12-year Temporal Trend in Referral Pattern and Test Results of Stress Echocardiography in a Tertiary Care Referral Center with Moderate Volume Activities and Cath-lab Facility

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Abstract

Background: Data on stress echocardiography (SE) time-related changes in referral patterns and diagnostic yield for detection of inducible ischemia could enhance Echo Lab quality benchmarks and performance measures. Aim: This study aims to evaluate temporal trends in SE test results among ambulatory patients with suspected or known coronary artery disease (CAD) in a tertiary care referral center with moderate (>100/year) volume SE activities and Cath-Lab facility. Methods: From January 2004 to December 2015, 1954 patients (mean age 62 ± 12 years, 42% women, 27% with known CAD) underwent SE (1673 exercise SE, 86%, 246 pharmacological SE, 12%, 35 pacing SE, 2%). Time was grouped into three 4 year periods, where clinical data and test results were evaluated. Results: Our series comprised low-to-intermediate pretest probability of CAD throughout the observation period (overall pretest probability of CAD 19% ± 15%). A progressive decline over time in the rate of pharmacological SE instead of a dramatic increment of exercise SE (79%–96%, \( P < 0.0001 \)) was noted. The use of beta-blockers increased (from 43% to 66%, \( P < 0.0001 \)), while the use of nitrates decreased (from 11% to 4%, \( P < 0.0001 \)) over time. We noted a very uncommon occurrence of abnormal test results with a further decrease in the last period (from 11% to 3%, \( P < 0.0001 \)). Conclusions: We observed, over a 12-year period, a progressive decrease in the frequency of inducible myocardial ischemia among patients with known or suspected CAD referred to our Echo Lab for SE with Cath-Lab facility, and this trend was parallel to changes in SE referral practice. These findings are particularly relevant if we consider the practical implications on diagnostic SE accuracy and risk assessment.

Keywords: Coronary artery disease, myocardial ischemia, stress echocardiography

Introduction

The most common sequence of events for evaluating patients with known or suspected coronary artery disease (CAD) is to perform a “gatekeeper” test followed by invasive coronary angiography in case of positive results of gatekeeper tests. However, only less than half of patients who undergo invasive coronary angiography for diagnostic purposes actually show obstructive CAD.[1]

Exercise electrocardiography (ECG) is currently the preferred test for evaluation of low-risk patients with atypical chest pain symptoms. Nonetheless, inconclusive results (due to equivocal ECG changes or discordance between symptoms and test results) limit the diagnostic ability of this noninvasive test.[2]

Stress echocardiography (SE) is a well-validated test that can diagnose the presence of obstructive CAD by visualizing stress-induced wall motion abnormalities, particularly in patients with an intermediate pretest probability of CAD.[3,4]

However, few data are available regarding time-related changes in referral patterns and diagnostic yield of SE for the detection of obstructive CAD. This information is clinically important since CAD mortality has decreased significantly over the last decades,[5] attributed to improved treatment and care of patients with CAD including wider availability of coronary angiography[1] and extensive use of invasive management.[7]

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Considering the simultaneous dramatic increase in the use of cardiac testing over time,\[8-10\] the diagnostic yield may have been reduced progressively in recent years influencing the clinical use of SE currently considered a useful “gatekeeper free-radiographic imaging and easy fruible technique test” and enhancing its high negative predictive value in low-risk patients with low pretest probability of CAD.\[11,12\] Therefore, we thought to evaluate the temporal trends in the use of SE in our area of reference among patients with suspected CAD with the aim of enhancing the echocardiography laboratory quality benchmarks and performance measure. Moreover, we analyzed our practice as measured by the prevalence of positive SE and the associations among clinical risk factors.

**Methods**

**Patients**

Using the retrospective Modena University Hospital Cardiovascular Echocardiography Laboratory Database, we identified all ambulatory patients who underwent SE. Between January 2004 and December 2015, a total of 1954 SE were performed in our unit, including 1673 exercise stress echocardiography (ESE) (86%) and 246 pharmacological stress tests (12%). The 12-year period was divided into three 4-year periods, where changes in demographics, clinical data, symptoms, and results of the tests across the different time periods were evaluated.

**Clinical variables**

Demographics, clinical data, and stress testing results were entered in our database prospectively. A history of CAD was defined as previous myocardial infarction, previous coronary revascularization, or prior angiographic documentation of any ≥50% coronary stenosis. Chest pain was classified as typical angina, atypical/probable angina, and nonischemic chest pain as previously described.

