Non-invasive assessment of myocardial ischaemia by using low amplitude oscillations of the conventional ECG signals (ECG dispersion mapping) during percutaneous coronary intervention

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Objective — The HeartVue™ 6S System is a recently developed novel technology that may provide non-invasive assessment of myocardial ischaemia by analysing low amplitude oscillations of the conventional ECG signals (ECG dispersion mapping). The available data to validate this new technology is limited. Therefore we performed a prospective study to assess the HeartVue™ 6S System for the detection of myocardial ischaemia during coronary occlusion in patients undergoing percutaneous coronary intervention (PCI).

Methods — A total of 101 patients undergoing cardiac catheterization were prospectively enrolled. HeartVue™ 6S System ECG dispersion mapping was obtained at baseline, and during the first balloon inflation and at the end of the procedure if PCI was performed. Parameters provided by the HeartVue™ 6S System were analysed.

Results — Fifty patients who underwent PCI comprised the final study population. The mean age was 63.7 ± 10 years and 58% were men. In 58% of cases the indication was acute coronary syndrome. In 98% of patients, PCI was successful. There were significant differences in the G7+G9 values between the first inflation and the end of the procedure, which reflect changes in ventricular depolarization (P = 0.02 by Wilcoxon signed rank test).

Conclusions — The HeartVue™ 6S System may have potential for a non-invasive assessment of ischaemia in patients with suspected coronary artery disease. Larger studies are warranted to confirm these preliminary findings.

Keywords: ECG dispersion map – myocardial ischaemia – percutaneous coronary intervention.
myocardial ischaemia during coronary occlusion (balloon inflation and/or stent deployment) in patients undergoing percutaneous coronary intervention (PCI).

Methods

INCLUSION AND EXCLUSION CRITERIA

In this single-centre prospective study, we enrolled patients scheduled for coronary angiography with possible percutaneous coronary intervention. Exclusion criteria included: (1) age < 18 years old; (2) known significant valvular or cardiomyopathic diseases; (3) previous pacemaker implantation; and (4) inability to give informed consent.

The study protocol was approved by the institutional review board. Informed consent was obtained from all patients prior to study participation.

Patient characteristics

101 patients were included in the study, 50 of them underwent PCI and comprised the analysed study population. Baseline characteristics are shown in table 1. Indication for catheterization was 58% unstable angina/non-ST-elevation myocardial infarction.

Table 1. – Baseline characteristics

<table>
<thead>
<tr>
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<th>Total population (n = 50)</th>
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<tr>
<td>Male sex</td>
<td>84%</td>
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<tr>
<td>Age, y</td>
<td>63.7 ± 10</td>
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<tr>
<td>DM</td>
<td>20%</td>
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<tr>
<td>Hypertension</td>
<td>74%</td>
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<td>Hyperlipidaemia</td>
<td>92%</td>
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<td>PVD</td>
<td>12%</td>
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<td>Smoker (current)</td>
<td>20%</td>
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<td>Previous MI</td>
<td>20%</td>
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Measurements

The general method of operating the HeartVue™ 6S System was as follows: (1) four electrodes were applied in accordance with the standard arrangement of ECG limb leads: one on each forearm and one on each lower leg; (2) ECG data acquisition was performed over 30 seconds; (3) an image of the heart was formed on screen together with quantitative and qualitative analysis of cardiac electrical activity; and (4) the HeartVue™ 6S System showed results in the form of a numeric dispersive characteristics range and a dispersive mapping. The dispersive mapping was a graduated colour-coded image of the heart in which green indicated healthy state and red represented pathological changes (figure 1).

The dynamics of the average micro fluctuations in the PQRS-complex are called dispersive characteristics. Dispersive characteristics were expressed by 9 analysed groups of deviations (G1-G9). In these groups the dispersive characteristics were analysed reflecting electrophysiological abnormalities in the depolarization and repolarization of the myocardium. Correspondence between groups G1-G9 and the QRST complex intervals are presented in figure 2. The study analysis was limited to groups G3-G9, which referred to the heart ventricles.

The manufacturer provided pre-specified parameters for the system: “myocardium” (measures the average micro alternans amplitude for both QRS and T wave), “G9” (measures the average micro alternans amplitude in the initial part of the QRS-complex), “G7+G9” (measures the average micro alternans amplitude in the middle part of the QRS-complex) and G3-G9 (measures the average micro alternans amplitude in the final stage of depolarization and repolarization) (figure 2).

ECG signal acquisitions were performed at baseline (prior to angioplasty), during the first coronary balloon inflation or stent deployment (by protocol all
inflations were at least 30 seconds) and at procedure end. If the patient did not proceed to angioplasty, then only baseline signal acquisitions were obtained. All signal acquisition was performed in the cardiac catheterization laboratory.

ENDPOINTS

The primary endpoint was to compare the average of the parameters provided by the HeartVue™ 6S System (myocardium, G9, G3-G9, G8+G7) at baseline, during artery occlusion (first balloon inflation or stent deployment) and at the end of the procedure.

