Comparison of cardiogoniometry and electrocardiography with perfusion cardiac magnetic resonance imaging and late gadolinium enhancement

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Aims
Cardiogoniometry (CGM) is a spatio-temporal five-lead resting electrocardiographic method utilizing automated analysis. The purpose of this study was to determine CGM’s and electrocardiography (ECG)’s accuracy for detecting myocardial ischaemia and/or lesions in comparison with perfusion cardiac magnetic resonance imaging (CMRI) and late gadolinium enhancement (LGE).

Methods and results
Forty (n = 40) patients with suspected or known stable coronary artery disease were examined by CGM and resting ECG directly prior to CMRI including adenosine stress perfusion (ASP) and LGE. The investigators visually reading the CMRI were blinded to the CGM and ECG results. Half of the patients (n = 20) had a normal CMRI while the other half presented with either abnormal ASP and/or detectable LGE. Cardiogoniometry yielded an accuracy of 83% (sensitivity 70%) and ECG of 63% (sensitivity 35%) compared with CMRI.

Conclusions
In this pilot study CGM compares more favourably than ECG with the detection of ischaemia and/or structural myocardial lesions on CMRI.

Keywords
Cardiogoniometry • Cardiac magnetic resonance imaging • CAD detection • Gadolinium enhancement

Introduction
There is an unmet need for a practical, cost-effective method to improve electrocardiological diagnosis of coronary artery disease (CAD) at rest in primary healthcare. In diagnosing CAD, standard 12-lead resting electrocardiography (ECG) can be inaccurate, particularly in stable and/or asymptomatic patients. Even in patients with acute coronary syndrome, the sensitivity of ECG for identifying non-ST-elevation myocardial infarctions and unstable angina pectoris is low (~20%). Therefore, exercise ECG has been established as the standard method in primary settings for detection of CAD in patients with suspected stable angina pectoris or without symptoms. In meta-analyses including patients with/without previous myocardial infarction, exercise ECG has shown a predictive accuracy of 73%/69%, a sensitivity of 68%/67%, and a specificity of 77%/72% for CAD diagnosis.2,3 However, exercise ECGs are often not meaningful due to limited stress capacity of the patient or are even contraindicated.2,3

Thus, ECG performed at rest is not an appropriate screening method for detecting myocardial ischaemia or structural myocardial lesions suggestive of CAD in the primary setting, and at the same time exercise ECG often cannot be performed appropriately due to its inherent limitations.

Alternatives to the standard 12-lead ECG have been proposed: vectorcardiography (VCG) has been in use since the late 1930s4 with many different lead-placing methods.5 The best-known and most frequently used VCG method is the seven-lead method developed by Frank.6 Vectorcardiography was mainly used to
perfusion is an established sensitive and specific non-invasive functional test for detection of ischaemia and LGE, a very sensitive test for detection of structural myocardial lesions. Thus, cardiac MRI (CMRI) is a very comprehensive reference for the comparison of two different electrocardiographic rest methods.

**Materials and methods**

**Patients**

A total of 40 patients with suspected or known stable CAD were examined in this study who had been scheduled for a medically indicated CMRI with adenosine perfusion and LGE in the Department of Cardiology, Schwarzwald-Baar-Klinikum, Villingen-Schwenningen, Germany. Patients were enrolled if they consented to an additional CMRI examination prior to CMRI. A standard 12-lead ECG was recorded after the CGM. The inclusion period spanned ~2 months in 2010.

**Cardiogoniometry**

The trigonometric principles of CGM have been published in detail elsewhere. In brief, four electrodes define two planes perpendicular to each other. Vectorial addition of the potentials measured between three electrodes in each plane yields a vector corresponding to the projection of the heart vector into this plane. Using the vector projections in the two orthogonal planes, the heart vector can be reconstructed for every millisecond. Vector orientation indicates direction and vector length the strength of the electrical field generated by the heart.

Cardiogoniometry uses different parameters compiled into specific sets based on gender and conduction characteristics (low T voltage, right bundle branch block, left bundle branch block, and atrial fibrillation). Analysis of all parameters is fully automated. The result of the automated analysis is dichotomous with respect to expected CAD.

