Accurate Health Risk Classification for Heart Disease using Point of Care Testing in a Health Screening and Wellness Environment and Lipid Quantitation

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Introduction: POCT Testing in Health Screening

The screening for cholesterol level in normal and apparently healthy populations is an integral part of a "Wellness Program". Such programs have gained increasing popularity in the United States and abroad. The use of Point of Care testing (POCT) is a desired element in many settings and an absolute necessity in remote test centers as analysis of fractionated cholesterol is an integral part in the determination of relative risk of Heart Disease (HD). The American Heart Association has established the clinical determination values which establish the relative HD risk. In a screening environment these measurements provide the basis for referral to a physician. The clinical limits which have been established are:

Total Cholesterol	
<200 mg/dL	Low risk
200-239 mg/dL	Borderline high
≥240 mg/dL	Higher risk

HDL Cholesterol	
<40 mg/dL	At risk
41-59 mg/dL	Borderline to near optimal
≥60 mg/dL	Optimal

Triglycerides	
<150 mg/dL	Normal
150 – 199 mg/dL	Borderline high
200 – 499 mg/dL	High
Greater than 500 mg/dL	Very high

Reference: Adult Treatment Panel (ATP) III guidelines. National Heart, Lung, and Blood Institute, Diseases and Condition Index. Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA. 2001;285(19):2486-2497.

Methods

The CardioChek uses either venous blood or capillary blood to quantitate cholesterol sub fractions. One of the most popular screening panels is the lipid panel which consist of a three-analyte test strip which simultaneously measures total cholesterol, HDL cholesterol and triglycerides and then using these measurements calculates the LDL cholesterol. The end point detection is based on reflectance. Blood added to the strip is vertically transported via gravity to cause a sequential red blood cell separation, cholesterol fractionation (in the case of HDL) and finally a enzymatic reaction in which the blood cholesterol esters are enzymatically degraded to produce by products which yield a colorimetric reaction in the presence of specific chromophore agents. The intensity of the color is recorded as reflectance.

Evaluation Protocol

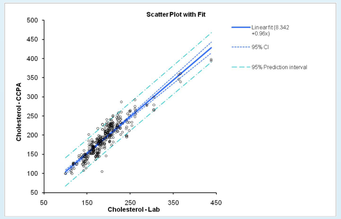
In a 4-site health screening setting we evaluated the comparative effectiveness of the CardioChek POCT (Lipid Panel) and a chemistry reference instrument (Olympus, Quest Labs) in heart disease risk classification based upon TC, HDL and Trig to assess whether the POCT device was a diagnostic equivalent. A total of 169 comparisons were conducted at geographically diverse centers using professional health screen organizations.

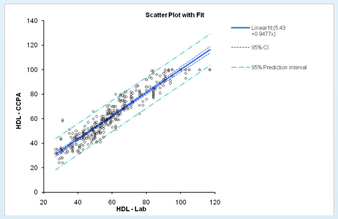
CardioChek® P·A

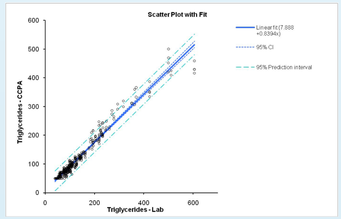
Results
Establishing the Correlation of the CardioChek Lipid Panel Assays and the Reference Laboratory

The correlation of the CardioChek to the reference analyzer is shown for the combined site data. The regression statistics for the individual cholesterol, HDL and Triglyceride for each lipid panel are used to describe the system bias. Bias is estimated using the difference of the reference value and the calculated CardioChek value at the respective clinical limits for each analyte.

Linear Regression (Combined Data)			Bias Estimation (Combined Data)			
	Statistics		Lab	CCPA	% Difference	Avg Bias
Cholesterol	slope	0.96	160	162	1.21	-0.04
	intercept	8.342	200	200	0.17	
	r^2	0.84	240	239	-0.52	
	r	0.92	280	277	-1.02	
HDL	slope	0.9477	40	43	8.35	3.48
	intercept	5.43	60	62	3.82	
	r^2	0.89	80	81	1.56	
	r	0.94	100	100	0.20	
Triglycerides	slope	0.8394	100	92	-8.17	-11.00
	intercept	7.888	150	134	-10.80	
	r^2	0.96	200	176	-12.12	
	r	0.98	250	218	-12.90	







