

Trends in Blood Mosaicism and Clinical Phenotype Score in Patients with Beckwith-Wiedemann Syndrome Evaluated for Tongue Reduction Surgery

Dominic J. Romeo MA MTS, Connor S Wagner BS, Benjamin B. Massenburg MD, Neil Reddy BS, Meagan Wu MA, Jinggang J. Ng MA, Madison DeMarchis, Eric C. Liao MD PhD, Jennifer M. Kalish MD PhD, Jesse A. Taylor MD

BACKGROUND

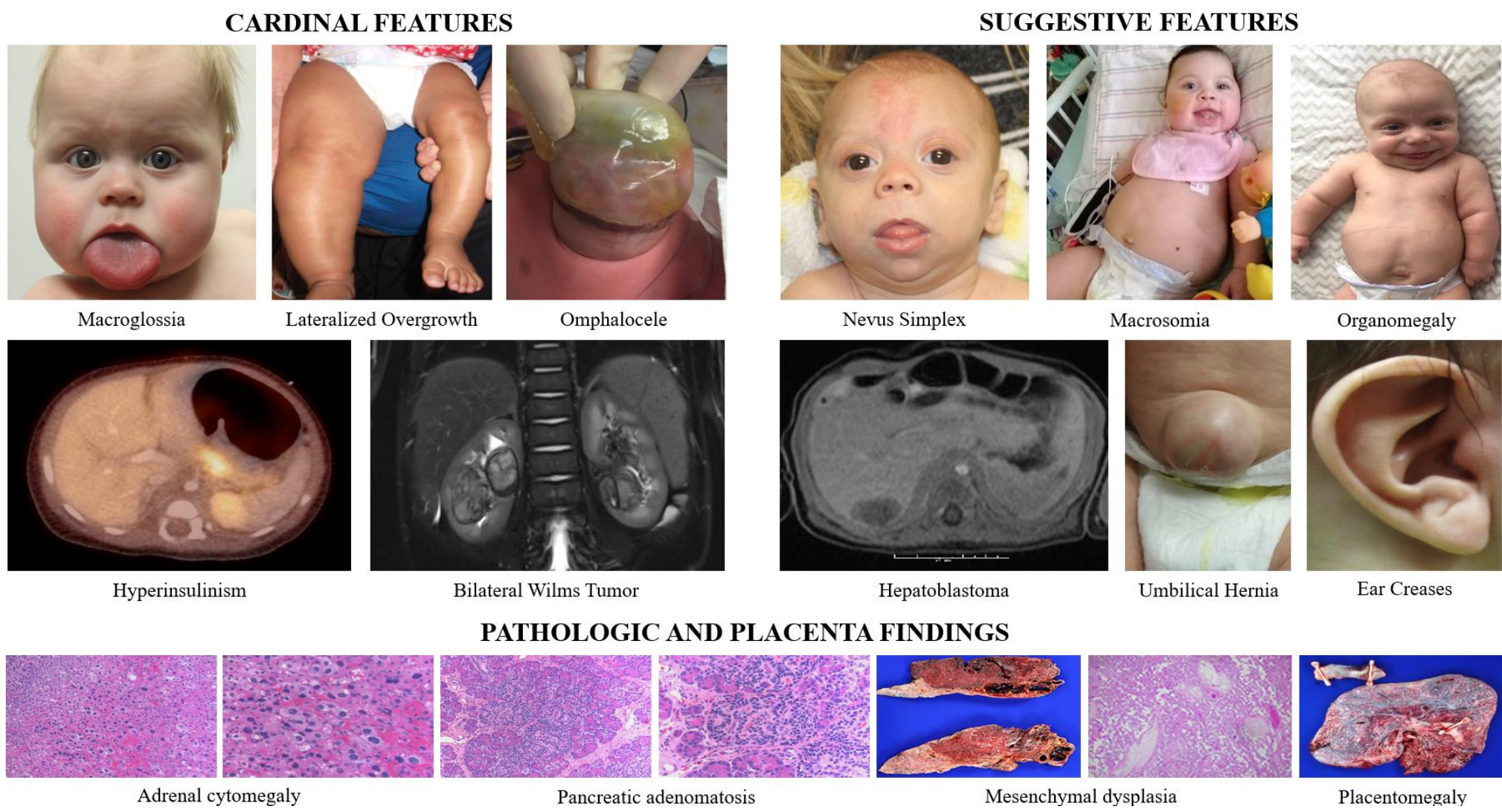
Most patients with Beckwith-Wiedemann syndrome (BWS) have macroglossia with some requiring tongue reduction surgery (TRS).

OBJECTIVES

This study reports correlations between levels of affected cells (mosaicism) and BWS clinical score in patients evaluated for TRS. We also show correlations of clinical score and mosaicism with obstructive sleep apnea (OSA) severity.

