The prediction by ECG dispersion mapping of clinical deterioration, as measured by increase in the Simple Clinical Score

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Key Points
- ECG dispersion mapping (ECG-DM) is a novel technique that analyzes low amplitude ECG micro-alternations that only takes a few seconds to perform and requires no skill to interpret.
- Clinical deterioration as measured by an increased Simple Clinical Score the day after admission to hospital is associated with a high mortality. This study identified ECG-DM changes during left ventricular re-polarization and nursing home residence as the only independent predictors of Simple Clinical Score increase the day after admission to hospital.

Abstract

Objective: ECG dispersion mapping (ECG-DM) is a novel technique that reports abnormal ECG micro-alternations. We report the utility of ECG-DM to predict clinical deterioration of acutely ill medical patients, as measured by an increase in the Simple Clinical Score (SCS) the day after admission to hospital.

Methods: 453 acutely ill medical patients (mean age 69.7 +/- 14.0 years) had the SCS recorded and ECG-DM performed immediately after admission to hospital.

Results: 46 patients had an SCS increase 20.8 +/- 7.6 hours after admission. Abnormal micro-alternations during left ventricular re-polarization had the highest association with SCS increase (p=0.0005). Logistic regression showed that only nursing home residence and abnormal micro-alternations during re-polarization of the left ventricle were independent predictors of SCS increase with an odds ratio of 2.84 and 3.01, respectively.

Conclusion: ECG-DM changes during left ventricular re-polarization are independent predictors of clinical deterioration the day after hospital admission.

Keywords
Hospital admissions, predictive scores, ECG dispersion.

Introduction
Intuition suggests that seriously ill patients are more likely to deteriorate and less likely to improve than those with mild illness. This, however, may not be the case. The Simple Clinical Score (SCS) is a reliable instrument that objectively assesses and measures severity of illness that has been independently validated in several different clinical settings. Approximately 12% of patients increase their SCS 24 hours after admission to hospital. We recently reported that low risk patients were just as likely to increase their SCS as high risk patients, and that an increased SCS was associated with a 5 fold increase in in-hospital mortality compared to patients with an unchanged SCS and a 20 fold increase in mortality compared to those with a decreased SCS. Only three features identified patients who increased their SCS: residence in a nursing home, the presence of heart failure and a Medical Admission Risk System (MARS) laboratory data score >0.10. ECG dispersion mapping (ECG-DM) is a recently developed technology that provides non-invasive assessment of myocardial pathology by analyzing low amplitude oscillations of conventional ECG signals.

The method examines not only the tiny fluctuations (micro-alternations) of the T-wave (T wave alternans) but also micro-alternations of the P wave and QRS complex. From the six traditional ECG leads of I, II, III, aVR, aVL and aVF patented formulae can quickly (i.e. within 30 seconds) and accurately determine micro-alternations not only of the T wave but of the entire PQRST complex. Nine groups of calculations (G1-G9) are then made that score in arbitrary units the extent of these micro-alternations in different areas of the heart, as well as those associated with intraventricular blocks and ventricular hypertrophy – a score of 0 indicates complete absence of abnormal micro-alternations, higher scores indicate increasing abnormality (Table 1). Micro-alternations reflect abnormalities in the myocardium at a metabolic level, which may include ischemia and other causes. ECG-DM, therefore, is not diagnostic but a non-specific indicator of myocardial health. The micro-alternations from all nine groups (G1-G9) combined represent the overall myocardial micro-alternation index (MMI) which is expressed as a percentage – if pathological micro-alternations are present throughout the entire myocardium the MMI is 100%, whereas an MMI of 0% indicates a total absence of abnormal micro-alternations in any part of the heart. ECG-DM is much more sensitive than the direct “beat to beat” measurement of ECG micro-alternations, and this allows measurements to be performed at rest. ECG-DM is a reliable instrument that objectively assesses and measures severity of illness that has been independently validated in several different clinical settings.
DM only takes a few seconds to perform and requires no skill to interpret and was primarily developed as a rapid screening test for heart disease. However, the role of this new technology in clinical medicine is still being defined. We recently reported on the ability of ECG-DM to predict in-hospital mortality. In this paper we report the ability of ECG-DM to predict clinical deterioration of acutely ill medical patients, as measured by an increase in the Simple Clinical Score the day after admission to hospital.

