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Performance of the CardioChek™ PA and Cholestech LDX® point-of-care analysers compared to clinical diagnostic laboratory methods for the measurement of lipids

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Summary

Point-of-care (POC) blood testing is intended to provide results more rapidly than can be obtained from a central laboratory. Precision and accuracy of the CardioChek PA and Cholestech LDX analysers were compared to clinical diagnostic laboratory methods. In 100 patients, total cholesterol (TC), triglycerides (TG), HDL cholesterol (HDL-C) and LDL cholesterol (LDL-C) levels were measured by both analysers and compared to those analysed by the National Health Laboratory Service (NHLS) laboratory. Data were evaluated for conformance with National Cholesterol Education Program (NCEP) guidelines.

Results were grouped into low, middle and high ranges and were similar to those obtained by the NHLS, except in the high range where TC and LDL-C levels were under-read by both analysers. All analytes measured by both analysers correlated significantly with NHLS ($p < 0.0001$). With the exception of LDL-C, both analysers showed reasonable compliance with NCEP goals for coefficients of variation and bias measurements. Both analysers met NCEP guidelines for all analytes at two clinical cut-off points.

We concluded that, compared to NHLS methods, performance of the CardioChek PA and Cholestech LDX analysers is acceptable and that they offer healthcare professionals a rapid, POC method for the measurement of lipids.

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Point-of-care (POC) blood testing, also known as near-patient testing, is intended to provide results more rapidly than can be obtained from a central laboratory. A fast POC analyser for testing lipids has several advantages. The healthcare professional can quickly identify an individual at risk for cardiovascular disease, monitor a patient's response to drug dosage and adjust his/her medication without delay.

Two such analysers are currently available in South Africa. The CardioChek PA [Polymer Technology Systems (PTS), Inc., Indianapolis, IN, USA] is a portable, hand-held, battery-operated instrument that uses a disposable test strip and requires a unique memory chip for each batch of strips. The Cholestech LDX (Cholestech Corporation, Hayward, CA, USA) is a small, lightweight, desktop device that operates using a disposable cassette. Both analysers measure total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and automatically calculate low-density lipoprotein cholesterol (LDL-C) from a small quantity (approximately 40 µl) of blood (finger prick or venous) within a few minutes. When a blood sample is applied to the strip or cassette, a chemical reaction is enzymatically induced, producing a colour change. The change in colour intensity is measured by reflectance photometry and the analyte concentration appears on the display screen.

Aim

There have been few evaluations of the CardioChek PA and Cholestech LDX analysers.[1-4] The number of samples tested with higher concentrations of lipids was relatively small. This study was undertaken, therefore, to analyse blood samples with a wide range of lipid levels, including some in the high range, and to compare the precision and accuracy of both analysers to clinical diagnostic laboratory methods.

Methods

Patients

One hundred patients were recruited from the lipid clinic at the Johannesburg Hospital. The majority were cases of familial hypercholesterolaemia (FH), a condition that is prevalent among the Afrikaner, Indian and Jewish populations in South Africa. All patients gave informed verbal consent to participate in the study.

Study design

Blood was drawn from each patient by venipuncture into a collection tube without anticoagulant for analysis by the Chemical Pathology Department of the National Health Laboratory Service (NHLS). An additional venous blood sample was collected into a lithium–heparin collection tube and used for measurement by the CardioChek PA and Cholestech LDX analysers.

Point-of-care analysis

Blood samples were tested simultaneously by the CardioChek PA and Cholestech LDX analysers according to the manufacturers' instructions. PTS Panels lipid panel test strips were used with the CardioChek PA analyser and results were available within two minutes. Cholestech LDX lipid profile cassettes were stored at 4°C, allowed to reach room temperature for 10 minutes before use, and results were available within 10 minutes. Both analysers calculated LDL-C values automatically.

Laboratory analysis

Enzymatic, colourimetric methods were used by the NHLS to measure TC, TG and HDL-C employing a Hitachi modular analyser and reagents supplied by Roche Diagnostics GmbH, Mannheim, Germany. Calculation of LDL-C values was based on the Friedewald equation.[5]

Precision and accuracy

Precision of the NHLS results was assessed externally by regular participation in the Royal College of Pathologists of Australia (RCPA) quality assurance programs. Intra-assay coefficients of variation (CV) of the CardioChek PA and Cholestech LDX analysers were determined by measurements of control samples with two levels of specified values, which were supplied by the manufacturer of each analyser.

