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Comparison between a traditional Holter system and AI-based automated analysis system based on ”Cortrium C3+ Holter monitor”-recordings

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BACKGROUND AND PURPOSE

Novel devices and technologies are being adopted and used in healthcare settings at an unprecedented rate[1]. The development of compact cableless and easy-to-use long term ECG recorders (Holter monitors) has a great potential in terms of lowering the resources required for screening and monitoring of arrhythmias in both ambulatory and in-hospital settings. As these new devices are introduced to the clinic, it is important to validate against current clinical methods[2].

Atrial fibrillation (AF) is the most common sustained arrhythmia[3] and is a major cause of stroke, heart failure, sudden death, and cardiovascular morbidity[4]. Moreover, the number of patients with AF is predicted to rise steeply in the coming years and AF is independently associated with a two-fold increased risk of all-cause mortality in women and a 1.5-fold increase in men[5–7].

The purpose of this study is to validate the quality of automated and non-subjective AI-based ECG-analysis based on data acquired using a novel 3 channel cableless ECG-device. The system is compared to a traditional 3-channel cabled Holter system where the analysis and interpretation is done by humans via a remote ECG-analysis service center.

The study is a method-comparison with the aim of answering the clinical question: can arrhythmias and cardiac events, such as ventricular beats, be measured by either method and get the same results[2]? In cases of disagreement between the two systems, a trained cardiologist specialized in electrophysiology reviewed the ECG-reports in order to establish ground truth.

METHODS

Investigation took place at the private hospital Aleris-Hamlet, Ringsted, Denmark. The hospital was responsible for inclusion, information, consent and data collection. Patients scheduled for outpatient long-term (24 hours to 48 hours) ECG registration during the study period were included in the study. Patients with pacemakers were excluded. Furthermore, patients who did not expect to be able to participate due to language or cognitive difficulties were excluded. Included patients were equipped with a Holtor monitor from both systems in order to perform simultaneous recordings.

The two Holter systems were:

1. Cortrium’s automated system consisting of the “C3+ Holter Monitor” (Cortrium ApS, Høje Taastrup, Denmark) and automatic ECG analysis software provided by “Cardiomatics” using report

version 2.8 (Cardiomatics, Kraków, Poland).
2. A traditional Holter system consisting of "Lifecard CF" (SpaceLabs, Washington, United States) and analysis provided by "Fysiologic ECG service" (Fysiologic, Amsterdam, Holland).

Both systems output one Holter report per recording. The reports comply with the European standard (IEC 60601-2-47). Based on the reports, the occurrences of events and arrhythmias were logged. A list of arrhythmias claimed to be detected by the automated ECG analysis software (Cardiomatics) is found below:

Table 1: Cardiomatics enables detection of the following parameters in ECG signals

1. Three classes of heartbeats:
    a. normal beat
    b. ventricular beat, including:
        i. premature ventricular contraction
        ii. ventricular escape beat
    c. supraventricular beat, including:
        i. aberrated atrial premature beat
        ii. nodal (junctional) premature beat
        iii. atrial premature contraction
        iv. nodal (junctional) escape beat
        v. atrial escape beat
2. Rhythms:
    a. normal sinus rhythm
    b. sinus bradycardia
    c. sinus tachycardia
    d. supraventricular rhythm
    e. atrial bigeminy
    f. atrial trigeminy
    g. atrial fibrillation
    h. atrial flutter
    i. supraventricular tachycardia
    j. supraventricular couplet
    k. idioventricular rhythm
    l. ventricular bigeminy
    m. ventricular trigeminy
    n. ventricular fibrillation
    o. ventricular flutter
    p. ventricular bradycardia
    q. ventricular tachycardia
    r. ventricular couplet

Binary outcomes, such as the occurrence of specific arrhythmias or cardiac events, were analyzed using McNemar's test, which is a non-parametric test to compare paired nominal proportions. It can be used to analyze retrospective case-control studies, where each case is matched to a particular control[8].

