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Use of the Sample-to-Cutoff Ratio (S/CO) to Identify Recency of HIV-1 Infection

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Background

Two FDA-approved 4th generation HIV assays currently available in US have the capability to detect both HIV-1/2 specific antibodies and HIV-1 p24 antigen, allowing for the diagnosis of acute HIV-1 infection (AHI). Both assays are considered reactive at sample/cutoff ratios (S/CO)≥1 and non-reactive at S/CO<1. Since the S/CO increases with the quantity of antigen and/or antibodies present in the sample, it should be possible to use the S/CO range to differentiate between negative, AHI, recent and established HIV infection status.

Objectives

- Determine the utility of the S/CO values from 4th generation HIV assays to identify HIV-1 infection status.
- Determine the correlation of S/CO values between 4th generation HIV assays.

Materials & Methods

- The Abbott ARCHITECT HIV Ag/Ab Combo (ARCHITECT) is a chemiluminescent magnetic microparticle based immunoassay (CMIA) while the Bio-Rad GS HIV Combo Ag/Ab (GSCOMBO) is an enzyme immunoassay (EIA).
- A retrospective analysis was done using our primary screening HIV diagnostic algorithm (ARCHITECT) and when sample volume was adequate, the GSCOMBO was also performed.
- Specimens were obtained from an academic hospital referral laboratory and a research HIV-1 vaccine clinic.
- Testing interpretation algorithm: S/CO<1 with negative nucleic acid amplification test (NAT) = negative; S/CO≥1 with Bio-Rad Multispot HIV-1/2 rapid test (MS) non-reactive and positive NAT = acute HIV-1 infection (AHI); S/CO≥1 with MS-reactive and confirmed Western blot (WB) without or with the band p31 present = recent or established infection, respectively.

Results

Updated values are in bold.

A total of **188** clinical specimens were evaluated. Ninety-nine samples with a S/CO<1 were confirmed as negative with an ARCHITECT and GSCOMBO S/CO median and interquartile range [IQR] of 0.11 [0.09-0.13] and 0.27 [0.25-0.28], respectively. **Eighty-nine** samples had a S/CO≥1, of which **33** confirmed as AHI (Fiebig II) with ARCHITECT and GSCOMBO S/CO median [IQR] of **16.4 [4.8-61]** and **11.7 [5.9-14]**, respectively, MS non-reactive and with a viral load median [IQR] of **1.45x10^6** RNA copies/mL **[4.48x10^5 - 10x10^6]**.

Of the **56** specimens that were MS reactive and WB positive, **10** were WB-p31 band negative, indicating recent infection (Fiebig V) and **46** specimens were WB-p31 band positive, indicating established infection (Fiebig VI). The ARCHITECT S/CO medians [IQR] for recent and established infections were **408 [374-449]** and **884 [684-1008]** respectively; the GSCOMBO S/CO ratios were the same for both recent and established infections (14 [14]). The GSCOMBO S/CO also reached 14 in **45.5%** of AHI (**15** samples).

There were statistically significant differences in the ARCHITECT S/CO median [IQR] between AHI, recent and established infection (Kruskal–Wallis, p<0.0001) but not for GSCOMBO (**Figure 1**).

In addition, there were statistically significant differences in the S/CO from negative samples between the two assays (Wilcoxon rank sum, p<0.0001), with an overall increment of 0.15 for the GSCOMBO with respect to the ARCHITECT (Bland-Altman analysis).