Accuracy was determined as the bias from NHLS results using the EP evaluator alternate method comparison, published by the Clinical and Laboratory Standards Institute.[10] Positive or negative bias was expressed in mmol/l and bias (%) was calculated as the difference between either the CardioChek PA or Cholestech LDX value and the NHLS value, expressed as a percentage of the NHLS value.

Although there are no specific criteria for acceptable performance of POC analysers, the American Heart Association recommends that they follow the National Cholesterol Education Program (NCEP) guidelines.[6-9] NCEP goals for lipids stated as total error are: ≤ 8.9% for TC; ≤ 15.0% for TG; ≤ 22.0% for HDL-C; ≤ 12.0% for LDL-C, which are consistent with CVs of ≤ 3.0% for TC; ≤ 5.0% for TG; ≤ 6.0% for HDL-C and ≤ 4.0% for LDL-C. Values at two NCEP clinical cut-off points for all analytes were calculated using each method's regression equation ($Y = A + B * X$) and bias at these points on the slope was expressed as a percentage. The NCEP clinical cut-off points used in the calculations were (mmol): TC 5.18 and 6.22; TG 1.69 and 2.26; HDL-C 1.03 and 1.55; LDL-C 3.36 and 4.13.

Data analysis

NHLS results were ranked in ascending order and divided into tertiles that designated clinical low, middle and high ranges. CardioChek PA and Cholestech LDX results for each patient were matched to their NHLS result and allocated to the same NHLS range for comparison. The ranges for TC were (mmol/l): low ≤ 5.0; middle 5.1–7.5; high ≥ 7.6. For TG the ranges were (mmol/l): low ≤ 1.5; middle 1.6–4.4; and high ≥ 4.5. HDL-C ranges were categorised as below 1.2 mmol/l or above 1.2 mmol/l. For LDL-C, the ranges were (mmol/l): low ≤ 3.0; middle 3.1–5.0 and high ≥ 5.1. NHLS methods measured these lipids over the entire range of values. CardioChek PA registered results in narrower ranges (mmol/l): TC 1.3–10.36; TG 0.28–5.65 and HDL-C 0.38–2.59. Cholestech LDX registered results in the following ranges (mmol/l): TC 2.59–12.93; TG 0.51–7.34 and HDL-C 0.39–2.59. LDL-C values could only be calculated by either instrument if the TC, TG and HDL-C results were within the assigned range. Consequently, some results that were above or below the measurable ranges were excluded from the statistical analysis, which was carried out on complete sets of results for each patient.

Statistical analysis

Comparisons of results in the low, middle and high ranges, as well as in the whole group were made by one-way analysis of variance and the Student's *t*-test using the GB-STAT program (Dynamic Microsystems, Inc., Silver Spring, USA). A value of $p < 0.05$ was considered significant. Results are expressed as mean ± SEM or mean ± SD where appropriate. CardioChek PA and Cholestech LDX values were compared to NHLS values using linear regression analysis and correlation coefficient calculations.

Results

Comparisons of low-, middle- and high-range lipid concentrations

Mean ± SEM for the ranges and the group as a whole are shown in Table I. Compared to NHLS, TC concentrations measured by both analysers were elevated in the low and middle ranges. The CardioChek PA level in the low range was increased by 0.5 mmol/l ($p < 0.0001$) and the Cholestech LDX level by 0.4 mmol/l ($p < 0.001$). In the middle range the increase was 0.2 mmol/l ($p < 0.05$) for CardioChek PA and 0.3 mmol/l ($p < 0.01$) for Cholestech LDX. TC concentrations in the high range were under-read by both analysers, by 0.5 mmol/l for Cholestech LDX and by 1.3 mmol/l for CardioChek PA ($p < 0.001$).

TG levels in the low and middle ranges were not significantly different from those of the NHLS, and no results were registered by any method in the high range.

