Unmasking Crohn's Disease: Anti-glycan antibodies (ACCA, ALCA, AMCA) may improve diagnostic accuracy while providing prognostic value, especially in ASCA-seronegative patients

Jane M. Yang[1], Ato O. Aikins[2], David Alfego[2] and Kelly Y. Chun[1]
[1]Labcorp Specialty Medicine, Calabasas, CA, USA; [2]Labcorp Data Science, Burlington, NC, USA

Introduction

Anti-glycan antibodies (AGA) include ACCA (Anti-chitobioside), ALCA (Anti-laminaribioside), and AMCA (Anti-mannobioside) and are antibodies specific to Crohn's Disease (CD) that target glycans (polysaccharides) found in microorganisms, such as *C. albicans* and *S. cerevisiae.* They may alter the immune response to fungal dysbiosis. Used together with gASCA (Anti-saccharomyces cerevisiae), the presence of AGA in patient serum differentiates CD from ulcerative colitis (UC) and non-IBD with about 85% specificity. Moreover, concomitant positivity of 2 or more AGA increases CD specificity (>95%) and predicts faster progression to more severe disease with strictures and fistulae. This diagnostic accuracy of AGA has been validated by more than a dozen independent, peer-reviewed studies in over 4,000 IBD patients.[1] More recent utilization and real-life performance of AGA in clinical practice have yet to be characterized.

Methods

We assessed the utilization and positivity of 4 AGA in 163,364 patient samples when ordered as the IBD Expanded Profile from January 2012 through March 2024. The antibodies, gASCA, ACCA, ALCA and AMCA, are detected in serum, quantitated by enzyme-linked immunosorbent assays (ELISA) using phophomannan, chitobioside, laminaribioside, and mannobioside, and reported in units where >50, >90, >60, and >100, respectively, are positive. gASCA utilizes an improved purified form of mannan and is comparable to conventional ASCA.

Results

Of a total of 163,394 patient samples, one quarter (25.2%) were positive for at least one AGA. Isolated positivity of only one AGA was found in 18.3% where gASCA alone was the most common (7.0%) followed by AMCA (6.1%).

Isolated Positivity of 1 AGA	n (% of total)	Concomitant Positivity of 2 AGA	n (% of total)	Concomitant Positivity of 3 or 4 AGA	n (% of total)
ACCA only	3623 (2.2%)	ALCA + gASCA	1,567 (1.0%)	ALCA + gASCA + AMCA	1,257 (0.8%)
ALCA only	4832 (3.0%)	ALCA + AMCA	2,609 (1.6%)	ALCA + gASCA + ACCA	185 (0.1%)
AMCA only	9888 (6.1%)	ACCA + ALCA	300 (0.2%)	ALCA + AMCA + ACCA	546 (0.3%)
gASCA only	11,508 (7.0%)	AMCA + gASCA	2,466 (1.5%)	gASCA + AMCA + ACCA	370 (0.2%)
		ACCA + gASCA	743 (0.5%)	gASCA + AMCA + ACCA + ALCA	437 (0.3%)
		ACCA + AMCA	891 (0.5%)		

Table 1. Anti-glycan antibodies in 163,394 patient serum samples.

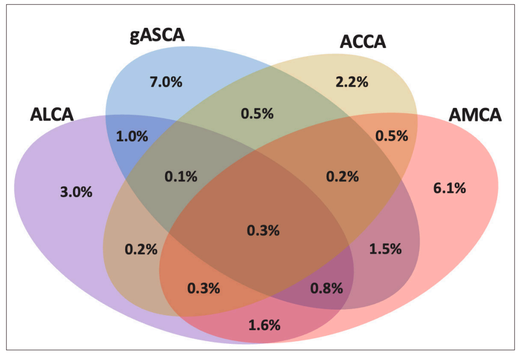

Figure 1. Concomitant positivity in 163,394 patient serum samples.
Anti-glycan antibodies (AGA):
ACCA: Anti-chitobioside carbohydrate antibodies
ALCA: Anti-laminaribioside carbohydrate antibodies
AMCA: Anti-mannobioside carbohydrate antibodies

Results (continued)

Concomitant positivity of 2 or more AGA occurred in only 7.0% of all samples with the most frequent co-occurrences, ALCA + AMCA and AMCA + gASCA. Individual AGA frequencies were gASCA (11.3%), AMCA (11.3%), ALCA (7.2%), and ACCA (4.3%). Median antibody levels (interquartile range) for positive samples were: gASCA 66.0 (57.0-84.0), ACCA 124.0 (104.0-167.0), ALCA 76.0 (67.0-92.0) and AMCA 147.0 (118.0-205.0).

Conclusion

Serum AGA were frequently positive in over 160,000 patient samples. One quarter (25.2%) of all samples were positive for at least one AGA supporting their potential usefulness in differentiating CD from UC and non-IBD. Most positivity (18.3%) occurred as one isolated positive AGA (~85% specific for CD). A smaller subset, 7.0%, had 2 or more AGA and as such, are associated with a very high specificity (>95%) for CD as well as an odds ratio of 3 for severe disease and need for abdominal surgery.[1,2]

Of note, most samples (88.7%) were seronegative for gASCA, reiterating the limited sensitivity of conventional IBD serology (only pANCA and ASCA). Of 144,864 gASCA-seronegative samples, a substantial number, 18,533 (13.9%), were positive for one or more of the novel AGA (ACCA, ALCA or AMCA). This result substantiates the potential incremental benefit of these novel anti-glycan antibodies in identifying those patients more likely to have CD and its disease complications.

References

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2. Kaul A, et al. Serum Anti-glycan Antibody Biomarkers for Inflammatory Bowel Disease Diagnosis and Progression: A Systematic Review and Meta-analysis. Inflamm Bowel Dis 2012;18(10):1872-1884.

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