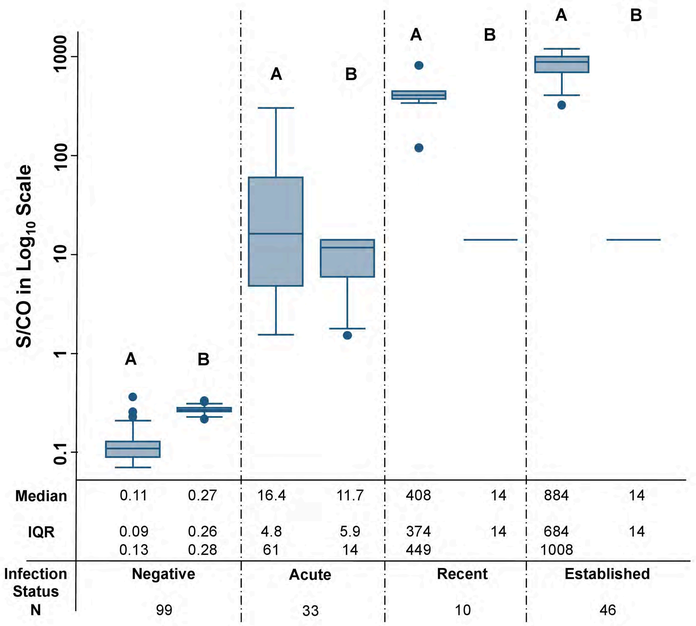

Figure 1: Distribution of S/CO values between (A) ARCHITECT and (B) GSCOMBO through different stages of HIV-1 infection.

Interpretation: **Although both assays distinguished negative from positive HIV infection equally well, only the range of the ARCHITECT S/CO values differentiated between AHI, recent and established HIV infection (Kruskal-Wallis, p<0.0001). The dynamic range of S/CO values for the ARCHITECT was two-logs greater than for the maximum GSCOMBO S/CO value of 14 which was reached for 45.5% of AHI and 100% of recent and established HIV infection.**

This difference was also observed in AHI samples through a model using fitted polynomial plots with both assays running in parallel until the S/CO of 5.8. This difference disappeared above the S/CO of 5.8 as the GSCOMBO S/CO approached its maximum value of 14 while the ARCHITECT S/CO continued to increase by more than one Log_{10} (**Figure 2**).

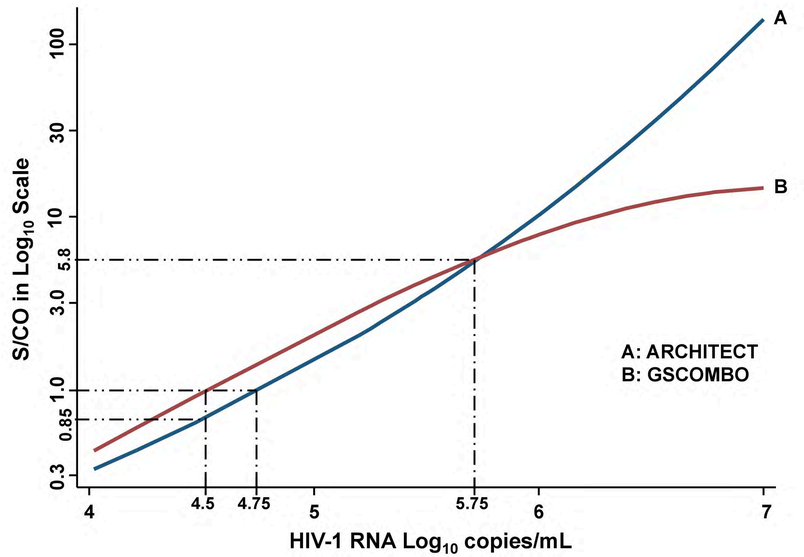

Figure 2: Fitted polynomial plots for HIV-1 RNA and the S/CO using 33 acute HIV infection results: (A) ARCHITECT and (B) GSCOMBO assays.

Interpretation: **Both the ARCHITECT and GSCOMBO Log10 S/CO values increased in parallel up to an HIV-1 plasma viral load of approximately 600,000 HIV-1 RNA copies/mL (S/CO of 5.8) after which the GSCOMBO S/CO plateaued while the ARCHITECT S/CO continued to increase by at least two more logs. In the model, the GSCOMBO becomes reactive at 31,600 HIV-1 RNA copies/mL, while the corresponding ARCHITECT S/CO would be 0.85. The model shows the ARCHITECT becoming reactive at 56,200 HIV-1 RNA copies/mL which reinforces the notion of creating a S/CO "grey zone" between 0.50 and 0.99 for the ARCHITECT. [Ramos EM. J Clin Virol. 2013;58(S1):e38-43]**

Conclusions

In this small study both the GSCOMBO EIA and ARCHITECT CMIA identified negative from positive HIV infection equally well but the ARCHITECT was able to further differentiate between AHI, recent and established infection. As such, the ARCHITECT's broader dynamic S/CO range compared to the GSCOMBO might be useful for identifying HIV-1infection incidence but requires confirmation in a larger study.

Acknowledgements

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