**Stress echocardiography**

Stress echo tests were performed according to the well-established protocols.\[3,4\] When possible, peak supine bicycle ESE was performed with patients who were not taking antiangina therapy. The exercise test was conducted with a variable load supine bicycle ergometer (Ergometrics 900 EL, Ergoline, Bitz, Germany) on a reclining seat at a 50° position to obtain the best echo windows for imaging. After recording a resting 2-dimensional echocardiogram from the standard views, patients pedalled at constant speed beginning at a workload of 25–50 W and increasing by 25W every 3 min. Two-dimensional images were obtained in four standard views (parasternal long-axis, parasternal short-axis, apical 4- and 2-chamber view) using Acuson Sequoia ultrasound systems (Mountain View, California, USA) in the supine position at baseline, at each workload and during the recovery phase, and recorded using a quad-screen cine-loop system. During each stage of exercise and recovery, symptoms (chest pain, shortness of breath, fatigue), blood pressure, heart rate, cardiac rhythm, a 12-lead ECG, and workload were recorded on the computerized database. Blood pressure, heart rate, cardiac rhythm, a 12-lead ECG, and workload were recorded on the computerized database.

Pharmacological SE tests were performed using dobutamine (up to 40 µg/kg/min with coadministration of atropine up to 1 mg) or dipyridamole (up to 0.84 mg over 10 min with coadministration of atropine up to 1 mg, or up to 0.84 mg over 6 min). Echocardiographic images were semiquantitatively assessed using a 16-segment, 4-point scale model of the left ventricle.\[13\]

A wall motion score index (WMSI) was derived by dividing the sum of individual segment scores by the number of interpretable segments. Ischemia was defined as stress-induced new and/or worsening of preexisting wall motion abnormality or biphasic response (i.e., low-dose improvement followed by high-dose deterioration). Resting hypokinesis that remained unchanged or improved at peak stress was considered a negative test. Necrotic pattern was akinetic or dyskinetic myocardium with no thickening during stress. Hypokinesis at rest was not considered scar. A test was considered abnormal in the case of inducible ischemia or necrotic pattern and normal in the case of no rest and stress wall motion abnormality.

Tests were supervised by specialist physicians.

**Clinical data**

Patients’ demographic and clinical characteristics including age, gender, cardiac risk factors, cardiovascular medications, and data were recorded at the time of supine bicycle ESE. Cardiac risk factors included current smoking or history of smoking, arterial hypertension (defined as untreated systolic blood pressure (BP) >140 mmHg or diastolic BP >90 mmHg or receiving anti-hypertension medication); diabetes mellitus (defined as fasting glucose ≥120 mg/dl or receiving medication for hyperglycemia); dyslipidemia (defined as total cholesterol >210 mg/dl, or LDL >130 mg/dl, or HDL <35 mg/dl or receiving medication for lipid control).

We used the CAD consortium scoring for determining the pretest likelihood of disease. This approach is also suggested by current North-American and European guidelines for tailoring the more appropriate stress testing approach in the individual patient with suspected CAD.\[6,14\]

**Statistical analysis**

Results were presented as mean ± SD for continuous variables and percentages for categorical variables. Patients were grouped according to three 4-year periods and compared with the use of the two-sided Student’s t-test for continuous variables, Wilcoxon rank-sum test for ordinal variables, the Chi-square for categorical variables, or Fisher’s exact tests for categorical variables when ≥1 cells have an expected frequency of ≤5. All tests were two-tailed. P < 0.05 was considered statistically significant. Analyses were performed using JMP version 9.0.1 (SAS Institute Inc., Cary, NC, USA).
Table 1: All cohort demographic and clinical data

