

Supplemental Online Content

Papa L, McKinley WI, Valadka AB, et al. Diagnostic performance of GFAP, UCH-L1, and MAP-2 within 30 and 60 minutes of traumatic brain injury. *JAMA Netw Open*. 2024;7(9):e2431115. doi:10.1001/jamanetworkopen.2024.31115

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Description of three patients with an initially unremarkable CT scan who required subsequent neurosurgical intervention.

Patient	Description
Patient 1	41-year-old male involved in an MVC with an initial GCS score of 12. The initial CT scan was negative and subsequent CT showed a subdural bleed. The patient had a craniotomy and was discharged from the hospital.
Patient 2	35-year-old male involved in an MVC with an initial GCS score of 11. The initial CT scan was negative and subsequent CT showed a subarachnoid bleed. The patient had a craniotomy and was discharged from the hospital.
Patient 3	35-year-old male with a fall from a height with an initial GCS score of 4. The initial CT scan was negative, but the patient had a thrombotic event, developed seizures and had an ICP monitor placed. The patient went into cardiac arrest, developed multiple organ failure, and died from non-TBI related complications.

eTable 2. Classification performance of GFAP concentration cutoff at 30pg/mL measured for the 241 patients who had samples later than 60-minutes of injury

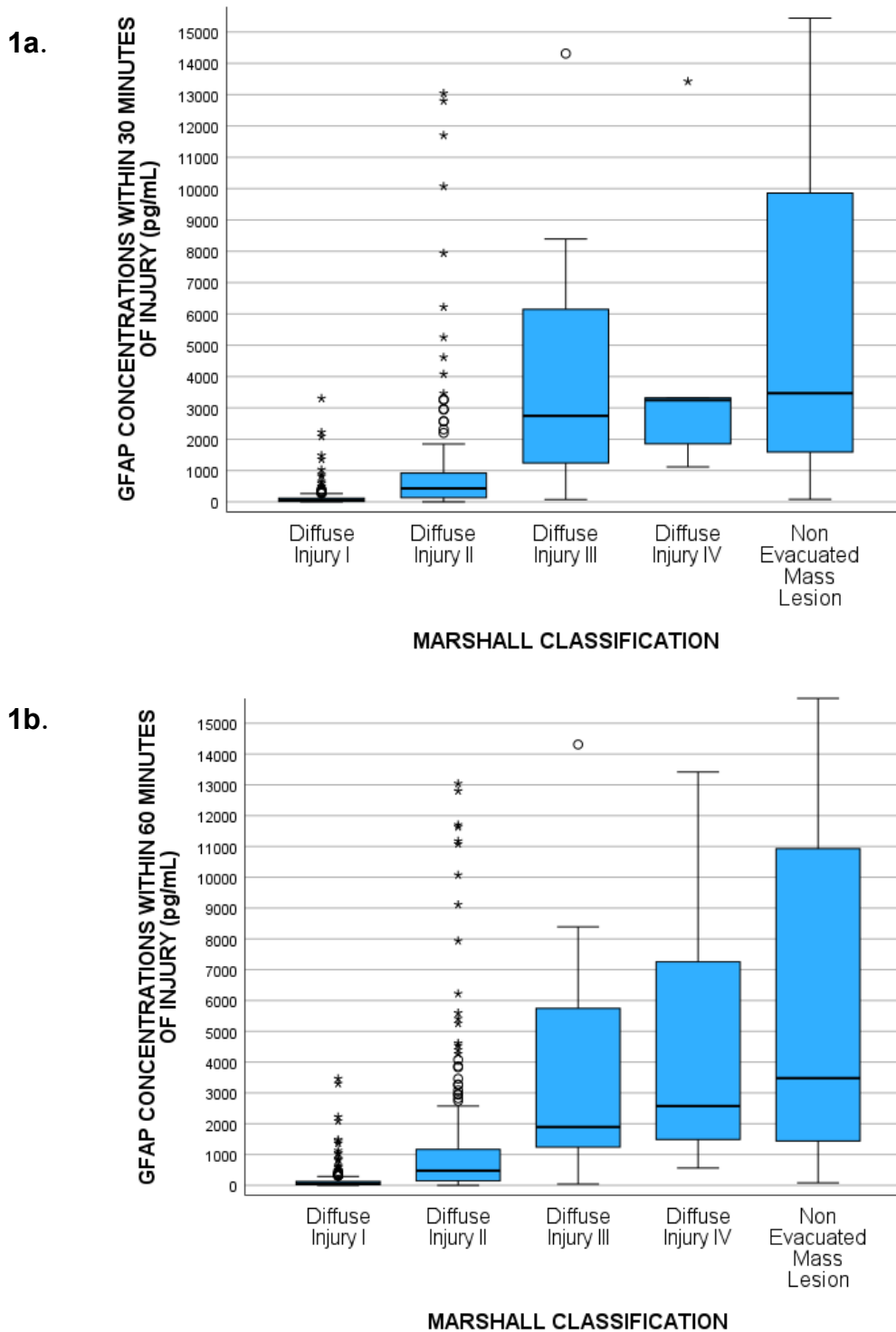
	Blood Sample Later than an Hour After Injury N=241	
CT SCAN	Injury on CT	No Injury on CT
GFAP Positive (≥30 pg/mL)	143	61
GFAP Negative (<30 pg/mL)	3	34
Sensitivity (%)	98% (94-99)	
Specificity (%)	36% (26-46)	
PPV	70% (63-76)	
NPV	92% (77-98)	
NEUROSURGICAL INTERVENTION WITHIN 24 HOURS	NSG Intervention	No NSG Intervention
GFAP Positive (≥30 pg/mL)	51	153
GFAP Negative (<30 pg/mL)	0	37
Sensitivity (%)	100% (91-100)	
Specificity (%)	19% (14-26)	
PPV	25% (19-32)	
NPV	100% (88-100)	
CLINICALLY IMPORTANT EARLY OUTCOME	Clinically Important Outcome	No Clinically Important Outcome
GFAP Positive (≥30 pg/mL)	81	123
GFAP Negative (<30 pg/mL)	0	37
Sensitivity (%)	100% (94-100)	
Specificity (%)	23% (17-31)	
PPV	40% (33-47)	
NPV	100% (88-100)	