Assessing Site Differences of Accuracy and Precision

Site Differences of Accuracy & Precision

	Analyte	Bias (%)	Precision (CV %)
Site A	Cholesterol	0.55	6.5
	HDL	3.79	7.3
	Triglyceride	-13.54	6.9
Site B	Cholesterol	3.56	3.0
	HDL	2.91	4.9
	Triglyceride	-11.84	5.6
Site C	Cholesterol	-2.07	4.7
	HDL	1.31	7.0
	Triglyceride	-5.83	5.1
Site D	Cholesterol	0.91	5.4
	HDL	8.55	8.8
	Triglyceride	-9.92	6.1

Overall (Average) Accuracy & Precision

	Cholesterol	HDL	Triglyceride
Bias	1.78%	4.14%	10.28%
Precision	4.9%	7.0%	5.93%

- Bias was minimal across the four sites for cholesterol and HDL.
- Bias for triglyceride was higher due to the initial lot calibration. Calibration can be controlled on a lot specific basis using the CardioChek MEMo Chip®.
- Precision estimates were measured using repetitive (N = 20) measurement of a single sample.

Risk Assessment

All individual analyte results were categorized based on the traditional risk category for the three analytes. These clinical decision limits are shown in the table for each analyte and the four sites. Cholesterol risk classification and striation was then assessed for each matched donor based upon the use of the POCT or Lab value (Table, Part 1). This showed nearly equivalent risk classification, by percent of the population across all analytes. To further assess risk categorization, a 3x3 clinical agreement table for each analyte was compiled using these same analyte specific striation levels and applying strict limits to quantify "Agreement". This analysis (Table, Part 2) shows the high degree of agreement of risk classification assignment between the two methods even when a small absolute value difference (i.e., Lab TC value of 199; POCT TC value of 205 (actual value in Site A) is recorded as a "1 Category Difference" yet the test result is not clinically different. Generally, across the study complete agreement is 80% or better (TC and HDL) and 90% for Trig. In only one instance (Site A, TC) is there a "2 Category Difference". Close analysis of the TC "1 Category Difference" at the clinical limit of 200 mg/dL shows that in the 19 matched pairs that contributed to this category the aggregate average difference was a clinically insignificant 16.6 mg/dL, reinforcing the stringent nature of this analysis and comparability of the methods.

Part 1		Risk Classification & Striation (% of population)								
		Cholesterol (mg/dL)			HDL (mg/dL)			Triglycerides (mg/dL)		
Source Value	Statistic	<200	200-240	>240	<40	40-60	>60	<150	150-200	>200
POCT	Avg + SD	62.9 ± 9.7	28.6 ± 9.4	8.5 ± 3.8	10.4 ± 10.1	44.1 ± 12.8	45.0 ± 13.4	77.1 ± 10.2	9.9 ± 3.6	13.0 ± 11.0
LAB	Avg + SD	64.3 ± 13.2	26.3 ± 10.9	8.9 ± 5.2	14.4 ± 8.1	44.1 ± 10.5	41.0 ± 15.2	72.9 ± 10.5	8.0 ± 2.9	18.6 ± 8.8
		Risk Classification Agreement Between Methods (%)								
Part 2		Cholesterol			HDL			Triglycerides		
	POCT vrs Lab	Agreement	1 Category Difference	2 Category Difference	Agreement	1 Category Difference	2 Category Difference	Agreement	1 Category Difference	2 Category Difference
Risk Assessment & Patient Classification	Site A	80.4	17.9	1.8	83.9	16.1	0	87.5	12.5	0
	Site B	76.7	23.3	0	90.0	10.0	0	93.3	6.7	0
	Site C	87.8	12.2	0	83.7	16.3	0	93.9	6.1	0
	Site D	82.4	17.6	0	67.6	32.4	0	91.2	8.8	0
	Average	**81.8**	**17.8**	**0.5**	**81.3**	**18.7**	**0**	**91.5**	**8.5**	**0**

Results Discussion and Conclusion

The critical part of any POCT testing in a health screening application is that the test properly categorizes patients with respect to health risk. Two different measurements for cholesterol derivatives (Total, HDL, Triglyceride) are never 100% aligned. POCT results are generally used for screening applications and the results of any wellness testing are to identify those patients that require further medical follow-up. Correlation studies help to initially establish the relationship of the POCT test to the laboratory reference but ultimately it is the categorization of patients to a health risk group that provides the true measure of a POCT test. The multi site study concluded here demonstrates that the CardioChek is an accurate means to properly categorize patients as to their heart disease risk category based on the level of cholesterol, HDL cholesterol and triglyceride.