| Characteristics    | 2004/2007 (n=847), n (%) | 2008/2011 (n=584), n (%) | 2012/2015 (n=523), n (%) | Total (n=1954), n (%) | P     | n     |
|--------------------|--------------------------|--------------------------|--------------------------|-----------------------|-------|-------|
| Age                | 62±12                    | 62±12                    | 62±11                    | 62±12                 | 0.7   | 1954  |
| Female sex         | 327 (39)                 | 256 (44)                 | 233 (45)                 | 816 (42)              | 0.04  | 1954  |
| Pretest probability of CAD (%) | 18±14                    | 20±15                    | 21±16                    | 19±15                 | 0.002 | 1954  |
| Indication         |                          |                          |                          |                       |       |       |
| CAD                | 249 (29)                 | 154 (26)                 | 133 (25)                 | 536 (27)              | 0.2   | 1954  |
| Suspected CAD      | 585 (69)                 | 412 (71)                 | 358 (68)                 | 1355 (69)             | 0.7   | 1954  |
| Dyspnea            | 13 (2)                   | 18 (3)                   | 31 (6)                   | 62 (3)                | <0.0001 | 1954 |
| Therapy            |                          |                          |                          |                       |       |       |
| Beta-blockers      | 248 (43)                 | 232 (62)                 | 211 (66)                 | 691 (54)              | <0.0001 | 1271*|
| Nitrates           | 74 (11)                  | 37 (71)                  | 22 (4)                   | 133 (8)               | <0.0001 | 1766*|
| Ca-channel blockers| 103 (21)                 | 81 (21)                  | 62 (20)                  | 246 (21)              | 0.8   | 1189* |
| Risk factors       |                          |                          |                          |                       |       |       |
| Smoke (current or previous) | 92 (11)                 | 100 (17)                 | 120 (23)                 | 312 (16)              | <0.0001 | 1954 |
| Diabetes mellitus  | 90 (11)                  | 87 (15)                  | 96 (18)                  | 273 (14)              | 0.0002 | 1954  |
| Dyslipidemia       | 239 (28)                 | 234 (40)                 | 260 (50)                 | 733 (38)              | <0.0001 | 1954 |
| Hypertension       | 416 (49)                 | 343 (59)                 | 324 (62)                 | 1083 (55)             | <0.0001 | 1954 |
| Family history of CAD | 58 (7)                  | 72 (12)                  | 86 (16)                  | 216 (11)              | <0.0001 | 1954 |
| Previous exercise ECG stress test: Doubt result | 82 (10)                  | 116 (20)                 | 249 (48)                 | 447 (23)              | <0.0001 | 1954 |

*In case of missing variables the N reported at the column heading is not applicable, the total is shown at the end of the table. CAD=Coronary artery disease, ECG=Electrocardiography

**RESULTS**

**Changes in stress echocardiography referral pattern**

Table 1 and show the demographic, clinical, and SE characteristics of the whole cohort of 1954 patients and of the three 4-year time groups’ patients. From the periods 2004–2007 to 2012–2015, we observed a gradual increase in the proportion of females (39%–42%, P = 0.04) with no change in the mean age (62 ± 12 years, P = 0.7). Classical risk factors and pretest probability of CAD progressively increased over time. Of note, our series comprised low-to-intermediate pretest probability of CAD throughout the observation period (overall pretest probability of CAD 19%±15%). The most frequent indication to SE in our series was suspected CAD (69%), followed by known CAD (27%) and these indications remained stable over time (all P > 0.2), whereas the indication for evaluating dyspnea increased significantly over time (from 2% to 6%, P < 0.0001). The prevalence of patients with a previous inconclusive result exercise ECG stress test dramatically raised (from 10% to 48%, P < 0.0001).

Regarding cardiovascular medications, in our series of patients, the use of beta-blockers increased (from 43% to 66%, P < 0.0001), while the use of nitrates decreased (from 11% to 4%, P < 0.0001) over time.

**Changes in stress echocardiography testing use and results**

A stark difference was noted in the stressor type used throughout the three 4-year periods: pharmacological SE significantly decreased from 18% to 3% (P < 0.0001), with a significant increase of exercise SE (from 79% to 96%, P < 0.0001), as shown in Table 2. This is accompanied by a significant increase in the double product (from 23075 ± 6156 to 24734 ± 5783, P < 0.0001). During the observed periods, we documented a gradual decrease in the frequency of myocardial ischemia detection by SE (from 11% to 3% respectively, P < 0.0001).

The same evidence emerged when the analysis was only addressed in the subgroup of patients undergoing exercise SE [Tables 3 and 4].

**DISCUSSION**

Over the last years, in our cohort of ambulatory patients referred for SE, we observed a progressive decline in the frequency of myocardial ischemia detection, implicating a very low diagnostic yield of SE. This decline in SE diagnostic yield occurred without significant changes in patients’ clinical and risk profile with the exception of an increased use of beta-blockers and decreased use of nitrates. Of note, this very uncommon occurrence of abnormal SE test results occurred in a population with low-to-moderate pretest probability of CAD throughout the study period.

