Value of Cardiogoniometry in Diagnosis of Coronary Artery Disease in Patients with Suspected Stable Ischemic Heart Disease
A Systematic Review and Meta-Analysis

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Summary
Cardiogoniometry (CGM) has been proposed as a new diagnostic tool for coronary artery disease (CAD) in recent years. Although different studies have evaluated the diagnostic value of CGM in CAD diagnosis, no pooled analysis of its diagnostic accuracy has been performed so far. This study aimed to assess the value of CGM in diagnosing CAD in patients with suspected stable ischemic heart disease (SIHD).

This was a systematic review and meta-analysis conducted on available literature until May 2018. Studies considered coronary angiography as the reference standard for CAD diagnosis and reported CGM diagnostic value parameters were included. No language and time restrictions for enrolling the studies were considered. Statistical analysis was performed using Meta-DiSc software.

The findings of the 10 studies published in 9 articles were enrolled in the meta-analysis. Overall pooled sensitivity was 71.7% (69.1 to 74.1; Cochrane Q = 39.5; P < 0.00001; I² = 77.3%), and pooled specificity was 78.8% (76.3 to 81.1; Cochrane Q = 37.39; P < 0.00001; I² = 75.9%). Regarding Egger's regression test (P = 0.32), there was no published bias in the studies.

It seems that CGM, as an easy-to-use and non-invasive modality, should be considered as a part of risk stratifying strategies for CAD in patients with SIHD, mainly in patients with contraindications for stress tests. However, further studies with a high quality of methodology are still needed to assess the diagnostic value of CGM for CAD in patients with suspected SIHD.

Key words: Diagnostic study

Ischemic heart disease (IHD) is the most common cause of death around the world, accounting for about 13% of total deaths worldwide. Over the last 25 years, the IHD mortality rate has dropped by half in high-income countries probably due to early diagnosis as well as the success of existing treatment options. Early, accurate and non-invasive diagnosis of coronary artery disease (CAD) in patients with suspected stable ischemic heart disease (SIHD) is one of the topics that has always attracted the attention of researchers and physicians. In cases of suspected SIHD, non-invasive tests are considered to be useful alongside history taking and physical examination. Exercise electrocardiography (ECG) is the most available method in the diagnosis of SIHD, with an estimated sensitivity of 70%-77% and specificity of 65%-80% in the general population. However, exercise-ECG testing for diagnosis of SIHD also has limitations that have made it difficult to use, especially in older adults. Moreover, stress echocardiography and cardiac stress magnetic resonance imaging (MRI) are other non-invasive methods; however, despite their high diagnostic value, they should only be performed by an expert with sufficient expertise and experience. In addition, cardiac computed tomography (CT), myocardial perfusion scintigraphy, and single-photon emission CT (SPECT) are other non-invasive methods, which have not yet been able to find a role as the first-choice among diagnostic tools for CAD, due to their high cost, user complexity, and the need for highly trained personnel, as well as the risk of radiation exposure. Therefore, efforts are continuing to find new diagnostic modalities, or promote the performance of existing diagnostic tools.

Cardiogoniometry (CGM) has been proposed as a new diagnostic tool for CAD in recent years. CGM is a simplified and modified form of vectorcardiography that creates a 3-dimensional (3D) image of the electrical activity of the heart within a few seconds using 4 to 5 surface electrodes. CGM, as a stress-free test, is often performed in the supine position to provide a spatial visualization of the movement of electrical waves in depolarization and repolarization processes.
polarization. CGM is performed in a resting position while interpreting the data immediately by mounted computer and simultaneously displaying the readings after the test, thereby providing on-time feedback to the patient and the medical operator. The variations in the direction of maximum vectors refer dominantly to deviations from the routine stimulus conduction characteristics in the CGM. It is accordingly claimed that myocardial ischemia can be diagnosed by sensitive indicators of the spatial orientation of these vectors and their angles relative to another. It seems that the first study evaluated the value of CGM in diagnosing CAD relates to 1983 by Saner, et al., who showed that CGM has a sensitivity of 79% and a specificity of 82% for CAD diagnosis. Following this study, more than 10 other studies have examined the value of CGM in CAD diagnosis in patients with stable angina and candidates for elective angiography, with their findings showing sensitivity of between 39% to 84% and specificity between 60% and 90%. Due to the diversity of studies conducted in this area and the lack of a relevant review article, there is still not a good overview of the position of CGM in diagnosing CAD in patients with SIHD manifestations. Therefore, this meta-analysis aimed to investigate the value of CGM in diagnosing CAD patients with suspected SIHD based on angiography findings.

