OVERVIEW – (https://cardis.io/studies)

Cardisiography^{TM}, the novel approach to vector-cardiography analyzed with artificial intelligence: Scientific foundations, evidence, and future perspectives.

Cardisiography – a Summary of Scientific Evidence

The following text provides an overview of the scientific evidence of Cardisiography (CSG), a non-invasive diagnostic tool for various heart pathologies. CSG is a 5-lead 3D vector cardiography with AI-based calculation, which examines 731 parameters to assess cardiovascular disease risk. CSG is an advancement of Cardiogoniometry (CGM)*, an adapted version of vectorcardiography first suggested in the 1920s [8–12].

Numerous studies on the performance of CGM have been conducted in the past [13-21, 23, 24]. The results of these studies proposing CGM as a new diagnostic tool for coronary artery disease were summarized in a meta-analysis [22]. The pooled overall sensitivity was 71.7%, and the pooled specificity was 78.8%. According to Egger regression tests (P = 0.32), there was no bias in the studies.

Multiple studies have demonstrated the promise of CSG as a diagnostic tool for coronary stenoses. For instance, a prospective study reported that CSG achieved a sensitivity of 95.4% and a specificity of 90% in identifying relevant coronary stenoses [25]. Similarly, another investigation found that CSG could diagnose coronary artery disease with a sensitivity ranging from 90% to 97% and a specificity between 74% and 76% [26]. These results were further validated by a study that employed myocardial scintigraphy [27].

Beyond its diagnostic accuracy, CSG has also shown potential in risk stratification for cardiovascular disease. An exploratory multicenter trial revealed that CSG could reliably differentiate between high- and low-risk patient groups. In this study, the CSG Index not only demonstrated a high negative predictive value of 0.91 but also outperformed classical risk factors in predicting cardiovascular risk [28].

Additional abstracts have been presented at the DGK Herbsttage, Bonn 2023 and American Heart Association Conference, November 2023, DGK Frühjahrstagung 2024, DGK Herbsttage, Hamburg, 2024. For further details see below.

** Please note that the Cardiogoniometry (CGM) technology is the proprietary technology of Cardisio GmbH*

Basis of Cardisiography (Vector-Cardiography, Cardiogoniometry*)

Non-invasive diagnosis of coronary heart disease is still underdeveloped and improvable. To date, there is no simple and cost-effective method for reliable diagnosis. Apart from expensive and elaborate imaging procedures, exercise electrocardiography (stress ECG) is the most important available diagnostic method, albeit with only unsatisfactory sensitivity and specificity [29]. Cardisiography (CSG) is a 5-lead 3D vector cardiography with AI-based calculation (5L3DVCG-AI) of 731 parameters, which enables risk assessment of cardiovascular disease in primary care through an algorithm. CSG originates from the field of Cardiogoniometry (CGM), which in turn is an adapted version of vector cardiography, first described by Sanz et al. in 1983 [30].

For the detection of ischemic indications, the technology behind CGM focuses on recognizing abnormalities in the T-wave, which originate from the disturbed repolarization of cardiomyocytes due to cardiac pathology. The potentials from the five electrodes are described by 350 parameters, including angles, amplitudes, and velocities of the P, R, and T loops, among others. Parameters showing significant deviations can indicate impaired cellular repolarization and thus perfusion disorders [18]. This allows for the interpretation of electrical leads from only three linear projections, providing information that cannot be extracted from the usual 12-lead ECG [31].

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So, what are the differences and, more importantly, the advantages of CSG over CGM?

Fundamentally, CSG processes the electrical heart activity more comprehensively, delivering a higher level of information compared to CGM. Simultaneously, CSG employs not only more advanced CGM-specific parameters, such as energy density in the QRS and T complex but also introduces new parameters that consider the change in excitation speed of the electrical 3D signal. However, the most significant distinction between CGM and CSG is the integration of cloud-based AI framework for signal evaluation and identification of pathological signal structures in electrical heart activity, patented under EP3850640. CSG is an advancement of the vector-cardiography and CGM, already being routinely employed by a large number of practicing physicians, specialized clinics and hospitals both nationally and internationally.

