Clinical validation and evaluation of a novel six-lead handheld electrocardiogram recorder compared to the 12-lead electrocardiogram in unselected cardiology patients (EVALECG Cardio)

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Background

Handheld electrocardiogram (ECG) machines are affordable, compact screening and diagnostic tools that are useful for the detection of atrial fibrillation, diagnosis of patients with palpitations, and evaluation of the QT interval

Kardia 6L (AliveCor Inc, Mountain View, CA, USA) is a novel handheld ECG device that has been approved by the US Food and Drug Administration for rhythm diagnosis and QT analysis and is Conformité Européenne (CE)-marked

The 12-lead ECG is the gold standard but can be challenging to perform as it requires trained personnel, an adequate clinical environment, ample time, and thorough cleaning of the cables

There is great need for easy-to-use, smaller, and portable handheld recorders for clinical use

This is the first large-scale comparison and validation study to compare Kardia 6L with the standard 12-lead ECG in an unselected cohort of cardiac patients

- Validation of Kardia 6L is important because it uses a different system than the 12-lead ECG (eg, absence of chest leads) and could potentially lead to diagnostic errors

Objectives

The objectives of this study were to validate the Kardia 6L device by comparing its diagnostic accuracy to the standard 12-lead ECG in terms of intermodality reliability using the kappa statistic for qualitative data; by comparing the percentage of leads that could be analyzed and determining the correlation between the 2 devices; and by detecting differences in area under the curve (AUC), identifying bias, and estimating agreement between the Kardia 6L and standard 12-lead ECG

Methods

- This was a prospective study of unselected cardiac patients (inpatients and outpatients) at Leeds General Infirmary (Leeds, UK) who required a 12-lead ECG
  - ECG recordings were taken by a qualified research doctor or nurse trained in recording a 12-lead ECG and in using the Kardia 6L
  - For the Kardia 6L, 2 hands hold the device in contact with the top 2 electrodes and a third electrode was placed on either the left thigh (>99% of cases) or left ankle; maximum recording time was 30 seconds
  - Both recordings were taken with a sweep speed of 25 mm/s, and an amplitude of 1 mm/mV
- ECG tests were performed sequentially with the standard 12-lead ECG performed first followed by the Kardia 6L recording immediately after
- ECG analysis was performed independently by 3 experienced observers (1 cardiologist and 2 cardiac physiologists)
  - Each ECG was read twice and measures of inter- and intra-observer analysis coefficient of variation analysis were calculated to ensure quality control
- For the statistical analysis, a Bland-Altman method was used for the principal analysis between 6- and 12-lead readings
  - For categorical variables, the kappa statistic was used to assess the intermodality reliability (the closer to 1, the better the association)
  - For continuous data, the initial comparison was done through a coefficient of determination of r^2 derived from a linear regression, which indicated the amount of variability of 12-lead ECG measurement explained by the Kardia 6L ECG
  - Performance of the Kardia 6L versus 12-lead ECG was assessed through sensitivity, specificity, binary receiver operating characteristic curve, and AUC for QT/QTc
    - A normal QT/QTc was defined a QT/QTc between 360 ms and 460 ms inclusive; values above and below these values were classified as abnormal

Results

A total of 1015 patients were recruited for this study; the average patient was 62 years of age, and 62.4% of the patients were male; the most common indications for ECG were coronary disease (47.1%), heart failure (25.8%), arrhythmia (11.4%), valve disease (11.4%), and inherited arrhythmia assessment (10.8%)

OBJECTIVE 1: To evaluate and compare the intermodality reliability using the kappa statistic for qualitative data (eg, ECG rhythm and abnormalities)

- For the Kardia 6L, excellent correlation with the 12-lead ECG was shown for rhythm analysis (eg, kappa statistic = 0.779 for sinus rhythm); and T-wave changes (kappa statistic = 0.895); however, the correlation was weak for ischemia (ST elevation: kappa statistic = 0.421; ST depression: kappa statistic = 0.340) and left ventricular hypertrophy (kappa statistic = 0.678) with the Kardia 6L (**Table 1**)