Data analysis of non-binary outcomes, such as comparing the amount of ventricular beats between methods, were conducted according to procedural example in the paper "Design, Analysis and Interpretation of Method-Comparison Studies" by Hanneman et al.[2], which includes visual examination of data patterns on graphs, Bland-Altman plots, and quantification of the estimate of the difference between methods and the accuracy of this difference, often referred to as bias and precision statistics[2].

RESULTS

Demographics: A total of 56 (n = 56) patients were included, with age ranging from 18 to 85

years. The average age was 53.5 years (SD +/- 18.2 years). The majority of the patients were females (n = 32, 57.1%).

Arrhythmias: The only arrhythmias detected in the recordings were atrial fibrillation / atrial flutter (AF) and non-sustained ventricular tachycardia (VT). The results are seen in Table 2. AF was found in the same 7 patients for both systems (12.25%), out of which 2 cases were paroxysmal AF and 5 cases were sustained AF (persistent or permanent). A trained electrophysiologist confirmed the diagnosis in all cases. For non-sustained VT, both systems found occurrences in the same 3 reports (5.36%). For the arrhythmias found in this dataset, no discordants (false negatives or false positives) were found, yielding a McNemar's coefficient of $X^2 = 1.00$, thus, the hypothesis that the two methods are equal for arrhythmia detection cannot be rejected.

Table 2: Comparison of arrhythmia detection

Arrhythmia	Both systems	Only Cortrium	Only Traditional	Com-ment
Paroxysmal AF	2	0	0	No diff.
Sustained AF	5	0	0	No diff.
Non-sustained VT	3	0	0	No diff.
Other	0	0	0	No diff.

Ventricular activity: The amount of premature ventricular beats/escape beats were detected by both systems and reported as a percentage of the recording (aka. Burden of ventricular beats) in the traditional Holter system reports and as an absolute number of beats in the automated system (Cortrium). To readily compare the detected burden of ventricular beats they were divided into three clinically relevant bins, of below 3%, between 3 and 10%, 10 and 20%, and above 20%. The results are summarized in the table below:

Table 3: Comparison of ventricular beats

Burden of ventricular beats	Cortrium	Traditional Holter
<3%	53 (94.6%)	54 (96.4%)
3-10%	1 (1.8%)	1 (1.8%)
10-20%	1 (1.8%)	1 (1.8%)
>20%	1 1 (1.8%)	0 (0%)

Comparison of maximum heart rate (HR): The max. heart rate was included in the reports from both systems and the paired data was compared in Figure 1 and 2.

Figure 1: Scatter plot of the paired max. HR data.

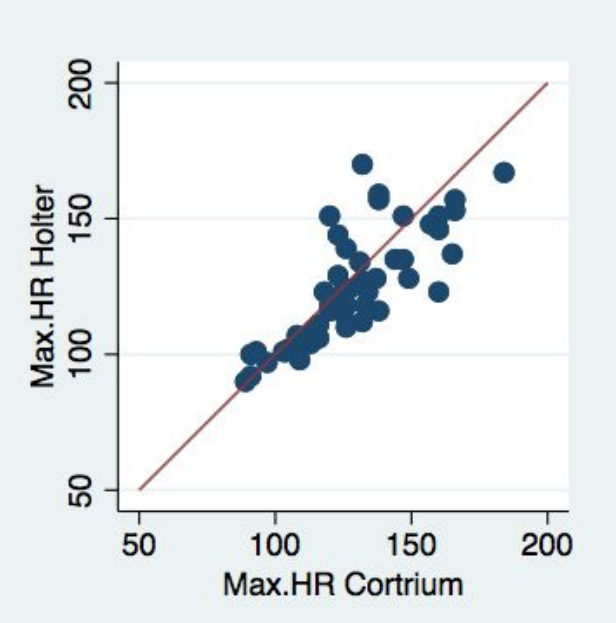
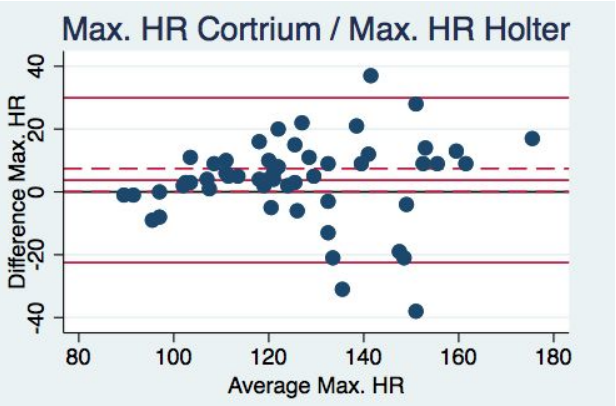


