Predictors of fatality in moderate to severe traumatic brain injury

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PhD NEUROSCIENCE

SPECIALIST NEUROSURGEON

- Study was carried out at the Nelson Mandela Academic Hospital and was financed through Walter Sisulu University for a doctor of philosophy study in basic neuroscience

- The study was conducted at the NMAH from March 2014- March 2017.

- Ethical and scientific approval was obtained from the institutional body

(WSU Protocol number 019/2013)

- Consent was obtained from relatives of patients

INCLUSION CRITERIA

patients with moderate to severe TBI (GCS ≤ 12) in whom neuromonitoring and surgical intervention were indicated.

patients whose relatives gave a clear informed consent to participate in the study.

Patients with intracranial pathology requiring surgical intervention and or temporary CSF drainage to lower intracranial pressure

EXCLUSION CRITERIA

Patients whose relatives refused to participate in the study

Patients with severe ballistic injuries with GCS=3, fixed and dilated pupils.

Patients for whom neuromonitoring was not carried out due to logistical problems

Patients not admitted to the neurosurgical service

Patients who died while still in the A/E or before admission

In OR: EVD inserted, craniotomy or craniectomy;burr hole done for Licox/ICP done

Daily ICP/PBO2 assessed

In ICU: daily blood and CSF analysed for CSF SOD, TAC, Malondialdehyde; serum IL-1β, IL-6 and IL-10;;Sedation protocol with morphine/dormicum or Propofol and fentanyl

: on day 14 blood samples taken

On day 14 and 90; GOS assessed Statistical analysis=SPSS 23

RESULTS

- 64 Patients with GCS ≤ 12

- After week 2 and before 3rd week ; 8 pts (12.5%) died, GOS 5=66%, GOS 4=11%, GOS 3=14%, GOS 2=9%

- By day 90: GOS 5=66%; 15% of patients had GOS 3 and less

- univariate correlates of fatality were identified using optimal cutoffs to discriminate recovery of functional status from fatality using ROC methods.
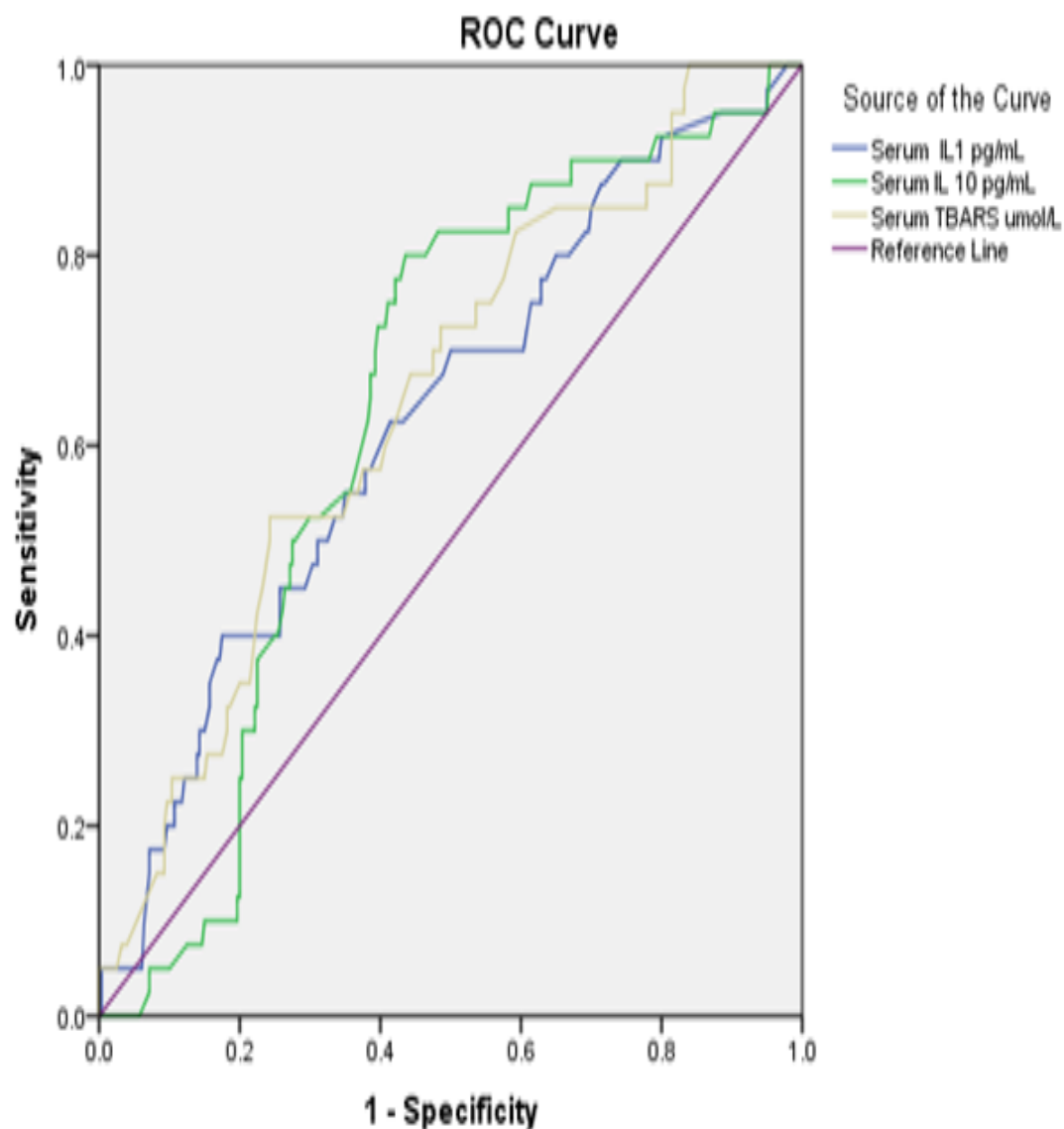
FACTOR IMPACTING ON GOS

