The Cerebrospinal Fluid HIV Risk Score for Assessing Central Nervous System HIV Activity

(410) 955-6328
ehammond@jhsph.edu

Edward R. Hammond[1], Rosa M. Crum[1], Glenn J. Treisman[1], Shruti H. Mehta[1], David B. Clifford[2], Ronald J. Ellis[3], Benjamin B. Gelman[4], Igor Grant[3], Scott L. Letendre[3], Christina M, Marra[5], Susan Morgello[6], David M. Simpson[6], Justin C. McArthur[1], for the CHARTER Group

[1]Johns Hopkins University, Baltimore, MD; [2]Washington University, St. Louis, MO; [3]University of California, San Diego, CA; [4]University of Texas, Medical Branch, Galveston, TX; [5]University of Washington, Seattle, WA; [6]Icahn School of Medicine at Mount Sinai, New York, NY.

Introduction

- Detectable cerebrospinal fluid (CSF) HIV RNA is associated with central nervous system (CNS) complications, including neurocognitive impairment and depression
- Measurement of CSF HIV RNA may have clinical utility under certain circumstances during HIV management
- Lumbar puncture procedures pose resource utilization challenges

Objective

- Develop a prediction model to estimate the risk of detectable CSF HIV RNA (threshold >50copies/ml) that will help identify patients who might benefit most from CSF monitoring

Methods

- The CNS HIV Anti-Retroviral Therapy Effects Research (CHARTER) is a six-center, US-based, prospective cohort study
- Cross-sectional data of 1,053 participants receiving combination antiretroviral therapy (cART) who underwent CSF evaluation at study entry (2004-2007)
- Multivariable logistic regression model to determine correlates of detectable CSF HIV RNA (threshold >50copies/ml), retained at a significance level of 0.157
- Internal validation by 5-fold cross-validation and bootstrapping
- CSF HIV Risk Score developed by weighting regression units for retained variables as integer points

Participant Characteristics

Table 1	n (%)	Mean (SD)	Median (IQR)
Age, years		44.3 (8.0)	
Male	822 (78.1)		
Race: White	414 (39.2)		
Black	504 (49.7)		
Hispanic/ Other	135 (12.8)		
Education, years		12.6 (2.5)	
CD4+ T-cell Nadir, cells/mm3		150.6 (147.1)	120.0 (29.0-218.0)
Current CD4 T-cell, cells/mm3		458.0 (290.7)	418.5 (248.0-610.0)
Log Plasma HIV RNA, c/mL		2.35 (1.04)	
Log CSF HIV RNA, c/mL		1.86 (0.49)	
CPE 2.0 Score		7.3 (1.7)	
Detectable CSF virus, n(%)	127 (15.7)		
Treatment duration, months		20.6 (23.0)	
Infection duration, months		130.1 (72.6)	
HIV Medication Adherence			
≥95%	915 (87.6)		
85-94%	46 (4.4)		
<85%	84 (8.0)		
Current MDD	140 (13.4)		
Lifetime MDD	527 (50.2)		

CPE2.0: CNS Penetration Effectiveness 2.0; MDD: Major Depressive Disorder

Retained Correlates of Detectable CSF HIV RNA

Table 2. Retained Correlates of Detectable CSF HIV RNA

Correlate		Odds Ratio (95% CI)	P-value	Risk Score
Race:	White	1.00		0
	Black	1.81(1.06, 3.09)	0.02*	3
	Other	2.39 (1.16, 4.95)	0.02*	4
Current MDD:	No	1.00		0
	Yes	2.25 (1.18, 4.28)	0.01*	4
Adherence:	≥95%	1.00		0
	85-94%	1.79 (0.67, 4.79)	0.23	3
	<85%	1.82 (0.90, 3.68)	0.10	3
CPE2.0 Score		0.77 (0.67, 0.88)	<0.001*	
	≥10			0
	5-9			6
	<5			9
Plasma RNA, c/mL		4.88 (3.91, 6.09)	<0.001*	
	<50			0
	50–199			2
	200-9,999			10
	>10,000			18
cART duration, months		0.99 (0.98, 1.00)	0.07	
	>36			0
	24-36			2
	13-24			3
	7-12			3
	<6			4