Methods

Protocol: This study was a systematic review and meta-analysis conducted in accordance with the principles set in the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement 2018.

Eligibility criteria and study selection: Inclusion criteria were: 1) angiography reference standard for CAD diagnosis (angiographically defined CAD); 2) sufficient information including at least a report of sensitivity and specificity for CGM; and 3) available sample size in both groups with and without CAD. Studies conducted on the patients with another diagnosis such as acute coronary syndrome and left bundle branch block (LBBB), or CGM in a non-resting state were excluded from the review article. Furthermore, articles that had no full text or had been published in the abstract format were also excluded. These articles were independently reviewed by two assessors to ensure full compliance with the study inclusion and exclusion criteria and were discussed and revised if disagreements arose.

Information sources and search: Databases including MEDLINE/PubMed, Scopus, Thomson Reuters’ Web of Science, the Cochrane Library, and Google Scholar, were searched since inception until May 2018 using the following keywords: “Coronary artery disease, Diagnostic Techniques and Procedures, Depolarization-repolarization variability, Cardiogoniometry, Myocardial Ischemia, Myocardial Infarction, Vectorcardiography, Coronary Angiography; Electrocardiography, Electrodiagnosis, Acute Coronary Syndrome, Angina, Stable, Non-Invasive Techniques (Elasticity Imaging Techniques), and Coronary Stenosis”. After finding the articles on the basis of searches in the databases, their abstracts and titles were reviewed, and then the articles unrelated in content were excluded. Next, the full text of the related articles was studied and the data were extracted. Also, the references of all included articles found were also reviewed in order to identify any relevant articles. No language restrictions were considered for the reviewed articles.

Data collection process: The required information from the articles was collected using a data extraction table, containing the first author’s name, year of publication, study nation, type of study design, reference standard and index tests for CAD diagnosis, sample size, mean age of the subjects studied, frequency distribution of gender, and the study outcomes including sensitivity, specificity, positive predictive value, and negative predictive value. This table was completed by the first author and checked by the second one for verifying.

Quality assessment: QUADAS-2 was used to assess the quality of eligible studies in two issues of “risk of bias” and “applicability”.

Summary measures and synthesis of results: The PRISMA declaration was followed for statistical analysis. Q statistics of the chi-square value test and I² index (inconsistency index) were used to evaluate the heterogeneity of individual studies contributing to the pooled estimate. I² > 50% suggested heterogeneity. P < 0.05 was considered statistically significant, suggesting the presence of heterogeneity. In the case of heterogeneity, a random effects model was used. One of the primary causes of heterogeneity in test accuracy studies is the threshold effect, which arises when differences in sensitivities and specificities or likelihood ratios (LHRs) occur due to different cut-offs or thresholds used in different studies to define a positive (or negative) test result. The presence of the threshold effect was evaluated with the typical pattern of “shoulder-arm” plot in a summary receiver operating characteristic (SROC) space. Moreover, in cases where there was a threshold effect, we expected a strong positive correlation between the logit of sensitivity and logit of 1-specificity. Probable sources of heterogeneity through the studies were explored using meta-regression and subgroup analysis. The probability of publication bias was evaluated through the Egger regression test and funnel plots. The funnel plots exhibit a graphical representation of possible publication bias so that any asymmetry in the
plot can represent publication bias, and Egger’s regression is also the statistical counterpart of this asymmetry.

The overall performance of CGM was reported using the SROC curve, calculating the area under the curve (AUC), and Q statistic of chi-square. The SROC curve expresses the overall performance of the test, and closer to the number 1 of AUC indicates a better test performance. Q is also a point on the SROC, with the sensitivity and specificity equal at that point, and a higher Q value represents a better test performance. Statistical analysis was performed using Meta-DiSc version 1.4.24) Publication bias analysis was performed using Comprehensive Meta-analysis version 2.

