HHV-8 Viral Load as Predictor for Cutaneous+Visceral Kaposi Sarcoma in PLWH: Multivariable Analysis

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1. INTRODUCTION

BACKGROUND:

Kaposi Sarcoma (KS) visceral involvement significantly worsens prognosis, yet validated predictive biomarkers have not yet been proposed. Human herpesvirus-8 (HHV-8) is the established etiologic agent, but its viral load's predictive utility for visceral involvement remains undefined.

- Clinical problem : >40% of KS cases develop visceral involvement[1].
- Current Gap: No tools for early identification of high risk cases.
- Study aim: Establish HHV-8 viral load cutoff for visceral prediction.

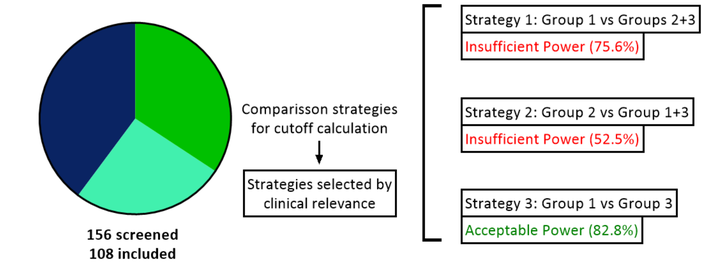
2. METHODS

DESIGN:

- Design: Cross-sectional diagnostic accuracy study.
- Setting: Single tertiary care center.
- Sample: 108 participants with histologically confirmed KS.
- IRB Approval: Num. C71-18.

GROUPS:

Figure 1. Groups by KS Involvement and Strategies for Sample Selection



Note. Of 156 patients screened, 108 were included. After power analysis, the optimal comparison was cutaneous-only (n=43) vs. cutaneous+visceral (n=37). Visceral-only (n=28) were excluded due to insufficient power (52.5%).

STATISTICAL ANALYSIS:

- Power: Post-hoc calculation (82.8% achieved).
- ROC Analysis: Youden's index for optimal cutoff.
- Multivariable logistic regression: Adjusted for age, gender, HIV viral load, Epstein-Barr and Cytomegalovirus viral load, and CD4+ T cell count.
- Validation: 70/30 train test split.
- Software: R 4.3.0 with pROC, pwr packages.

For PLWH with cutaneous KS, **HHV-8 viral load >3.0log10 copies/mL predicts visceral involvement with high specificity (87.8%).** This blood test provides a validated tool for **early identification of high-risk people** who need more aggressive evaluation.

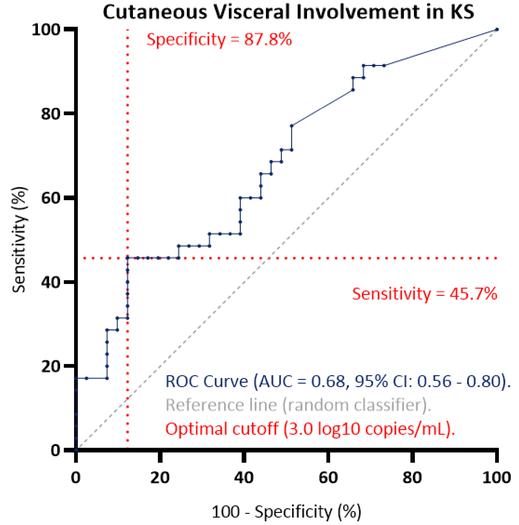
3. RESULTS

Table 1. Characteristics of the study groups

	Cutaneous-only (n =43)	Visceral-only (n = 28)	Cutaneous+visceral (n = 37)	p-value
Age—yr. (IQR)	36 (31-43)	35 (26-41)	32 (27-39	0.3512
Gender—no. (%) MSM	42 (98)	28 (100)	37 (100)	0.3447
HIV VL—log10copies/mL	5.1 (4.0-5.7)	5.1 (4.1-5.7)	4.9 (3.3-5.6)	**0.0364**
EBV VL—log10copies/mL	2.2 (1.5-2.7)	2.3 (1.6-3.2)	2.1 (1.0-2.8)	0.8465
CMV VL—log10copies/mL	2.5 (1.6-3.4)	2.4 (1.3-3.0)	1.6 (1.3-3.1)	0.3906
HHV-8 VL—log10copies/mL	2.4 (1.6-2.9)	2.7 (1.9-3.9)	2.8 (1.6-3.7)	**0.0368**
CD4—cells/mcL (IQR)	22 (11-42)	48 (16-127)	48 (16-110)	**0.0053**

Note. Values are median (IQR) or n (%). P-values: Kruskal–Wallis test for continuous variables; Chi-square test for categorical variables. Abbreviations: yr, years; HIV, human immunodeficiency virus; VL, viral load (log_{10} copies/mL); EBV, Epstein–Barr virus; CMV, cytomegalovirus; HHV-8, human herpesvirus 8; CD4, CD4+ T-cell count (cells/μL).