eTable 3. Threshold concentrations of GFAP for the outcome measures.

CT Scan Lesions	Sensitivity (30 minutes)	Specificity (30 minutes)	Sensitivity (60 minutes)	Specificity (60 minutes)
30 pg/mL (Optimize Sensitivity)	98% (95-99)	34% (27-42)	99% (97-100)	36% (30-42)
110 pg/mL (Optimize Sensitivity & Specificity)	88% (83-92)	74% (67-81)	89% (85-92)	73% (67-79)
2300 pg/mL (Optimize Specificity)	32% (26-95)	99% (95-100)	33%(28-38)	99% (96-100)
Neurosurgical Intervention				
55 pg/mL (Optimize Sensitivity)	98% (90-100)	26% (21-31)	98% (92-100)	26% (22-30)
500 pg/mL (Optimize Sensitivity & Specificity)	74% (61-84)	71% (65-76)	77% (67-85)	71% (66-75)
6200 pg/mL (Optimize Specificity)	18% (10-30)	94% (91-96)	18% (11-27)	94% (91-96)
Clinically Important Early Outcomes				
55 pg/mL (Optimize Sensitivity)	99% (94-100)	31% (25-37)	99% (95-100)	31% (26-36)
485 pg/mL (Optimize Sensitivity & Specificity)	80% (72-87)	80% (75-85)	79% (72-85)	79% (75-83)
6200 pg/mL (Optimize Specificity)	23% (16-32)	99% (96-100)	23% (17-30)	99% (97-100)
Mortality within 7 Days				
60 pg/mL (Optimize Sensitivity)	100% (83-100)	27% (22-32)	100% (83-100)	26% (23-30)
1000 pg/mL (Optimize Sensitivity & Specificity)	100% (83-100)	79% (74-83)	97% (73-100)	77% (74-81)
15000 pg/mL (Optimize Specificity)	29% (13-51)	99% (97-100)	40% (24-58)	99% (97-100)

