ORIGINAL RESEARCH

Clinical Practice Variations in the Management of Ischemia With No Obstructive Coronary Artery Disease

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BACKGROUND: Ischemia with no obstructive coronary artery disease is a condition associated with major adverse cardiovascular outcomes. To date, there are no specific American Heart Association or American College of Cardiology guidelines. The objective of this survey is to better understand the clinical practice and knowledge gaps that exist nationally.

METHODS AND RESULTS: Participant-specific links for a survey with 11 questions and 3 reminders were sent between September and October 2020 to the American College of Cardiology CardioSurv Panel. The panel consists of randomly selected cardiologists (n=437) who represent the current profile of the American College of Cardiology US membership. The survey received a 30% response rate. Of the 172 respondents, 130 (76%) indicated that they have treated patients with ischemia with no obstructive coronary artery disease. Although the majority (69%) are generally confident in their ability to manage this condition, 1 of 3 report lack of confidence or are neutral. The American College of Cardiology/American Heart Association Chronic Stable Angina Guidelines are the most commonly used reference for treating ischemia with no obstructive coronary artery disease (81%), with most cardiologists wanting additional clinical guidance, such as randomized controlled trials (61%). More than 4 of 5 cardiologists rarely or never order advanced imaging modalities to assess coronary flow reserve. Approximately 2 of 3 of respondents frequently prescribe statins (68%), aspirin (66%), calcium channel blockers (63%), and β blockers or α/β blockers (55%). However, nearly 70% never prescribe angiotensin-converting enzyme inhibitors or angiotensin receptor blockers.

CONCLUSIONS: This survey demonstrates heterogeneity in the management of ischemia with no obstructive coronary artery disease among US cardiologists, identifies support for guideline development, and outlines knowledge gaps for research and education in the therapeutic management of this condition.

Key Words: angina ■ guidelines ■ ischemia with no obstructive coronary arteries ■ ischemic heart disease ■ nonobstructive ■ stable coronary syndromes

For decades, the primary focus when managing patients with angina has been to verify obstructive coronary stenosis. However, in recent years, a new paradigm has emerged for ischemic heart disease, with increasing recognition of patients who present having signs and symptoms of ischemia with no obstructive coronary arteries (INOCA). INOCA is a broad term that emphasizes the significance of coronary syndromes beyond obstructive epicardial coronary artery disease (CAD), with multiple incompletely understood, contributing mechanisms, such as hypertension, severe anemia, severe aortic stenosis, myocardial bridging, coronary anomalies, or coronary vasomotor disorders.

INOCA is not benign, as it is estimated that >4 million Americans (the majority, >60% women) have symptoms despite normal or <50% stenoses on coronary angiograms, with a surmounting economic burden...
CLINICAL PERSPECTIVE

What Is New?
- Ischemia with no obstructive coronary artery disease is a condition with adverse prognosis and is managed heterogeneously among practicing US cardiologists.
- Many cardiologists rarely or never order advanced imaging modalities to assess coronary flow reserve to rule out coronary microvascular dysfunction as an underlying cause of ischemia with no obstructive coronary artery disease.
- Most cardiologists never prescribe angiotensin-converting enzyme inhibitors or angiotensin receptor blockers for patients with ischemia with no obstructive coronary artery disease.

What Are the Clinical Implications?
- Additional high-quality research studies are needed for guideline development.
- US consensus documents can potentially unify approaches to diagnostic workup and medication strategies, and educate clinicians in the management of ischemia with no obstructive coronary artery disease.

Nonstandard Abbreviations and Acronyms

| Abbreviation | Definition |
|--------------|------------|
| ACC          | American College of Cardiology |
| AHA          | American Heart Association |
| INOCA        | ischemia with no obstructive coronary artery disease |

of health care costs similar to those of obstructive CAD.6,7 Despite the considerable evidence documenting adverse prognosis associated with INOCA and established European Society of Cardiology guidelines for this population, no specific American College of Cardiology (ACC) or American Heart Association (AHA) guidelines exist to direct therapeutic strategies.1,8,9 We hypothesized that clinical equipoise remains for INOCA management, with little known about the US experience. Therefore, for the first time, we developed and administered a survey to a representative sample of practicing cardiologists to better understand the clinical practice variations and current knowledge gaps that exist in the management of INOCA.

METHODS

Because of the nature of the data collected for this study, requests to access the data set from qualified researchers trained in human subject confidentiality protocols may be sent to the coauthor collaborator at the ACC (ptheriot@acc.org).

The focused survey was developed by expert clinicians from a dedicated women’s heart center who routinely manage patients with INOCA at a single, tertiary-care hospital in the United States. The survey consisted of 11 questions designed to gather a general understanding from US cardiologists of their perceptions on the treatment and management of patients with INOCA (Table S1). Before distribution, the survey was reviewed by collaborating ACC staff with experience and expertise in survey design.

To capture a broad representation of practicing cardiologists in the nation, the ACC CardioSurve Panel was used. The ACC CardioSurve Panel consists of 437 US-based fellows of the ACC members who have voluntarily agreed to participate in monthly research surveys for a 2-year term. Panelists are selected at random from ACC’s membership database of active (ie. not retired) US-based fellows and invited to participate in the CardioSurve program. Although the selection of members is random, the composition of the CardioSurve Panel is stratified and modeled via demographic information to ensure that the design of the panel represents the demographic segmentation of ACC’s database of US-based fellows at the time of selection. At the end of each 2-year panel term, the current panel is retired and a fresh panel is recruited to participate in a new 2-year term. Per the ACC mandate set in 2010, the CardioSurve Panel surveys attempt to achieve an n=130 to 200 per each monthly survey. From the ACC’s Market Intelligence department’s response rate estimate calculations (based on prior research), this requires maintenance of a panel size of approximately n=350 to 450 at all times. To attain the n=437 panelists for the 2020 to 2021 CardioSurve Panel, 3500 email invitations were sent to randomly selected current, active US-based ACC fellows, of which n=437 accepted the invitation and completed the enrollment survey.

Participant-specific links to the INOCA survey and 3 reminders were emailed from September 11 to October 8, 2020.

Statistical Analysis

Data were collected and analyzed using Verint EFM 15.1 (Melville, NY) and SPSS 23 (Armonk, NY). Unless otherwise stated, data is descriptively presented as proportions with percentages.

