Clinical Biochemistry xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Clinical Biochemistry

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

Short Communication

Validating laboratory results in a national observational cohort study without field centers: The Reasons for Geographic and Racial Differences in Stroke cohort

Sarah R. Gillett [a], Rebekah H. Boyle [b], Neil A. Zakai [a,b], Leslie A. McClure [c], Nancy S. Jenny [b], Mary Cushman [a,b,*]

[a] Department of Medicine, University of Vermont College of Medicine, 208 South Park Dr., Colchester, VT 05446, USA
[b] Department of Pathology, University of Vermont College of Medicine, 208 South Park Dr., Colchester, VT 05446, USA
[c] University of Alabama at Birmingham, 1665 University Blvd., Birmingham, AL 35233, USA

ARTICLE INFO

Article history:
Received 30 May 2014
Received in revised form 29 July 2014
Accepted 3 August 2014
Available online xxxx

Keywords:
Quality control
Blood chemical analysis
Biological markers
Blood specimen collection
Cohort studies

ABSTRACT

Objectives: The REasons for Geographic and Racial Differences in Stroke (REGARDS) study is a prospective cohort of 30,239 Americans in the contiguous United States; the first of this scale to use home visits to obtain, process, and ship biologic samples to a core laboratory. Pre-analytical factors resulting from this study design may affect the results of some laboratory assays. We investigated the impact of REGARDS processing on a variety of analytes.

Design and methods: In REGARDS, blood samples were processed in the field by technicians who were trained on standardized methods for phlebotomy and sample processing. Field processing included centrifugation using varying non-uniform equipment and shipping overnight on ice to the University of Vermont, where samples were re-centrifuged for 30,000 ×g-minutes and stored at −80 °C. We assessed the effects of REGARDS sample handling by processing split samples from 20 volunteers using either ideal procedures or simulated REGARDS procedures. Assays for 19 analytes for potential study in REGARDS were then run on both samples and results compared.

Results: Spearman correlation coefficients for analytes measured in ideal versus REGARDS processed samples ranged from 0.11 to 1.0. Thirteen of 19 analytes were highly correlated (>0.75), but platelet proteins were more variable.

Conclusions: Simulation of non-optimal field processing and shipment to a central laboratory showed high variability in analytes released by platelets. The majority of other analytes produced valid results, but platelet contamination in REGARDS samples makes measurement of platelet proteins unadvisable in these samples. Future analytes considered by REGARDS or similar studies should undergo similar pilot testing.
© 2014 The Canadian Society of Clinical Chemists. Published by Elsevier Inc. All rights reserved.

Introduction

Unlike epidemiologic studies that use study centers for clinical exams and blood sample collection, the REasons for Geographic and Racial Differences in Stroke (REGARDS) study conducted in-home visits with participants. This allowed recruitment of a nationally representative sample. While standardized training and methods were used, since field processing and sample shipping may affect the quality of samples [1–5], the validity of assays run on these samples required investigation. Here, we provide results on analyte validity using split samples from 20 volunteers, and results on sample yield and quality from >30,000 REGARDS participants from a baseline in-home visit.

Materials and methods

REGARDS enrolled 30,239 adults ≥45 years old, 42% black and 58% white, 45% men and 55% women, 56% from the stroke belt (Alabama, Arkansas, Georgia, Louisiana, Mississippi, North Carolina, South Carolina, and Tennessee) and 44% from the 40 other contiguous United States [6]. Institutional review boards approved the study. After written informed consent, Examination Management Services, Inc. (EMSI) (Scottsdale, AZ) technicians collected biologic samples following telephone-based screening and enrollment. Trained technicians followed detailed

Abbreviations: ADAMTS-13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; CV, coefficient of variation; EDTA, ethylenediaminetetraacetic acid; ELISA, enzyme-linked immunosorbent assay; EMSI, Examination Management Services, Inc.; ERL, Enzyme Research Laboratories; HGF, hepatocyte growth factor; IL, interleukin; PAI-1, plasminogen activator inhibitor 1; PDGF, platelet-derived growth factor; REGARDS, REasons for Geographic and Racial Differences in Stroke; SCAT-1, sample collection/anticoagulant tube; s-EPCR, soluble endothelial protein C receptor; TGFβ1, transforming growth factor beta 1; vWF, von Willebrand factor.

