

Supplemental Files

Supplemental Table 1. Logistic regression model evaluating relation of laboratory parameters with >1 type of acute complication in pediatric and adult cohort combined

>1 type of acute complication**				Total cohort		
Laboratory parameters	Odds ratio			Adjusted odds ratio		
	OR	95% CI	P-value	aOR	95% CI	P-value
PoS (10 mmHg ↑)	1.60	1.22 – 2.11	0.001*	1.77	1.32 – 2.37	<0.0001*
El _{min} (0.1 EI ↑)	0.44	0.31 – 0.65	<0.0001*	0.43	0.31 – 0.65	<0.0001*
El _{max} (0.1 EI ↑)	0.62	0.45 – 0.85	0.002*	0.58	0.43 – 0.80	0.001*
Blood viscosity (1.0 cP ↑) [‡]	n/a	n/a	n/a	n/a	n/a	n/a
HVR	n/a	n/a	n/a	n/a	n/a	n/a
Hb (1.0 g/dL ↑)	0.98	0.79 – 1.21	0.821	0.98	0.79 – 1.22	0.885
HbF (10.0% ↑) [†]	0.56	0.37 – 0.87	0.009*	0.50	0.31 – 0.82	0.005*
MCV (10 fl ↑)	1.07	0.86 – 1.33	0.550	1.00	0.82 – 1.32	0.705
MCHC (1.0 g/dL ↑)	1.03	0.86 – 1.23	0.781	1.05	0.87 – 1.28	0.602
MCH (pg)	0.99	0.94 – 1.05	0.808	0.98	0.93 – 1.05	0.588
ARC (100 x10 ⁹ /L ↑)	1.27	0.999 – 1.61	0.051	1.26	0.98 – 1.62	0.076
Dense RBCs (1.0% ↑)	n/a	n/a	n/a	n/a	n/a	n/a

Supplemental Table 2. Logistic regression model evaluating relation of laboratory parameters with vaso-occlusive episode in pediatric and adult cohort combined

Vaso-occlusive episode				Total cohort		
Laboratory parameters	Odds ratio			Adjusted odds ratio		
	OR	95% CI	P-value	aOR	95% CI	P-value
PoS (10 mmHg ↑)	1.57	1.20 – 2.05	<0.001*	1.57	1.20 – 2.05	0.001*
El _{min} (0.1 EI ↑)	0.58	0.43 – 0.80	<0.001*	0.58	0.43 – 0.80	<0.001*
El _{max} (0.1 EI ↑)	0.68	0.49 – 0.93	0.013*	0.68	0.49 – 0.93	0.015*
Blood viscosity (1.0 cP ↑) [‡]	n/a	n/a	n/a	n/a	n/a	n/a
HVR	n/a	n/a	n/a	n/a	n/a	n/a
Hb (1.0 g/dL ↑)	1.00	0.82 – 1.22	0.991	0.99	0.82 – 1.21	0.949
HbF (10.0% ↑) [†]	0.42	0.27 – 0.64	<0.0001*	0.41	0.26 – 0.64	0.0001*
MCV (10 fl ↑)	0.92	0.76 – 1.12	0.452	0.93	0.77 – 1.13	0.513
MCHC (1.0 g/dL ↑)	1.10	0.93 – 1.31	0.253	1.10	0.92 – 1.31	0.292
MCH (10.0 pg ↑)	0.61	0.35 – 1.08	0.086	0.61	0.34 – 1.10	0.100
ARC (100 x10 ⁹ /L ↑)	1.22	1.00 – 1.49	0.035	1.22	1.00 – 1.49	0.028
Dense RBCs (1.0% ↑)	n/a	n/a	n/a	n/a	n/a	n/a

Supplemental Table 3. Logistic regression model evaluating relation of laboratory parameters with acute chest syndrome in pediatric and adult cohort combined

Acute Chest Syndrome	Total cohort					
	Odds ratio			Adjusted odds ratio		
Laboratory parameters	OR	95% CI	P-value	OR	95% CI	P-value
PoS (10 mmHg ↑)	1.28	0.995 – 1.66	0.051	1.63	1.22 – 2.19	0.001*
El _{min} (0.1 EI ↑)	0.52	0.38 – 0.71	<0.0001*	0.46	0.33 – 0.64	<0.00001*
El _{max} (0.1 EI ↑)	0.73	0.54 – 0.97	0.037	0.61	0.44 – 0.85	0.003*
Blood viscosity (1.0 cP ↑) [‡]	n/a	n/a	n/a	n/a	n/a	n/a
HVR	n/a	n/a	n/a	n/a	n/a	n/a
Hb (1.0 g/dL ↑)	0.97	0.80 – 1.17	0.723	1.01	0.83 – 1.23	0.919
HbF (10.0% ↑) [†]	0.76	0.52 – 1.10	0.135	0.58	0.38 – 0.90	0.016*
MCV (10 fl ↑)	1.13	0.93 – 1.37	0.205	1.08	0.89 – 1.32	0.451
MCHC (1.0 g/dL ↑)	0.90	0.76 – 1.07	0.224	0.99	0.83 – 1.20	0.948
MCH (10.0 pg ↑)	1.02	0.59 – 1.77	0.951	0.85	0.47 – 1.53	0.603
ARC (100 x10 ⁹ /L ↑)	1.25	1.02 – 1.52	0.014	1.19	0.98 – 1.45	0.057
Dense RBCs (1.0% ↑)	n/a	n/a	n/a	n/a	n/a	n/a