Methods

All patients were recruited from the unselected acutely ill medical patients admitted to Nenagh Hospital between July 30th 2009 and 31st March 2010. Of the 1702 patients admitted during this period 453 (26.6%) were included in the study – the only criterion for study inclusion was that one of the authors was able to perform an ECG-DM on them within 10 to 20 minutes of hospital admission. ECG-DM (HeartVue system, Medical Computer Systems Ltd., Moscow) is a non-invasive procedure that takes 30 seconds to perform, and only requires the placement of the four standard ECG limb leads.

All patients had their presenting complaint and the clinical data required to calculate the Simple Clinical Score (SCS) recorded at the time of admission by the nursing staff of the hospital’s medical admission unit. The nursing staff of the hospital has been fully trained in the use of the SCS since 2007 – implementation of this training process has been reported in a previous publication. The SCS can be quickly performed at the bedside and requires no additional information or investigation other than a 12 lead ECG. In order to prevent errors the SCS was calculated by a computer program. The SCS includes the classic vital signs expressed as categorical variables: a blood pressure below 100 mmHg, a pulse rate greater than systolic blood pressure, hypo or hyperthermia, a respiratory rate over 20 breaths per minute, and oxygen saturation below 95%. In addition the score contains the following variables: breathlessness, altered mental status, prior illness (requiring some part of the daytime to be spent in bed), being unable to stand without help, nursing home residence, a new stroke, any ECG abnormality and diabetes.

Nenagh Hospital is small general hospital in rural Ireland serving a population of 60,000. It has a 36 bed acute medical unit with 2,800 admissions per year almost all of which are unplanned emergencies. It is served by four consultant physicians each assisted by a team of three
physicians in training - each team is on-call every fourth day. The hospital has a five bed ICU capable of cardiac monitoring, external and temporary transvenous pacing, non-invasive and invasive ventilation. Renal dialysis, hematology and oncology units are available at Limerick Regional Hospital, 25 miles away. The overall in-hospital mortality rate for acute medical patients is 3.7% and not significantly different from the rate of 3.3% reported by the Limerick Regional Hospital, the nearest teaching hospital and tertiary referral center.

Routine laboratory investigations performed at the time of admission were used to calculate the MARS laboratory score on each patient. The MARS laboratory data score only requires a full blood count, electrolytes and urea level determination and, hence, adds considerable value to these ubiquitous investigations at no extra cost. Approximately 24 hours after admission (20.8 +/- 7.6 hours) each patient was reviewed by the nursing staff and the SCS re-calculated. All data was corrected for errors and then entered into an Epi-Info version 6.0 database (Center for Disease Control and Prevention, USA). The ICD10 coded diagnoses recorded at discharge or death were also entered into this database.

The continuous variables of age, MMI, G1-G9 etc were converted into categorical variables by determining the thresholds levels with the highest odds ratio for predicting in-hospital mortality. This was done by a process of trial and error. Continuous variables were compared by Student’s t test and categorical variables by Chi-square analysis that applied Yates continuity correction – all calculations were performed using Epi-Info version 6.0 (Center for Disease Control and Prevention, USA), and statistical significance was set at a p value <0.05. The independence of variables was tested by logistic regression using Logistic Version 3.11E software (G.E. Dallal, Andover MA). This study was performed while the services in the hospital were undergoing reconfiguration part of which was the diversion after midnight of seriously ill patients directly to Limerick Regional Hospital. This resulted in the majority of patients being admitted between 3 and 9 pm. Patients studied had the same age (68.0 +/- 16.7 vs. 66.2 +/- 19.0 years, p = 0.07), length of hospital stay (6.7 +/- 7.0 vs. 7.2 +/- 7.8 days, p = 0.24) and in-hospital mortality (3.5% vs. 3.5%, p = 0.99) as the other patients admitted during the study period.

Ethical approval of the study was obtained from the Mid-Western Regional Hospital Complex Scientific Research Ethics Committee, which granted exemption for patient consent.