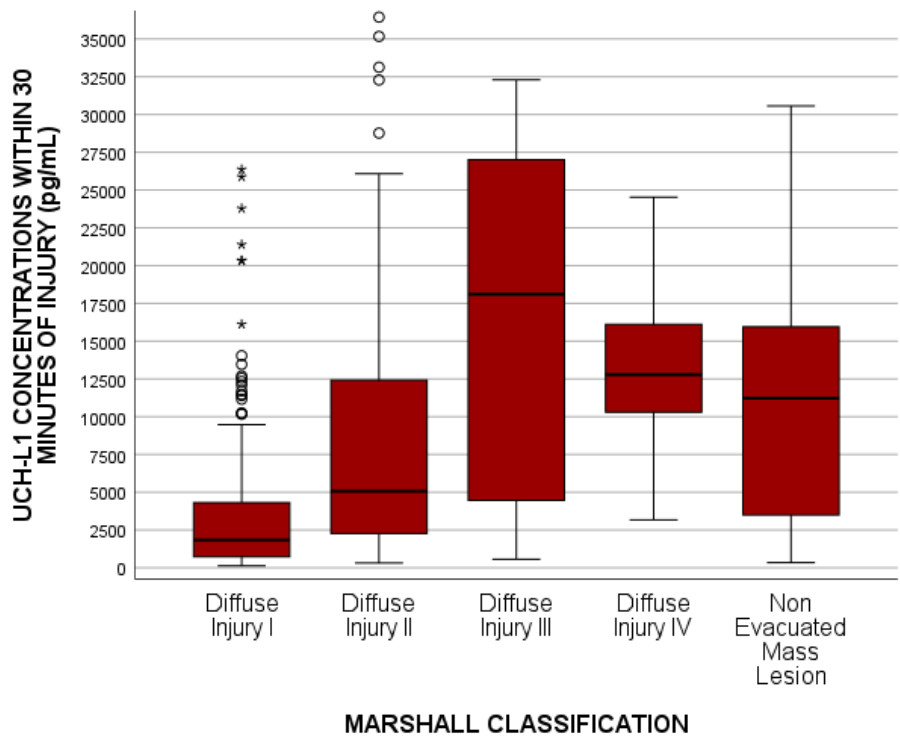
eFigures

eFigure 1. Boxplots of GFAP concentrations measured within 30 and 60 minutes of injury relative to the categories of Marshall Classification of CT scan Lesions

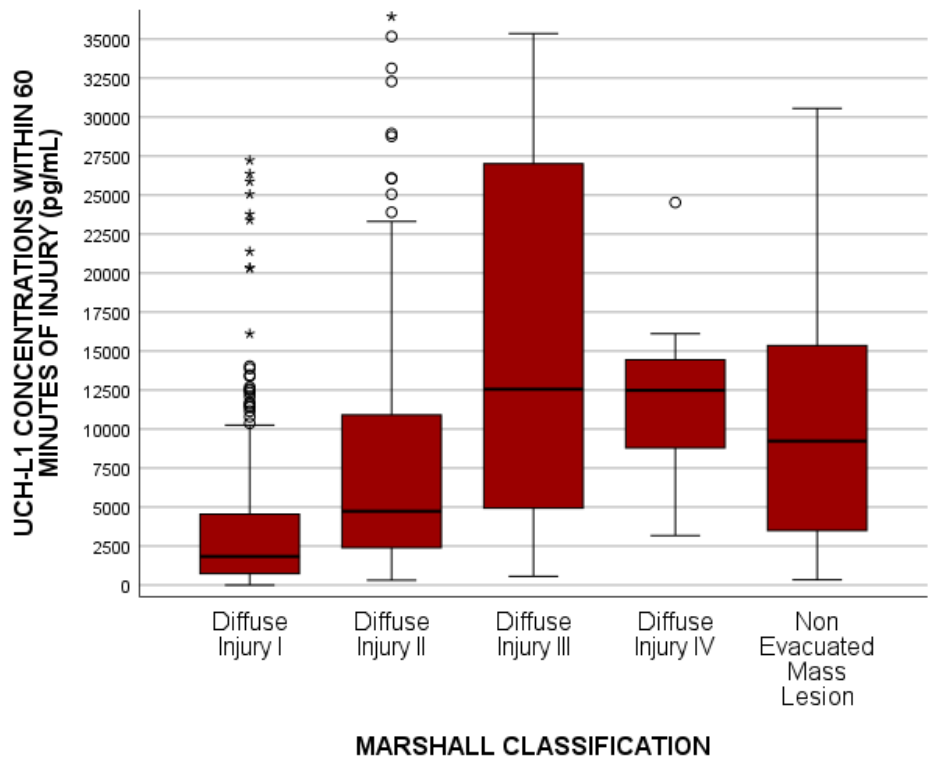


eFigure 2. Boxplots of UCH-L1 concentrations measured within 30 and 60 minutes of injury relative to the categories of Marshall Classification of CT scan Lesions