Supplemental Table 4. Logistic regression model evaluating relation of laboratory parameters with cerebral infarction in pediatric and adult cohort combined

Cerebral infarction	Total cohort					
	Odds ratio			Adjusted odds ratio		
Laboratory parameters	OR	95% CI	P-value	OR	95% CI	P-value
PoS (10 mmHg ↑)	1.63	1.06 – 2.51	0.027	1.60	0.99 – 2.56	0.056
El _{min} (0.1 EI ↑)	0.35	0.16 – 0.73	0.005*	0.34	0.16 – 0.73	0.006*
El _{max} (0.1 EI ↑)	0.41	0.24 – 0.68	0.0005*	0.41	0.24 – 0.69	0.0009*
Blood viscosity (1.0 cP ↑) [‡]	n/a	n/a	n/a	n/a	n/a	n/a
HVR	n/a	n/a	n/a	n/a	n/a	n/a
Hb (1.0 g/dL ↑)	1.06	0.74 – 1.53	0.758	1.02	0.70 – 1.48	0.922
HbF (10.0% ↑) [†]	0.61	0.28 – 1.33	0.217	0.71	0.31 – 1.62	0.428
MCV (10 fl ↑)	1.15	0.79 – 1.67	0.461	1.17	0.82 – 1.67	0.381
MCHC (1.0 g/dL ↑)	0.96	0.71 – 1.30	0.807	0.89	0.67 – 1.19	0.437
MCH (10.0 pg ↑)	0.91	0.32 – 2.58	0.870	0.97	0.34 – 2.80	0.952
ARC (100 x10 ⁹ /L ↑)	1.02	0.89 – 1.65	0.220	1.32	0.95 – 1.84	0.093
Dense RBCs (1.0% ↑)	n/a	n/a	n/a	n/a	n/a	n/a

Supplemental Table 15. Correlations of oxygen gradient ektacytometry-derived biomarkers with laboratory parameters

Laboratory parameters	Adult cohort			Pediatric cohort		
	PoS	El _{min}	El _{max}	PoS	El _{min}	El _{max}
Hemoglobin (g/dL)	$r = -0.09$	$r = 0.08$	$r = 0.24$	$r = -0.48\ddagger$	$r = 0.54\ddagger$	$r = 0.62\ddagger$
HbF (%)	$r = -0.50^{\S}$	$r = 0.63\ddagger$	$r = 0.65\ddagger$	$r = -0.70\ddagger$	$r = 0.81\ddagger$	$r = 0.79\ddagger$
MCV (fL)	$r = -0.12$	$r = 0.43\ddagger$	$r = 0.29^*$	$r = 0.05$	$r = -0.05$	$r = 0.00$
MCHC (g/dL)	$r = 0.02$	$r = 0.08$	$r = 0.04$	$r = 0.16^*$	$r = -0.20\ddagger$	$r = -0.19^*$
MCH (pg)	$r = -0.09$	$r = 0.34^*$	$r = 0.29^*$	$r = 0.00$	$r = -0.02$	$r = 0.04$
Dense RBC (%)	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	$r = 0.65\ddagger$	$r = -0.73\ddagger$	$r = -0.80\ddagger$
ARC (10.9/L)	$r = 0.41\ddagger$	$r = -0.51^{\S}$	$r = -0.63\ddagger$	$r = 0.35\ddagger$	$r = -0.44\ddagger$	$r = -0.47\ddagger$
WBC (10.9/L)	$r = 0.34^*$	$r = -0.47^{\S}$	$r = -0.54\ddagger$	$r = 0.24\ddagger$	$r = -0.31\ddagger$	$r = -0.42\ddagger$
TCD Left MCA	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	$r = 0.27\ddagger$	$r = -0.34^{\S}$	$r = -0.32^{\S}$
TCD Right MCA	<i>n/a</i>	<i>n/a</i>	<i>n/a</i>	$r = 0.31^{\S}$	$r = -0.30\ddagger$	$r = -0.40^*$

Supplemental Table 5. Correlations of oxygen gradient ektacytometry-derived biomarkers with laboratory parameters and TCD values. $\ddagger p < 0.0001$, $\S p < 0.001$, $\ddagger p < 0.01$, $* p < 0.05$. PoS, point of sickling; El_{min}, minimum deformability; El_{max}, maximum deformability; HbF, fetal hemoglobin; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin concentration; MCH, mean corpuscular hemoglobin; RBC, red blood cell; ARC, absolute reticulocyte count; WBC, white blood cell; TCD, trans cranial Doppler; MCA, media cerebral artery; *n/a*, not addressed;

Supplemental Table 6. Intra patient variability

PoS	Mean CV	SD CV
No therapy (n=6)	5.1%	6.9%
Hydroxyurea (n=5)	7.8%	6.0%
All (n=11)	6.3%	6.4%

Supplemental Table 6. Intra patient variability of PoS measured at two or three different time points.

PoS, point of sickling; CV, coefficient of variance; SD, standard deviation