Poster Board 9
Abstract 45
2016 HIV Diagnostics Conference
March 21-24, 2016
Atlanta, Georgia

Distribution of the ARCHITECT Sample to Cutoff Ratio (S/CO) by Fiebig Stage of HIV-1 Infection

Eric M. Ramos*, José Ortega*, Glenda Daza*, Socorro Harb*, Joan Dragavon* and Robert W. Coombs*†

Departments of *Laboratory Medicine and †Medicine, University of Washington, Seattle, Washington, USA.

Robert W. Coombs, MD PhD
Eric M. Ramos, MD MSc
Virology Specialty Laboratory
300-9th Ave, Room 706 C
Seattle, WA, 98104-2499
(T): (206) 897-5205 or 5202
(E): bcoombs@uw.edu
emramos@uw.edu

Background

It is important to distinguish recent from established HIV-1 infection quickly and efficiently to assess seroincidence and to inform iniation of antiretroviral treatment (ART) early in infection. ART will rapidly reduce the viral load and thus limit the size of the cellular viral reservoir, improve immune function and reduce the forward transmission of HIV-1 infection.

"Recent HIV-1 infection" refers to an approximate three-month time interval following HIV-1 acquisition and represents part of an infection continuum described by the Fiebig staging schema.[1] This staging relies on the detection of HIV-1 RNA, p24 antigen and sequential immunoassay reactivity to specific viral antigens.

Objectives

The broad dynamic range of the sample to cutoff (S/CO) ratio for the fourth generation ARCHITECT HIV Ag/Ab Combo chemiluminescent magnetic microparticle based immunoassay (CMIA) (ARCHITECT; Abbott, Chicago, IL), correlates with the level of HIV-1 p24-antigen and antibody.[2]

Although the high viremia levels associated with acute HIV-1 infection (AHI) contribute to S/CO values of ≤15, it is common to see S/CO values >15 when the Western blot (WB) is negative during recent infection because the ARCHITECT will detect low-level HIV-1 specific antibody below the WB sensitivity.[3]

We sought to characterize the association between the ARCHITECT S/CO ratio, Fiebig stage and recency of HIV-1 infection in clinical specimens.

Materials & Methods

Specimens were obtained from an academic hospital referral laboratory and research HIV vaccine trials.

A retrospective analysis of specimens obtained be-tween May 2011 to September 2015 used a 4th generation HIV-1/2 diagnostic al-gorithm comprised of the ARCHITECT, Multispot (Bio-Rad), Western blot (Bio-Rad) and HIV-1/2 plasma RNA (Abbott m2000).[4]

The HIV-1 testing algorithm interpretation for the S/CO and Fiebig stage (FS) was as follows:

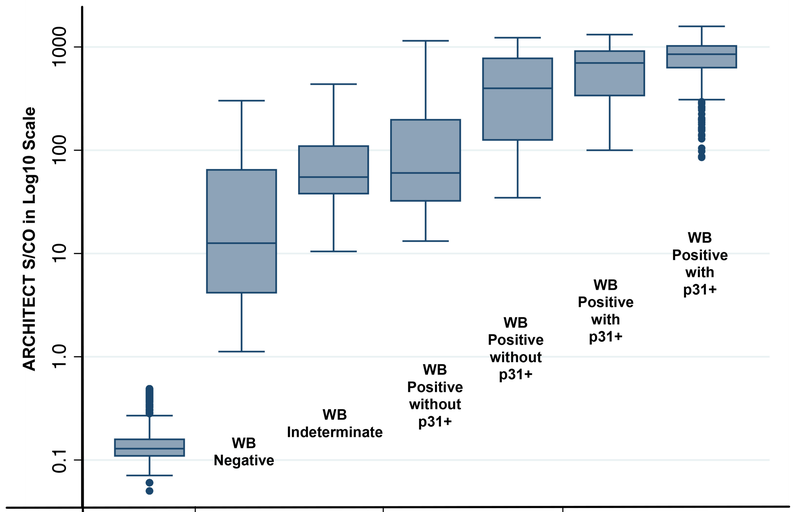
- Negative infection: S/CO <1.0
- Acute infection (AHI) or FS I-II: S/CO ≥1, Bio-Rad Multispot HIV-1/2 rapid test (MS) non-reactive and a positive plasma HIV-1 RNA.
- Recent early infection or FS III-IV: S/CO ≥1, MS reactive with negative or indeterminate WB.
- Recent infection or FS V: S/CO ≥1, positive HIV-1 WB without a p31 band.
- Established infection or FS VI: S/CO ≥1, positive HIV-1 WB with a p31 band present.