RESULTS

A total of 172 of 437 (39%) panelists completed the screening question on the survey on whether they have currently or in the past treated patients with INOCA.
However, 42 of those panelists were excluded, as they indicated they have never treated patients with INOCA. Therefore, the fielding of the data collection instrument ultimately achieved n=130 panelists who indicated that they currently or in the past have treated patients with INOCA, for a response rate of 30%. Characteristics of the entire CardioSurve panelists are shown in the Table, which included surveyed (n=172) and nonsurveyed (n=265) cardiologists from a broad range of sub-specialties, locations, patient populations, and work-settings.

### Table  Baseline Characteristics of the Surveyed (n=172) and Nonsurveyed (n=265) ACC CardioSurve Panelists

| Demographics                  | Surveyed panelists (n=172) | Nonsurveyed panelists (n=265) |
|-------------------------------|---------------------------|-------------------------------|
| **Sex**                       |                           |                               |
| Men                           | 148 (86)                  | 226 (85)                      |
| Women                         | 24 (14)                   | 39 (15)                       |
| **Race or ethnicity**         |                           |                               |
| White                         | 93 (54)                   | 136 (51)                      |
| Asian                         | 50 (29)                   | 78 (29)                       |
| Hispanic/Latino               | 10 (6)                    | 14 (5)                        |
| Black                         | 6 (4)                     | 14 (5)                        |
| Native American               | 1 (1)                     | 1 (0.4)                       |
| Native Hawaiian               | 2 (1)                     | 2 (1)                         |
| **Time in practice, y**       |                           |                               |
| Early career (1–7 y)          | 55 (32)                   | 86 (33)                       |
| Mid career (8–21 y)           | 46 (27)                   | 84 (32)                       |
| Late career (≥22 y)           | 66 (38)                   | 76 (28)                       |
| **Board certification**       |                           |                               |
| Electrophysiology             | 19 (11)                   | 21 (8)                        |
| General cardiology            | 88 (51)                   | 129 (49)                      |
| Interventional cardiology     | 46 (27)                   | 91 (34)                       |
| Pediatric cardiology          | 11 (6)                    | 12 (5)                        |
| **Primary work setting**      |                           |                               |
| Cardiovascular practice       | 76 (44)                   | 127 (48)                      |
| HMO/industry                  | 0 (0)                     | 5 (2)                         |
| Hospital                      | 28 (16)                   | 48 (18)                       |
| Medical school                | 39 (23)                   | 51 (19)                       |
| Multispecialty group          | 23 (13)                   | 31 (12)                       |
| **Practice size (No. of cardiologists)** |             |                               |
| Large (≥26)                   | 58 (43)                   | 84 (32)                       |
| Medium (11–25)                | 51 (30)                   | 62 (23)                       |
| Medium small (5–10)           | 32 (19)                   | 51 (19)                       |
| Small (1–4)                   | 28 (16)                   | 54 (20)                       |
| **Location**                  |                           |                               |
| Rural                         | 19 (11)                   | 24 (9)                        |
| Suburban                      | 57 (33)                   | 111 (42)                      |
| Urban                         | 95 (56)                   | 122 (46)                      |

Data are given as number (percentage). ACC indicates American College of Cardiology; and HMO, health maintenance organization.

### Scope of Practice
Approximately 3 of 4 respondents (130/172 [76%]) have previously or are currently treating patients with INOCA in their practice. This is generally consistent among cardiologists across all tenure levels, including those in early career (1–7 years), mid career (8–21 years), and late career (≥21 years). However, as much as 30% (17/55) of early career, 17% (8/46) of mid career, and 21% (14/66) of late career respondents do not manage patients with INOCA in their practice. Of the 130 cardiologists who manage patients with suspected INOCA, ≈3/5 of cardiologists surveyed (59%) currently treat <10 patients, and this proportion was consistent across the different tenure levels (Figure S1).

### Use of Guidelines and/or References for Managing INOCA
Of the 130 cardiologists, the overwhelming majority use guidelines and/or references to help manage patients with suspected INOCA, with only a small proportion of respondents (2%; 3/130) who report not using any materials. More than 4 of 5 cardiologists (81%; 105/130) report using the AHA/ACC Chronic Stable Angina Guidelines, whereas approximately half (52%; 68/130) use the AHA/ACC Cholesterol Clinical Practice Guidelines. Other reported references include the AHA/ACC Guideline for Primary Prevention of Cardiovascular Disease (35%; 46/130) and UpToDate (28%; 36/130) (Figure S2).

### Confidence in Management of INOCA
Most cardiologists (69%; 90/130) express some degree of confidence in their ability to manage stable patients with suspected INOCA. However, only 1 of 4 (24%; 31/130) report being very confident. In addition, ≈1 of 3 (27%; 35/130) respondents are not confident or neutral when managing patients with INOCA. In general, mid to late career cardiologists more often report feeling very confident in their clinical management compared with early career cardiologists. In addition, cardiologists who see ≥11 patients with INOCA (39%; very confident) have a higher degree of confidence than those who see ≤10 patients (16%; very confident) (Figure 1).

### Investigations for Patients With Suspected INOCA
Almost half or more of the 130 cardiologists have rarely/never ordered the tests and measures cited for their patients with INOCA (Figure 2). Furthermore, only a small proportion have ordered specific testing to measure coronary flow reserve or myocardial blood flow, including invasive coronary function testing (21%; 27/130), stress cardiac positron emission
tomography (14%; 18/130), or stress cardiac magnetic resonance imaging (11%; 14/130). Approximately one fifth have always/often ordered an invasive coronary angiogram (23%; 30/130) or a noninvasive computed tomographic coronary angiogram (15%; 20/130) to presumably rule out nonobstructive coronary artery disease. About one third have always/often ordered a transthoracic echocardiogram (35%; 46/130) or a stress single-photon emission computed tomogram (34%; 44/130). The frequency for ordering the above cardiac investigations varies across different levels of confidence (Figure S3A), tenure levels, and scope of practice (Figure S3B).