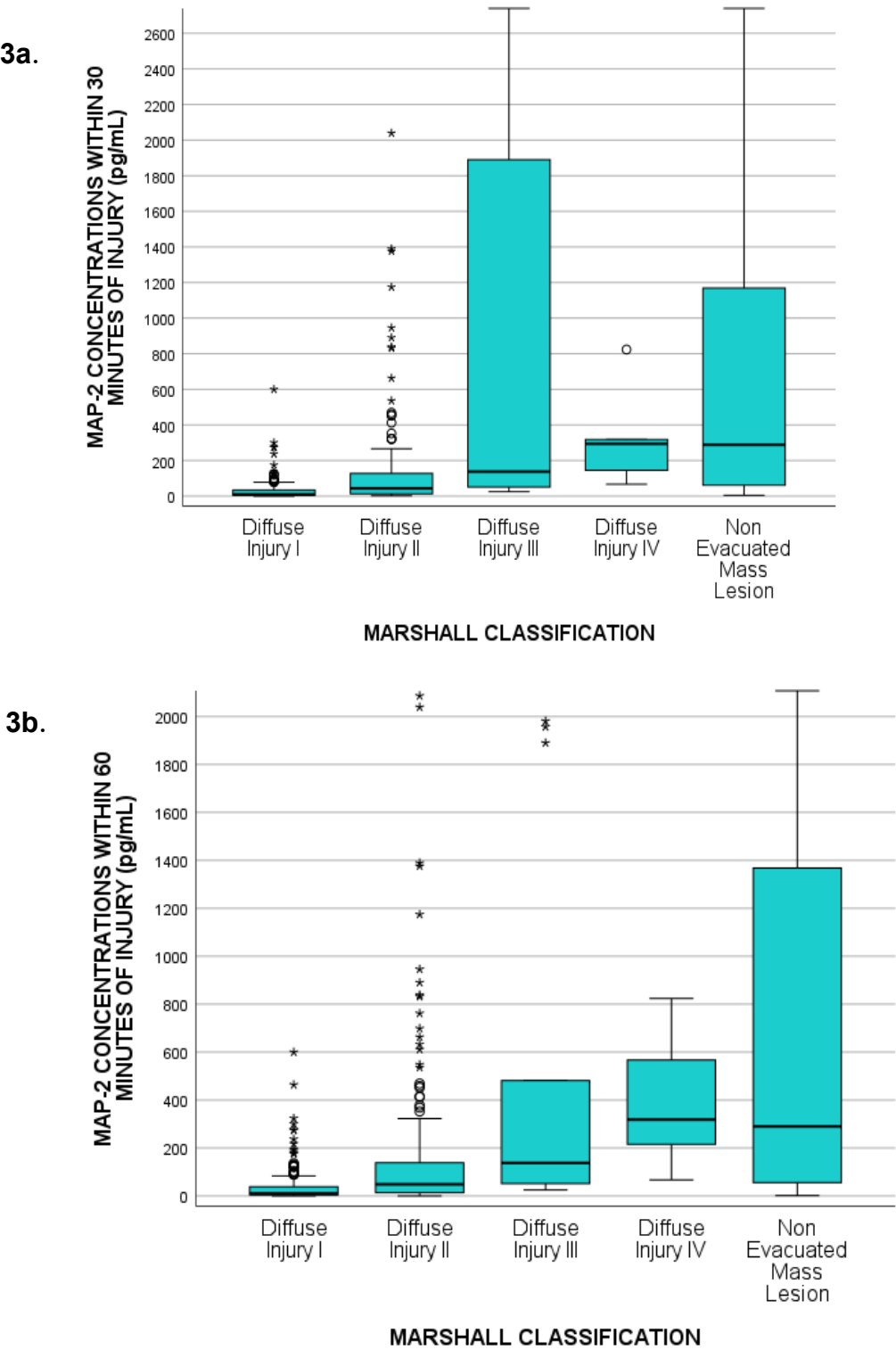
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2b.

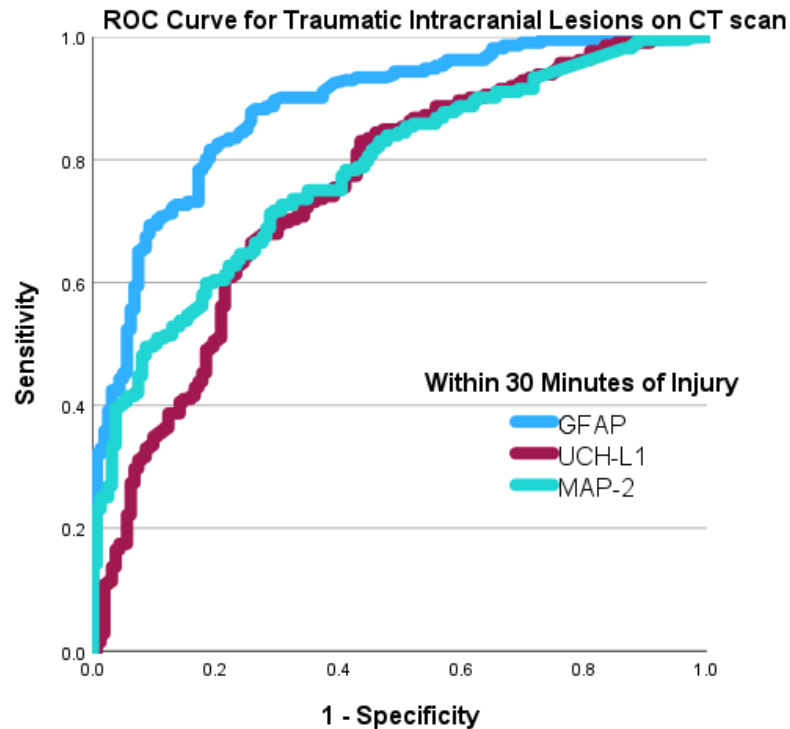


eFigure 3. Boxplots of MAP-2 concentrations measured within 30 and 60 minutes of injury relative to the categories of Marshall Classification of CT scan Lesions

