Evaluating Frailty and Epigenetic Tests for Predicting Complications Following Adult Spinal Deformity Surgery

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INTRODUCTION: Age is a critical factor in evaluating surgical risk for adult spinal deformity (ASD). Emerging evidence suggests that frailty indices and epigenetics may be a more accurate predictor. This study evaluates multiple aging metrics to determine their predictive value for perioperative complications.

METHODS: ASD patients undergoing ≥7-level fusion or 3-column osteotomy were recruited and monitored for 30-day complications. Blood samples were collected on the day of surgery, and DNA methylation of PBMCs was analyzed. Epigenetic age (EA) was assessed using Horvath's DNAmAge, Levine's DNAmAge (LevD), and Levine's PhenotypicAge (LevP). This study examines frailty and aging metrics, including Edmonton Frailty (EFI), DNAmAge, LevP, LevD, and the differences between chronological (CA) and epigentic age calculators, to evaluate their predictive value for postoperative complications. Correlation analyses with univariate and multivariate models assessed the predictive power of each metric for complication rates.

RESULTS: 40 surgical ASD patients were enrolled. 23 (57.5%) were revisions. 29 patients (72.5%) received all-posterior and 11 (27.5%) underwent anterior-posterior surgery. 10 (25%) received a three-column osteotomy and average levels fused was 11.5. Complications were pulmonary emboli (N=2), death (N=1), reoperation for dehiscence (N=1), altered mental status (N=6), and acute kidney injury (N=5). There were no 30-day readmissions. Univariate analysis revealed that CA, EFI, EA, LevP, LevD did not predict complication rates (all p-values>0.1). However, CA-EA (p=0.015), CA-LevP (p=0.033), and CA-LevD (p=0.045) all demonstrated a predictive value. Multivariate model revealed that CA-EA was the only significant predictor of complication rate (p = 0.029). Odds ratio (OR) of CA-EA was 1.03, meaning a 3% increase in complication rate for every year that DNAmAge was greater than CA.

DISCUSSION AND CONCLUSION: Traditional frailty indices and absolute age metrics, both chronological and epigenetic, did not predict 30-day complications. However, the gap between chronological and epigenetic age (specifically CA–EA) was significantly associated with complication rates, with a 3% increased risk for each year EA exceeded CA. This suggests that epigenetic age acceleration may serve as a more sensitive marker of physiological vulnerability. Larger studies are needed to validate these findings and support the integration of biologically informed metrics into surgical risk assessment.

UNIVARIATE	Mean Age Difference Complication vs No Complication	2.5% CI	97.5% CI	p-value
Chronological Age (CA)	-2.25	-2.57	4.57	0.240
Edmonton Frailty Index	-0.36	-1.09	1.82	0.614
Epigenetic Age (EA)	2.09	-2.59	6.76	0.372
Levine PhenoAge (LevP)	3.83	-3.83	11.48	0.312
Levine DNA Methylation (LevD)	3.49	-8.62	1.33	0.190
CA-EA	3.05	0.88	7.79	**0.015**
CA-LevD	-5.89	-9.36	0.02	**0.045**
CA-LevP	-6.09	-10.07	-0.17	**0.034**
MULTIVARIATE	OR	2.5% CI	97.5% CI	p-value
CA-EA	1.03	1.004	1.057	**0.029**
CA-LevD	1.09	0.872	1.37	0.445
CA-LevP	0.94	0.761	1.15	0.533

Table 1. Univariate and multivariate correlation of frailty indices and epigenetic age calculators with complication rate.