TABLE 1. Kappa Statistic for Qualitative Data

ECG rhythm and abnormalities	Kappa statistic
Sinus rhythm	0.779
Atrial fibrillation	0.986
Atrial flutter	0.917
IVCD	0.970
Junctional rhythm	1.000
Paced	0.894
Left ventricular hypertrophy	0.678
2nd degree or 3rd degree AV block	1.000
Ectopy	0.666
T-wave changes	0.895
ST elevation	0.421
ST depression	0.340

IVCD, intraventricular conduction delay.

Results (cont'd)

OBJECTIVE 2: To evaluate the percentage of leads that could be analyzed and the correlation between the Kardia 6L and the standard 12-lead ECG

- Measurement of the PR interval, QRS duration, cardiac axis, and QRS amplitude was obtained in the majority of the patients using the Kardia 6L (**Table 2**)
  - The r^2 (coefficient of determination) for these parameters ranged from 59.5% to 85.0%
- The median QT interval in the sample was 380 ms (interquartile range 360–420 ms, and minimum and maximum QT of 260 ms and 640 ms, respectively)
  - A strong correlation was observed between the Kardia 6L and 12-lead ECG for most measurements of QT with the r^2 (coefficient of determination) of ≥72.9% reported in the majority of measurements (**Table 2**)
    - The correlation between the Kardia 6L and 12-lead ECG was weaker for QTc with the r^2 ranging from 44.1% to 51.7%

TABLE 2. Percentage of Leads Analysis Possible and Fitted Logistic Linear Regression Analysis Comparing 12-Lead ECG and 6L Measurements

	% ECG leads that could be analyzed		
Leads	**12L**	**6L**	**r^2**
PR interval	75.9%	71.5%	83.4%
QRS duration	92.2%	87.6%	85.0%
Axis	91.6%	89.9%	78.0%
QRS amplitude lead I	97.9%	97.1%	59.5%
QRS amplitude lead II	98.1%	97.3%	73.9%
QRS amplitude lead III	98.0%	97.1%	73.6%
QRS amplitude lead AVR	97.9%	97.2%	70.4%
QRS amplitude lead AVL	98.1%	97.4%	67.4%
QRS amplitude lead AVF	98.1%	97.1%	75.8%
QT lead I	67.9%	71.6%	75.8%
QTc lead I	67.9%	71.5%	46.2%
QT lead II	76.6%	72.8%	77.8%
QTc lead II	76.6%	72.8%	48.1%
QT lead III	55.4%	51.4%	72.9%
QTc lead III	55.4%	51.3%	48.5%
QT lead AVR	68.6%	71.9%	73.5%
QTc lead AVR	68.6%	71.8%	44.1%
QT lead AVL	58.2%	66.1%	75.5%
QTc lead AVL	58.2%	66.0%	46.1%
QT lead AVF	61.5%	57.0%	72.9%
QTc lead AVF	61.5%	56.9%	45.8%
Longest QT	80.4%	75.9%	78.8%
QTc longest lead	80.4%	75.9%	51.7%

OBJECTIVE 3: To evaluate differences in AUC, identify bias, and estimate agreement between the Kardia 6L and standard 12-lead ECG using Bland-Altman analysis and receiver operator analysis

- The mean differences between the Kardia 6L and 12-lead ECG were small for PR interval, QRS duration, and cardiac axis, with a receiver operator analysis AUC of >80% for each
- Mean differences for QT and QTc between the Kardia 6L and 12-lead ECG were also small, with AUCs of >75% and >60%, respectively
- For the Kardia 6L device, Bland-Altman analysis demonstrated overall acceptable agreement with few outliers (<6% in all parameters) and little bias compared with the 12-lead ECG (**Table 3**)