The analysed parameters can be divided into the following main classes: angles, amplitudes, shapes, and eccentricities describing the P-, R-, and T-loops, potential distributions of the P-, R-, and ST/T-loops in octants and velocities (both absolute and ratios) of the P-, R-, and T-loops. In addition, variability of all parameters is analysed.

Prior to CMRI, the study data were collected by resting five-lead CGM on the supine patient using a commercial CGM device (Cardiologic Explorer, Enverdis GmbH, Jena, Germany) equipped with software running at a 1016 Hz sampling rate and 22-bit resolution. During the recording, the patients were requested to hold their breath for 12–15 s after normal expiration. If this was not possible, they were asked to perform shallow breathing and keep their thoracic excursions to a minimum. The software automatically detected any ectopic and irregular beats occurring during the recording and excluded them from the analysis. The CGM results were recorded by an independent investigator blinded to all patient data. Cardiogoniometry provided an automatic dichotomous result, i.e. either normal (score \( = 0 \)) or abnormal (score \( \neq 0 \)).

**Twelve-lead electrocardiography**

The resting 12-lead ECG (GE MAC Resting ECG) was recorded after the CMG and prior to the CMRI. All ECGs were analysed by one independent investigator blinded to all patient data. A pathologic ECG was assumed whenever electrocardiographic criteria suspicious of myocardial ischaemia or prior myocardial infarction were present. These criteria were defined as horizontal or down-sloping ST depression \( \geq 0.05 \) mV in two contiguous leads; and/or T inversion \( \geq 0.1 \) mV in
Figure 2 Cardiogoniometry taken directly prior to cardiac MRI (see Figure 1). (A) Overall CGM findings: upper left, maximum vector view (cf. C), below, potential view, calculated from $\text{SQR}(X_1^2 + Y_1^2 + Z_1^2)$. Centre: spatial vector loops (R-loop blue, T-loop green) in the three projection planes YX, XZ, and YZ. On the right, the automatic overall finding and the parameters used for normal regions (green) and abnormal regions (yellow, red). A patient is classified as normal when all parameters are located within the normal (green) range. (B) CGM maximum vectors: spherical view depicting the maximum vectors (points of the longest distance from the vector loops to the coordinate origin) of the spatial R-loops (blue squares) and T-loops (green triangles) representing each heart cycle of recording lasting a total of 12 s. This is generated from the XZ projection with a view to the apex by folding out the basal regions of the heart (like the ellipsis created by flattening out a globe). The blue field represents the normal range of the R-maximum vectors and the green field the normal range of the T-maximum vectors. CGM identifies deficient perfusion on the mirror image of the contralateral side when the T-maximum vectors are located outside of the green (normal) area.
Patients gave their informed consent.

Pathological ASP and/or the presence of subendocardial LGE. Presence of CAD based on the CMRI findings was assumed if there was stress perfusion (ASP) and/or the presence of LGE on CMRI.

Cardiac magnetic resonance imaging (CMRI) was performed at rest (without adenosine). During each perfusion study 0.1 mmol/kg gadoteridol (PROHANCE 0.5 M) was administered. Image acquisition was performed with a 3D/2D inversion recovery fast gradient echo sequence. Cardiac magnetic resonance imaging images were analysed visually and the investigators blinded to the CGM results.

Cardiogoniometry and ECG findings were compared against adenosine stress CMRI. Presence of CAD based on the CMRI findings was assumed if there was a pathological ASP and/or the presence of subendocardial LGE.

The study was approved by the local ethics committee and all patients gave their informed consent.

Table 1 Baseline clinical characteristics of patients presenting for perfusion cardiac magnetic resonance and late gadolinium enhancement examination (n = 40)

<table>
<thead>
<tr>
<th></th>
<th>Normal adenosine perfusion and no late enhancement on MRI (n = 20)</th>
<th>Pathological adenosine perfusion and/or late enhancement on MRI (n = 20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62 ± 13</td>
<td>67 ± 7</td>
<td>n.s.</td>
</tr>
<tr>
<td>Female gender</td>
<td>45% (n = 9/20)</td>
<td>25% (n = 5/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Diabetes</td>
<td>15% (n = 3/20)</td>
<td>10% (n = 2/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Current smoker</td>
<td>5% (n = 1/20)</td>
<td>15% (n = 3/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Arterial hypertension</td>
<td>80% (n = 16/20)</td>
<td>100% (n = 20/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>70% (n = 14/20)</td>
<td>60% (n = 12/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Known CAD</td>
<td>45% (n = 9/20)</td>
<td>85% (n = 17/20)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>0% (n = 0/20)</td>
<td>45% (n = 9/20)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>30% (n = 6/20)</td>
<td>80% (n = 16/20)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>5% (n = 1/20)</td>
<td>15% (n = 3/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
<td>10% (n = 2/20)</td>
<td>5% (n = 1/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Previous stroke/TIA</td>
<td>10% (n = 2/20)</td>
<td>15% (n = 3/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Reduced global ejection fraction*</td>
<td>0% (n = 0/20)</td>
<td>20% (n = 4/20)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Data are presented as mean value ± SD or percentage of patients.