Results
The day after admission no patients had died, 46 (10.2%) had increased their SCS by 2.2 +/- 1.5 points, in 209 (46.1%) the SCS was unchanged, in 162 (35.8%) it was decreased by 2.5 +/- 1.6 points and 36 (7.9%) patients had already been discharged home. Patients with an increased SCS were older and had a longer length of hospital stay. They also had a higher MARS laboratory score and a higher MMI, and were more likely to have heart failure and to be admitted from a nursing home. There was no association, however, between the SCS on admission and SCS increase. The in-hospital mortality of patients with an increased SCS was 21.7%, compared with 2.4% for those with no change in their SCS and 0.6% for those patients with a reduced SCS – an increase in SCS was highly significantly associated with increased mortality (OR 18.6, CI 95% 5.7-62.2, p<0.001) (Table 2).
Table 3. Comparison of ECG-DM findings of patients with and without an increase in the Simple Clinical Score (SCS) within 24 hours of hospital admission.

<table>
<thead>
<tr>
<th></th>
<th>SCS not increased</th>
<th>SCS increased</th>
<th>p</th>
<th>Odds ratio (CI 95%)</th>
<th>Chi-square</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial micro-alternation index &gt;36%</td>
<td>14.0%</td>
<td>28.3%</td>
<td>0.02</td>
<td>2.4 (1.1-5.2)</td>
<td>6.4</td>
</tr>
<tr>
<td>G1 &gt;=3</td>
<td>54.3%</td>
<td>71.7%</td>
<td>0.04</td>
<td>2.1 (1.0-4.5)</td>
<td>4.4</td>
</tr>
<tr>
<td>G2 &gt;=5</td>
<td>31.7%</td>
<td>52.2%</td>
<td>0.001</td>
<td>2.4 (1.2-4.6)</td>
<td>6.9</td>
</tr>
<tr>
<td>G3 &gt;=4</td>
<td>18.9%</td>
<td>30.4%</td>
<td>0.10</td>
<td>1.9 (0.9-3.9)</td>
<td>2.7</td>
</tr>
<tr>
<td>G4 &gt;=6</td>
<td>12.3%</td>
<td>19.6%</td>
<td>0.25</td>
<td>1.7 (0.7-4.1)</td>
<td>1.3</td>
</tr>
<tr>
<td>G5 &gt;=1</td>
<td>31.0%</td>
<td>47.8%</td>
<td>0.03</td>
<td>2.0 (1.1-4.0)</td>
<td>4.6</td>
</tr>
<tr>
<td>G6 &gt;=5</td>
<td>28.0%</td>
<td>54.3%</td>
<td>0.0005</td>
<td>3.1 (1.6-6.0)</td>
<td>12.3</td>
</tr>
<tr>
<td>G7 &gt;=5</td>
<td>21.4%</td>
<td>39.1%</td>
<td>0.01</td>
<td>2.4 (1.2-4.7)</td>
<td>6.4</td>
</tr>
<tr>
<td>G8 &gt;=1</td>
<td>4.4%</td>
<td>6.5%</td>
<td>0.79</td>
<td>1.5 (0.3-5.8)</td>
<td>0.1</td>
</tr>
<tr>
<td>G9 &gt;=20</td>
<td>2.2%</td>
<td>0.0%</td>
<td>0.64</td>
<td>0.0 (0.0-5.4)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

An MMI >36%, G1 >=3, G2 >=5, G5 >=1, G6 >=5 and G7 >=5 were associated with SCS increase (Table 3). Patients with G6 values >=5 had an odds ratio of 3.1 (CI 95% 1.6-6.0, Chi square 12.3, p 0.0005) for SCS increase the day after admission. The majority of patients had a G6 value of 0 or 1, and no patients had G6 values of 2,3 or 4. There are, therefore, two distinct patient populations and a G6 value >=5 clearly identified those patients most likely to increase their SCS (Figure 1).

Numerous logistic regression models were tested that included the discharge diagnosis of heart failure, the MARS laboratory score >0.10 and nursing home residence (i.e. the three variables previously identified as independent predictors of SCS increase)5 as well as each of the ten ECG-DM variables, both as continuous variables and using the cut-off values in Table 3 (i.e. MMI >36% and G1 >=3, G2 >=5, G3 >=4, G4 >=6, G5 >=1, G6 >=5, G7 >=5, G8 >=1 andG9 >=20). Only a G6 value >=5 and nursing home residence remained as independent predictors of SCS increase (Table 4).

