Clinical Biochemistry 46 (2013) 119–122

Contents lists available at SciVerse ScienceDirect

Clinical Biochemistry

journal homepage: www.elsevier.com/locate/clinbiochem

Performance characteristics of the ARCHITECT Galectin-3 assay

Sonia L. La'ulu [a], Fred S. Apple [b], MaryAnn M. Murakami [b], Ranka Ler [b], William L. Roberts [a,c], Joely A. Straseski [a,c,*]

[a] ARUP Institute for Clinical and Experimental Pathology, Salt Lake City, UT, United States
[b] Department of Laboratory Medicine and Pathology, Hennepin County Medical Center and Minneapolis Medical Research Foundation, Minneapolis, MN, United States
[c] Department of Pathology, University of Utah, Salt Lake City, UT, United States

ARTICLE INFO

Article history:
Received 6 June 2012
Received in revised form 10 September 2012
Accepted 13 September 2012
Available online 23 September 2012

Keywords:
Galectin-3
Heart failure
Immunoassay
Method comparison
Reference interval
Imprecision
Linearity
ARCHITECT

ABSTRACT

Objectives: Galectin-3 is an emerging biomarker that is commonly increased in patients with heart failure and/or patients at risk for cardiovascular disease. We evaluated the Galectin-3 assay on the Abbott ARCHITECT $i1000_{SR}$ and ARCHITECT $i2000_{SR}$ at 2 testing sites.

Design and methods: Imprecision (%CV), interference, limits of blank (LoB), detection (LoD), and quantitation (LoQ), linearity, method comparison to an ELISA method, comparisons between plasma and serum, and reference intervals were evaluated. Imprecision was performed based on two runs of duplicate testing conducted daily. Verification of LoB, LoD, and LoQ was performed according to Clinical and Laboratory Standards Institute guidelines. Linearity was evaluated by making 5 dilutions of a high patient EDTA plasma pool with a low patient pool. Reference intervals were established using EDTA plasma collected from self-reported healthy volunteers. A second lot of reagent was used at one site for method comparison and imprecision studies.

Results: Total CV's were ≤6.0%. A positive interference was observed for hemolyzed samples over 2.0 g/L hemolysate. The LoB ranged from 0.1 to 0.3 ng/mL, the LoD from 1.4 to 2.1 ng/mL and the LoQ from 3.0 to 3.3 ng/mL. Linearity studies had slopes and correlation coefficients equal to 1.0. Comparison of the $i1000_{SR}$ and $i2000_{SR}$ to the ELISA method demonstrated slopes of 1.0 to 1.2 and correlation coefficients of 0.93 to 0.97. The 97.5th percentile of the reference interval was 18.7 and 17.9 ng/mL for the $i1000_{SR}$ and $i2000_{SR}$, respectively.

Conclusions: The Abbott Galectin-3 assay demonstrated acceptable analytical performance on both the ARCHITECT $i1000_{SR}$ and ARCHITECT $i2000_{SR}$.

Introduction

Nearly 6 million people in the United States suffer from heart failure (HF), resulting in 281,000 deaths per year. Prevalence has been estimated to increase 25% in the next 20 years leading to an additional 3 million people who will be diagnosed with HF [1]. Currently, B-type natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP) are the most commonly used biomarkers to aid in the diagnosis of HF. Galectin-3 is an emerging biomarker that is directly associated with cardiac remodeling and is therefore considered a "culprit" biomarker since it participates in the pathogenesis of HF [2]. Due to its involvement with adverse cardiac remodeling, galectin-3 has potential as a therapeutic target to slow and possibly prevent the development of HF [2,3]. Recent studies have demonstrated that galectin-3 has particular value in predicting prognosis rather than clinical diagnosis of HF [4,5]. Using galectin-3 independently or in conjunction with measurement of BNP, NT-proBNP, and/or cardiac troponin has been demonstrated to aid in prognosis determination, risk stratification, and management of patients presenting with symptoms of HF [4–7].

As galectin-3 continues to show promise as a biomarker for HF, appropriate high volume testing platforms are needed. An enzyme-linked immunosorbent assay (ELISA) is commercially available and a comprehensive evaluation has been performed previously [8]. However, automated methods can facilitate faster turn-around-times and are less laborious. The purpose of the current study was to evaluate the analytical performance of the Galectin-3 assay on the Abbott ARCHITECT $i1000_{SR}$ and ARCHITECT $i2000_{SR}$.