Medical Therapies for Management of INOCA

More than half of the 130 cardiologists treating patients with INOCA are always/often prescribing statins (68%), aspirin (66%), calcium channel blockers (63%), nitrates (60%), or β blockers or α/β blockers (55%). However, consistent across all tenure levels, only 1 of 4 respondents are prescribing/recommending angiotensin-converting enzyme inhibitors or angiotensin receptor blockers (ACE-Is/ARBs) (25%; 33/130). About one fourth are regularly prescribing/recommending ranolazine (27%; 35/130) or cardiac rehabilitation (24%; 31/130) to their patients (Figure 3). Consistent across all tenure levels or scope of practice, cardiologists rarely/never use third- or fourth-line therapies, including iv- abradine, L-arginine, or enhanced external counter pulsation. Likewise, early career cardiologists are less inclined to prescribe nitrates (47%; 61/130) compared with their more tenured colleagues (mid career, 68%; late career, 63%). Early career (68%; 88/130) and mid career (71%; 92/130) cardiologists are twice as more likely to use β blockers or α/β blockers compared with their peers (late career, 33%; 43/130) (Figure S4A). Similarly, cardiologists who feel most confident in managing patients with INOCA more often prescribe statins, aspirin, calcium channel blockers, nitrates, and β blockers or α/β blockers, compared with those with
Of those respondents who do not feel very confident managing patients with INOCA, only 7% (1/15) routinely prescribe ACE-Is/ARBs and 0% (0/15) prescribe cardiac rehabilitation (Figure S4B).

Follow-Up and Referral for Patients With INOCA
Most of the 130 cardiologists (81%) follow up with their patients with INOCA within the first 3 months after initial evaluation or diagnosis; most of them do so in the third month (42%). This is true across all of the audiences (Figure S5). Similarly, most cardiologists (75%; 98/130) rarely or never refer their patients with INOCA to other colleagues or centers, whereas about one fifth (19%; 25/130) sometimes make referrals for these patients. This is consistent across all audiences (Figure S6).

Perceived Characteristics and Risk Factors
According to the 130 cardiologists who have treated patients with INOCA, the top perceived characteristic is that these patients are women (77%), whereas the top risk factors are hypertension (60%) and diabetes (54%). Interestingly, cardiologists who are treating ≥11 patients with INOCA were more likely to identify a larger number of traits in their patients with INOCA than those who treat <10 patients (Figure S7).

Areas for Improvement
Almost all of the 130 cardiologists (97%) believe that additional clinical guidance for treating patients with INOCA is needed. According to these cardiologists who have treated patients with INOCA, the top resources needed to accurately diagnose and treat INOCA are randomized controlled trials for treatment (61%; 79/130), guidelines specific to INOCA (58%; 75/130), and US guidelines or expert consensus for diagnosis and management (50%; 65/130) (Figure S8).

DISCUSSION
Among a representative cohort of practicing cardiologists in the United States, we describe, for the first time, the general perceptions about management and treatment of patients with INOCA. Our study demonstrates heterogeneity in the clinical practice of INOCA and illustrates potential for future research and education to guide our treatment.
The baseline demographics of the cardiologists who completed the survey compared with those who did not complete the survey were similar across all captured variables. Most CardioSurve panelists (and survey respondents) are men, which is consistent with real-world experience, where cardiology remains a male-dominant profession with a smaller proportion of female cardiologists. In our study, we found nearly 25% of cardiologists have never treated patients with INOCA and as much as 60% of the surveyed respondents treat <10 patients with INOCA in their practice. This is likely not an accurate representation of the actual number of patients with suspected INOCA, as up to 70% of individuals undergoing invasive angiography have nonobstructive CAD, and because these patients present with a wide spectrum of symptoms and signs, they may potentially be mislabeled with noncardiac diagnoses and not followed up by cardiologists routinely.

Our results indicate a lack of uniformity among cardiologists in the diagnosis and management of INOCA, which is expected considering that a standard definition for INOCA has not been unequivocally established. The clinical triad of anginal chest pain, evidence of ischemia by noninvasive stress testing, followed by normal-appearing coronary arteries on angiography has been reported in literature for several decades and was first described using the now outdated term of cardiac syndrome X. Currently, there remains ongoing confusion with respect to uniform terminology to describe these patients and lack of standardized diagnostic criteria. One approach has been to anatomically (using computed tomography or invasive coronary angiography) describe these patients as having no obstructive CAD, which comprises 2 groups: normal coronary arteries and diffuse nonobstructive CAD (defined as 1%–49% stenosis in any epicardial coronary artery). Patients labeled with no apparent CAD may be defined visually as having normal-appearing coronary arteries, but when measured by quantitative methods, have evidence of minimal stenosis that is <20% diameter narrowing.

In contemporary clinical studies, such as the WARRIOR (Women’s Ischemia Trial to Reduce Events in Nonobstructive Coronary Artery Disease) trial, enrolled participants have symptomatic (chronic angina or equivalent) with nonobstructive CAD, defined as <50% diameter reduction of a major epicardial vessel or Fractional flow reserve >0.80 (using computed tomography or invasive coronary angiography). Similarly, in the clinical trial CorMicA (Coronary Microvascular Angina), INOCA is further defined functionally using invasive coronary reactivity testing in participants with symptoms of angina, in the absence of obstructive CAD (≥50% diameter stenosis and/or Fractional flow reserve ≤0.80), and other noncoronary pathologic conditions, such as valve disease or hypertrophic
obstructive cardiomyopathy. In CorMicA, researchers have shown that coronary vasomotor dysfunction is common in patients with INOCA, with over three quarters having microvascular and/or vasospastic angina. The presence of coronary microvascular dysfunction, defined by abnormal coronary flow reserve (<2.0) using positron emission tomography, echocardiographic Doppler, or cardiac magnetic resonance imaging in patients without obstructive CAD, has also been referenced as diagnostic criteria for INOCA.

From a pragmatic perspective, anatomically defined terminologies, such as ANOCA (angina with nonobstructive CAD), NOCAD (nonobstructive CAD), and INOCA, or functionally defined terminologies, such as coronary microvascular dysfunction, and coronary vasomotor disorders, can generally all refer to the same entity in the clinical setting.