### Discussion

Although there are several well validated scoring systems that can predict imminent death,15,16 determining the factors associated with clinical deterioration (or failure to respond to treatment) has proved difficult. Despite examining numerous variables in our original study we found only three features identified patients who increased their SCS: residence in a nursing home, the presence of heart failure and an elevated MARS laboratory data score. This study found, however, that only increased micro fluctuations associated with left ventricular re-polarization (i.e. G6 values >=5) and nursing home residence were independent predictors of clinical deterioration as measured by SCS increase the day after hospital admission. Therefore, although the risk of deterioration cannot be excluded in any patient, it would appear to be between two and three times more likely in a patient with abnormal micro fluctuations during left ventricular re-polarization and/or those admitted from a nursing home.

Table 4. logistic regression models that include the three variables previously reported as independent predictors of an increase in the Simple Clinical Score (SCS) (i.e. nursing home residence, heart failure and a Medical Admission Risk System (MARS) laboratory data score >0.10) and ECG-DM G6 values >=5. Only nursing home residence and a G6 value >=5 are independent predictors of SCS increase.

<table>
<thead>
<tr>
<th>Coefficient</th>
<th>SE</th>
<th>Odds ratio</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constant</td>
<td>-2.9842</td>
<td>0.2720</td>
<td>-</td>
</tr>
<tr>
<td>Nursing home residence</td>
<td>0.9419</td>
<td>0.4545</td>
<td>2.56</td>
</tr>
<tr>
<td>G6 &gt;=5</td>
<td>0.9024</td>
<td>0.1360</td>
<td>2.47</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0.4831</td>
<td>0.3596</td>
<td>1.62</td>
</tr>
<tr>
<td>MARS laboratory score &gt;0.10</td>
<td>0.5111</td>
<td>0.1298</td>
<td>1.67</td>
</tr>
<tr>
<td>Constant</td>
<td>-2.7463</td>
<td>0.2364</td>
<td>-</td>
</tr>
<tr>
<td>Nursing home residence</td>
<td>1.0446</td>
<td>0.4482</td>
<td>2.84</td>
</tr>
<tr>
<td>G6 &gt;=5</td>
<td>1.3018</td>
<td>0.3183</td>
<td>3.01</td>
</tr>
</tbody>
</table>

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The prediction by ECG dispersion mapping of clinical deterioration

There were 46 patients with an increased SCS (i.e. 46 events) and four variables (i.e. ECG-DM measurements, heart failure, nursing home residence and the MARS laboratory score) tested for independence by logistic regression. This is close to the minimal number of acceptable events per variable than should be included in a logistic regression model.17 It is possible, therefore, that a larger study might show several other variables to be independent predictors of SCS increase. Nevertheless, our results suggest that nursing home residence and a G6 value >=5 will remain the major predictors of SCS increase.

The relationship between the SCS and other early warning systems is not clear. In this small study we found the ViEWS score18 of patients with an increased SCS was the same as those without an increase (i.e. 2.8 +/- 2.4 vs 2.9 +/- 2.7, p 0.78). Also of the 46 patients who increased their SCS only 32 had and increased ViEWS score 24 hours after admission, while 68 patients who increased their ViEWS score did not have an increase in their SCS. Furthermore, an increase in ViEWS score was not associated with any increased risk of mortality (OR 2.2, CI 95% 0.7–6.8, Chi square 1.5, p 0.23). Unlike early warning scores such as MEWS and ViEWS the SCS also considers the co-morbid condition of diabetes, functional status and ECG changes. Therefore, changes in the SCS may not capture the same clinical information as changes in other scores. Furthermore, although it appears that a rise of the SCS of a single point is of clinical significance, this may not be the case for other scoring systems in which far larger changes may be required to be of importance.

Although other ECG-DM changes also appear related to SCS increase changes in G6 were the most apparent. The pathophysiology of these findings can only be speculated on. Left ventricular re-polarization is an active energy consuming process and it is reasonable to postulate that a “sick” myocardium might be more likely to demonstrate subtle abnormalities during this phase of the cardiac cycle. Changes in G6 will, therefore, reflect left ventricular health. Although increased micro-alternations during left ventricular re-polarization was a more powerful predictor of clinical deterioration than heart failure, we diagnosed this clinically and not by echocardiography or BNP testing. It may be that these techniques would have been better predictors of clinical deterioration than changes in G6, but would not have been cheaper, quicker and easier to perform.

Conclusion

ECG-DM changes during left ventricular re-polarization and nursing home residence are independent predictors of clinical deterioration as measured by SCS increase within 24 hours of admission. ECG-DM is inexpensive, only takes a few seconds to perform and requires no skill to interpret.

References