Results

Study selection: A total of 61 abstracts were retrieved in databases and manual cross-checking of reference lists (Figure 1). Thirty-two articles were omitted after reviewing the title and abstract, so the full texts of the remaining 29 articles were studied in detail. After reading the full texts, 19 of the articles were excluded. Finally, the findings of the 11 studies in 10 articles were enrolled in the meta-analysis (Figure 1). One study had two different subgroups of patients and each subgroup was considered as a separate study. Additionally, Seeck, et al. had reported the diagnostic value of CGM based on two different methods in the same population, so only the better results for CGM were selected.

Excluded studies: Nineteen studies were excluded after reviewing the original text for the following reasons: The population of the study was other than candidates for elective angiography (n = 6), including Poorzand, et al. in patients with psoriasis, Spiliopoulos, et al. in patients who received a heart transplant, Tölg, et al. and Khamis, et al. in patients with acute coronary syndrome, Herrmann, et al. in patients with left bundle branch block (LBBB); lack of reporting required diagnostic value parameters that could be used to construct or calculate true positive (TP), false positive (FP), true negative (TN), and false negative (FN) results (n = 4); different types of articles including case reports, narrative reviews or congress abstracts with insufficient diagnostic parameters (n =
Weber, et al. noted that other than CAD stenosis in angiography (significant coronary stenosis;45) however, the primary aim of this study was to assess the ability of CGM to detect physiologically significant coronary stenosis defined by fractional flow reserve (FFR).

**Study characteristics:** This study was performed on 2461 patients (1330 CAD, 1131 non-CAD) with a mean age of 63.1 ± 2.8 years. Main coronary artery stenosis over 50% was considered as significant stenosis in the majority of studies, and stenosis over 70%12,17 and 75%20 was defined as significant stenosis in 3 others. Only Seeck, et al.15 reported no definition of coronary artery stenosis based on angiography. The lowest sample size was 48,13 and the largest one was Huebner16 with 658 patients. The first article was published in 1983,15 and the latest published articles were published in 2017.18,20 (Table I) Moreover, the methods of CAD diagnosis based on CGM were also different among the studies and included automated interpretation,13,20,21,22 diagnostic score,14 deviation from mean normal values,12,13 and other specified methods.15,16

**Results of individual studies:** The sensitivity and specificity were reported in all studies. The highest reported sensitivity for CGM in CAD was 84%17,33 and the highest specificity was 90%.13,33 Also, the lowest reported sensitivity and specificity were 39%20 and 60%,18 respectively. The positive predictive value (29% to 88%) and negative predictive value (58% to 89%) were reported in only 5 articles.13,15,17,19,20 CGM accuracy was also reported in 5 papers13,15,17,19,20 with the highest value of 86%15 and the lowest value of 64%.18 (Table I)

**Quality assessment:** The studies in the current meta-analysis were not of the same quality. (Figure 2) All the studies have the same target population. However, there were some differences in the inclusion criteria of 3 studies.12,13,19 Although most of the studies had consecutive recruitment, one study had a random sampling method,18 and in one study it was not reported apparently.19 A case-control approach was not used in any of the studies. Index test and reference standard blinding were reported in all of the studies but one.19 The diagnostic criteria based on the reference standard were somehow different in 3 studies, using 70-75% of stenosis instead of 50% as the definition of CAD.12,19,20 Risk of Bias was acceptable among our included studies, where only two articles were considered high risk in the domains of “patient selection”19 and “follow and timing”.20 However, 3 different studies12,19,20 in the domain of “reference standard”, as well as two different studies in the domains of “patient selection”19 and “index test”18 were assessed to have a high risk of applicability concerns.