As with CGM, studies have been conducted for CSG. Substantial study results are available in which CSG was compared against various common examination methods.

CSG specific studies

In 2019, a total of 595 patients with clinical indications for catheterization were measured using CSG, and the diagnosis was confirmed through coronary angiography. The diagnosis was independently evaluated by two investigators. The study revealed that CSG could identify coronary artery disease (significant stenosis) at rest with a sensitivity of 90 ± 4% in females and 97 ± 3% in males. The specificity was 74 ± 10% (female) and 76 ± 9% (male). Hence, the overall diagnostic accuracy was 82 ± 6% (female) and 91 ± 3% (male) [26].

In 2020, Erkenov et al. conducted a prospective study involving 106 patients who underwent CSG measurements, following various exclusion criteria. All included patients had a clinical indication for coronary angiography, which was subsequently performed. The study demonstrated that CSG identified relevant stenoses with a sensitivity of 95.4% and a specificity of 90%. [25]

Apart from coronary angiography, CSG was also compared against myocardial scintigraphy. In 2022, a study with 112 consecutive patients showed a strong trend towards accuracy of 5L3DVCG-AI related to pathological MPS (Chi2: 3.2, p=0.07) with a sensitivity of 75% of 5L3DVCG-AI for a moderately or highly pathological MPS, a specificity of 58% and a negative predictive value (NPV) of 97% [27].

In the subgroup of 76 patients with clinically suspected CVD, significant accuracy of 3D-VCG related to MPS was seen with a sensitivity 83%, specificity 66%, and NPV 98%. Thus, in a preselected study group of patients with clinically suspected, or known CHD, 5L3DVCG-AI has the potential to identify those patients not requiring interventional procedures as detected by MPS, with a significant NPV of 96%. [27]

In an exploratory study (presented in the poster session at the ESC 2023, Amsterdam), we analyzed patients in a national, multicenter trial [28]. 468 Patients were recruited from general cardiology practices and a radiology center with patients referred for further diagnosis of suspected or confirmed CVD. Based on the CSG-Index, patients were either classified as high, medium, or low risk for CVD (medium + high defined as high CVD-risk). Confirmation of CAD was performed according to the practitioners' discretion blinded to the CSG-Index. Number of risk factors (mod. PROCAM score) were compared between the high- and low-risk group using an independent t-test. The number of cardiovascular risk factors was significantly higher in the high-risk CVD-group as defined by CSG-Index compared to low CVD-risk (4.0 [3.0 – 5.0] vs. 3.5 [2.0 – 4.0], $p < 0.05$). CSG-Index differentiated between suspected CVD with or without consequent PCI or CABG (Chi2 = 4.02, $p<0.05$).

Conclusions: AI based 3D VCG is an innovative diagnostic tool that can help determine a patient's cardiovascular risk in resting condition for clinical and research purposes. CSG-Index reliably identified healthy controls (negative predictive value = 0.91) without signs or symptoms of CHD. The CSG-Index differentiated those with no signs and symptoms of CHD and patients with CHD and is a better predictor for cardiovascular risk than the classical risk factors.