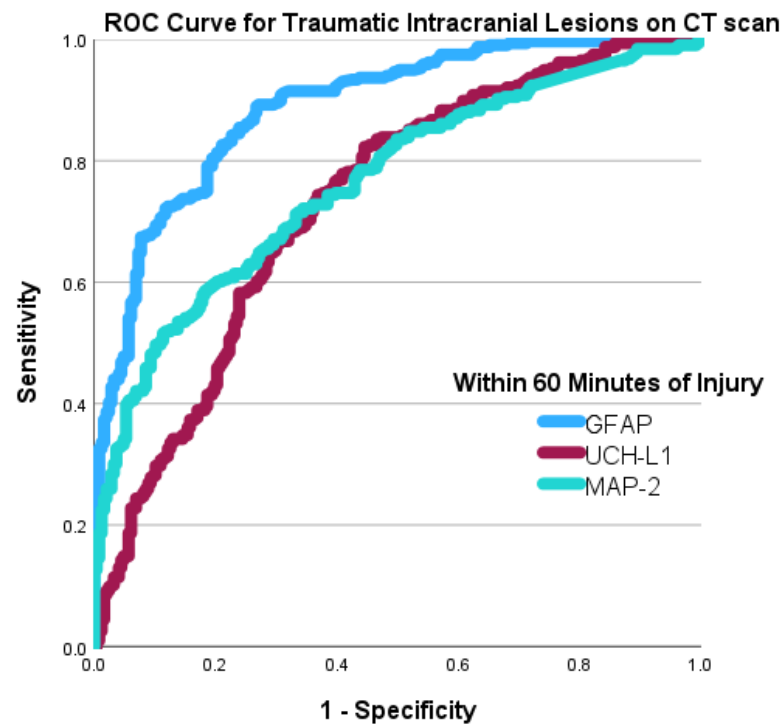


eFigures 4. Area under the ROC (AUROC) Curve for GFAP, UCH-L1 and MAP-2 measured with 30 and 60 minutes of injury for Detecting Intracranial Lesions on CT Scan (primary outcome)

4a.

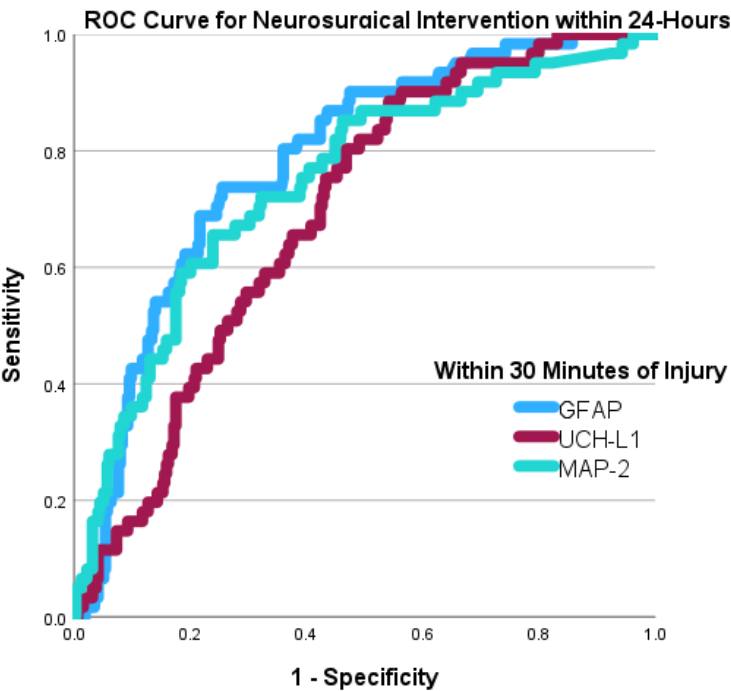


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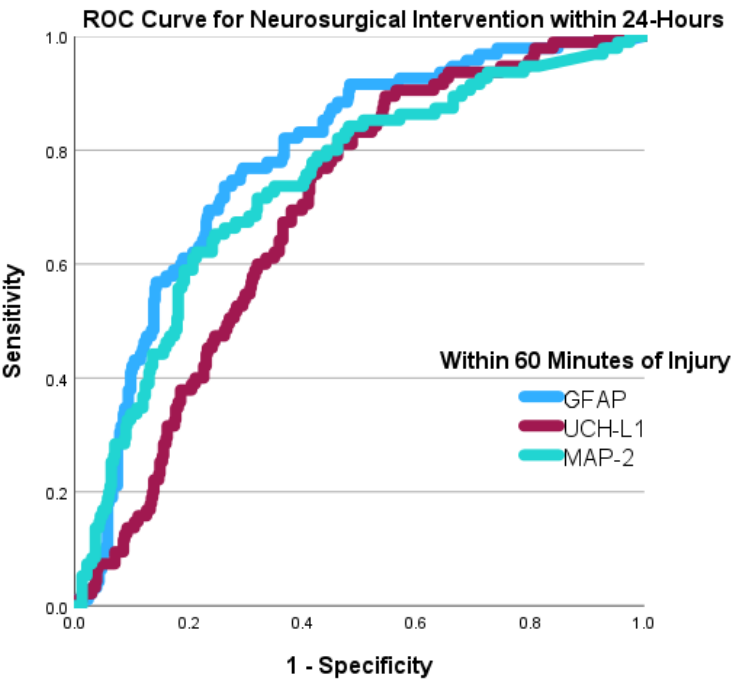