More recently, the European Association of Percutaneous Cardiovascular Interventions published an expert consensus document on INOCA, specific to the management of microvascular and vasospastic angina. This expert consensus document formulates a diagnostic/investigational approach to INOCA, emphasizing the role of functional imaging and invasive functional coronary angiography in tailoring effective treatments for patients. Although current imaging modalities do not directly visualize the coronary microcirculation, available techniques can evaluate physiological surrogates of the microvasculature, such as coronary flow reserve or myocardial perfusion reserve index.

We found only a small minority (<10%) of cardiologists routinely order invasive coronary function testing, stress cardiac positron emission tomography, or stress cardiac magnetic resonance imaging for assessment of coronary flow reserve or myocardial perfusion reserve index. Specifically, abnormal stress perfusion cardiac magnetic resonance imaging-derived myocardial perfusion reserve index has been shown to be an independent imaging predictor of adverse cardiovascular events in patients with INOCA.

More important, in patients with nonobstructive CAD, researchers have shown that a negative noninvasive stress test, such as exercise electrocardiography, stress echocardiography, or stress nuclear imaging, has limited diagnostic accuracy to rule out coronary vasomotor dysfunction. Specifically, when compared with the reference standard of invasive coronary function testing, traditional noninvasive stress tests had only 41% sensitivity and 57% specificity to predict coronary vasomotor dysfunction. However, stress single-photon emission computed tomography and stress echocardiography were among the most common investigations ordered for patients with suspected INOCA by the surveyed cardiologists.

Alternatively, in many cases in the clinical setting, the diagnosis of INOCA is made after a presentation of nonclassic anginal symptoms (breathlessness, pain between the shoulder blades, indigestion, nausea, extreme fatigue, weakness, vomiting, and/or sleep disturbances), triggering a stress test (with or without imaging), which shows positive results that then lead to subsequent coronary angiography revealing no obstructive CAD. For some cardiologists, this constellation of findings would be labeled as a “false-positive stress test,” leading to reassurance, risk factor modification, a trial of antianginal medication, and no further testing. We recognize that this paradigm is not necessarily one of ignorance or lack of knowledge about the clinical entity of INOCA, but potentially one of disbelief about the presence of ischemia on the part of some cardiologists. However, we emphasize that failure to appropriately diagnose underlying vasomotor dysfunction may lead to misguided therapeutic strategies. As a result, patients with INOCA continue to have a high burden of angina and reduced quality of life, exacerbated by poor clinical outcomes and increased health care costs related to repeated hospitalizations and coronary angiography.

The overwhelming majority of surveyed cardiologists believe that additional clinical guidance is needed to accurately diagnose and treat patients with INOCA, with over half wanting US-specific guidelines or expert consensus for diagnosis and management. Presently, most surveyed cardiologists rely on preexisting references, including the AHA/ACC chronic stable angina and the cholesterol clinical practice guidelines. As a result of the knowledge gaps related to an inherently heterogeneous condition, as much 1 of 3 cardiologists in early to mid career report being neutral or lacking confidence in their ability to manage patients with INOCA. To help educate and provide a summary of findings and recommendations for this clinical entity, we refer the audience to other available published resources, including the 2019 European Society of Cardiology Chronic Coronary Syndrome Guidelines, a State of the Art White Paper by Bairey Merz and colleagues, and State of the Art Review articles by lead authors Ford and Mathew. The Japanese Circulation Society has also previously published guidelines for the management of vasospastic angina.

Despite a plethora of data demonstrating increased events in the follow-up of patients with INOCA, there have been no therapies shown to improve their prognosis. Currently, the management strategy for INOCA remains unclear, but emerging evidence from clinical trials is available. Specifically, the randomized control trial, CorMicA, has recently shown that a stratified medical approach using targeted antianginal medications guided by interventional diagnostic procedure with coronary function testing significantly improves angina and quality of life in patients with INOCA at 1-year follow-up. Accordingly, most surveyed respondents are prescribing antianginal
medications as patients with INOCA often have persistent angina.31 The role of aspirin is extrapolated from the AHA/ACC chronic stable angina guidelines, as most patients have at least some evidence of atherosclerosis based on intravascular ultrasound examination.38 A review of the literature further suggests the potential roles for statins and ACE-Is to improve coronary endothelial or vascular smooth muscle function in patients with INOCA.39–41 Accordingly, 3 of 5 cardiologists are always/often prescribing statins and aspirin. However, we found only 1 of 4 respondents are prescribing ACE-Is or ARBs to their patients with suspected INOCA, despite expert consensus and support for this recommendation. The frequency for prescribing ACE-Is or ARBs increases to ~1 of 3 respondents who see more patients with suspected INOCA in their practice or who report having more confidence in managing these patients.

In anticipation of much needed large-scale clinical trials to guide therapeutic strategies, the first multicenter randomized control trial, WARRIOR, is recruiting patients to evaluate whether intensive medical therapy with statins, aspirin, and ACE-Is or ARBs versus usual care will reduce major adverse coronary events in women with INOCA (https://clinicaltrials.gov/ct2/show/NCT03417388).6 Furthermore, researchers from Sweden are leading an international, multicenter randomized control trial to determine whether the addition of oral β-blockade and ACE-Is/ARBs reduces major adverse events in patients discharged with myocardial infarction with nonobstructive coronary arteries and no clinical signs or evidence of heart failure (https://clinicaltrials.gov/ct2/show/NCT03686696; Randomized Evaluation of Beta Blocker and ACE/ARB Treatment in MINOCA Patients-MINOCA-BAT).42 These clinical trials will aim to provide evidence-based treatment strategies for patients with stable and acute nonobstructive coronary syndromes.

**Study Limitations**

The survey was distributed to a small sample of ACC cardiologists across the United States and may not accurately represent the viewpoints of the collective cohort of cardiologists. However, the moderately high response rate and strategic collaboration with the ACC to use the CardioSurve database increases the likelihood that our survey was able to capture a representative sample of practicing cardiologists in the nation. Second, responses were self-reported, with potential susceptibility to recency bias, and may not reflect real-life practice patterns for INOCA.

**CONCLUSIONS**

Although there is increased recognition and understanding of the poor prognosis related to INOCA, the management of this condition remains largely based on expert opinion and consensus. This study demonstrates heterogeneity in the management of INOCA in the United States, identifies support for guideline development, and outlines knowledge gaps for further research and education to improve clinical outcomes.