CGM, coronary artery bypass graft; n.s., not significant; PCI, percutaneous coronary intervention; TIA, transient ischaemic attack.

*Ejection fraction measured by any method; reduced ejection fraction was defined as <55%; no patient with EF <40% in the study cohort.

Cardiac magnetic resonance imaging

For detection of ischaemia, a perfusion scan with adenosine stress (140 μg/kg/min) was performed. Analysis was done in three short axis planes acquired with a FGRE-ET sequence (GE Signa EXCITE® HD). Around 20 min later a second perfusion scan was performed at rest (without adenosine). During each perfusion study 0.1 mmol/kg gadoteridol (PROHANCE® 0.5 M) was administered at a rate of 5 mL/sec. For detection of late enhancement, a total amount of 0.2 mmol/kg gadoteridol was administered. Image acquisition was performed with a 3D/2D inversion recovery fast gradient echo sequence. Cardiac magnetic resonance imaging images were analysed visually and the investigators blinded to the CGM results.

Cardiogoniometry and ECG findings were compared against adenosine stress perfusion (ASP) and/or the presence of LGE on CMRI. Presence of CAD based on the CMRI findings was assumed if there was a pathological ASP and/or the presence of subendocardial LGE.

The study was approved by the local ethics committee and all patients gave their informed consent.

Results

Forty patients (n = 40) were included in the study. Half of the patients (n = 20) had a normal CMRI finding. The other half (n = 20) presented with either an abnormal perfusion scan during adenosine stress and/or a detectable LGE (pathological perfusion and late enhancement n = 5, late enhancement only n = 13, and pathological perfusion only n = 2). The clinical baseline characteristics of the two patient cohorts differed significantly with respect to the prevalence of known CAD, previous myocardial infarction and previous percutaneous coronary intervention. More details are given in Table 1.

In accordance with the difference in baseline clinical characteristics patients with a pathological finding on CMRI had numerically more pathological Q waves and/or QS waves on standard 12-lead ECG and numerically more regional wall motion abnormalities on echo (Table 2).

Cardiogoniometry yielded a total accuracy of 83%, a sensitivity of 70%, a specificity of 95%, a positive predictive value (PPV) of 93%, and a negative predictive value (NPV) of 76% according to Table 3. The defined ECG criteria for detection of ischaemia prior to myocardial infarction yielded a total accuracy of 63%, a sensitivity of 35%, a specificity of 90%, a PPV of 93%, and a NPV of 58% (Table 3).

Discussion

Non-invasive diagnostics raise the suspicion of CAD when tentative proof is provided of ischaemia or presumably ischaemia-related myocardial damage. Certain limitations make conventional resting ECG unsuitable for detecting stable
The findings of our pilot study suggest that CGM is increasingly used as an imaging method in the primary setting, especially on patients physically unable to undergo stress testing provided that these findings are confirmed in larger prospective studies which are already prepared.

Table 2 Resting electrocardiography and echocardiographic findings

<table>
<thead>
<tr>
<th>No irregular findings on resting ECG (nos. 1–3)</th>
<th>Normal adenosine perfusion and no late enhancement on MRI (n = 20)</th>
<th>Pathological adenosine perfusion and/or late enhancement on MRI (n = 20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Resting ECG with path. Q waves and/or QS waves and/or pers. ST-segment depression</td>
<td>65% (n = 13/20)</td>
<td>50% (n = 10/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>2. Resting ECG with negative T waves and/or ST-segment depression</td>
<td>0% (n = 0/20)</td>
<td>30% (n = 6/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>3. Resting ECG with any type of bundle branch block</td>
<td>10% (n = 2/20)</td>
<td>5% (n = 1/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Left anterior hemiblock</td>
<td>25% (n = 5/20)</td>
<td>15% (n = 3/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Left bundle branch block</td>
<td>15% (n = 3/20)</td>
<td>10% (n = 2/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Right bundle branch block</td>
<td>5% (n = 1/20)</td>
<td>0% (n = 0/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Bifascicular block</td>
<td>5% (n = 1/20)</td>
<td>5% (n = 1/20)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Regional wall movement abnormality on echo</td>
<td>0% (n = 0/14)</td>
<td>50% (n = 8/16)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