**Synthesis of results:** Overall pooled sensitivity was 71.7% (69.1 to 74.1; Cochrane Q = 39.5; P < 0.00001; F = 77.3%), and pooled specificity was 78.8% (76.3 to 81.1; Cochrane Q = 37.39; P < 0.00001; F = 75.9%) (Figure 3). SROC analysis showed an AUC of 0.81 and Q* of 0.75. Pooled negative LHR was reported to be 0.37 (0.28 to 0.48; Cochrane Q = 60.79; P < 0.00001; F = 85.2%), and 3.12 for positive LHR (2.27 to 4.29; Cochrane Q = 52.7; P < 0.00001; F = 82.9%) (Figure 4). Lastly, the diagnostic odd ratio (OR) was calculated to be 8.70 (4.99 to 15.17; Cochrane Q = 57.48; P < 0.00001; F = 84.3%) (Figure 5).

**Heterogeneity assessment and publication bias:** Considering the Q statistic of the chi-square value test and P index > 50%, there were possible sources of heterogeneity among studies. So, probable sources of heterogeneity were explored by using meta-regression and subgroup analysis with the following covariates: diagnosis of CAD based on % stenosis in angiography; year of publication; location of study; and method of CAD diagnosis based on CGM (Table II). Moreover, according to the points’ pattern in ROC space plot, we did not find “shoulder-arm” shape, indicating the possibility of the threshold effect (Spearman correlation coefficient = −0.527, P = 0.117; Figure 6). Regarding Egger’s regression test (P = 0.943), there was no published bias in the studies.

**Discussion**

**Summary of evidence:** The present meta-analysis aimed to determine the diagnostic value of CGM in detecting CAD in patients with suspected SIHD. Our findings demonstrated that the CGM is a tool with overall high specificity (79%) and relatively high sensitivity (72%) from 10 studies. The specificity is used to rule in the disease, and the sensitivity is used to rule out the disease.46 Theoretically, if the result of a test with high specificity is positive, that person will most likely have a tested disease; while if the result of a test with high sensitivity is negative, that person most likely will not have a tested disease.46 In our study, the specificity and sensitivity of CGM were approximately 80% and 70%, respectively, which seems acceptable for a cardiac diagnostic test. These findings may indicate that a negative result of the CGM will not be a definite rejection and a positive result will not be a definite verification in CAD detection. In fact, we also did not expect a 100% specificity and sensitivity of CGM, since this tool was not supposed to be the replacement of angiography. Moreover, even considering this amount of sensitivity, the CGM can be a useful tool for exploring the likelihood of the CAD along with other diagnostic measures, and it can find a new position among existing instruments. The sensitivity and specificity of other diagnostic tests also indicate that the simultaneous sensitivity and specificity of a non-invasive cardiac diagnostic test have not been reported more than 80-90%, except in individual cases, even in the ideal conditions and despite applying large quantities of contrast agents and radiation.47 This means that there is no diagnostic test with high sensitivity and specificity simultaneously close to 100% since in this case, it will become a diagnostic gold standard.

Positive and negative LHRs are considered as essential characteristics of a diagnostic test contributing to rule in or out the presence of a disease in a person. In our study, the positive likelihood ratio was reported to be close to 3.5, which is approximately equal to that reported
### Table 1. The Characteristics of Included Studies