METHODS

Blood mosaicism levels and BWS clinical score were recorded in patients with macroglossia referred to plastic surgery for evaluation. Associations among blood mosaicism, BWS clinical score, TRS, and OSA were assessed with appropriate statistics.



RESULTS SUMMARY

Of the 225 patients included, BWS blood testing was available in 128 (56.9%). Mosaicism levels were higher in those who underwent TRS compared to those who did not (85.9 85.9 (56.5-95.9)% vs. 29.7 (2.8-73.1)%, $p<0.001$). BWS clinical score was also higher in those requiring TRS (9.0 (8.0-11.0) versus 7.0 (6.0-9.0), $p<0.001$). There was a positive correlation between clinical score and obstructive apnea-hypopnea index ($r=0.320$, $p=0.011$). Receiver operating characteristic curve analysis showed a clinical score ≥ 11 had 100% specificity and 36.4% sensitivity for detecting patients requiring TRS. Blood mosaicism $\geq 80\%$ had 63.6% sensitivity and 83.6% specificity for predicting surgery. A combined criteria of BWS clinical score ≥ 11 or mosaicism $\geq 80\%$ had 72.7% sensitivity and 83.6% specificity for predicting TRS.

Table. BWS Clinical Score and Surgical Indication

Indication	BWS Score (n)	N	BWS Score (n)	N	p
	TRS Cohort		Non-TRS Cohort		
TRS Cohort vs No TRS	9.0 (8.0-11.0)	55	7.0 (6.0-9.0)	73	<0.001
Upper Airway Obstruction (UAO) vs Patients without TRS	9.0 (8.0-11.0)	43	7.0 (6.0-9.0)	73	<0.001
Cranio-dental Developmental Concerns (CDDC) vs Patients without TRS	8.5 (7.0-11.0)	12	7.0 (6.0-9.0)	73	0.020
UAO vs CDDC					0.190
TRS: tongue reduction surgery, UAO: upper airway obstruction, CDDC: cranio-dental developmental concerns, BWS: Beckwith-Wiedemann Syndrome					
*Values reported as Median (Interquartile Range)					

Table. Blood Mosaicism Percent and Surgical Indication

Indication	Blood Mosaicism (%)	N	Blood Mosaicism (%)	N	p
	TRS Cohort		Non-TRS Cohort		
TRS Cohort vs No TRS	85.9 (56.5-95.9)	55	29.7 (2.8-73.1)	73	<0.001
Upper Airway Obstruction (UAO) vs Patients without TRS	85.7 (56.5-95.7)	43	29.7 (2.8-73.1)		<0.001
Cranio-dental Developmental Concerns (CDDC) vs Patients without TRS	89.6 (67.3-96.3)	12	29.7 (2.8-73.1)		0.002
UAO vs CDDC					0.998
TRS: tongue reduction surgery, UAO: upper airway obstruction, CDDC: cranio-dental developmental concerns					
*Values reported as Median (Interquartile Range)					

Figure. Percent of Patients Undergoing Tongue Reduction Surgery by Blood Mosaicism Level

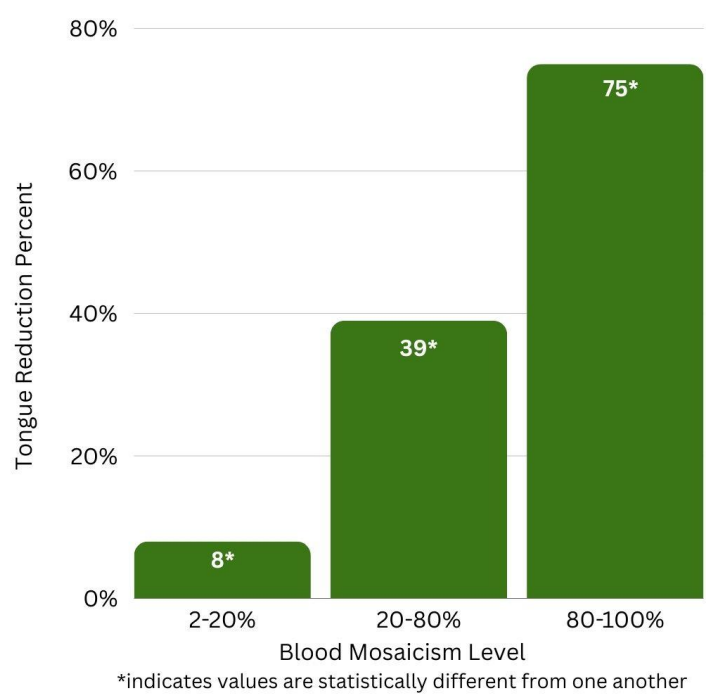


Figure. Percent of Patients Undergoing Tongue Reduction Surgery by Beckwith-Wiedemann Clinical Score