Data are presented as absolute numbers and percentage of patients.

n.s., not significant.

Table 3 Diagnostic yield of cardiogoniometry and rest electrocardiography compared with physiological or pathological findings on cardiac magnetic resonance perfusion and/or late enhancement

<table>
<thead>
<tr>
<th>CGM</th>
<th>12-lead ECG suspicious for CAD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity 70% (n = 14/20)</td>
<td>35% (n = 7/20)</td>
</tr>
<tr>
<td>Specificity 95% (n = 19/20)</td>
<td>90% (n = 18/20)</td>
</tr>
<tr>
<td>PPV 93% (n = 14/15)</td>
<td>93% (n = 7/9)</td>
</tr>
<tr>
<td>NPV 76% (n = 19/25)</td>
<td>58% (n = 18/31)</td>
</tr>
<tr>
<td>Accuracy 83% (n = 33/40)</td>
<td>63% (n = 25/40)</td>
</tr>
</tbody>
</table>

Data are presented as absolute numbers and percentage of patients.

CAD, coronary artery disease.

*ECG changes suspicious for CAD were defined as: pathological Q waves and/or QS waves and/or negative T waves and/or pers. ST-segment depression.

CAD: ECG is neither sensitive nor specific with respect to ST segment depressions and inverted T waves; furthermore, pathological Q or QS waves although quite specific for previous myocardial infarction are not frequently found in the entire patient cohort with chronic stable CAD. This is the reason why the use of stress ECG is a common practice to detect ischaemia in stable patients. A major problem with physical stress testing in our ageing and increasingly overweight population, however, is that many patients do not have the capacity to be stressed on adequate levels.24 Obviously, pharmacological stress in conjunction with advanced imaging methods (echo, nuclear scans, or MRI) is a valuable alternative but not broadly available in the primary setting. Hence, we have an unmet need for resting ECG examinations that show a markedly higher sensitivity and specificity for detecting stable CAD. The findings of our pilot study suggest that CGM is significantly superior to 12-lead resting ECG for identification of patients with functional myocardial ischaemia and/or myocardial scars presumably caused by past ischaemic events.

Corresponding to all other contemporary electrocardiographic methods CGM interpretation is based on phenomenology with a limited understanding of the cellular mechanisms underlying the transient or persisting changes seen on the sum electrocardiogram. The T-wave memory after tachyarrhythmias is a well-known example for this.25 Similarly, our knowledge of the transient or persisting mechanical abnormalities in acute or chronic myocardial ischaemia like stunning or hibernating myocardium is limited to the cellular level.26 Keeping this in mind it is well conceivable that we are able to detect more electrical phenomena at rest related to chronic myocardial ischaemia as we are accustomed to do at present with the use of a more sensitive electrocardiographic probe. This might overcome the paradigm that electrocardiographic methods need necessarily be combined with stress to detect chronic ischaemia.

The major limitations of this study are the small overall sample size and the fact that of the seven patients with pathological ASP, five also had an LGE. Thus, our observation does not allow us to draw a substantiated conclusion as to what extent detection of CAD by CGM is driven by detection of myocardial scars or detection of chronic ischaemia.

Conclusions

In this pilot study, CGM compares favourably with the combination of ASP and LGE in terms of detecting signs of stable CAD and clearly outperforms resting ECG. Given its simplicity, this new examination performed at rest appears suitable for use in the primary setting, especially on patients physically unable to undergo stress testing provided that these findings are confirmed in larger prospective studies which are already prepared.
Conflict of interest: The authors were not supported by any grants for this research. R.B., R.T., U.Z., and R.W. have already participated in a previous trial sponsored by Enverdis company and received speaker fees.

References