| Study               | Location     | Total, n (CAD / non-CAD) | Diagnostic Criteria $^1$ | Sensitivity | Specificity | Male, n | Main Inclusion Criteria                                                                 | Main Exclusion Criteria                                                                 |
|---------------------|--------------|--------------------------|--------------------------|-------------|-------------|---------|------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|
| Saner, 1983 (12)    | Switzerland  | 50 (39/11)               | > 70%                    | 79%         | 81%         | N/A     | Sinus rhythm, absence of left bundle branch block (BBB), left ventricular (LV) hypertrophy, or digits induced ST-T changes | Not reported                                                                             |
| Meier, 1987 (13)    | Switzerland  | 48 (39/9)                | > 50%                    | 63%         | 67%         | 41      | 30 < age < 65 years, absence of: angina at rest, LV failure, cardiomyopathy, valvular lesions, LV hypertrophy, digits treatment, frequent ventricular premature complexes or BBB | Technical problems for CGM$^*$ measurements                                               |
| Schipbach (Retro$^*$), 2008 (14) | Switzerland | 461 (264/197)            | > 50%                    | 73%         | 87%         | 307     | Not reported                                                                             | Atrial fibrillation (AF), left BBB, valvular heart disease, previous cardiac surgery     |
| Schipbach (Pros$^*$), 2008 (14) | Switzerland | 332 (207/125)            | > 50%                    | 64%         | 82%         | 216     | Not reported                                                                             | Same as above                                                                            |
| Seeck, 2008 (15)    | Germany      | 109 (47/62)              | N/A                      | 81%         | 90%         | 0       | Not reported                                                                             | Not reported                                                                             |
| Huebner, 2010 (16)  | Switzerland  | 658 (405/253)            | > 50%                    | 72%         | 76%         | 432     | Not reported                                                                             | Atrial fibrillation (AF), left BBB, severe valvular heart disease, previous cardiac interventions or myocardial infarction |
| Ghadrdoost, 2015 (17)| Iran         | 390 (127/263)            | > 70%$^*$                | 84%         | 81%         | 316     | Not reported                                                                             | Same as above                                                                            |
| Seyedian, 2016 (18) | Iran         | 190 (130/60)             | > 50%                    | 73%         | 60%         | 107     | Not reported                                                                             | Acute coronary syndromes (ACS)                                                           |
| Zeljković, 2017 (19)| Croatia      | 114 (32/82)              | > 70%                    | 75%         | 74%         | 0       | 18 < age < 85 without angina symptoms at rest and ECG without signs of ischemia, and normal cardioselective enzymes | Angina symptoms, known CAD, ACS, left BBB, cardiac arrhythmia, previous cardiothoracic surgery, congenital heart disease, valvular disease, renal failure grade III, COPD, life-expectancy of less than 1 year, anemia, alcohol and/or drug addiction, urgent state, pregnant women |
| Weber, 2017 (20)    | Germany      | 109 (31/78)              | >75%                     | 39%         | 63%         | 67      | Symptoms of stable angina pectoris or a positive exercise ECG result with preserved systolic function | Previous CAD, renal insufficiency, or the inability to undergo physical stress            |

$^*$ Retro: Retrospective study, and Pros: Prospective study; $^1$ Coronary artery disease; $^1$ Diagnostic criteria for CAD (Stenosis %); $^*$CGM: Cardiogoniometry. Note 1: All studies' target populations were patients suspected with stable ischemic heart disease referred for elective coronary angiography. Note 2: Angiography was the only reference standard and cardiogoniometry was the only index test.
by other diagnostic tests, except for CT angiography.\textsuperscript{37-40} Therefore, considering the positive LHR in addition to the high specificity, we believe that the CGM is a tool whose abnormal findings can be at least equal to other available diagnostic methods for CAD risk-assessment. Additionally, the negative LHR was close to 0.3, which is approximately equal to the reported amount of stress echocardiography and slightly more than other diagnostic measures.\textsuperscript{16,47-49} Therefore, by referring to the definitions of positive and negative LHR, it can be concluded that CGM is a tool whose positive findings based on the presence of CAD are more valuable than its negative findings based
on the absence of disease, a fact which is a very important issue for a CAD screening test for patients with suspected SIHD.

Causes of heterogeneity: The essential requirement for simple pooling of each of the diagnostic parameters including overall specificities and sensitivities, in addition to positive and negative LHRs, is the homogeneity of the studies’ results; an issue which was not established in our statistical pooling. Therefore, it was necessary to explore the possible source of heterogeneity to evaluate the suitability of statistical pooling of accuracy estimates from different studies. First of all, we evaluated the threshold effect; which was not present in our study. We attempted to explore the heterogeneity sources in other factors than the threshold effect. We performed meta-regression and subgroup analysis on factors that can cause variations in accuracy estimates through a variety of test accuracy studies in our review. However, we were restricted to choose a variety of possible factors, since the available data in the published articles were too low. We assumed the diagnostic criteria for angiographically defined CAD, methods of CAD diagnosis based on CGM, the location of studies, and the year of publication as the possible sources. Although subgroup analysis showed a lower I^2 in studies published before 2000 seconds, which considered abnormal CGM results based on an angle deviation of more than two standard deviations from a mean value obtained previously from 100 healthy volunteers, no other subgroups showed a homogeneity.