Furthermore, Cardisiography study results have been presented at the following Cardiology Congresses/Events in fall 2023:

1. **DGK Herztage, 05.10 – 07.10.2023 World Conference Center Bonn**
   - An innovative artificial intelligence-driven 3D vectorcardiography method for the non-invasive prediction of obstructive coronary artery disease

   - Sensitivity and Specificity of the Artificial Intelligence-Based 5-Lead 3D Vectorcardiography in Patients with Suspected or Confirmed Coronary Heart Disease

2. **American Heart Association Conference, November 11–13, Pennsylvania Convention Center**

   [**Abstract 16473: Validation of the Artificial Intelligence-Based 5-Lead 3D Vectorcardiography in Comparison to the 12-Lead ECG in a Mixed Population**]()

   [**Abstract 15181: Sensitivity and Specificity of the Artificial Intelligence-Based 5-Lead 3D Vectorcardiography in Patients With Suspected or Confirmed Coronary Heart Disease**]()

In April 2024, updated study results have been presented at the German Society for Cardiology Jahrestagung 2024 – "5L3DVCG-AI (Cardisiography) for identification of cardiac pathology in a mixed population" [32]. The goal was to identify patients at risk for CVD and cardiac pathology. 299 patients with clinical indication for the detection of CVD were included in this monocentric, retrospective observational study.

The study showed that AI further improves the easy-to-use and inexpensive 5L3DVCG (CSG) and that CSG is superior to CVRF-Score in differentiating people at risk of CVD or cardiopathology, especially for women and hard-to-reach population (NPV: 88%). Thus, 5L3DVCG-AI opens up a diagnostic window for early detection of CVD.

Link to Abstract

In **October 2024,** the results of a National Health Service (NHS), SBRI Healthcare study have been presented: Assessing the impact of using community-based heart testing in primary care to detect early signs of cardiovascular disease through a novel, quick, low- cost test which uses sophisticated AI-based analysis [33].

The SBRI study (SBRIH21P3013) investigated how the Cardisiography could be incorporated into the NHS, focusing on its application within Primary Care to enhance early detection of cardiovascular issues and improve the efficiency of patient referrals to Secondary Care.

628 asymptomatic, elevated-risk individuals were recruited from three primary care settings (GP practice, in-pharmacy setting, and outreach pharmacy) in the West Midlands, UK. Test outcomes were compared with standard care to assess diagnostic accuracy, and the impact on secondary care referrals was analyzed.

The results demonstrated a high diagnostic accuracy (sensitivity of 73.8%, specificity of 94.4%, PPV of 80%, and NPV of 90.4%. A strong correlation was found between Cardisio results and clinical decisions for secondary care referrals ($p<0.001$).

In conclusion, the Cardisio test is a highly accurate, cost-effective, and user-friendly tool for early detection of CVD in primary care. Its strong PPV and NPV values, ability to reduce unnecessary secondary care referrals, opportunities for remote and community testing, and positive environmental and social outcomes make it an ideal tool for early diagnosis and decision-making in healthcare settings.

Link to study report

In **October 2024** an oral presentation was held at the DGK Herztage on the topic of "AI-based 5-lead 3D-vectorcardiography (5L3DVCG-AI) detecting cardiac pathologies at rest may replace conventional 12-lead ECG with potential additional value" [34].

In this multicentre retro- and prospective study, recordings from 5L3DVCG-AI were externally validated against automated 12-lead ECG in 287 patients with and without cardiac pathologies. 5L3DVCG-AI derived 12-lead ECG (VCG-ECG) was reconstructed from 5L3DVCG-AI with an algorithm and time intervals were derived from 5L3DVCG-AI. Two independent specialist cardiologists masked for 12-lead ECG results interpreted VCG-ECG qualitatively and quantitatively. The following variables were compared between 5L3DVCG-AI and 12-lead ECG: electric heart axis and rhythm, HR, and time intervals for P, PQ, QT, QTcB. Presence of cardiac pathology (CP) was categorised as exclusion of any CP (control), mild CP or overt CP by 2 independent cardiologists from clinical practice with a follow-up period of 16.2 ± 7.5 months.

In summary, 5L3DVCG-AI is an easy-to-use and feasible technology with good accuracy and reproducibility for electric heart axis, ECG-parameters and intervals and thus offers additional value in detecting individuals with cardiac pathologies or cardiac risks. 5L3DVCG-AI may replace conventional 12-lead ECG in the General Practice or cardiological outpatient departments. Especially for women this may offer additional value.