Figure 2. ROC Curve: HHV-8 Viral Load for Predicting Cutaneous Visceral Involvement in KS



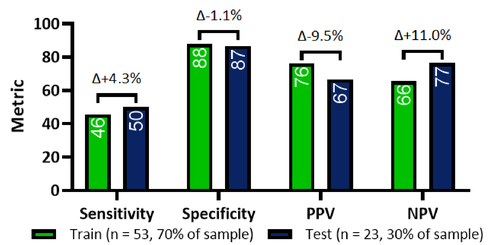
Note. Optimal cutoff: 3.0 log10 copies/mL (Sens = 45.7%, Spec = 87.8%, PPV =7 6.2%). Model validation showed consistent performance (test set: Sens = 50.0%, Spec=86.7%). Groups differed significantly (p = 0.017).

Table 2. HHV-8 VL Cutoff Diagnostic performance

Metric	Value (95%CI)
AUC	0.67 (0.55-0.79)
Sensitivity—%	45.7 (32.1-59.3)
Specificity- %	**87.8 (76.4-95.9)**
PPV—%	76.2 (61.5-87.5)
NPV—%	65.5 (53.7-76.1)

Note. HHV-8 ≥3.0 log10 predicted visceral KS with high specificity (87.8%) and good PPV (76.2%). AUC 0.678, sensitivity 45.7%, LR+ 3.75. High specificity enables confident clinical decision-making for rule-in.

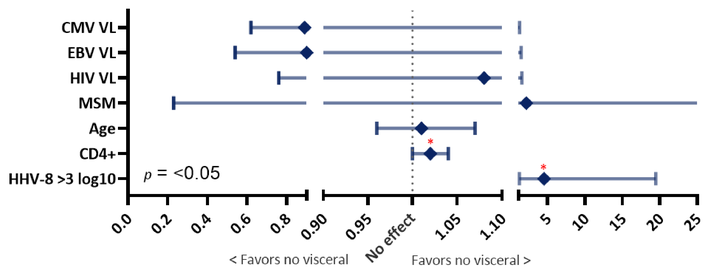
Figure 3. Validation train/test



Note. Model performance remained stable across training (n=53) and validation (n=23) sets. Specificity was nearly identical (87.8% vs 86.7%), confirming robustness and generalizability of the 3.0 log10 cutoff.

Figure 4. Multivariable Predictors of Visceral Involvement in KS

Logistic regression adjusted for all covariates



Note. HHV-8 >3.0 log10 (OR 4.53) and CD4 (OR 1.02) were significant independent predictors. Other covariates not significant. Log scale; dashed line = OR 1.0 (no effect).

Table 3. Multivariable predictors

Variable	Coefficient	Odds Ratio	95% CI
HHV-8 >3.0 log VL	1.510	4.53	**1.21 - 19.47***
CD4+ cells/mcL	0.021	1.02	**1.00 - 1.04***
Age (per year)	0.009	1.01	0.96 - 1.07
Male gender	0.766	2.15	0.23 - 51.83
HIV viral load	0.077	1.08	0.76 - 1.56
EBV viral load	-0.102	0.90	0.54 - 1.47
CMV viral load	-0.117	0.89	0.62 - 1.25

Note. *Significant at p<0.05. Multivariable model adjusted for age, gender, HIV VL, EBV VL, CMV VL, and

4. Discussion

Key findings:

- HHV-8 >3.0 log10 is an independent predictor of visceral disease.
- High specificity enables rule-in for visceral involvement.
- Superior multivariable model: AUC improved from 0.66 to 0.79.
- Robust validation: Consistent performance in external test set.

Clinical utility:

- Proposed algorithm: HHV-8 >3.0 log10 → Aggressive visceral workup
- Resource optimization: Target expensive diagnostics to high-risk patients.
- Early intervention: Potential for improved outcomes with timely treatment.

5. Conclusions

HHV-8 viral load >3.0 log10 copies/mL independently predicts visceral Kaposi sarcoma (OR 4.53). Its high specificity (87.8%) enables confident clinical decision-making, providing a practical tool for risk stratification and targeted use of diagnostic resources.