Figure 2: Bland-Altman plot of maximum HR. The dashed horizontal lines represent 95% confidence limits (agreement boundaries).



The average difference between max. HR is 3.6 beats per minute (BPM) (CI -0.05; 7.23 and SD ±13.29 (CI 11.17; 16.40) resulting in a P-value of 0.004. The mean difference in max. HR between the two systems is not statistically significant from 0. It is noted that 3 of 56 (5%) data points are outliers and exceed the limits of agreement.

Recording durations: The average recording time for the automated Holter system (Cortrium) was 39:20 hours (SD ±13:00 hours) compared to 42:06 hours (SD ±11:11 hours) for the traditional Holter system. Note that the recording times cannot be directly compared, as several cases were found where the two systems were not set to record for the same duration, ie. one system was programmed to record for 24 hours while the other was programmed to record for 48 hours.

Signal quality: Signal quality and noise levels in the recordings are categorized differently in the between the two systems. The automated system (Cortrium) reports noise as the percentage of recording that is "non-diagnostic," while the traditional holter report categorizes the signal quality into four groups: good, sensible, mediocre, or poor. The categorization can be subjective. To compare the two measurements for signal quality, the percentages of the "non-diagnostic" parts of the reports were divided into quartiles. The results are shown in the table below:

Table 3: Comparison of noise in quintiles

Signal quality/noise level	Cortrium	Traditional Holter
“Good signal” or above 75% diagnostic part	39 (69.6%)	18 (32.1%)
“Reasonable signal” or between 50% and 75% diagnostic part	12 (21,4.2%)	20 (35.7%)
“Mediocre signal” or between 25% and 50% diagnostic part	4 (7.1%)	9 (16.1%)
“Poor signal” or below 25% diagnostic part	0 (0%)	9 (16.1%)

DISCUSSION

The study serves to validate the two systems against each other and not to validate against a ground truth established by having experts thoroughly review all ECG signals. Only reports where AF was found in one or both systems were thoroughly reviewed and the diagnosis was confirmed by an expert reader, there could potentially be cases of AF or other arrhythmias that were false negatives in both systems.

The demographics of the patients included is representative of the background population expected to undergo Holter-monitoring in an ambulatory setting.

The maximum HR difference between the two systems, seen as outliers in Figure 2, can be due to differences in the time frame used in the calculation of HR as it is unknown if the traditional system, like the automated systems, averages over 60 seconds.

Signal quality/noise level cannot be directly compared as the authors cannot rule out that the noise grading of the traditional system might rely on a subjective evaluation.

Known limitations: Only two types of arrhythmias were identified in the data. Thus the study cannot be used to compare performance for other arrhythmias. It should be noted that the ECG analysis algorithm used in the automated system (Cardiomatics) only claims to detect the events and arrhythmias mentioned in Table 1.

CONCLUSION

In this study, both systems detected AF in the same 7 patients and non-sustained VT in the same 3 patients, thus there was no significant difference in arrhythmia detection rates (AF and non-sustained VT) between Cortrium's automated Holter system and the traditional Holter system with manual, human interpretation. Further, the detected ventricular activity, max. HR, and noise levels were comparable between the systems.

In conclusion, the study suggests that, based on the evaluation metrics, there is no significant difference in performance between the two systems and that Cortrium's automated system can replace traditional Holter systems with manual interpretation.

CONFLICTS OF INTEREST

The study was financed by Cortrium ApS and both authors are employed at Cortrium ApS.

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