- Significant independent predictors of variations of GOS (adjusted R^2=12.5%) were serum IL-1↓), serum IL-10 (↓), Serum TAC (↑), and serum SOD (↑)
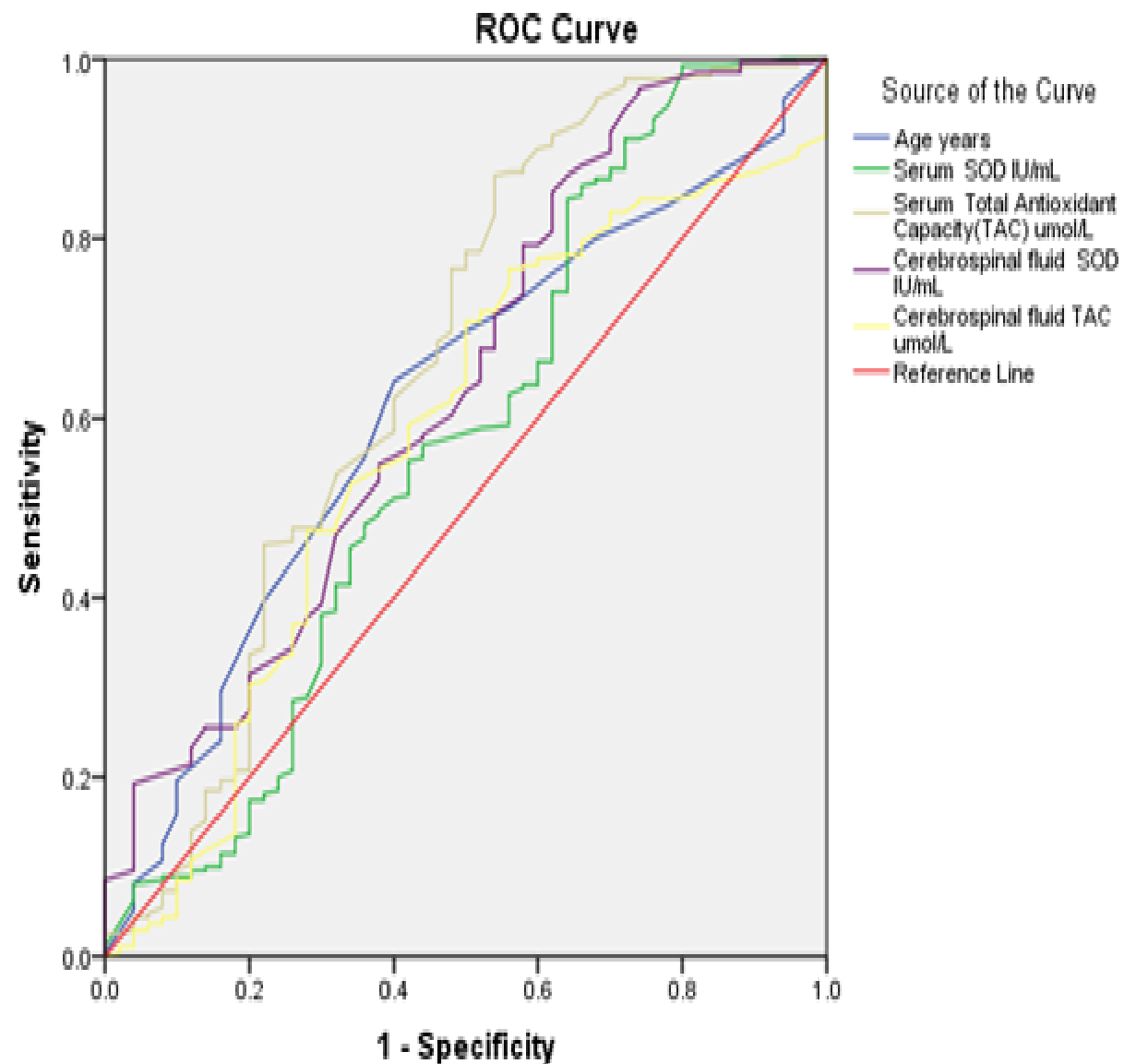
	Unstandardized		Standardized	P-Value
	B	Std. Error	β	
Constant	10.387	1.565		<0.0001
Serum IL-1	-0.059	0.024	-0.159	0.013
Serum IL-10	-0.055	0.010	-0.331	<0.0001
Serum TAC	0.004	0.002	0.197	0.008
Serum SOD	3.965	1.706	0.133	0.021

