors for complications reasonably related to a patient's biology. Parametric and non-parametric analyses were used to assess significance.

RESULTS:

30 surgical ASD patients were enrolled. 15 (50%) were revisions. 21 patients (70%) received all-posterior and 9 (30%) underwent anterior-posterior surgery. 7 (23%) received a three-column osteotomy and average levels fused was 11.9 (SD=3.7). Complications were pulmonary emboli (N=2), death (N=1), reoperation for dehiscence (N=1), altered mental status (N=5), and acute kidney injury (N=4). There were no 30-day readmissions. Mean EA and CA were significantly different (71.2 vs 68.4, p=0.009). For patients who experienced a post operative complication (N=14, 47%) there was an association with EA>CA (86%) compared to CA>EA (14%, p = 0.038). The difference between EA and CA (EA-CA) was greater in patients that had a complication (5.07 vs 0.87, p=0.029). There was no association of EFI for frailty between complication groups. Between complication groups, there was no difference in mean CA (67.7 vs 69.0, p=0.596), EA (73.0 vs 69.7, p=0.12), or EFI (4.3 vs 3.7, p=0.468).

DISCUSSION AND CONCLUSION:

Preliminary findings suggest EA>CA has greater association with perioperative complication after ASD surgery than EFI, EA, or CA alone. Further studies with more patients are warranted to investigate epigenetic stressors linked to changes in EA. These patient-specific factors can be used to improve risk-stratification in ASD surgeries.

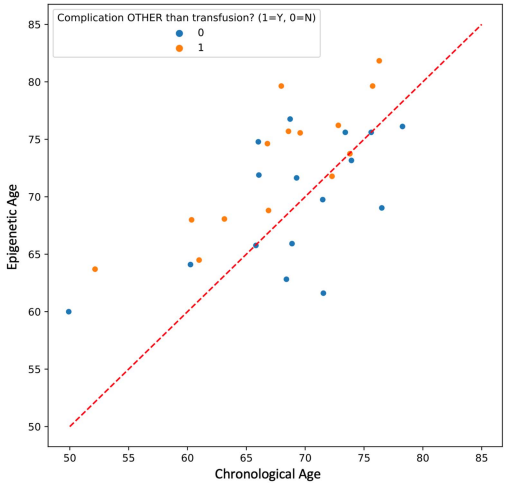

Figure 1: Scatterplot of patients that experienced complications (orange) and no complications (blue). The dotted line represents equal EA (DNAmAge) and CA.