eFigures 5. Area under the ROC (AUROC) Curve for GFAP, UCH-L1 and MAP-2 measured with 30 and 60 minutes of injury for Predicting Neurosurgical Intervention within 24 hours of injury (secondary outcome)

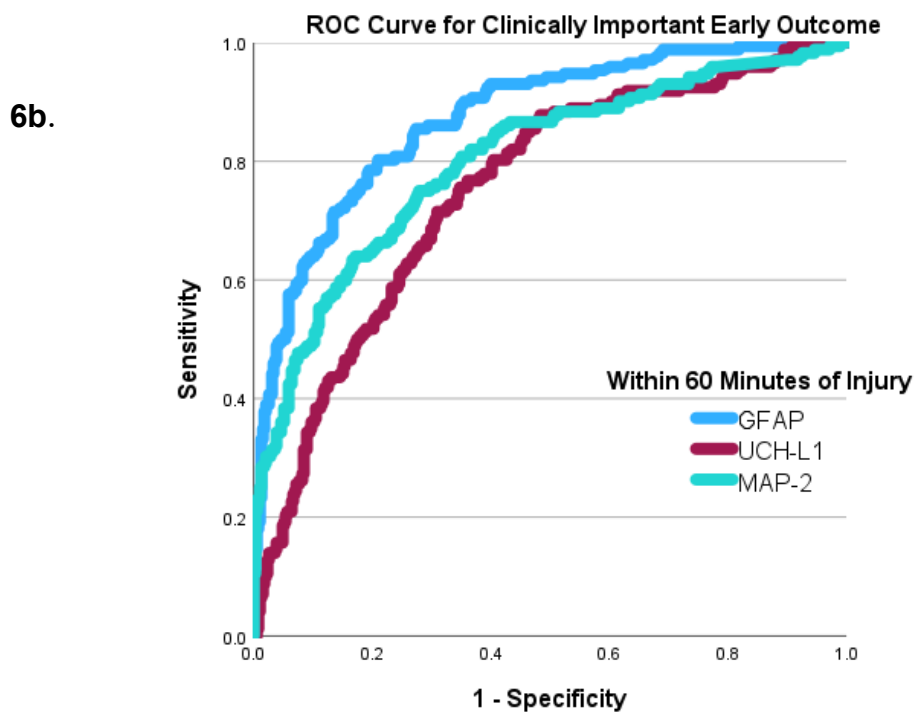
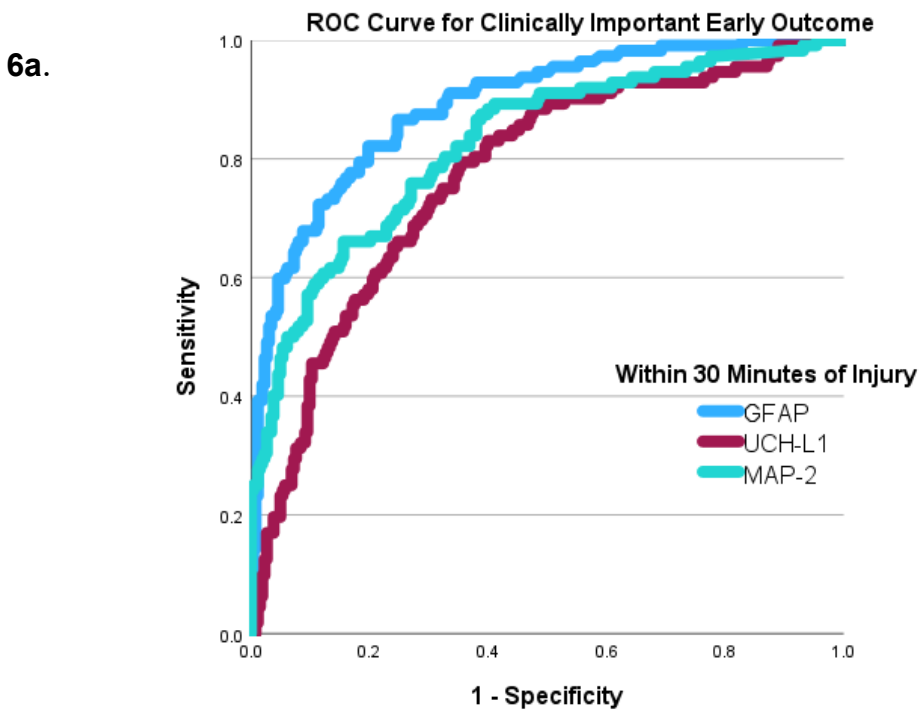