Adjusted for serum IL-6

UNIVARIATE PREDICTORS OF TBI FATALITY USING ROC CURVES

optimal cut off for serum IL-1β≥45pg/mL Area under curve (AUC) 0.629; 95% CI 0.537-0.721 SE 0.0047 P=0.008 sensitivity 70%, specificity 51% according to ROC

optimal cutoff for serum MDA (TBARS) ≥1.4μmol/L with prognostic and diagnostic performance defined by Area under curve (AUC) 0.649; 95% CI 0.561-0736; SE=0.045; P value=0.002; sensitivity 73%; specificity =51%, according to ROC

ROC methods were used to obtain optimal cutoff for CSF SOD ≤0.3IU/mL; AUC=0.647; 95% CI=0.548-0746; SE=0.051, P value=0.003, sensitivity 70%, specificity=50% according to ROC

ROC Methods were used to obtain optimal cutoff for serum IL 10≥60pg/mL AUC=0.639; 95% CI=0.560-0.719, SE=0.041, P<0.004, sensitivity=75%, specificity=68% according to ROC

ROC Methods were used to obtain optimal cutoff for serum TAC ≥450 μmol/mL, AUC 0.724; CI=0.629-0.819 SE=0.048, P<0.0001, sensitivity=70%, specificity=60% according to ROC