**REFERENCES**

1. Jespersen L, Hvelplund A, Abildstrøm SZ, Pedersen F, Galatius S, Madsen JK, Jørgensen E, Kelbaek H, Prescott E. Stable angina pectoris with no obstructive coronary artery disease is associated with increased risks of major adverse cardiovascular events. Eur Heart J. 2012;33:734–744. doi: 10.1093/eurheartj/ehs331

2. Blumgart HL, Schlesinger MJ, Davis D. Studies on the relation of the clinical manifestations of angina pectoris, coronary thrombosis, and myocardial infarction to the pathologic findings: with particular reference to the significance of the collateral circulation. Am Heart J. 1940;19:1–91. doi: 10.1016/S0002-8703(40)90305-2

3. Bairey Merz CN, Pepine CJ, Walsh MN, Fleg JL. Ischemia and no obstructive coronary artery disease (INOCA): developing evidence-based therapies and research agenda for the next decade. Circulation. 2017;135:1075–1092. doi: 10.1161/CIRCULATIONAHA.116.024534

4. Mehta P, Wei J, Bairey Merz N. Chapter 25: angina in patients with evidence of myocardial ischemia and no obstructive coronary artery disease. In: Braunwald E, ed. Braunwald’s Heart Disease: A Textbook of Cardiovascular Medicine. 10th ed. Philadelphia, Pa: Elsevier/Saunders; 2014.

5. Ford TJ, Yli E, Siddik N, Good R, Rocchiccioli P, McIntegart M, Watkins S, Eteiba H, Shaukat A, Lindsay M, et al. Ischemia and no obstructive coronary artery disease: prevalence and correlates of coronary vasomotion disorders. Circ Cardiovasc Inter. 2019;12:e008126. doi: 10.1161/CIRCINTERVENTIONS.119.008126

6. Handberg EM, Merz CNB, Cooper-Dehoff RM, Wei J, Conlon M, Lo MC, Boden W, Frayne SM, Villines T, Spertus JA, et al. Rationale and design of the Women’s Ischemia Syndrome Evaluation. Circulation. 2006;114:894–904. doi: 10.1161/CIRCULATIONAHA.105.609990

7. Sediak TL, Lee M, Izadnegahdar M, Merz CN, Gao M, Humphries KH. Sex differences in clinical outcomes in patients with stable angina and...
no obstructive coronary artery disease. Am Heart J. 2013;166:38–44. 

doi: 10.1016/j.jahj.2013.05.015

9. Gulati M, Cooper-DeHoff RM, McClure C, Johnson BD, Shaw LJ, Handberg EM, Zineh I, Kelsey SF, Arnsdorf MF, Black HR, et al. Adverse cardiovascular outcomes in women with nonobstructive coronary artery disease: a report from the Women’s Ischemia Syndrome Evaluation Study and the St James Women Take Heart Project. Arch Intern Med. 2009;169:843–850. doi: 10.1001/archinternmed.2009.50

10. Lewis SJ, Mehta LS, Douglas PS, Gulati M, Limacher MC, Pappas A, Walsh MN, Rzeszut AK, Duvernoy CS; American College of Cardiology Women in Cardiology Leadership Council. Changes in the professional lives of cardiologists over 2 decades. J Am Coll Cardiol. 2017;69:452–462. doi: 10.1016/j.jacc.2016.11.027

11. Patel MR, Peterson ED, Dai D, Bremann JM, Redberg RF, Anderson HV, Brindis RG, Douglas PS. Low diagnostic yield of elective coro-

nary angiography. N Engl J Med. 2010;362:886–895. doi: 10.1056/NEJMoa0907272

12. Jespersen L, Abildstrom SZ, Hvelplund A, Madsen JK, Galatus S, Pedersen F, Holjerg B, Prescott E, Burden of hospital admission and repeat angiography in angina pectoris patients with and without coronary artery disease: a registry-based cohort study. PLoS One. 2014;9:e93170. doi: 10.1371/journal.pone.0093170

13. Eastwood J-A, Johnson BD, Rutledge T, Bittner V, Whittaker KS, Krantz DS, Cornell CE, Etelba W, Handberg E, Vido D, et al. Anginal symp-
toms, coronary artery disease, and adverse outcomes in Black and White women: the NHLBI-sponsored Women’s Ischemia Syndrome Evaluation. With J Womens Health. 2015;22:724–732. doi: 10.1089/jwh.2012.4231

14. Kemp HG. Left ventricular function in patients with the anginal syn-
drome and normal coronary arteriograms. Am J Cardiol. 1973;32:375–376. doi: 10.1016/S0002-9149(73)80510-X

15. Pepine CJ, Ferdinand KC, Shaw LJ, Light-McCroy KA, Shah RJ, Gulati M, Duvernoy C, Walsh MN, Bairey Merz CN; ACC CVD in Women Committee. Emergence of nonobstructive coronary artery disease: a woman’s problem and need for change in definition on angiography. J Am Coll Cardiol. 2015;66:1918–1933. doi: 10.1016/j.jacc.2015.08.876

16. Sharaf B, Wood T, Shaw L, Johnson BD, Kelsey S, Anderson RD, Pepine CJ, Bairey Merz CN. Adverse outcomes among women pre-
senting with signs and symptoms of ischemia and no obstructive coro-

nary artery disease: findings from the National Heart, Lung, and Blood Institute-sponsored Women’s Ischemia Syndrome Evaluation (WISE) angiographic core laboratory. Am Heart J. 2013;166:134–141. doi: 10.1016/j.jahj.2013.04.002

17. Ford TJ, Stanley B, Good R, Rocchiccioli P, McEntegart M, Watkins S, Etelba H, Shaukat A, Lindsay M, Robertson K, et al. Stratified medi-
cal therapy using invasive coronary function testing in angina: the CorMiCa trial. J Am Coll Cardiol. 2018;72:2841–2855. doi: 10.1016/j.ijcard.2017.08.068