Although no sources of heterogeneity were found with our analysis by using meta-regression and subgroup analysis, we believe that one of the most important causes of heterogeneity might be the pre-test probability of having CAD on angiography. However, the baseline characteristics were inadequately reported in studies to explore the role of pre-test probability as a source of heterogeneity in this meta-analysis. Moreover, the CGM diagnostic value in detecting the CAD may vary depending on the type of coronary vessel involved. Also, the presence of ventricular hypertrophy, bundle branch block, atrial fibrillation, and previous myocardial infarction (MI) seem to be the other items inducing the heterogeneity; however, in
few studies, they were excluded. Another possible cause of the heterogeneity in studies is the differences in non-CAD groups among different studies, and other comorbidities in patients with CAD. In the majority of studies, the non-CAD group did not include “truly healthy individuals.”

**CGM versus other non-invasive tests:** Reported values of sensitivity and specificity for the CGM as a screening tool in detecting CAD are noticeable when compared with the diagnostic features of the current screening tools in detecting CAD in patients with suspected SIHD. Among non-invasive cardiac functional tests, exercise ECG is the cheapest and most accessible intervention. Although this test is most often used as the first diagnostic procedure, it is subject to restrictions because of the inability to exercise to obtain exercise ECG in all patients, and due to false positive changes in the ST segment after taking drugs like digoxin. Also, the presence of some baseline ECG abnormalities, such as left bundle branch block (LBBB) and depolarization abnormalities of left ventricular hypertrophy, makes it impossible to analyze the exercise ECG in all subjects. Interestingly, exercise ECG, as a method of vectorography, is one of the most important criteria in deciding to nominate patients for angiography in many treatment centers, with a sensitivity and specificity of 62% and 68% in patients with suspected CAD. So the reported sensitivity and specificity of CGM in our meta-analysis showed a higher sensitivity and specificity of about 10% in comparison with exercise ECG. Additionally, the sensitivity and specificity of the stress echocardiography have been reported respectively to be 85% and 77%, which are somehow comparable with CGM; however, due to the low-quality and operator-dependent images, the use of stress echocardiography is not on the rise. Although there are more non-invasive diagnostic tools such as positron emission tomography (PET), SPECT, and Cardiac MRI, their application has also been restricted due to the limited availability, high

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**Table II.** Predefined Subgroup Analysis of Indices (with 95% Confidence Intervals) and Subsequent Meta-Regression on Diagnostic Odds Ratio (DOR) of Cardiogoniometry

| Subgroups                                      | No. of studies | Sensitivity pooled | Specificity pooled | DOR pooled | I² (%) | RDOR       | P       |
|------------------------------------------------|----------------|--------------------|--------------------|------------|--------|------------|---------|
| **Study location**                             |                |                    |                    |            |        |            |         |
| Europe                                         | 8              | 70.0 (67.1-72.7)    | 79.5 (76.5-82.2)    | 8.409      | 83.1   | 1.28 (0.06;27.72) | 0.852   |
| Non-Europe                                     | 2              | 78.6 (73.1-83.5)    | 77.1 (72.1-81.6)    | 9.702      | 93.5   |            |         |
| **% Stenosis for CAD diagnosis in coronary angiography** |                |                    |                    |            |        |            |         |
| 50%                                            | 6              | 70.7 (67.8-73.4)    | 78.4 (75.2-81.3)    | 8.106      | 66.6   | 1.46 (0.24;8.76) | 0.630   |
| Other                                          | 4              | 75.9 (70.1-81.0)    | 79.5 (75.2-83.3)    | 11.314     | 92.8   |            |         |
| **Year of publication**                        |                |                    |                    |            |        |            |         |
| Before 2000s                                   | 2              | 71.8 (60.5-81.4)    | 75.0 (50.9-91.3)    | 7.511      | 45.1   | 1.18 (0.10;13.98) | 0.878   |
| After 2000s                                    | 8              | 71.6 (69.1-74.1)    | 78.9 (76.3-81.2)    | 8.887      | 87.4   |            |         |
| **Method of CGM**                              |                |                    |                    |            |        |            |         |
| Automated interpretation                       | 4              | 73.6 (68.4-78.2)    | 74.7 (70.5-78.5)    | 5.610      | 92.2   | 1.62 (0.79;3.35) | 0.158   |
| Diagnostic score                               | 2              | 69.0 (64.6-73.2)    | 84.8 (80.4-88.6)    | 11.947     | 79.5   |            |         |
| Deviation from mean normal values              | 2              | 71.8 (60.5-81.4)    | 75.0 (50.9-91.3)    | 7.511      | 45.1   |            |         |
| Others                                         | 2              | 73.0 (68.7-77.0)    | 79.0 (74.1-83.4)    | 16.501     |        |            |         |