ROC Methods were used to obtain optimal cutoff for GCS ≤7 area under curve (AUC) =0.867; 95%CI=0.827-0.907, SE=0.020, P value <0.0001, sensitivity 84%, specificity=70 according to ROC methods
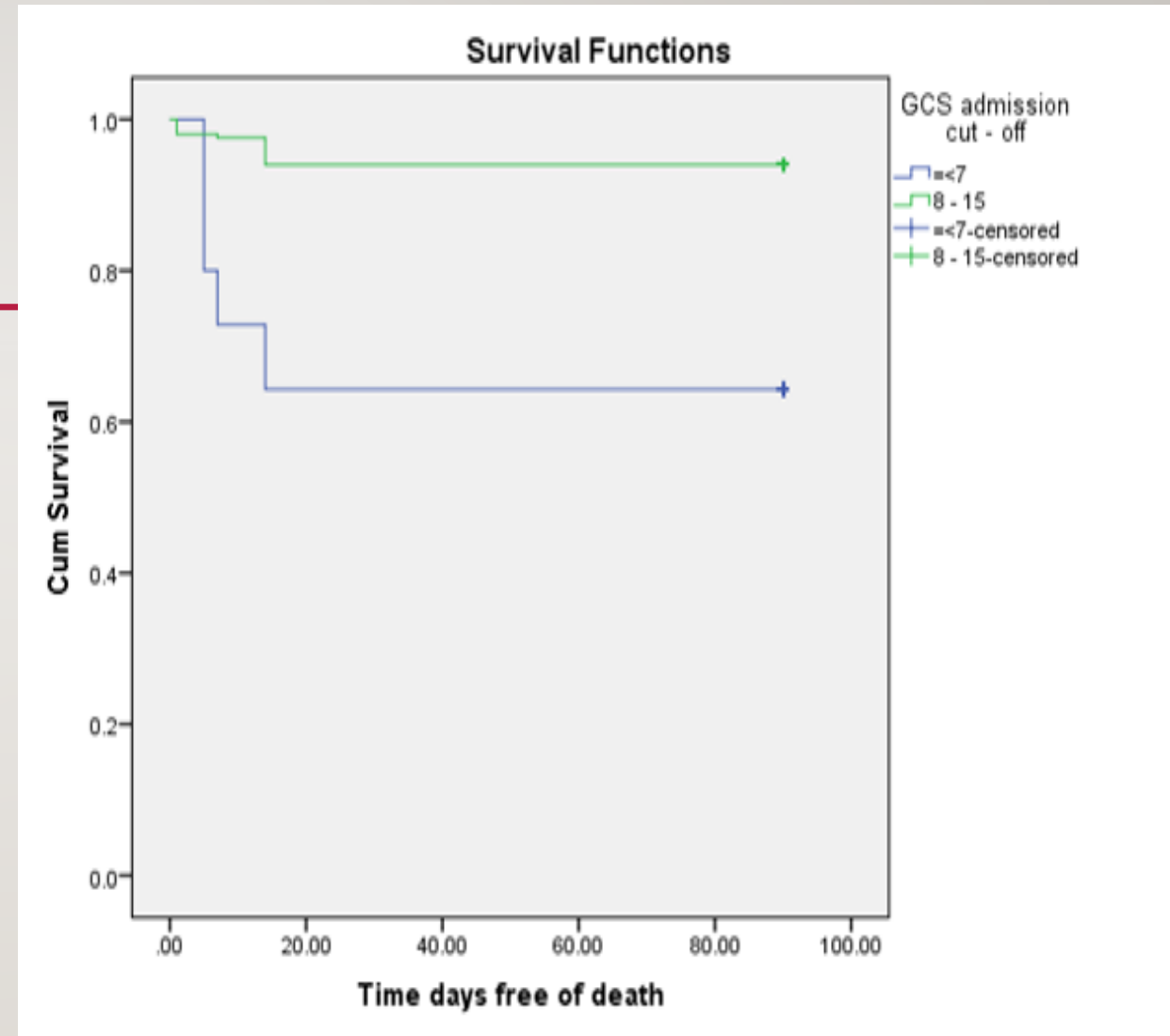
CUTOFF VALUES AS PREDICTORS OF FATAL OUTCOME IN TBI

Variable	Optimal Cutoff	Relative risk RR	95% CI	P-Value
Admission GCS	≤7	6	3.3-10.7	<0.0001
AGE group	≤20 years	1.2	1.03-1.3	<0.001
Serum-IL1 pg/ml	≥35	1.4	1.2-1.5	<0.0001
Serum TBARS µmol/L	≥1.4	1.3	1.2-1.5	<0.0001
Serum SOD IU/mL	≤0.3	1.5	1.3-1.8	<0.0001
Serum TAC µmol/L	≤450	1.4	1.2-1.6	<0.0001
CSF SOD IU/ml	≤0.3	1.7	1.4-2.0	<0.0001
CSF TAC µmol/L	≥300	1.6	1.3-1.8	<0.0001