* Corresponding author at: Department of Medicine, University of Vermont College of Medicine, 208 South Park Dr., Colchester, VT 05446, USA.
E-mail address: mary.cushman@uvm.edu (M. Cushman).

http://dx.doi.org/10.1016/j.clinbiochem.2014.08.003
0009-9120/© 2014 The Canadian Society of Clinical Chemists. Published by Elsevier Inc. All rights reserved.

ARTICLE IN PRESS

instructions for phlebotomy and sample processing using centrally assembled kits. Fasting morning blood was drawn using butterfly needle systems in the following order: 1 9-mL serum separator tube (SST; BD, Franklin Lakes, NJ), 1 10-mL EDTA plasma tube (BD), 1 5-mL sample collection/anticoagulant tube (SCAT-1) plasma tube (Hematologic Technologies, Inc., Essex Junction, VT), and 1 4-mL SST. SCAT-1 tubes are designed to prevent in vitro clotting activation and contain, in whole blood, 4.5 mmol/L EDTA, 0.15 kIU/L aprotinin, and 20 mol/L D-Phe-Pro-Arg-chloromethylketone [7]. All tubes were placed in a biohazard bag with absorbent pad and placed in a styrofoam mailer on frozen gel ice packs (0 °C) for the remainder of the EMSI visit. Processing was required within 120 minutes of phlebotomy; centrifugation was for 10 minutes, then serum or plasma, and packed cells from the EDTA and SCAT-1 tubes were transferred into mailer tubes. Specimens were shipped overnight with two frozen gel ice packs to the University of Vermont Laboratory for Clinical Biochemistry Research. Upon receipt, samples were catalogued and serum and plasma re-centrifuged at 4 °C for 30,000 $\times g$-minutes, then stored at −80 °C.

Real-time feedback on sample condition was provided to EMSI. Sample redraws were required for errors including mislabeled tubes, missing or extra tubes, whole blood sent instead of serum or plasma, <2 ice packs, spilled/leaked specimens, or samples not shipped the day of draw. Redraws were not requested due to participant refusal of phlebotomy, technical problems with phlebotomy, shipping delay attributed to the shipping carrier, or central laboratory processing errors.

To determine whether analytes proposed for measurement in REGARDS could be accurately measured, split samples from 20 volunteers were processed using both ideal (immediate) procedures and a simulated REGARDS processing protocol. Ideal processing included allowing the SST tube to clot at room temperature for 30 minutes before centrifuging for 30,000 $\times g$-minutes at 4 °C; EDTA and SCAT tubes were placed on ice for <5 minutes following phlebotomy then centrifuged for 30,000 $\times g$-minutes at 4 °C. Serum and plasma were then immediately stored at −80 °C. To simulate REGARDS processing, draw tubes were placed in an insulated cooler with 2 gel ice packs for 60–120 minutes, and then centrifuged for 5000 $\times g$-minutes at room temperature. Plasma and serum were separated into mailer tubes and sealed in an insulated shipping container with 2 gel ice packs overnight. The following day, mailer tubes were re-centrifuged for 30,000 $\times g$-minutes at 4 °C, and plasma and serum stored at −80 °C. Ideal and REGARDS processed samples from each individual were then assayed for analytes listed in Table 1.

Results and discussion

Between February 2003 and December 2007, 31,170 sample kits (including re-draws) were received at the core laboratory (Supplemental Fig. 1), representing 96% of the cohort. Errors occurred for 8.2% of the kits; 3.2% from shipper delay, and 5% ($n = 1,575$) from technician errors that triggered redraw requests. Technician errors were misprocessing

Table 1
Correlations between plasma samples processed in REGARDS vs. ideal fashion.