Discrimination and Calibration of CSF HIV RNA Risk Score

Figure 1. Discrimination Plot

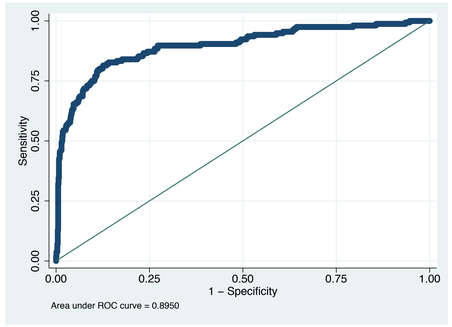


Figure 1. Discrimination plot from 5-fold validation displays Sensitivity vs. 1-Specificity of CSF HIV RNA Risk Score indicated by the curved line. The area under the curve represents discriminative ability.

Figure 2. Calibration Plot

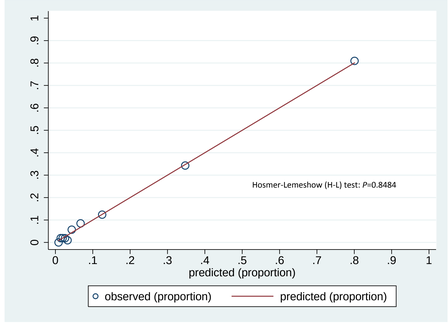


Figure 2. Circles represent risk class corresponding with predicted (X-axis) and observed (Y-axis) risk of detectable CSF HIV RNA. Predicted and observed risks do not differ across classes, H-L $P=0.848$.

Distribution of the CSF HIV RNA Risk Score

Figure 3.

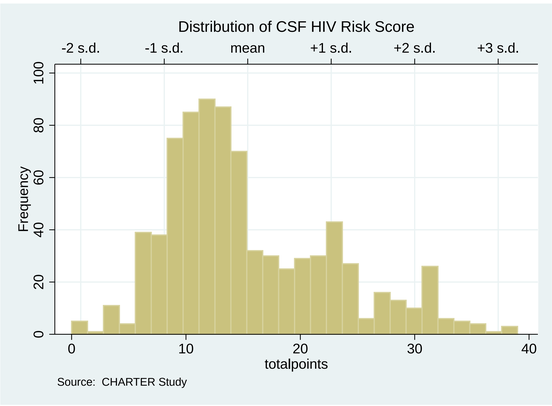


Figure 3. The CSF HIV Risk Score ranges from 0-39 points. Higher risk scores indicate greater probability of detecting CSF HIV RNA.

Distribution of CSF Viral Load by Risk Score

Figure 4.

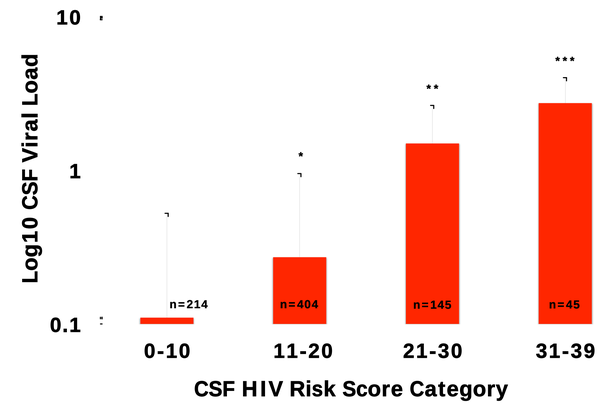


Figure 4. Higher CSF HIV Risk Score category associated with higher CSF viral load. *$P<0.001$ for CSF Risk Score category 2 vs. category 3 & 4; **$P<0.001$ for category 3 vs. category 1, 2 & 4; **$P<0.001$ for category 4 vs. 1, 2 & 3.

Conclusions

- The CSF HIV Risk Score correlates with detection of HIV RNA in the CSF, an advance in HIV management and monitoring of CNS effects of HIV
- The CSF HIV Risk Score may enable clinicians to better identify persons who may most benefit from lumbar puncture