In **November 2024,** researchers at Hospital IGESP (Sao Paulo, Brazil) assessed the accuracy of 5L3DVCG-AI (Cardisiography) for diagnosing acute coronary syndrome in patients with chest pain in the emergency department [publication under way].

This prospective, monocentric, double-blinded study with predefined hypotheses was carried out on 46 consecutive patients in a general hospital emergency unit. After admission for acute chest pain, the patients were clinically assessed, following the institutional protocol for chest pain, and the 5L3DVCG-AI recordings were also collected. After collection, the 5L3DVCG-AI signals were automatically decoded and analyzed. Investigators were blinded to the patients' clinical data or 5L3DVCG-AI results, respectively prior to databank close. Diagnostic accuracy of the 5L3DVCG-AI was validated using clinical cardiological diagnosis (clinical symptoms, ECG, troponin T, Angio-tomography, coronary angiography, as clinically indicated) as the gold standard.

The results showed a sensitivity of 93%, specificity of 64%, a PPV of 62% and a NPV of 93% with a diagnostic accuracy for diagnosis of acute coronary syndrome as the cause of chest pain of 75% (AUC ROC).

In conclusion, the high specificity presented by 5L3DVCG-AI for the diagnosis of acute coronary syndrome in this population suggests that this method may be suitable for screening patients with acute chest pain in emergency departments for planning further diagnostic measures.

In **early 2025** an abstract for the DGK-Jahrestagung 2025 has been accepted for presentation: "Evaluation of new Vector Electrocardiography Algorithms for identifying Patients with reduced Left Ventricular Ejection Fraction and Left Ventricular Hypertrophy" [35].

Reduced left ventricular ejection fraction (LV-EF) and left ventricular hypertrophy (LVH) are associated with high mortality and morbidity. Early and accurate diagnosis is essential, but non-invasive, cost-effective diagnostic tools are still needed for clinical application. This study evaluated the diagnostic performance of CSG for detecting reduced LV-EF and LVH.

This prospective, single-center, case-control study included patients with reduced LV-EF (< 40%), and LVH, defined as indexed LV mass > 55 g/m², compared with controls without cardiac pathology. Cardiac magnetic resonance imaging (CMR) was performed as part of routine clinical care and used as the reference standard for measuring LV-EF and LV mass. Patients were enrolled consecutively. In total, 583 parameters per heartbeat were analysed to classify cardiac status.

A total of 280 patients were included in the analysis. The group with reduced LV-EF (n=40) had a mean age of 56 ± 16 years and was predominantly male (78%), with a median LV-EF of 31.5% (IQR: 23.4-36.3%). The LVH group (n=209) had a mean age of 60 ± 16 years (87% male) with an indexed LVM of 67g/m² (IQR: 61-77 g/m²). Controls (n=31) had a mean age of 50 ± 16 years (61% male), normal LV-EF of 62 ± 5.6% and indexed LV mass of 40g/m² (IQR: 35-47g/m²). Using 15 VCG parameters demonstrated a **sensitivity of 80.0%** and **specificity of 85.7%** for **detecting reduced LV-EF (accuracy 82.9%).** For detecting LVH, it achieved a sensitivity of 74.5% and specificity of 68.6% (accuracy 73.6%). In cases with patients having both reduced LV-EF and LVH (n=64), the VCG demonstrated a sensitivity of 79.3% and a specificity of 85.7% (accuracy 82.8%).

In conclusion, the modified VCG algorithm showed notable diagnostic value for detecting reduced LV-EF and LVH. The VCG could serve as a fast, non-invasive, and cost-effective method to assist clinicians in identifying significant cardiac conditions and guiding further diagnostic steps. Further optimization of the VCG algorithm is necessary to improve differentiation between healthy individuals and those with cardiac disease, enhancing its clinical application.

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