INDEPENDENT PREDICTORS OF FATALITY BY COX REGRESSION

Independent predictors	B	SE	Wald	HR(95%CI)	P-Value
Serum IL-1					
≥45pg/ml	0.856	0.350	5.973	2.4(1.2-4.7)	0.015
≤45pg/ml				1 reference	
Serum TBARS					
≥1.4μmol/L	0.692	0.338	4.186	2(1.03-3.9)	0.041
≤1.4μmol/L				1 reference	
Serum IL-10					
≥60pg/ml	1.300	0.375	12.026	3.7(1.76-7.7)	<0.001
≤60pg/ml				1 reference	
GCS admission					
≤7	1.682	0.338	24.702	5.4(2.77-10.4)	<0.0001
>7				1 reference	

KAPLAN MEIER ANALYSIS

The probability of survival based GCS>7 was higher than

that when GCS ≤ 7; proportion of patients with GCS ≤ 7

surviving by day 90 was =64.3%: survival duration

60.6±4.7 days: This was significantly less than when GCS

>7 (94%; mean duration = 85.2±1.2 days). p value of

<0.0001.

Survival Functions

Survival Functions

Serum IL 10 cut - off
- ≥ 60 pg/mL
- < 60 pg/mL
- ≥ 60 pg/mL-censored
- < 60 pg/mL-censored

Cum Survival vs *Time days free of death*
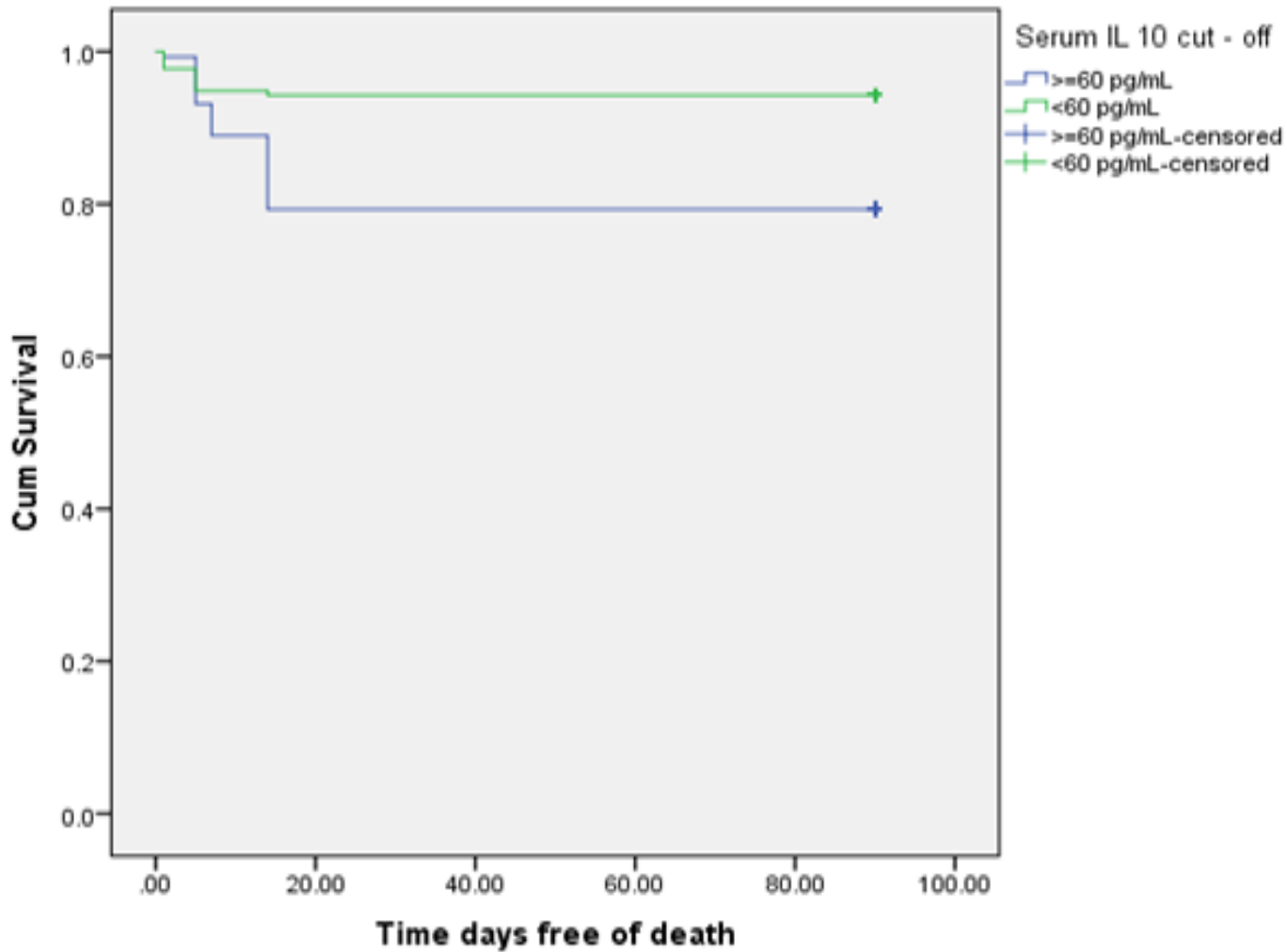
- proportion of patients surviving by day 90 with serum IL-10<60pg/ml, = 94.3% , mean survival duration=85.1±1.5 days; this was significantly > than the proportion of patients surviving with IL-10>60pg/ml; survival duration =73.3±2.7 days. p-value <0.0001.