TABLE I. COMPARISON OF LIPID CONCENTRATIONS MEASURED BY TWO POC ANALYSERS AND THE NHLS. VALUES ARE MEAN ± SEM

	Low range	*Middle range*	*High range*	*Whole group*
Total cholesterol (mmol/l)	≤ 5.0 (*n* = 32)	5.1–7.5 (*n* = 52)	≥ 7.6 (*n* = 16)	3.8–12.6 (*n* = 100)
CardioChek PA	5.11 ± 0.15^{++}	6.02 ± 0.12*	8.23 ± 0.23^{+}	6.08 ± 0.13
Cholestech LDX	5.00 ± 0.07^{+}	6.07 ± 0.10**	9.04 ± 0.35	6.20 ± 0.15^{+}
NHLS	4.57 ± 0.05	5.79 ± 0.09	9.45 ± 0.32	5.99 ± 0.18
Triglyceride (mmol/l)	≤ 1.5 (*n* = 45)	1.6–4.4 (*n* = 55)	≥ 4.5 (*n* = 0)	0.8–3.8 (*n* = 100)
CardioChek PA	1.06 ± 0.05	2.21 ± 0.08	–	1.70 ± 0.07^{+}
Cholestech LDX	1.17 ± 0.04	2.45 ± 0.10	–	1.88 ± 0.08^{++}
NHLS	1.12 ± 0.03	2.35 ± 0.09	–	1.80 ± 0.08
HDL cholesterol (mmol/l)	≤ 1.2 (*n* = 41)	–	> 1.2 (*n* = 59)	0.6–2.3 (*n* = 100)
CardioChek PA	1.25 ± 0.05^{++}	–	1.72 ± 0.05**	1.53 ± 0.04^{++}
Cholestech LDX	0.96 ± 0.03*	–	1.45 ± 0.04^{++}	1.25 ± 0.04^{++}
NHLS	1.03 ± 0.02	–	1.59 ± 0.04	1.36 ± 0.04
LDL-cholesterol (mmol/l)	≤ 3.0 (*n* = 38)	3.1–5.0 (*n* = 44)	≥ 5.1 (*n* = 18)	1.7–10.5 (*n* = 100)
CardioChek PA	2.69 ± 0.10*	3.85 ± 0.11	5.80 ± 0.23^{++}	3.76 ± 0.13
Cholestech LDX	2.93 ± 0.07^{++}	4.02 ± 0.09^{++}	6.77 ± 0.32	4.10 ± 0.15^{++}
NHLS	2.43 ± 0.06	3.67 ± 0.08	7.04 ± 0.34	3.80 ± 0.18

*$p < 0.05$ **$p < 0.01$ $^{+}p < 0.001$ $^{++}p < 0.0001$.
HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol.

Both analysers had similar levels to those of the NHLS in the low range, while in the middle range the CardioChek PA level was 0.2 mmol/l lower and the level for Cholestech LDX was 0.1 mmol/l higher than that of the NHLS.

In the low range, the HDL-C concentration measured by CardioChek PA was raised by 0.3 mmol/l ($p < 0.0001$) and the Cholestech LDX level was virtually the same as that of the NHLS. Both analysers recorded a difference of 0.1 mmol/l in the high range, with CardioChek PA being higher ($p < 0.01$) and Cholestech LDX being lower than the NHLS value ($p < 0.0001$).

LDL-C levels measured by both analysers were higher than NHLS values in the low and middle ranges. The CardioChek PA value was increased by 0.3 mmol/l ($p < 0.05$) and the Cholestech LDX value was 0.5 mmol/l higher in the low range ($p < 0.0001$). Middle-range readings were 0.2 mmol/l higher for CardioChek PA and 0.3 mmol/l higher for Cholestech LDX ($p < 0.0001$). In the high range both analysers under-read values, by 0.2 mmol/l for Cholestech LDX and by 1.2 mmol/l for CardioChek PA ($p < 0.0001$).