TABLE 3. Bland-Altman and Receiver Operator Analysis for Quantitative Data

Leads	Mean bias	SD	CI upper limit	CI lower limit	Outliers (%)[a]	AUC[b]
PR interval (ms)	0.76	12.00	24.28	-22.76	13 (1.8)	0.91
QRS duration (ms)	0.29	8.47	16.89	-16.32	21 (2.4)	0.98
Axis (degrees)	4.24	22.11	47.57	-39.08	34 (4.3)	0.85
QRS amplitude lead I (mm)	-1.47	2.91	4.23	-7.17	41 (4.2)	NA
QRS amplitude lead II (mm)	0.96	2.07	5.02	-3.10	31 (3.1)	NA
QRS amplitude lead III (mm)	-0.16	2.73	5.18	-5.50	40 (4.1)	NA
QRS amplitude lead AVR (mm)	-0.33	1.80	3.19	-3.85	34 (3.4)	NA
QRS amplitude lead AVL (mm)	-1.13	2.56	3.90	-6.15	39 (4.0)	NA
QRS amplitude lead AVF (mm)	0.94	2.11	5.06	-3.19	37 (3.7)	NA
QT lead I (ms)	6.29	21.68	48.69	-36.21	29 (4.0)	0.79
QTc lead I (ms)	-0.27	28.17	54.93	-55.48	29 (4.0)	0.70
QT lead II (ms)	7.03	19.81	45.87	-31.80	22 (3.0)	0.82
QTc lead II (ms)	0.62	26.82	53.19	-51.95	37 (5.1)	0.69
QT lead III (ms)	6.47	23.99	53.48	-40.54	19 (3.7)	0.79
QTc lead III (ms)	1.15	28.67	57.35	-55.05	25 (4.9)	0.66
QT lead AVR (ms)	7.06	21.18	48.57	-34.46	20 (2.8)	0.81
QTc lead AVR (ms)	-0.03	27.11	53.10	-53.15	37 (5.2)	0.70
QT lead AVL (ms)	5.45	22.50	49.56	-38.65	21 (3.2)	0.80
QTc lead AVL (ms)	-2.02	28.38	53.61	-57.65	28 (4.2)	0.67
QT lead AVF (ms)	8.49	23.00	53.57	-36.59	17 (3.0)	0.77
QTc lead AVF (ms)	2.35	29.14	59.46	-54.76	31 (5.4)	0.64
Longest QT (ms)	11.76	20.69	52.31	-28.79	24 (3.2)	0.80
QTc longest lead (ms)	5.71	27.11	58.85	-47.42	43 (5.7)	0.74

AUC, area under the receiver operating characteristic curve (the normal range was set at a QT/QTc of between 360 and 460 ms); CI, 95% confidence interval for upper and lower limit on Bland-Altman analysis; NA, not applicable; SD, standard deviation.

[a]Outlier percentage compared to the number of ECGs analyzed rather than total sample.

[b]Higher values (max of 1.00) suggest that the Kardia 6L performs similarly to the 12-lead ECG and far from the random diagnosis based on an established threshold.

Conclusions

In this study, Kardia 6L was validated against the gold standard 12-lead ECG. Several parameters recorded by the Kardia 6L performed similarly to the gold standard 12-lead ECG, including QT interval in all 6 leads, rhythm detection, PR interval, QRS duration, and cardiac axis. However, that consistency weakened for left ventricular hypertrophy, QRS amplitudes, and ischemic changes

This study had several limitations including: recordings were made sequentially, not simultaneously, so complexes were not directly compared; assessments were performed on ECG graph paper at a rate of 25 mm/s which could have introduced some error; for the Kardia 6L device, differences in position of the third electrode (thigh or ankle) may have introduced an error

Results from this study support the continued assessment of Kardia 6L compared with the standard 12-lead ECG in large-scale clinical trials

Importance to AliveCor

This study demonstrated that Kardia 6L performs similarly to the gold standard 12-lead ECG for many parameters including rhythm and QT interval analysis, which is consistent with previous reports

The portability, size, cost, and storage and transfer of data make Kardia 6L potentially useful in practices where 12-lead ECG recorders are not available or difficult to perform