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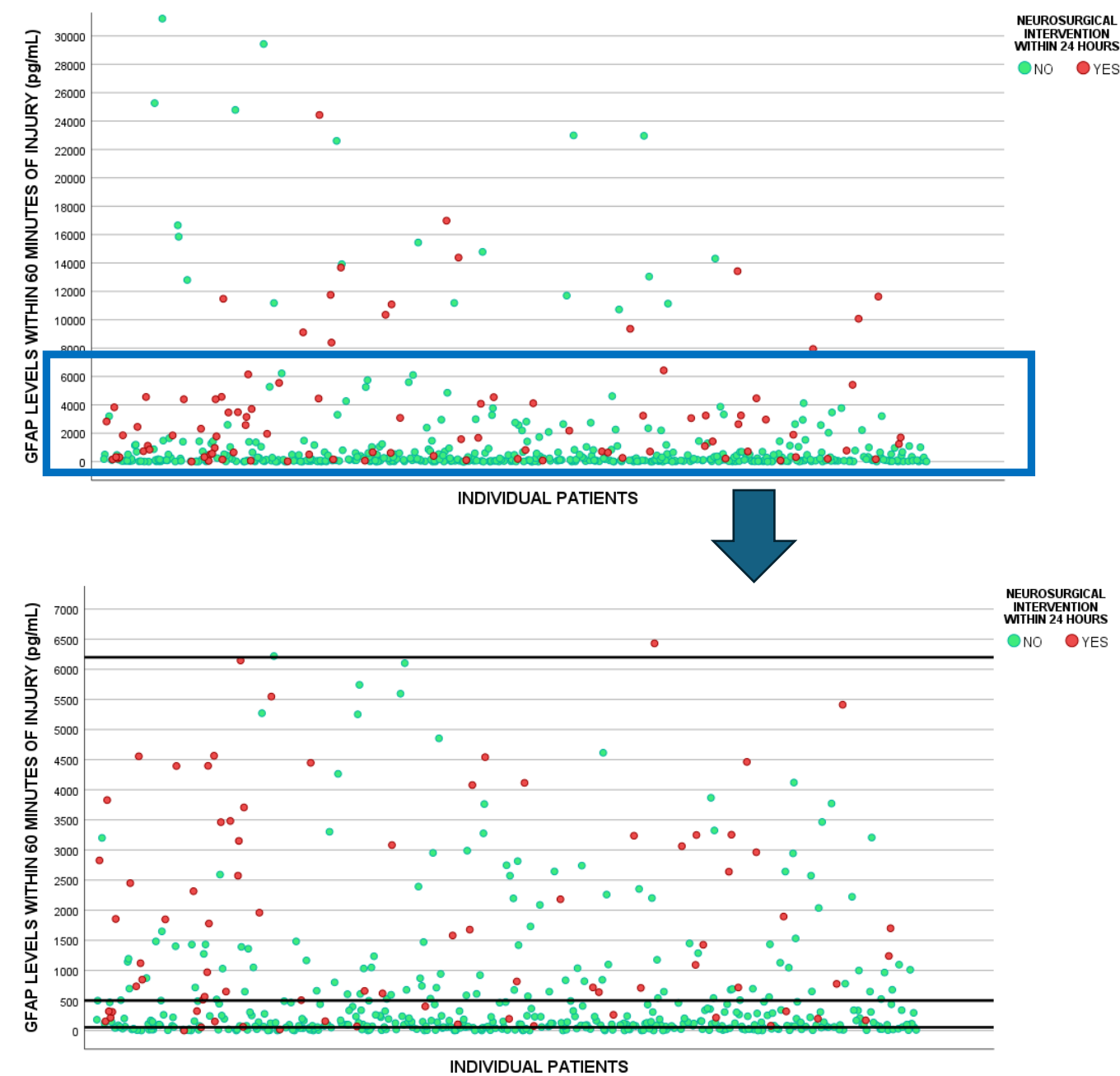
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eFigures 6. Area under the ROC (AUROC) Curve for GFAP, UCH-L1 and MAP-2 measured with 30 and 60 minutes of injury for Predicting Clinically Important Early Outcomes (tertiary outcome)