We believe that our study cohort is representative of a current typical population undergoing SE in laboratories with Cath-Lab facility, and several explanations of this decline in SE diagnostic yield might account for the change in referral patterns, although substantially speculative as untestable in this study. Indeed, in these realities, it might be a reduction in the threshold for direct referral to coronary angiography without noninvasive testing.[1] On the other hand, clinicians frequently refer high-risk patients directly to invasive angiography rather than noninvasive testing.[15]
Another possible explanation is that increasing awareness of the limitations of exercise ECG may have led to a reduction in the threshold for referring patients to SE, as evidenced by the fact that in our population, the percentage of patients with a previous inconclusive exercise ECG has quadrupled in the last 4 years. In addition, the progressive acceptance of the policy to perform cardiac stress under anti-ischemic therapy may have masked ischemic response. In our cohort, the proportion of patients studied on beta-blockers increased from 43% in the first time period to 61% in the last 9 years). Even in this setting, there was a progressive decline over time in the rate of SE positivity from 42% (1983–1991) to 22% (2001–2009), with a relative increase of patients with low pretest probability of disease (from 5% to 27%). In accordance with our observations, the percentage of patients with prior myocardial infarction and noninterpretable electrocardiograms declined.[17]

Carpeggiani et al. in Italy expanded these findings in 2007 hospitalized patients without previous myocardial infarction or coronary revascularization who performed SE in a high-volume tertiary care referral center over a wider time window (from 1983 to 2009), with different forms of stress imaging (mostly pharmacological SE with dipyridamole). In our cohort, the proportion of patients studied on beta-blockers increased from 43% in the first time period to 66% in the last time period.

Our result corroborates the very low diagnostic yield already described for cardiac stress scintigraphy by Rozanski et al. in which the rates of ischemic studies dropped from 29.6% in 1991 to only 5% in 2009[16] and support recent findings which have demonstrated a marked decline in SE diagnostic performance over the last few years.[17,18]

A single-center Spanish cohort study of 12,339 outpatients referred for exercise SE between 1997 and 2012 observed a gradual decrease in the frequency of detection of myocardial ischemia from 35.3% in 1997–2000 to 25.4% in 2009–2012 (P < 0.001). There was also a progressive increase in the prevalence of cardiovascular risk factors, while the proportion of patients with prior myocardial infarction and noninterpretable electrocardiograms declined.[17]

Carpeggiani et al. in Italy expanded these findings in 2007 hospitalized patients without previous myocardial infarction or coronary revascularization who performed SE in a high-volume tertiary care referral center over a wider time window (from 1983 to 2009), with different forms of stress imaging (mostly pharmacological SE with dipyridamole). Even in this setting, there was a progressive decline over time in the rate of SE positivity from 42% (1983–1991) to 22% (2001–2009), with a relative increase of patients with low pretest probability of disease (from 5% to 27%). In accordance with our observations, the percentage of patients studied with SE under anti-ischemic therapy increased markedly (from 8% in the first time period to 61% in the last 9 years).[18]

In our center, the percentage of patients studied with pharmacological SE significantly decreased over time leaving...
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the place to a sharp increase in exercise SE, which is now being performed in almost all patients. Exercise SE is cheaper in general, it is quicker to perform and more tolerable than pharmacological SE. It is noteworthy that patients with a