Comparisons of the group as a whole showed that TC concentrations measured by both analysers were slightly higher than those of the NHLS. The CardioChek PA level was increased by 0.1 mmol/l and the Cholestech LDX level was 0.2 mmol/l higher ($p < 0.001$). Both analysers registered small differences in TG values, CardioChek PA being 0.1 mmol/l lower ($p < 0.001$) and Cholestech LDX being 0.1 mmol/l higher ($p < 0.0001$). Differences of 0.1 mmol/l in HDL-C levels were also measured by both analysers ($p < 0.0001$). The CardioChek PA level of LDL-C was virtually the same as that of the NHLS, while the Cholestech LDX level was 0.3 mmol/l higher ($p < 0.0001$).

Some individual TC, TG, HDL-C and LDL-C values measured by both analysers differed from NHLS results in our designated ranges. Most of these differences occurred at the extreme ends of the low and high ranges (CardioChek PA up to 22.8%; Cholestech LDX up to 11.5%).

Precision and accuracy

Mean ± SD and CVs are shown in Table II. At the two levels of control samples, CardioChek PA complied with NCEP guidelines for TC and HDL-C; TG values were slightly above 5.0%. Cholestech LDX exceeded the TC goal for both control samples, and was well within the limits for TG and HDL-C. Neither analyser met the LDL-C goal of ≤ 4.0%.

Mean bias (mmol/l and %) for both analysers versus NHLS, and bias (%) at the two NCEP clinical cut-off points for all analytes are shown in Table III. Compared to NHLS, both analysers showed small variations in mean bias, all of which were < 0.3 mmol/l. Mean biases (mmol/l) measured by Cholestech LDX were larger than for CardioChek PA for TC and LDL-C. HDL-C bias for CardioChek PA was larger than Cholestech LDX, and TG bias was similar for both analysers. Both analysers showed a positive bias from NHLS values for TC. Bias for TG and LDL-C was negative for CardioChek PA and positive for Cholestech LDX. This pattern was reversed for HDL-C where CardioChek PA showed a positive bias, and Cholestech LDX had a negative bias. Mean bias (%) for Cholestech LDX was lower than for CardioChek PA for all analytes. NCEP guidelines were met for TC and TG by Cholestech LDX but they were not met by CardioChek PA. Both analysers were within the limit for HDL-C and neither analyser met the goal for LDL-C.

At the first NCEP clinical cut-off point, bias (%) for TC and HDL-C was greater for CardioChek PA than for Cholestech LDX. At the second clinical cut-off point, Cholestech LDX had greater bias than CardioChek PA for TC, TG and HDL-C, whereas CardioChek PA showed greater bias for LDL-C. Overall, both analysers complied with NCEP guidelines for all analytes at both clinical cut-off points.

TABLE II. PRECISON OF THE CARDIOCHEK PA AND CHOLESTECH LDX POC ANALYSERS

	CardioChek PA		*Cholestech LDX*	
Analyte (mmol/l)	*Control level 1* (n = 7) *Mean ± SD CV (%)*	*Control level 2* (n = 7) *Mean ± SD CV (%)*	*Control level 1* (n = 7) *Mean ± SD CV (%)*	*Control level 2* (n = 7) *Mean ± SD CV (%)*
Total cholesterol	4.48 ± 0.11 (2.5)	6.27 ± 0.15 (2.4)	4.36 ± 0.22 (5.0)	6.45 ± 0.29 (4.5)
Triglyceride	1.55 ± 0.08 (5.2)	2.69 ± 0.15 (5.6)	1.70 ± 0.03 (1.8)	2.88 ± 0.06 (2.1)
HDL cholesterol	2.54 ± 1.00 (3.9)	2.59 ± 0.10 (0.1)	0.91 ± 0.01 (1.1)	1.89 ± 0.06 (3.2)
LDL cholesterol	1.20 ± 0.17 (14.2)	2.44 ± 0.16 (6.6)	2.67 ± 0.21 (7.9)	3.23 ± 0.29 (9.0)

HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol.