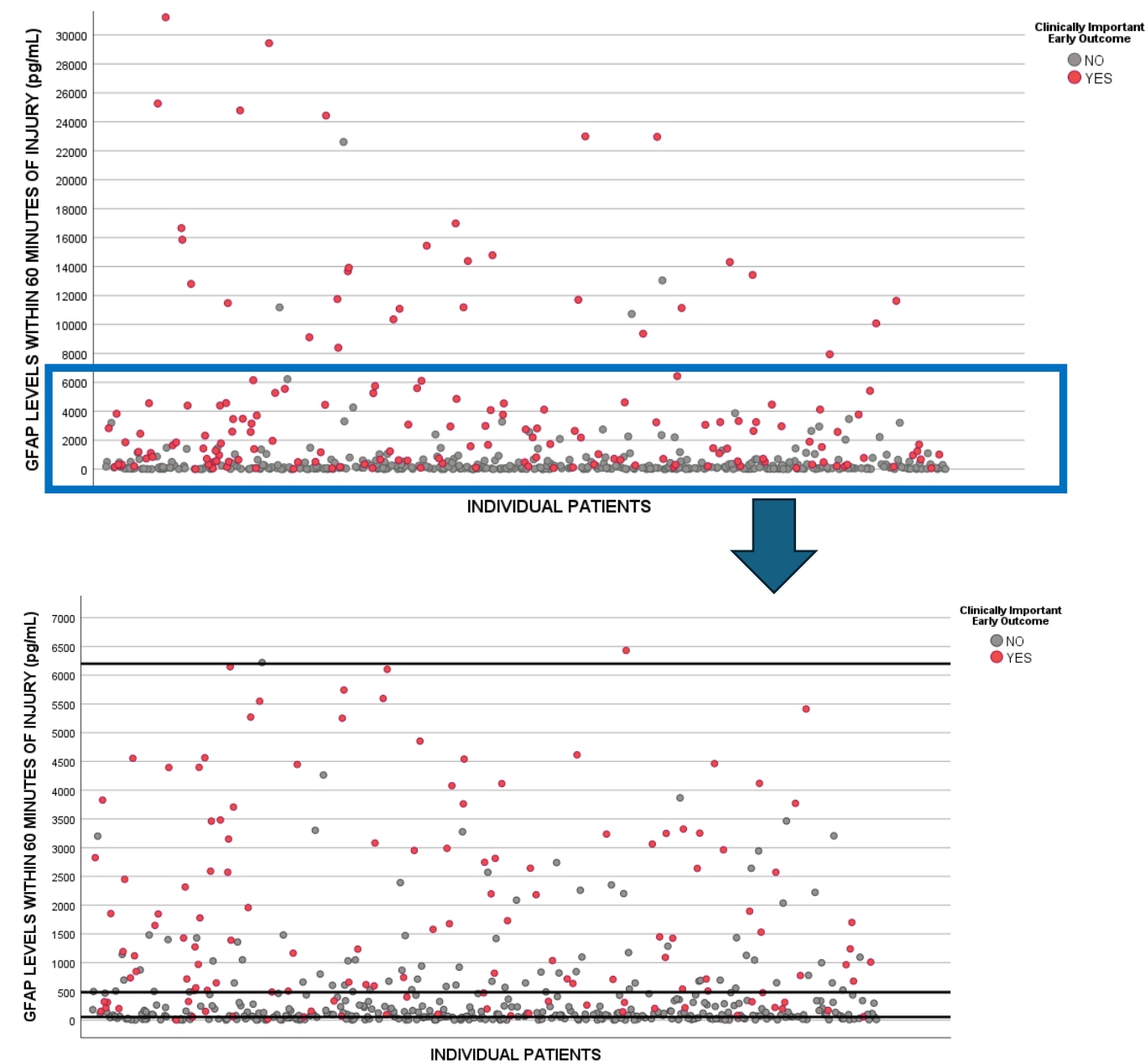


eFigure 7. Scatterplot exploring cutoff thresholds of GFAP for having neurosurgical intervention



GFAP Cutoffs for Neurosurgical Intervention	Sensitivity (30 minutes)	Specificity (30 minutes)	Sensitivity (60 minutes)	Specificity (60 minutes)
55 pg/mL (Optimize Sensitivity)	98% (90-100)	26% (21-31)	98% (92-100)	26% (22-30)
500 pg/mL (Optimize Sensitivity & Specificity)	74% (61-84)	71% (65-76)	77% (67-85)	71% (66-75)
6200 pg/mL (Optimize Specificity)	18% (10-30)	94% (91-96)	18% (11-27)	94% (91-96)

eFigure 8. Scatterplot exploring cutoff thresholds of GFAP for clinically important early outcome within 7 days of injury



GFAP Cutoffs for Clinically Important Early Outcomes	Sensitivity (30 minutes)	Specificity (30 minutes)	Sensitivity (60 minutes)	Specificity (60 minutes)
55 pg/mL (Optimize Sensitivity)	99% (94-100)	31% (25-37)	99% (95-100)	31% (26-36)
485 pg/mL (Optimize Sensitivity & Specificity)	80% (72-87)	80% (75-85)	79% (72-85)	79% (75-83)
6200 pg/mL (Optimize Specificity)	23% (16-32)	99% (96-100)	23% (17-30)	99% (97-100)