18. Ford TJ, Corcoran D, Oldroyd KG, McEntegart M, Rocchiccioli P, Watkins S, Brooksbank K, Padmanabhan S, Sattar N, Briggs A, et al. Rationale and design of the coronary microvascular angina cardiac magnetic resonance imaging (CorCMR) diagnostic study: the CorMiCa CMR sub-

try. Open Heart. 2018;5:e000924. doi: 10.1136/openheart-2018-000924

19. Kessel CK, Chen G, Southern DA, Galbraith PD, Anderson TJ; APPROACH Investigators. Impact of clinical presentation and pres-
ence of coronary sclerosis on long-term outcome of patients with non-obstructive coronary artery disease. BMC Cardiovasc Disord. 2018;18:187. doi: 10.1186/s12973-018-0908-z

20. Ong P, Camici PG, Beltrame JF, Crea F, Shimokawa H, Sechtem U, Kasic JC, Bairey Merz CN; Coronary Vasomotion Disorders International Study Group (COVADIS). International standardization of diagnostic criteria for microvascular angina. Int J Cardiol. 2018;250:16–20. doi: 10.1016/j.ijcard.2017.08.008

21. Beltrame JF, Crea F, Kasic JC, Ogawa H, Ong P, Sechtem U, Shimokawa H, Bairey Merz CN; Group, Coronary Vasomotion disorders inter-
national study. International standardization of diagnostic criteria for vasospastic angina. Eur Heart J. 2017;38:2565–2568. doi:

10.1093/eurheartj/ehv351

22. Kunadian V, Chiefo A, Camici PG, Berry C, Escaned J, Maas AHM, Prescott E, Karam A, Appelman Y, Fraccaro C, et al. An EAPCI ex-
pert consensus document on Ischaemia with non- obstructive coro-
nary arteries in collaboration with European Society of Cardiology Working Group on Coronary Pathophysiology & Microcirculation Endorsed by Coronary Vasomotor Disorders International Study Group. EuroIntervention. 2021;16:1049–1069. doi: 10.4244/EIJY20M07_01

23. Mathew RC, Bourque JM, Salerno M, Kramer CR. Cardiovascular imag-
ing techniques to assess microvascular dysfunction. JACC Cardiovasc Imaging. 2020;12:1577–1590. doi: 10.1016/j.jcicin.2019.09.006

24. Zhou W, Lee JCY, Leung ST, Lai A, Lee T-F, Chiang JB, Cheng YW, Chan H-L, Yu K-H, Goh VKM, et al. Long-term prognosis of patients with coronary microvascular disease using stress perfusion cardiac magnetic resonance. JACC Cardiovasc Imaging. 2021;14:602–611. doi: 10.1016/j.jcicin.2020.09.034

25. Cassar A, Chareonthaitawee P, Rihal CS, Prasad A, Lennon RJ, Lerman LO, Lerman A. Lack of correlation between non-invasive stress tests and invasive coronary vasomotor dysfunction in patients with nonobstruc-
tive coronary artery disease. Circ Cardiovasc Inter. 2009;2:237–244. doi: 10.1161/CIRCINTERVENTIONS.108.841056

26. Johnson BD, Shaw LJ, Pepine CJ, Reis SE, Kelsey SF, Sopko G, Rogers WJ, Mankad S, Sharaf BL, Bittner V, et al. Persistent chest pain predicts cardiovascular events in women without obstructive coronary artery disease: results from the NIH-NHLBI-sponsored Women’s Ischaemia Syndrome Evaluation (WISE) study. Eur Heart J. 2006;27:1408–1415. doi:

10.1093/eurheartj/ehl040

27. Gibbons RJ, Chattjee K, Daley J, Douglas JS, Finn SD, Gardin JM, Grenwald MA, Levy D, Lytle BW, O’Rourke RA, et al. ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina: executive summary and recommendations. Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Stable Chronic Angina). Circulation. 1999;99:2829–2848. doi: 10.1161/01.CIR.99.21.2829

28. Grundy SM, Stone NJ, Bailey AL, Beam C, Bircher KK, Blumenthal RS, Braun LT, de Ferranti S, Failla-Tommaso J, Forman DE, et al. 2018 AHA/ACC/AACVP/AA/ABCP/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines. Circulation. 2019;139:e1082–e1143. doi: 10.1161/CIR.0000000000006025

29. Knutti J, Wiins W, Saraste A, Capodanno D, Barbato E, Funck-

Brentano C, Prestcott E, Storey RF, Deaton C, Cuijss T, et al. 2019 ESC guidelines for the diagnosis and management of chronic coronary syn-
dromes. Eur Heart J. 2020;41:407–477. doi: 10.1093/eurheartj/ehaa245

30. Ford TJ, Ong P, Sechtem U, Beltrame J, Camici PG, Crea F, Kasic JC, Bairey Merz CN, Pepine CJ, Shimokawa H, et al. Assessment of vascu-
lar dysfunction in patients without obstructive coronary artery disease: why, how, and when. JACC Cardiovasc Interv. 2020;13:1847–1864. doi: 10.1016/j.jcin.2020.03.010

31. Ford TJ, Stanley B, Sidik N, Good R, Rocchiccioli P, McEntegart M, Watkins S, Etelba H, Shaukat A, Lindsay M, et al. 1-year outcomes of angina management guided by invasive coronary function testing
38. Lee B-K, Lim H-S, Fearon WF, Yong AS, Yamada R, Tanaka S, Lee DP, Yeung AC, Tremmel JA. Invasive evaluation of patients with angina in the absence of obstructive coronary artery disease. Circulation. 2015;131:1054–1060. doi: 10.1161/CIRCULATIONAHA.114.012636

39. Caliskan M, Erdogan D, Gullu H, Topcu S, Ciftci O, Yildirim A, Muderrisoglu H. Effects of atorvastatin on coronary flow reserve in patients with slow coronary flow. Clin Cardiol. 2007;30:475–479. doi: 10.1002/clc.20140

40. Eshtehardi P, McDaniel MC, Dhawan SS, Binongo JN, Krishnan SK, Golub L, Corban MT, Raggi P, Quyyumi AA, Samady H. Effect of intensive atorvastatin therapy on coronary atherosclerosis progression, composition, arterial remodeling, and microvascular function. J Invasive Cardiol. 2012;24:522–529.