DOR indicates diagnostic odds ratio; RDOR, relative diagnostic odds ratio; and I², inconsistency value.
cost, need for exposure to radiation, and technical restrictions, especially when using pharmacologic stress agents. Among non-invasive anatomical tests, CT coronary angiography, despite the disadvantages associated with and without irradiation and contrast media, has shown a specificity of 64%-83% in detecting CAD that is roughly equivalent to that determined by CGM in our study. Interestingly, except for exercise ECG as mentioned earlier, the review of other non-invasive diagnostic methods reveals that the reported specificity of CGM is about 40% higher than coronary artery calcium scoring (CACS), and is almost equivalent to the specificity of SPECT and CT angiography; and its sensitivity is almost equal to Stress MRI and SPECT.

Although many patients are admitted for elective coronary angiography to check for the presence or absence of CAD, “no significant CAD” is the final report of around 45% of them (within the range of 0-77%). This means that around half of the patients with suspected SIHD who undergo elective angiography have merely tolerated potential risks and complications such as contrast-induced nephropathy without any clinical benefit. Therefore, one of the leading concerns in the management of ISHD patients is the attempt to find more criteria based on non-invasive diagnostic tools, like what we attempted to do, toward a better decision-making strategy for the possibility of coronary stenosis.

Comparison with other meta-analysis: This was the first meta-analysis on the diagnostic value of CGM in detecting CAD in people with suspected SIHD and who are candidates for elective angiography. Hence, its findings can be useful in determining the approach of physicians compared to this non-invasive modality. No other meta-analysis has yet examined the effectiveness of CGM in detecting CAD or other diseases. Therefore, the findings of this meta-analysis are incomparable to another review study.

Study limitations: Due to the presence of numerous inclusion and exclusion criteria, many studies were not included in our final analysis, resulting in a narrower range of investigated samples. Also, all studies had an observational design, which itself has no high position among the valuable pyramid of studies. Most of the studies had a single-center design and small sample size. Another limitation in the studies was the presence of referral bias so that all patients had been referred to a particular treatment center for cardiac assessments. Several factors such as age, anthropometric status, and their cardiac risk assessment could be useful in the determination of CAD prevalence and possibly CGM, but we failed to consider their effect on the final analysis in this study due to the inadequate reporting of these variables in all studies. Lastly, due to the novelty of CGM, the number of high-quality studies investigating its value in CAD diagnosis is still limited; so the number of included studies in this meta-analysis was also limited.
Conclusions

Implications for future research: Further studies with a high quality of methodology are still needed to assess the diagnostic value of CGM for CAD in patients with suspected SIHD. Moreover, this hypothesis that there is a relationship between the CGM accuracy and the type of involved coronary artery should be evaluated in other studies. The majority of previous studies examined the diagnostic value of CGM in detecting CAD in patients with suspected SIHD, and limited studies examined the value of CGM in detecting coronary artery stenosis in patients with acute coronary syndrome manifestations.

Application of study findings for clinical practitioners: According to the results of this meta-analysis, CGM seems to be a non-invasive, easy-to-use, and risk-free action that can be used to detect stable CAD; however, further studies are needed for a better understanding about its real accuracy. CGM can be applied as a part of the diagnostic algorithm for the screening of patients with suspected SIHD, especially those with contraindications for stress tests. All the efforts of this study have been driven to introduce the capabilities of a new diagnostic approach to increase the decision-making accuracy of selecting candidates among patients with suspected SIHD for angiography. Our suggestion to physicians, especially those who are active in areas with fewer facilities, is to use CGM along with physical examination, history taking, and exercise tests for a better risk assessment to nominate patients for elective angiography.

Disclosure

Conflicts of interest: None.

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