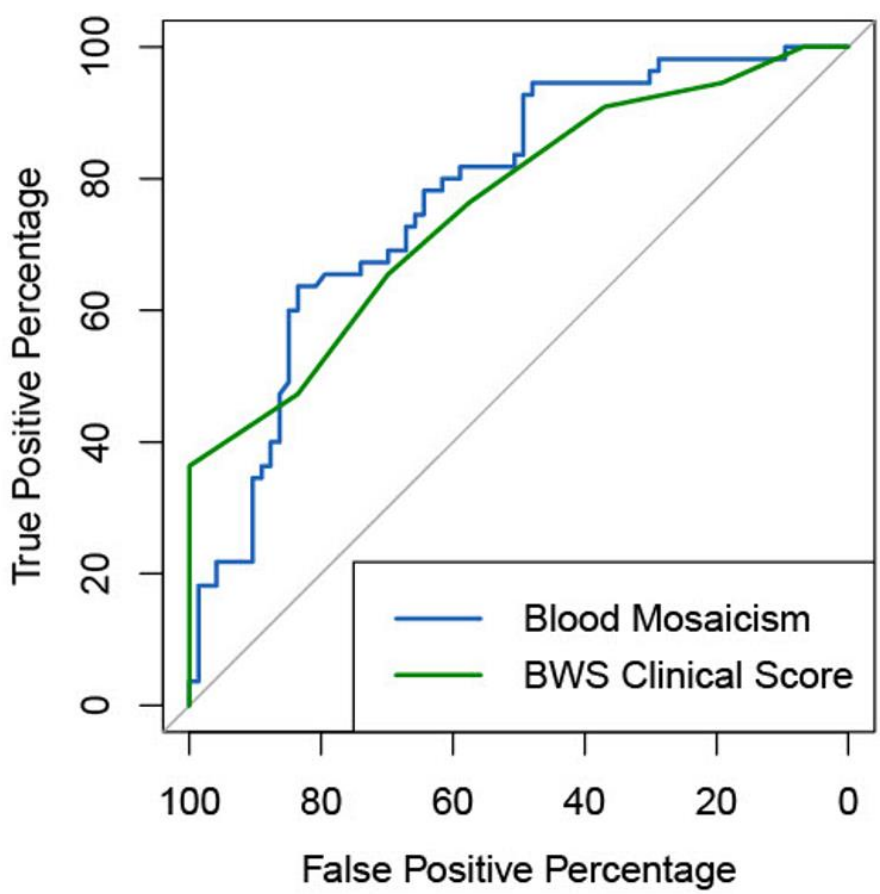
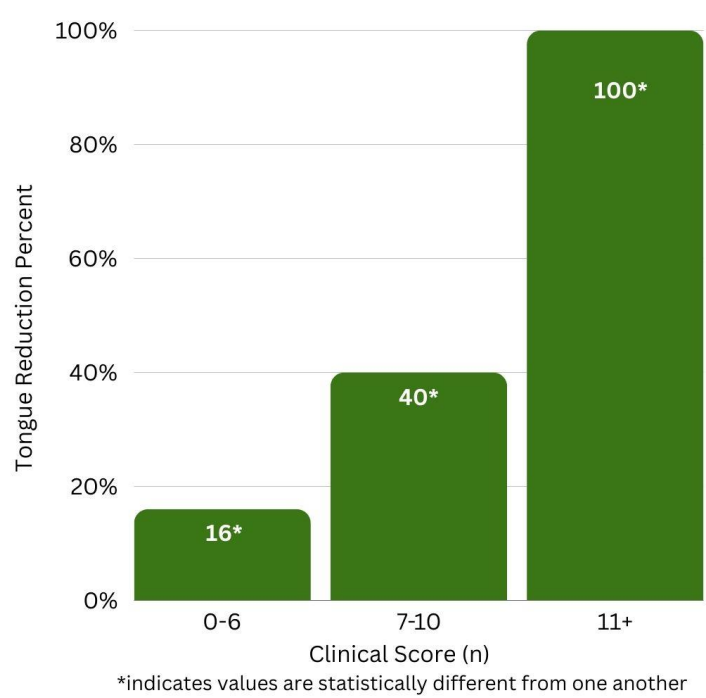


Figure. Receiver Operator Characteristic Curve Predicting Surgery Based on Blood Mosaicism and Beckwith-Wiedemann Syndrome (BWS) Clinical Score

Blood Mosaicism at $\geq 80\%$:

- Sensitivity 63.6%
- Specificity 83.6%
- AUC: 0.77

BWS Clinical Score at ≥ 11 :

- Sensitivity: 36.4%
- Specificity: 100%
- AUC: 0.76

CONCLUSION

Blood mosaicism levels and higher BWS clinical scores appear associated with a greater frequency of having surgery in patients with macroglossia referred for surgical evaluation. Elevations in BWS clinical scoring are associated with increased OSA severity while increased blood mosaicism is not.