Assay	Inter-assay CV	Reference range	Sample type	Spearman rank correlation (ρ)	Coefficient of determination (R^2)	% Bias	Linear regression equation
ADAMTS-13*	8%**	0.6–1.6 μg/mL	EDTA	0.61	0.27	20%	$y = 0.74x - 0.01$
Adiponectin	4–13%	3 to 14 μg/ml	EDTA	0.92	0.87	−11%	$y = 0.87x + 1.29$
			SCAT	0.98	0.97	−1%	$y = 0.96x + 0.76$
D-Dimer*	5–17%	0.22–4.0 μg/mL	EDTA	0.77	0.57	33%	$y = 0.77x - 0.26$
			SCAT	0.75	0.72	0%	$y = 0.99x - 0.18$
Factor VII antigen	6–9%	70–130%	SCAT	0.93	0.93	−8%	$y = 0.94x - 2.22$
Factor VIII antigen (ERL)	4–7%	40–145%	EDTA	0.89	0.83	3%	$y = 0.86x + 17.1$
			SCAT	0.92	0.80	7%	$y = 0.94x + 12.1$
Factor IX antigen (ERL)	9–15%	80.3–152%	EDTA	0.90	0.93	1%	$y = 0.90x + 7.87$
			SCAT	0.88	0.90	0%	$y = 0.87x + 10.4$
Factor XI antigen (ERL)	6–9%	40–111.4%	EDTA	0.91	0.85	0%	$y = 0.86x + 16.9$
			SCAT	0.75	0.72	0%	$y = 0.80x + 27.2$
Fibrinogen antigen	3–8%	180–350 mg/dl	EDTA	0.87	0.71	6%	$y = 1.13x - 22.6$
			SCAT	0.96	0.94	−2%	$y = 0.94x + 14.0$
HGF	3–10%	80–380 pg/mL	EDTA	0.88	0.67	−20%	$y = 0.77x + 5.02$
			SCAT	0.94	0.77	17%	$y = 1.07x + 10.3$
IL-8*	3–7%	1.2–16.7 pg/mL	EDTA	0.69	0.45	30%	$y = 0.93x + 0.17$
			SCAT	0.90	0.86	10%	$y = 0.92x + 0.10$
IL-10*	4–11%	0.16–12.70 pg/mL	EDTA	0.88	0.73	1%	$y = 0.08x + 1.16$
			SCAT	0.99	0.84	0%	$y = 0.10x + 1.11$
Leptin*	1–4%	2000–11,100 pg/mL	EDTA	1.0	1.0	−4%	$y = 1.02x - 0.20$
			SCAT	1.0	1.0	3%	$y = 1.00x + 0.00$
PAI-1	4–16%	5–66 ng/mL	SCAT	0.65	0.33	676%	$y = 1.10x + 59.0$
PDGF	6.5–8.5%	155.7–643.0 pg/mL	EDTA	0.23	0.02	253%	$y = 0.32x + 1855.2$
Protein C* antigen (ERL)	9%	70–140%	EDTA	0.53	0.29	4%	$y = 0.37x + 2.61$
			SCAT	0.62	0.44	−8%	$y = 0.50x + 0.13$
Protein C antigen (Stago)	5–8%	70–140%	EDTA	0.94	0.87	1%	$y = 1.04x - 3.85$
			SCAT	0.61	0.48	1%	$y = 0.50x + 73.8$
Resistin	2–6%	6.39–26.4 ng/ml	EDTA	0.59	0.29	−10%	$y = 0.38x + 6.52$
			SCAT	0.73	0.53	−5%	$y = 0.39x + 6.22$
s-EPCR*	6–7%	65.3–197.3 ng/mL	EDTA	0.93	0.96	1%	$y = 0.93x + 0.37$
TFG-β1	6.4–9.3%	100.0–1234.0 pg/mL	EDTA	0.11	0.03	126%	$y = 4.12x + 16,110$
			SCAT	0.31	0.06	64%	$y = 0.85x + 16,031$
vWF antigen	3–13%	50–160%	EDTA	0.60	0.48	−18%	$y = 0.94x - 13.4$

CV = coefficient of variation, SCAT = sample collection/anticoagulant tube, EDTA = ethylenediaminetetraacetic acid, ADAMTS-13 = A disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13, ERL = Enzyme Research Laboratories, HGF = hepatocyte growth factor, IL = interleukin, PAI-1 = plasminogen activator inhibitor 1, PDGF = platelet-derived growth factor, s-EPCR = soluble endothelial protein C receptor, TFG-β1 = transforming growth factor beta-1, vWF = von Willebrand factor.
* Log transformed for linear regression.
** Based on 2 plates.

Please cite this article as: Gillett SR, et al, Validating laboratory results in a national observational cohort study without field centers: The Reasons for Geographic and Racia..., Clin Biochem (2014), http://dx.doi.org/10.1016/j.clinbiochem.2014.08.003

Download English Version:

https://daneshyari.com/en/article/8317312

Download Persian Version:

https://daneshyari.com/article/8317312

Daneshyari.com