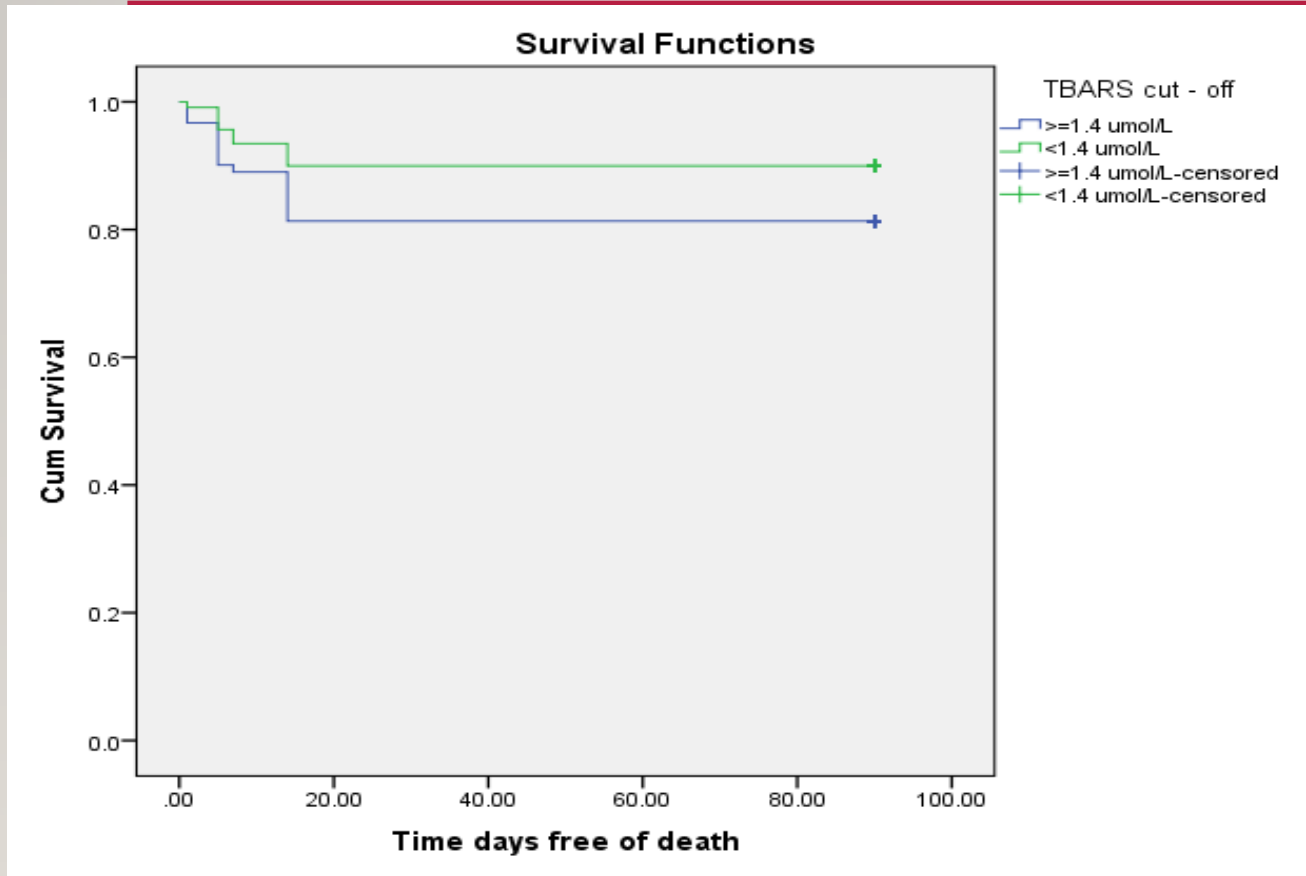## KAPLAN MEIER CURVES FOR SERUM IL-10

KAPLAN MEIER CURVES FOR SERUM IL-1B

Survival Functions
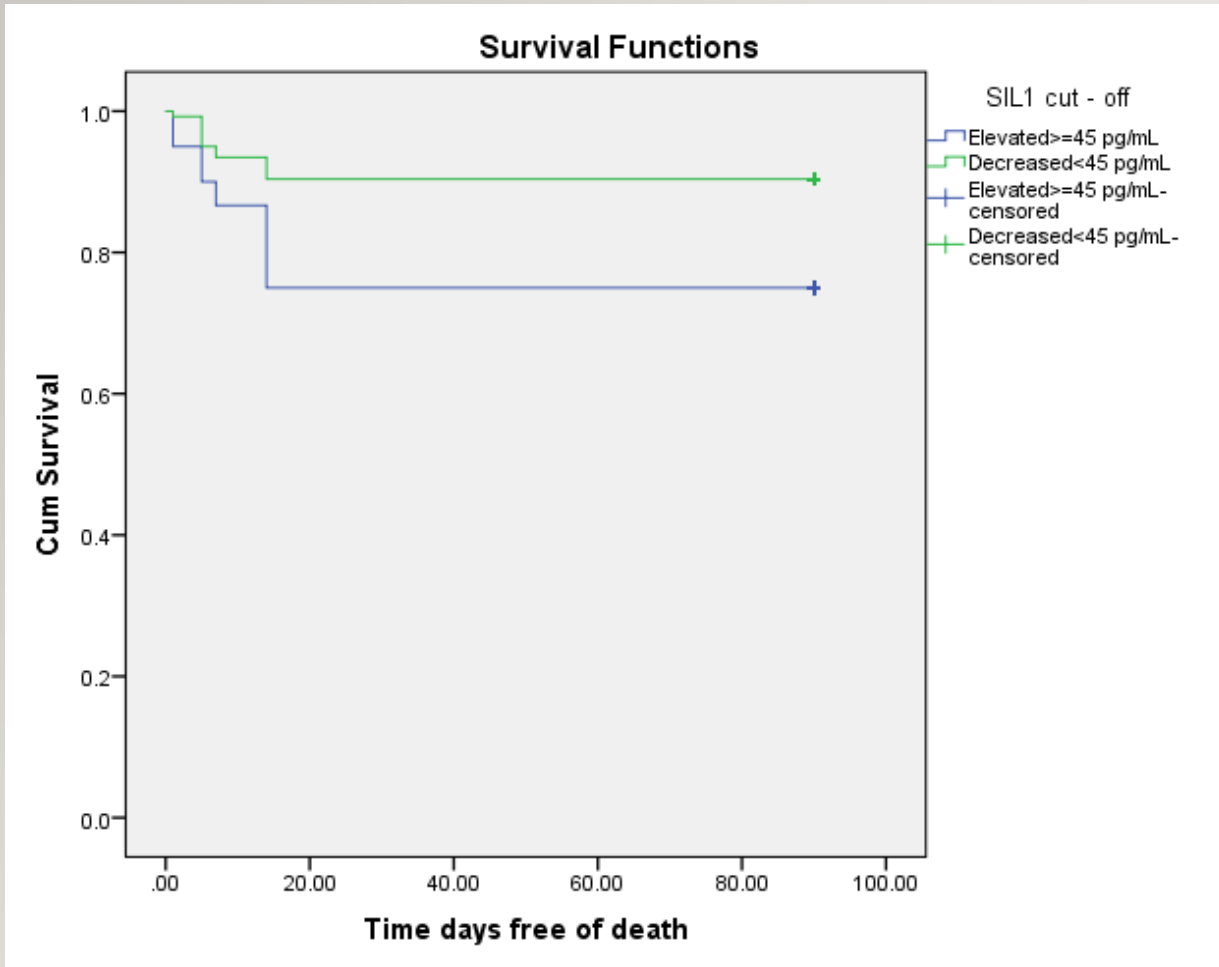
- The proportion of patients with IL-1β > 45 pg/ml surviving by day 90 = 75% ; mean survival duration =69.7±4.6 days; this was less than when IL-1β levels < 45 pg/ml were the proportion surviving = 90.4%; survival duration =82.1±1.5 days. $p < 0.001$.