| Table 3: ESE cohort demographic and clinical characteristics |
|-------------------------------------------------------------|
| **Characteristics**                                         | **2004/2007 (n=672), n (%)** | **2008/2011 (n=499), n (%)** | **2012/2015 (n=502), n (%)** | **Total (n=1673), n (%)** | **P** | **n** |
| Age                                                        | 60±12                         | 61±12                         | 62±11                         | 61±12                         | 0.02  | 1673  |
| Female                                                     | 243 (36)                      | 209 (42)                      | 216 (43)                      | 667 (40)                      | 0.03  | 1673  |
| Pretest probability of CAD (%)                             | 17±14                         | 19±15                         | 21±16                         | 19±15                         | 0.0002| 1673  |
| Indication                                                |                               |                               |                               |                               |       |       |
| CAD                                                        | 201 (30)                      | 129 (26)                      | 130 (26)                      | 460 (28)                      | 0.2   | 1673  |
| Suspected CAD                                              | 458 (68)                      | 352 (72)                      | 340 (68)                      | 1155 (69)                     | 0.3   | 1673  |
| Dyspnea                                                    | 13 (2)                        | 13 (3)                        | 31 (6)                        | 57 (3)                        | 0.0002| 1673  |
| Therapy                                                    |                               |                               |                               |                               |       |       |
| Beta-blockers                                              | 199 (44)                      | 202 (62)                      | 204 (66)                      | 605 (56)                      | <0.0001| 1088* |
| Nitrates                                                   | 44 (8)                        | 27 (6)                        | 19 (4)                        | 90 (6)                        | 0.02  | 1534* |
| Ca-channel blockers                                        | 76 (19)                       | 64 (20)                       | 58 (19)                       | 198 (19)                      | 0.9   | 1035* |
| Risk factors                                               |                               |                               |                               |                               |       |       |
| Smoke (current or previous)                                | 74 (11)                       | 82 (16)                       | 116 (23)                      | 272 (16)                      | <0.0001| 1673  |
| Diabetes mellitus                                          | 63 (9)                        | 62 (12)                       | 91 (18)                       | 216 (13)                      | <0.0001| 1673  |
| Dyslipidemia                                               | 204 (30)                      | 201 (40)                      | 248 (49)                      | 653 (39)                      | <0.0001| 1673  |
| Hypertension                                               | 321 (48)                      | 285 (57)                      | 308 (61)                      | 914 (55)                      | <0.0001| 1673  |
| Family history of CAD                                      | 49 (7)                        | 62 (12)                       | 84 (17)                       | 195 (12)                      | <0.0001| 1673  |
| Previous exercise ECG stress test: Doubt result            | 77 (11)                       | 112 (22)                      | 248 (49)                      | 437 (26)                      | <0.0001| 1673  |

*In case of missing variables, the N reported at the column heading is not applicable, the total is shown at the end of the table. CAD=Coronary artery disease, ECG=Electrocardiography, ESE=Exercise stress echocardiography

| Table 4: ESE cohort, SE characteristics                     |
|-------------------------------------------------------------|
| **Characteristics**                                         | **2004/2007 (n=672), n (%)** | **2008/2011 (n=499), n (%)** | **2012/2015 (n=502), n (%)** | **Total (n=1673), n (%)** | **P** | **n** |
| Symptoms                                                   | 101 (15)                      | 81 (16)                       | 60 (12)                       | 243 (15)                      | 0.1   | 1673  |
| Angor                                                      | 34 (5)                        | 17 (3)                        | 10 (2)                        | 61 (4)                        | 0.02  | 1673  |
| Atypical chest pain                                       | 27 (4)                        | 26 (5)                        | 19 (4)                        | 72 (4)                        | 0.5   | 1673  |
| Dyspnea                                                   | 29 (4)                        | 29 (6)                        | 23 (5)                        | 81 (5)                        | 0.5   | 1673  |
| Other symptoms                                             | 15 (2)                        | 14 (3)                        | 10 (2)                        | 39 (2)                        | 0.6   | 1673  |
| Inducible ischemia                                         |                               |                               |                               |                               |       |       |
| Negative                                                  | 579 (86)                      | 459 (92)                      | 481 (96)                      | 1519 (91)                     | <0.0001| 1673  |
| Positive                                                  | 79 (12)                       | 24 (5)                        | 16 (3)                        | 119 (7)                       |       | 1673  |
| Doubt                                                      | 14 (2)                        | 16 (3)                        | 5 (1)                         | 35 (2)                        |       | 1673  |
| LVEF (%)                                                   |                               |                               |                               |                               |       |       |
| Rest                                                       | 57±6                          | 57±6                          | 57±6                          | 57±6                          | 0.3   | 1564* |
| Peak of exercise                                          | 66±11                         | 69±9                          | 71±9                          | 69±10                         | <0.0001| 1312* |
| WMSI                                                       |                               |                               |                               |                               |       |       |
| Rest                                                       | 1.06±0.90                     | 1.07±0.22                     | 1.05±0.17                     | 1.06±0.19                     | 0.1   | 1673  |
| Peak of exercise                                          | 1.08±0.21                     | 1.07±0.22                     | 1.05±0.20                     | 1.07±0.21                     | 0.05  | 1673  |
| BP (mmHg) peak of exercise                                 |                               |                               |                               |                               |       |       |
| Systolic                                                   | 186±25                        | 190±25                        | 194±26                        | 189±25                        | <0.0001| 1617* |
| Diastolic                                                  | 89±11                         | 92±13                         | 94±12                         | 92±12                         | <0.0001| 1617* |
| Double product                                             | 24424±5687                    | 24268±5579                    | 25050±5580                    | 24568±5623                    | 0.07  | 1615* |
| Interruption reason                                        |                               |                               |                               |                               |       |       |
| Fatigue                                                    | 352 (66)                      | 331 (82)                      | 415 (88)                      | 1098 (78)                     | <0.0001| 1409* |
| High blood pressure                                        | 15 (3)                        | 14 (3)                        | 14 (3)                        | 43 (3)                        | 0.8   | 1409* |
| Chest pain                                                 | 11 (2)                        | 3 (1)                         | 5 (1)                         | 19 (1)                        | 0.2   | 1409* |
| ECG/ECHO changes                                           | 10 (2)                        | 2 (1)                         | 1 (0.2)                       | 13 (1)                        | 0.01  | 1409* |
| Other                                                      | 148 (28)                      | 53 (13)                       | 40 (8)                        | 241 (17)                      | <0.0001| 1409* |