STATISTICAL ANALYSIS

No formal power calculation was performed for this study, as there were no previous data. Continuous variables are expressed as mean ± standard deviation and categorical variables as percentages. The Kolmogorov-Smirnov test showed that the distribution of the variables was not normal. Therefore, the Wilcoxon signed rank test was used to compare the differences in myocardium, G9, G3-G9, and G8+G7 between the baseline, first inflation and at procedure end. A significance level of 0.05 was used and 2-tailed test were applied. Analyses were performed using the Statistical Package for Social Scientists (SPSS Inc, 15.0 for Windows).

Result

HEARTVUE™ 6S SYSTEM PARAMETERS

In all the patients we obtained baseline data. Among the 50 patients who underwent PCI the first inflation data (balloon inflation or stent deployment) and post-procedure data were obtained in 44 (88%) and 48 (96%) patients respectively.

DISPERSE MAPPING

At baseline in 80% of cases, the dispersive figures had a great variability and fluctuating form. These baseline findings prevented us from performing any comparison using dispersive mapping.

DISPERSE CHARACTERISTICS

There were no statistically significant differences in the parameters myocardium, G3-G9 and G9 provided by the system between baseline, first inflation and at the end of the procedure. However, there were significant differences in G8+G7 parameter between the first inflation and procedure end (table 2, figure 3).

Discussion

In this prospective study we showed that there are differences in the parameter G7+G9 provided by the HeartVue™ 6S System between baseline and at the end of the procedure. The HeartVue™ 6S System may have potential for a non-invasive assessment of ischaemia in patients with suspected coronary artery disease undergoing PCI.

The sensitivity of the standard ECG for detection of CAD is limited1,2, several methods have been proposed and developed to enhance sensitivity and

<table>
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<th>Table 2. – Comparison of differences in G7+G9 parameter between baseline, first inflation and end of the procedure</th>
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specificity of the resting ECG for diagnosis of symptomatic and asymptomatic CAD.

Diagnostic ECG computer programmes have been developed. However, they have not yet been shown to be superior to the specialist physician’s judgment. The results of a device that amplified and digitized the analogue ECG signal have been described. This device has shown a good sensitivity and specificity for the detection of patients with haemodynamically relevant stenosis. The sensitivity and specificity of an ECG for the detection of CAD can be improved by exercise testing. The exercise ECG has a reported specificity of over 80% under ideal conditions. Clinically, however, sensitivity is typically less than 50-60%. While these approaches provided significantly better diagnostic performance than the standard ECG, it appears that none of these methods has been implemented in broad clinical practice.

The ECG dispersion mapping method is a novel approach to ECG signal analysis. Using conventional ECG signals obtained from limb leads, low amplitude oscillations of the ECG signals are digitally amplified and assessed over several cardiac cycles. Patients with coronary heart disease display greater ECG signal fluctuation reflecting abnormal regional depolarization and repolarization processes within the myocardium. Thus dispersive changes in ECG signals may potentially reflect myocardial ischaemia.

The HeartVue™6S System was developed as a non-invasive screening device for coronary heart disease. However, available data is limited and this device has not been validated prospectively in a clinical study. We performed this study using the HeartVue™6S System to determine if it detects myocardial ischaemia during coronary occlusion (balloon inflation and/or stent deployment) in patients undergoing PCI. Among several different approaches to validate the system we opted for coronary occlusion to eliminate potential confounding variables.

In this study we could not use the dispersive mapping data due to its great variability and fluctuating form. Further modifications of the system may help with this problem.

When we analysed the dispersive characteristics, we found significant differences in the G7+G9 parameter during first balloon inflation compared to procedure end. The G7+G9 parameter reflects the middle stages in ventricular depolarization, so potentially it could be the most sensitive parameter for detecting myocardial ischaemia.

This system was developed as a screening tool, it was not designed for PCI monitoring. During PCI there are factors that can influence the measurements of the HeartVue™6S System: the patients receive several medications that can reduce the amplitude of microfluctuations and the presence of compensatory mechanisms could reduce the ability of the system to detect ischaemia. The ECG’s micro-alternans amplitude measured by the HeartVue™6S System could reflect not only local myocardium hypoxia but compensatory myocardium reaction through collateral and microcirculatory mechanisms. Therefore modifications in the system may be needed to improve its ability to detect acute ischaemia during PCI. Continuous monitoring, instead of 30 sec recording, with trend analysis of the microfluctuations may be a better approach in the setting of PCI (a dynamic intervention).

Limitations

This is a single-centre study with a small number of patients. Ischaemia was induced during coronary occlusion by balloon inflation or stent deployment, ischaemia caused by platelet aggregation or spasm may induce a different type of response.

Conclusion

The HeartVue™6S System may have potential for a non-invasive assessment of ischaemia in patients with suspected coronary artery disease undergoing PCI. Larger studies and modifications of the system are warranted to confirm these preliminary findings.

Acknowledgements

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Conflict of interest

Dr Ik-Kyung Jang MD, PhD received a research grant from Heart View, LLC, Cleveland, Ohio.

References