41. Pauly DF, Johnson BD, Anderson RD, Handberg EM, Smith KM, Cooper-DeHoff RM, Sopko G, Sharaf BM, Kelsey SF, Merz CNB, et al. In women with symptoms of cardiac ischemia, nonobstructive coronary arteries, and microvascular dysfunction, angiotensin-converting enzyme inhibition is associated with improved microvascular function: a double-blind randomized study from the National Heart, Lung and Blood Institute Women’s Ischemia Syndrome Evaluation (WISE). Am Heart J. 2011;162:678–684. doi: 10.1016/j.ahj.2011.07.011

42. Nordenskjöld AM, Agewall S, Atar D, Baron T, Beltrame J, Bergström O, Erlinge D, Gale CP, López-Pais J, Jernberg T, et al. Randomized evaluation of beta blocker and ACE-inhibitor/angiotensin receptor blocker treatment in patients with myocardial infarction with non-obstructive coronary arteries (MINOCA-BAT): rationale and design. Am Heart J. 2021;231:96–104. doi: 10.1016/j.ahj.2020.10.059
SUPPLEMENTAL MATERIAL
Table S1. Questions included in the survey.

| Question                                                                 | Options                                                                 |
|-------------------------------------------------------------------------|-------------------------------------------------------------------------|
| 1. Where do you currently practice? (Pull down option to pick state)    | Cardiology group, Medical school/University, Non-government hospital, Multi-specialty group, Solo practice, Government hospital/agency, Other work setting |
| 2. In what setting do you primarily carry out your practice             | Cardiology group, Medical school/University, Non-government hospital, Multi-specialty group, Solo practice, Government hospital/agency, Other work setting |
| 3. Have you previously or currently manage patients with INOCA in your practice? | Yes, No, Do not treat patients (THANK AND TERMINATE) |
| 4. What guidelines or references do you use when managing these patients? | ACC/AHA Chronic stable angina guidelines, ACC/AHA Cholesterol clinical practice guidelines, ACC/AHA Primary prevention cardiovascular disease (CVD) guidelines, ACC/AHA NSTE-ACS guidelines, CCS (Canadian Cardiovascular Society) Refractory angina guidelines, CCS Dyslipidemia CVD prevention guidelines, ESC (European Society of Cardiology) Stable angina pectoris guidelines, ESC Dyslipidemia guidelines, ESC Primary prevention CVD guidelines, ESC NSTE-ACS guidelines, UpToDate, Reference and/or review articles such as ESC Expert consensus document on INOCA, Other, I do not use any guidelines or references |
| 5. How confident are you with managing stable patients with INOCA in your practice? | Very confident, Somewhat confident, Neutral, Somewhat confident, Not very confident |
| 6a. Which of the following investigations do you order for your INOCA patients? | Exercise Treadmill Test, Transthoracic Echocardiogram, Stress Echocardiogram, Stress SPECT, Stress Cardiac PET with or without coronary flow reserve measurement |
Stress Cardiac MRI with or without myocardial perfusion reserve index measurement
- Invasive Coronary Angiogram
- CT Coronary Angiogram
- Invasive coronary function testing (coronary flow reserve and/or index of microcirculatory resistance)
- I do not order any investigations
- Other, please specify: ____________
- Not sure

6b. Which often do you order the investigations for your INOCA patients?

7a. Which of the following medications/treatment do you prescribe/recommend for your INOCA patients?
- Beta blockers, or alpha/beta blockers
- ACEi/ARBs
- Diuretics
- Calcium channel blockers
- Statins
- Nitrates
- Aspirin
- Antiplatelets (Plavix or Ticagrelor)
- Ranolazine
- Ivabradine
- Oral anticoagulation (i.e., warfarin or direct-oral anticoagulants)
- Enhanced External Counter Pulsation (EECP)
- L-arginine
- Hormone therapy
- Cardiac rehabilitation
- I do not prescribe any medications or treatments
- Other, please specify: ________________
- Not sure

7b. How often do you prescribe/recommend the medications/treatments for your INOCA patients?

8. When do you follow up with these patients after the initial evaluation or diagnosis?
- 1 month
- 2 months
- 3 months
- >6 Months
- Other, please specify: ____________
- I do not follow-up with them
- Not sure

9. How often do you refer patients with INOCA to other colleagues or centers?
- Always
- Often
- Sometimes
- Rarely
10. In your practice, what are the common patient characteristics and/or risk factors that you encounter in INOCA patients?

Demographics:
- Female
- Male
- Older Age > 65 years of age
- Black or African American Ethnicity/Race
- White/Caucasian Ethnicity/Race
- Hispanic Ethnicity/Race
- Asian Ethnicity/Race
- Other Ethnicity/Race

Past or present medical conditions:
- Diabetes
- Hypertension
- Dyslipidemia
- Family history premature CAD
- Past or current smoking
- Mental health disorders (i.e. depression or anxiety)
- Obesity
- Menopause
- Adverse pregnancy outcomes (gestational HTN, gestational DM, pre-eclampsia/eclampsia, preterm before 37 weeks delivery, small or large for gestational age)
- Chemotherapy/Radiation therapy
- Autoimmune diseases

Socioeconomic position
- Low socioeconomic status
- Lack of access to healthcare providers
- Lack of medical insurance coverage

- Other, please specify: ________________________________
- None
- Not sure

11. In your opinion, what do you think is needed for clinicians to accurately diagnose and treat INOCA?

- US guidelines or expert consensus for diagnosis and management
- Randomized controlled trials for treatment
- High-quality systematic reviews/meta analyses
- Workshops or dedicated forums at the major cardiology conferences
- Guidelines specific to INOCA
- Other, please specify: ________________________________
- No further improvements are needed
|   |   |
|---|---|
| **Not sure** |   |
Figure S1. Current Number of INOCA Patients Managed by Surveyed Cardiologists. Results reported by tenure level (early, mid, late career) and total respondents (n=172).
Figure S2. Guidelines/References Used When Managing INOCA Patients. Results reported by surveyed cardiologists (n=130).