Results

Updated values are in bold.

From **43,264** specimens tested, **42,543** were considered negative with a S/CO median and interquartile range [IQR] of 0.13 [0.11-0.16]. A total of **721 (1.7%)** specimens were ARCHITECT reactive; however, only 43 **(6.0%)** were MS non-reactive and confirmed as AHI by HIV-1 RNA with a S/CO median [IQR] of 12.5 [4.2-65] and a viral load median [IQR] of 1.45x10^6 RNA copies/mL [4.48x10^5 – 10.0 x10^6].

Of the **678** MS-reactives, 19 were WB indeterminate with a S/CO median [IQR] of 55 [38-110] and were considered to be recent early infections. The rest were divided in two groups; **111** were WB-positive without p31 (recent HIV infection) and 548 were p31-positive (established HIV infection) with a S/CO median [IQR] of **139 [51-603]** and **826 [584-1023]**, respectively.



Median	0.13	12.5	55	60	399	701	850
IQR	0.11 0.16	4.2 65	38 110	32 200	126 781	342 919	630 1034
Infection Status	Negative	Acute	Recent Early	Recent	Recent	Established	Established
N	42,543	43	19	56	55	80	468
WB Bands	No bands	No bands	1 - 2 bands	2 - 3 bands	≥ 4 bands	≤ 7 bands	≥ 8 bands
Fiebig Stage		FS I - II	FS III - IV	FS V	FS V	FS VI	FS VI

Figure 1: Association between ARCHITECT sample to cutoff ratio (S/CO) values and Fiebig stage of HIV-1 infection for 43,264 specimens tested by the UW 4th generation HIV-1 algorithm between 2011 and 2015.

Interpretation: ARCHITECT S/CO values distinguish between AHI, recent early, recent and established HIV-1 infection (Kruskal-Wallis, p<0.0001). ARCHITECT S/CO values increased in association with the number of WB bands present in the sample.

There were statistically significant differences among Fiebig stages (Kruskall-Wallis, p<0.0001); between acute (FS I & II), recent-early (FS III & IV) and recent (FS V) HIV-1 infections compared to established HIV-1 infection (FS VI) (Wilcoxon Mann-Whitney, p<0.0001); and between recent-early and early HIV-1 infection (Wilcoxon-Mann-Whitney, p=0.004).

In the recent (FS V) and established (FS VI) HIV-1 infection groups, we were able to further categorize the samples according to the number of WB bands present between the two groups (Figure 1). We divided the recent infection category with the p31 band absent into two sub groups: one subgroup with three or fewer bands and and another subgroup four or more bands with a S/CO median [IQR] of 60 [32-200] and 399 [126-781], respectively. Similarly, we divided the established infection group with the p31 band present into two subgroups: one with seven or fewer bands and the other with eight or more bands and with a S/CO median [IQR] of 701 [342-919] and 850 [630-1034], respectively.

The ARCHITECT S/CO signal increased in parallel with the number of WB bands as expected; thus, there were statistically significant differences among each group (Wilcoxon Mann-Whitney, p<0.0001), except between recent-early infection and recent infection with only 2 or 3 WB bands (Wilcoxon Mann-Whitney, p=NS) due to only a single WB band difference between the two groups.

Conclusions

The broad range of ARCHITECT S/CO values can be used to presumptively differentiate between AHI, recent and established HIV infection while awaiting confirmation by other methods. In conjunction with a rapid orthogonal confirmatory test, the S/CO information may be helpful to accurately assign HIV-1 infection recency and emphasize to the clinician the urgency for considering the use of early antiretroviral therapy during the acute and recent HIV-1 infection periods. The use of the S/CO ratio for this purpose requires further validation in the clinical laboratory setting.

Acknoledgements

Funding support from the ACTG Virology Specialty Laboratory (UM1-AI-068636; UM1-AI-106701), HVTN HIV Diagnostic Laboratory (UM-AI-068618) and UW CFAR Clinical Retrovirology Core (P30-AI-027757). We also would like to thank Public Health - Seattle and King County (Paul Swenson, PhD and Joanne Stekler, MD, MPH) for contributing patient samples for the study.

References

1. Fiebig EW, et al. AIDS. 2003;17(13):1871-79.
2. Brennan CA, et al. J Clin Virol. 2013;57(2):169-72.
3. Ramos EM, et al. 22nd Conference of Retrovirus Opportunistic Infection. 2015.
4. Ramos EM, et al. J Clin Virol. 2013;58 Suppl 1:e38-43.