Materials and methods

Imprecision (%CV), interference, limits of blank (LoB), detection (LoD), and quantitation (LoQ), linearity, method comparison to an ELISA method, comparisons between plasma and serum, and reference intervals were evaluated using the Galectin-3 assay on the ARCHITECT $i1000_{SR}$ and ARCHITECT $i2000_{SR}$ (Abbott Diagnostics, Abbott Park, IL) at 2 different sites: ARUP Laboratories, Salt Lake City, UT (site A), and

* Corresponding author at: University of Utah/ARUP Laboratories, 500 Chipeta Way, Mail Code 115, Salt Lake City, UT 84108, United States. Fax: +1 801 584 5207.
E-mail address: joely.a.straseski@aruplab.com (J.A. Straseski).

0009-9120/$ – see front matter
http://dx.doi.org/10.1016/j.clinbiochem.2012.09.014

Hennepin County Medical Center, Minneapolis, MN (site B). Testing was performed on both the $i1000_{SR}$ and $i2000_{SR}$ at site A and on the $i2000_{SR}$ at site B according to manufacturer's instructions, employing the same reagent lot at both sites. A second lot of reagent was used at site A for method comparison and imprecision studies. The Galectin-3 STAT assay uses 25 μL of sample and has an 18 minute process time to first result. All studies involving the use of human specimens were approved by the Institutional Review Board at the respective sites.

Imprecision was evaluated at each site using 3 concentrations of manufacturer's quality control (QC) material run in duplicate. Two runs were performed daily, for 20 days, with a minimum of 2 hours separating each run. A second lot of reagent was used to perform a 5 day imprecision study. Interference studies were performed as previously described on the $i2000_{SR}$ at site A [9]. Briefly, EDTA plasma pool aliquots, with a galectin-3 concentration close to the clinical cutoff of 17.8 ng/mL [7] was supplemented with 2.0 g/L RBC hemolysate; or 766 μmol/L (44.8 mg/dL) bilirubin; or 20% Intralipid to a final triglycerides concentration of 34.3 mmol/L (3034 mg/dL). A measured galectin-3 concentration ±10% of the expected concentration was considered acceptable. Verification of LoB, LoD, and LoQ was performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines (EP17-A) on each analyzer at both sites. For LoB, 20 replicates of blank material (Calibrator A, 0.0 ng/mL) were tested. For LoD verification, 20 replicates of a sample with a concentration close to the manufacturers claimed LoD were used. LoQ was verified by testing a minimum of 30 replicates of a sample with a concentration near the claimed LoQ. Linearity was assessed by making 5 dilutions of a high patient EDTA plasma pool containing an analyte concentration near the upper end of the analytical measurement range (AMR), with a low patient EDTA plasma pool. Each dilution was tested in duplicate on all methods and different sample pools were used at each site.

The ARCHITECT analyzers were compared to a Galectin-3 ELISA (BG Medicine, Waltham, MA) [8]. The ARCHITECT and ELISA reagents utilize the same monoclonal antibody clones as well as the same capture antibody and conjugate. A total of 190 EDTA plasma samples were tested at site A using 2 lots of ARCHITECT reagents and 129 samples at site B with one lot of reagent. Samples were thawed in batches, mixed thoroughly, centrifuged, checked for clots, and analyzed by the ARCHITECT methods and the ELISA on the same day. Comparison of EDTA plasma to serum was evaluated by testing 11 paired samples on both the $i1000_{SR}$ and $i2000_{SR}$. Reference intervals were established non-parametrically using EDTA plasma samples collected from 122 self-reported healthy adult volunteers from site A (62 females; 60 males; 19–65 years of age; median age 31 years) and 120 subjects from site B (60 females; 60 males; 20–79 years of age; median age 39 years) with no history of myocardial infarction, coronary artery bypass surgery, angioplasty, coronary stent placement, and/or stroke. Participants also reported no diagnosis or treatment for cancer, diabetes mellitus, hypertension, hypercholesterolemia, and/or hyperlipidemia.

Imprecision, linearity, and reference intervals were evaluated using EP Evaluator (Release 8, David G. Rhoads Associates, Kennett Square, PA). Verification of LoB, LoD, and LoQ was performed using StatisPro (version 1.13.00, Clinical and Laboratory Standards Institute, Wayne, PA). Passing–Bablok and linear regression was generated by Analyse-it (version 2.26, Analyse-it Software, Leeds, England). GraphPad Prizm (version 5.04) was used to calculate p values.