TABLE III. ACCURACY OF TWO POC ANALYSERS COMPARED TO THE NHLS

Analyte	*NHLS versus*	*Correlation coefficient (r)*	*Mean bias (mmol/l)*	*Mean bias (%)*	*Bias at NCEP cut-off points (%)*	
Total cholesterol	CardioChek PA	0.8323	0.0960	13.2	7.5	0.2
	Cholestech LDX	0.9414	0.2183	8.6	6.9	2.9
Triglyceride	CardioChek PA	0.9382	–0.0940	20.6	–5.2	–7.3
	Cholestech LDX	0.9833	0.0860	15.0	14.6	11.8
HDL cholesterol	CardioChek PA	0.7244	0.1602	21.1	21.6	8.7
	Cholestech LDX	0.8717	–0.1132	12.9	–6.6	–9.2
LDL cholesterol	CardioChek PA	0.8634	–0.0430	18.6	3.8	–8.9
	Cholestech LDX	0.9426	0.2980	16.2	5.8	1.9

NCEP: National Cholesterol Education Program; HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol.

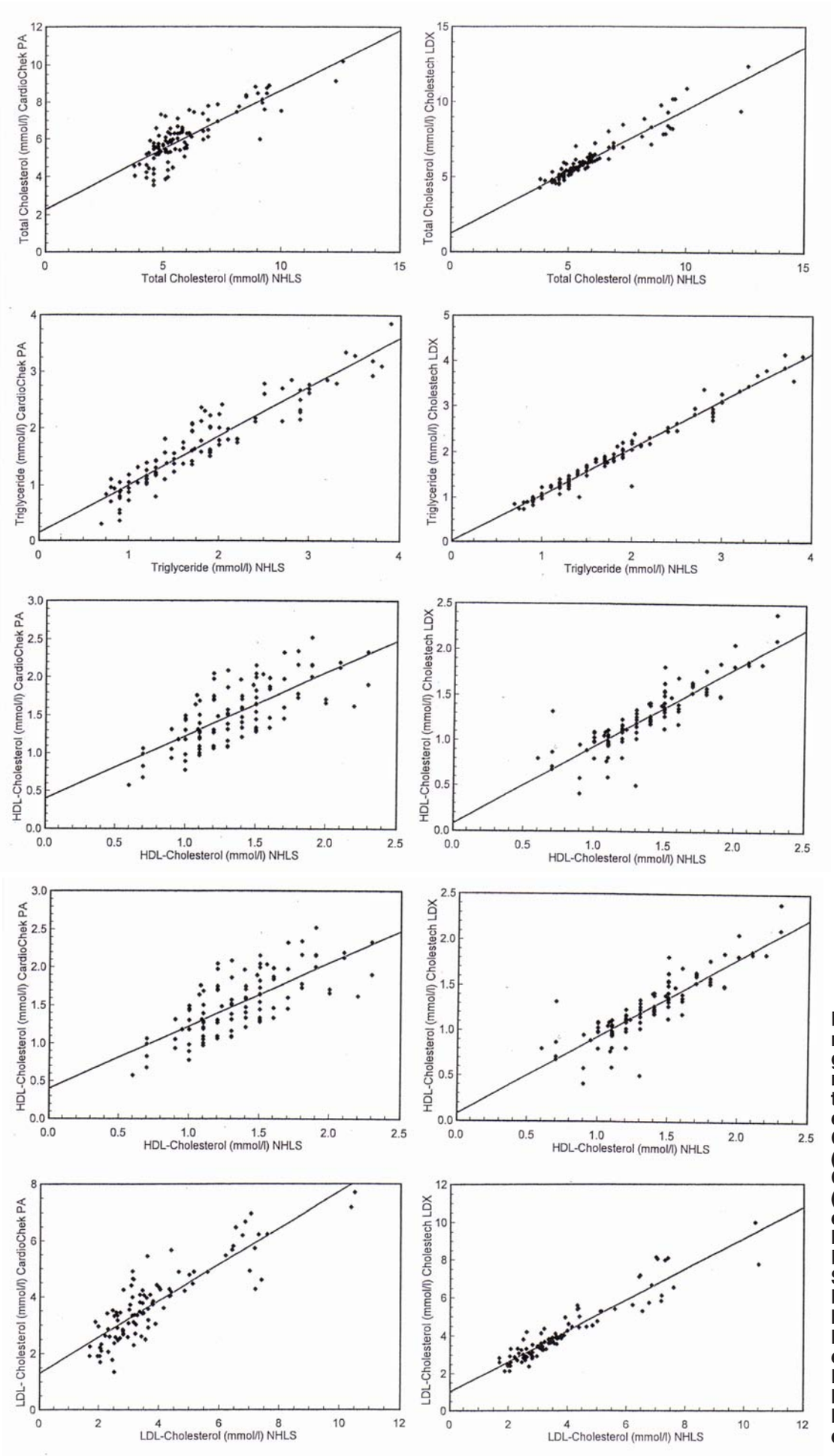

Fig. 1. Linear regression graphs of lipids measured by two point-of-care analysers, CardioChek PA (left panel) and Cholestech LDX (right panel) compared to the National Health Laboratory Service (NHLS). HDL cholesterol: high-density lipoprotein cholesterol; LDL cholesterol: low-density lipoprotein cholesterol.

Linear regression

Linear regression graphs of TC, TG, HDL-C and LDL-C results for both analysers compared to NHLS values are displayed in Fig. 1 and correlation coefficients (r) are shown in Table III. All analytes measured by both analysers correlated significantly with NHLS methods ($p < 0.0001$). The closest correlations were found for TG values (CardioChek PA: $r = 0.9382$; Cholestech LDX: $r = 0.9833$). There was good agreement between values from both analysers and those of the NHLS for TC and LDL-C, while HDL-C correlation coefficients were slightly weaker (CardioChek PA: $r = 0.7244$; Cholestech LDX: $r = 0.8717$).

Discussion

In general, lipid levels in the low and middle ranges, measured by the CardioChek PA and Cholestech LDX analysers agreed satisfactorily with NHLS results. Both analysers, however, registered some patients' results that differed from NHLS results in our designated ranges, mostly at the extreme ends of the low and high ranges.

Although some mean values differed statistically, the differences were small and clinically unimportant. The exception was our finding that in the high range, TC and LDL-C results were under-read by both analysers, by a larger margin in the case of CardioChek PA. Reasons for these discrepancies might be our inclusion of more samples with elevated lipid levels and that the ranges measurable by the analysers were limited. However, patients with levels outside these ranges would usually be referred for confirmatory measurements by a clinical diagnostic laboratory.