*In case of missing variables, the N reported at the column heading is not applicable, the total is shown at the end of the table. LVEF=Left ventricular ejection fraction, WMSI=Wall motion score index, BP=Blood pressure, ESE=Exercise stress echocardiography
negative pharmacologic stress echocardiogram have somewhat higher event rate than patients with negative exercise SE, explained by the higher risk status of patients who are unable to perform exercise stress test, as this group tends to be older with more comorbidities.[3]

Our policy therefore is to emphasize the importance of exercise stress testing to allow reproduction of symptoms and their correlation with ECG and imaging findings as well as the comparison of functional capacity to the extent of ischemia and prognostication since functional capacity is the strongest predictor of survival in patients with and without known CAD and ischemic stress-induced ST segment downsloping.[19,20] Accordingly, a negative exercise SE has a long-term favorable prognostic value.[21]

Our findings may have numerous practical implications. Although it is likely that a more thorough application of appropriateness guidelines would improve the yield of SE,[18] we are inevitably seeing changes in SE referral practices which leads to an “epidemiological transition” characterized by acceptance of patients with low pretest probability of CAD with atypical clinical symptoms and previous inconclusive exercise ECG. Of note, SE has been proposed in some guidelines for the assessment of chest pain with any pretest probability in case of wide availability and also for the assessment of atypical chest pain.[22]

The low pretest probability of CAD limits the usefulness of SE in these individuals making the presence of ischemia not prognostically important even in those with positive test results[23] since most of the patients with events had normal findings on SE. Elhendy et al. studied a group of 1,618 patients with a pretest probability of CAD of <25% during a mean follow-up period of 3 years. They had only 19 cardiac events, for an annualized event rate of approximately 0.4%. Moreover, only half with cardiac events were identified by abnormal results on exercise SE.[24]

However, although the low percentage of abnormal test results and the low event rate limit the usefulness of exercise SE in these individuals, we thought that exercise SE is better than exercise ECG for saving resources because of the smaller number of invasive downstream procedures with the former strategy[25] reserving exercise SE for those with abnormal findings during exercise ECG testing in only a minority of the patients initially submitted to exercise ECG testing.

**Limitations**

Our study has the limitations inherent to an observational single-center study with retrospective design. In particular, we cannot rule out the possibility that referral bias or local changes in clinical management might account for at least part of the trends observed. In addition, local differences in the availability of noninvasive cardiac imaging techniques[26] may compromise the generalizability of our findings.

In general, a positive noninvasive test is independently related to the presence of obstructive CAD.[11] However, we cannot evaluate the performance of noninvasive testing because we have no information on patients who underwent noninvasive testing but were not referred for catheterization, a situation that was probably more common among patients with negative or equivocal test results.

Finally, if testing is used extensively in low-risk patient populations, Bayesian principles dictate that many SE positive test results will be false positive results rather than true positive results, and this may have severely limited the ability of this noninvasive testing to add incremental value for the identification of obstructive CAD.

**Conclusions**

Invasive strategies are widely employed nowadays for CAD management. We observed, over a 12-year period, a progressive decrease in the frequency of inducible myocardial ischemia among patients with known or suspected CAD referred to our Echo Lab for SE with Cath-Lab facility, and this trend was parallel to changes in SE referral practice. These findings are particularly relevant if we consider the practical implications on diagnostic SE accuracy and risk assessment.

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**Conflicts of interest**

There are no conflicts of interest.

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