Results and discussion

Imprecisions of the ARCHITECT methods were assessed by using the manufacturer's QC materials. Total CVs were ≤6.0% for all methods, demonstrating favorable imprecision, and results were comparable between the two testing sites and two lots of Galectin-3 reagent (Table 1). Overall, the high level of QC (average concentration 73.9 ng/mL) was the most precise and the low level (average concentration 9.3 ng/mL) was the least precise. The medical decision point of 17.8 ng/mL for galectin-3 [7] is close to the concentration of the medium level of QC, where total observed CVs were ≤3.4%. Total CVs on the ARCHITECTs were lower than the reported CVs for the ELISA (5.6 to 16.9%) [8].

Table 1
Imprecision of the ARCHITECT Galectin-3 assay.

Method/ site/lot	QC	Mean concentration (ng/mL)	Total SD	CV (%)		
				Within run	Between day	Total
$i1000_{SR}$	Low	9.3	0.4	4.1	1.2	4.2
Site A	Medium	19.7	0.6	2.0	0.8	2.9
Lot 1[a]	High	73.5	1.7	1.2	0.7	2.3
$i2000_{SR}$	Low	9.4	0.5	4.9	0.0	5.0
Site A	Medium	19.4	0.6	3.0	1.1	3.2
Lot 1[a]	High	74.1	1.9	2.4	0.8	2.6
$i2000_{SR}$	Low	9.4	0.6	5.2	0.0	6.0
Site B	Medium	19.6	0.6	2.5	2.1	3.3
Lot 1[a]	High	73.6	2.0	1.8	1.4	2.8
$i1000_{SR}$	Low	9.1	0.4	4.0	1.9	4.5
Site A	Medium	19.4	0.5	2.1	1.5	2.6
Lot 2[b]	High	73.8	1.3	1.3	1.1	1.8
$i2000_{SR}$	Low	9.5	0.5	4.8	0.6	4.8
Site A	Medium	19.5	0.5	2.5	0.9	2.7
Lot 2[b]	High	74.7	1.7	1.9	0.6	2.2

[a] 20 day imprecision study.
[b] 5 day imprecision study.

Interference studies for icterus and lipemia demonstrated <10% interference detected by the highest concentration of each substance tested. Presence of hemolysis at concentrations ≥2.0 g/L RBC hemolysate caused a significant positive interference. Interference from hemolyzed samples has been reported previously [8].

Verification of manufacturer's claimed LoB, LoD, and LoQ was performed and analyzed according to CLSI guidelines. The mean concentrations determined were 0.3, 0.2, and 0.1 ng/mL for LoB; 2.1, 1.6, and 1.4 ng/mL for LoD; and 3.3, 3.0, and 3.1 ng/mL for LoQ on the $i1000_{SR}$ and $i2000_{SR}$ at site A and $i2000_{SR}$ at site B, respectively (Table 2). The intended concentration for each linearity sample was calculated based on the concentrations of the low and high patient EDTA plasma pools used to make the dilutions. The maximum deviation from the target recovery ranged from 11.9% to 14.3% (Table 3). The concentration where the maximum deviation occurred was different between the 2 sites. Repeated linearity studies performed showed deviations occurring at various concentrations along the AMR, ranging from 12.6 to 55.6 ng/mL, but never exceeded 15.8% at either site. The assay was linear across the entire AMR with both slopes and correlation coefficients equal to 1.0 for all methods at both sites.

Method comparisons were performed using the BG Medicine Galectin-3 ELISA as the comparator method. Testing was performed with the $i1000_{SR}$ and $i2000_{SR}$ at site A and with the $i2000_{SR}$ at site B. Comparison of the $i2000_{SR}$ to the ELISA was evaluated by each site independently as well as combined (Fig. 1, Panels B, C, D). EDTA plasma specimens demonstrated acceptable agreement between methods with correlation coefficients of ≥0.93 and slopes ranging from 1.0 to 1.2. The $i1000_{SR}$ and $i2000_{SR}$ methods tested at site A showed a slight positive bias relative to the ELISA method with slopes of 1.2 (Fig. 1,

Table 2
LoB, LoD, and LoQ of the ARCHITECT Galectin-3 assay.

Method/site		n	Mean (ng/mL)	Median (ng/mL)	Total SD	CV (%)
$i1000_{SR}$	LoB	20	0.3	0.2	0.2	99.5
Site A	LoD	20	2.1	2.0	0.1	5.1
	LoQ	30	3.3	3.3	0.2	6.2
$i2000_{SR}$	LoB	20	0.2	0.1	0.2	130.7
Site A	LoD	20	1.6	1.6	0.1	8.0
	LoQ	30	3.0	3.0	0.2	7.0
$i2000_{SR}$	LoB	20	0.1	0.0	0.2	154.0
Site B	LoD	20	1.4	1.4	0.2	14.5
	LoQ	30	3.1	3.1	0.2	6.7