Standardisation of methods, including precision and accuracy of measurements, are considered to be of paramount importance for lipid analysis. CardioChek PA and Cholestech LDX analysers were capable of reproducible results and linear regression data indicated that there was a close correlation between both analysers and NHLS methods. Although there are no specific criteria for acceptable performance of POC analysers, the American Heart Association recommends that they follow the NCEP guidelines.[6-9] In this study, neither CardioChek PA nor Cholestech LDX conformed completely to these guidelines. However, with the exception of LDL-C, both analysers complied reasonably well with the presently accepted goals for CVs and bias measurements.[6-9] Moreover, NCEP guidelines were met for all analytes at the two clinical cut-off points.

In this study, both POC analysers tested venous blood containing heparin as an anticoagulant. EDTA, because of its osmotic effect, causes an artefactual fall in most lipid concentrations, but a paradoxical rise in HDL.[11] Heparin does not produce fluid shifts and is, therefore, an acceptable anticoagulant for lipid measurements. Healthcare professionals would normally use POC analysers such as the CardioChek PA and Cholestech LDX to measure capillary blood samples obtained by finger prick. Provided that a standardised protocol is followed, e.g. the manufacturer's package insert,[12,13] results comparable to those obtained by the clinical diagnostic laboratory can be achieved. It is extremely important, however, that the analytical factors be well controlled so that at-risk patients are correctly identified and lipid-lowering therapy decisions are based on credible data.

In summary, CardioChek PA and Cholestech LDX analysers provided accurate lipid measurements in the low and middle ranges. In the high ranges, however, TC and LDL-C levels registered by both analysers were lower than those of the NHLS. In this instance, the results would serve simply as a screening test and should supplement, but not replace, analysis by a clinical diagnostic laboratory. We concluded that compared to NHLS methods, performance of the CardioChek PA and Cholestech LDX analysers is acceptable, and that both analysers offer healthcare professionals a rapid, point-of-care method for the measurement of lipids.

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