KAPLAN MEIER CURVES FOR SERUM MDA

- The cumulative proportion of patients with MDA by (TBARS) level ≥ 1.4μmol/L surviving by day 90 was 81.3% Mean duration to survival =74.7±3.3 days, this was lower than the survival of 90% in patients with MDA level < 1.4μmol/L, with a mean duration of survival of 81.6±1.6 days. The comparisons based on Log Rank Mantel Cox revealed a p value =0.033.

FATALITY PREDICTORS
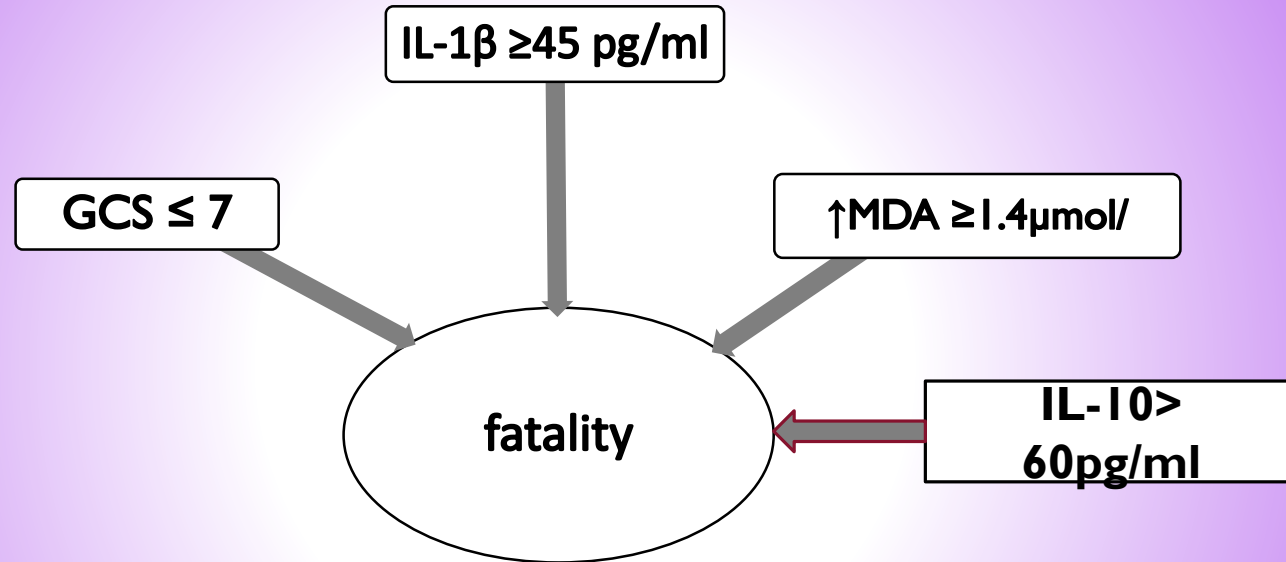
CONCLUSION

GCS, Inflammatory response and oxidative stress biomarkers are important predictors of fatality in TBI patients

A SIMILAR STUDY

- "Predictors of recovery in moderate to severe traumatic brain injury" (JNS17-2185), is in the active phase of production. In the (JNSPG).

ACKNOWLEDGEMENTS