| Reference Type                                                   | Percentage |
|------------------------------------------------------------------|------------|
| ACC/AHA Chronic stable angina guidelines                         | 81%        |
| ACC/AHA Cholesterol clinical practice guidelines                 | 52%        |
| ACC/AHA Primary prevention cardiovascular disease (CVD) guidelines | 35%        |
| UpToDate                                                         | 28%        |
| Reference and/or review articles (e.g. ESC Expert Consensus document) | 22%        |
| ACC/AHA NSTE-ACS guidelines                                      | 18%        |
| ESC (European Society of Cardiology) Stable angina pectoris guidelines | 12%        |
| ESC Primary prevention CVD guidelines                            | 4%         |
| ESC Dyslipidemia guidelines                                      | 2%         |
| CCS (Canadian Cardiovascular Society) Refractory angina guidelines | 2%         |
| CCS Dyslipidemia CVD prevention guidelines                       | 2%         |
| ESC NSTE-ACS guidelines                                          | 2%         |
| Other                                                            | 1%         |
| I do not use any guidelines or references                       | 2%         |
Figure S3a: Frequency of Investigations Ordered for INOCA Patients Heat Map.
Summary table of responses for “always and/or often” only, reported by level of confidence in managing stables patients with INOCA.

| Procedure                                                                 | Not very confident | Neutral | Somewhat confident | Very confident |
|---------------------------------------------------------------------------|--------------------|---------|--------------------|----------------|
| Transthoracic Echocardiogram                                              | 20%                | 35%     | 37%                | 42%            |
| Stress SPECT                                                              | 40%                | 40%     | 32%                | 32%            |
| Invasive Coronary Angiogram                                               | 7%                 | 30%     | 19%                | 32%            |
| Stress Echocardiogram                                                     | 20%                | 35%     | 15%                | 23%            |
| CT Coronary Angiogram                                                     | 7%                 | 35%     | 8%                 | 16%            |
| Exercise Treadmill Test                                                   | 13%                | 15%     | 12%                | 19%            |
| Invasive coronary function testing (coronary flow reserve and/or index of microcirculatory resistance) | 7%                 | 10%     | 7%                 | 13%            |
| Stress Cardiac PET with or without coronary flow reserve measurement      | 0%                 | 10%     | 5%                 | 6%             |
| Stress Cardiac MRI with or without myocardial perfusion reserve index measurement | 0%                 | 5%      | 2%                 | 0%             |
| Other                                                                     | 0%                 | 0%      | 2%                 | 0%             |
| N-Size                                                                    | n=15               | n=20    | n=59               | n=31           |

Heat Map Legend:
- Less used
- More used
Figure S3b. Frequency of Investigations Ordered for INOCA Patients Heat Map.
Summary table of responses for “always and/or often” only, reported by tenure level and number of INOCA patients seen in practice.

| Summary Table of "Always/Often" | Tenure Level | # of INOCA Patients |
|----------------------------------|--------------|---------------------|
|                                  | Early Career (1-7 years) | Mid-Career (8-21 years) | Late Career (22+ years) | 10 or less patients | 11 or more patients |
| Transthoracic Echocardiogram     | 50%          | 29%                | 29%             | 26%              | 49%              |
| Stress SPECT                    | 24%          | 39%                | 37%             | 30%              | 34%              |
| Invasive Coronary Angiogram      | 18%          | 29%                | 22%             | 14%              | 34%              |
| Stress Echocardiogram           | 11%          | 21%                | 27%             | 17%              | 24%              |
| CT Coronary Angiogram           | 18%          | 13%                | 12%             | 18%              | 7%               |
| Exercise Treadmill Test         | 11%          | 18%                | 14%             | 7%               | 24%              |
| Invasive coronary function testing (coronary flow reserve and/or index of microcirculatory resistance) | 13%          | 8%                | 8%              | 8%               | 12%              |
| Stress Cardiac PET with or without coronary flow reserve measurement | 5%          | 5%                | 6%              | 7%               | 5%               |
| Stress Cardiac MRI with or without myocardial perfusion reserve index measurement | 0%          | 0%                | 4%              | 1%               | 2%               |
| Other                            | 3%           | 0%                 | 0%              | 1%               | 0%               |

(n=38) (n=38) (n=51) (n=76) (n=41)

Heat Map Legend:
- Less used
- More used
Figure S4a. Frequency of Medications Ordered for INOCA Patients Heat Map. Summary table of responses for “always and/or often” only, reported by tenure level and number of INOCA patients seen in practice.

| Medication                                      | Early Career (1-7 years) | Mid-Career (8-21 years) | Late Career (22+ years) | 10 or less patients | 11 or more patients |
|------------------------------------------------|---------------------------|--------------------------|-------------------------|---------------------|---------------------|
| Statins                                         | 63%                       | 82%                      | 67%                     | 64%                 | 73%                 |
| Aspirin                                         | 63%                       | 71%                      | 67%                     | 66%                 | 66%                 |
| Calcium channel blockers                        | 55%                       | 74%                      | 61%                     | 55%                 | 71%                 |
| Nitrates                                        | 47%                       | 68%                      | 63%                     | 55%                 | 61%                 |
| Beta blockers, or alpha/beta blockers           | 68%                       | 71%                      | 33%                     | 53%                 | 51%                 |
| Ranolazine                                      | 21%                       | 29%                      | 29%                     | 20%                 | 34%                 |
| ACEi/ARBs                                       | 18%                       | 34%                      | 25%                     | 16%                 | 37%                 |
| Cardiac rehabilitation                          | 21%                       | 32%                      | 20%                     | 18%                 | 29%                 |
| Antiplatelets (Plavix or Ticagrelor)            | 11%                       | 26%                      | 12%                     | 12%                 | 22%                 |
| L-arginine                                      | 0%                        | 0%                       | 4%                      | 1%                  | 0%                  |
| Ivabradine                                      | 3%                        | 3%                       | 0%                      | 1%                  | 2%                  |
| Enhanced External Counter Pulsation (EECP)      | 0%                        | 3%                       | 0%                      | 1%                  | 0%                  |
| Oral anticoagulation (i.e., warfarin or direct-oral anticoagulants) | 0% | 0% | 0% | 0% | 0% |
| Diuretics                                       | 0%                        | 0%                       | 0%                      | 0%                  | 0%                  |
| Hormone therapy                                 | 0%                        | 0%                       | 0%                      | 0%                  | 0%                  |
| Other                                           | 3%                        | 0%                       | 0%                      | 0%                  | 0%                  |

(n=38) (n=38) (n=51) (n=76) (n=41)
Figure S4b. Frequency of Medications Ordered for INOCA Patients Heat Map. Summary table of responses for “always and/or often” only, reported by level of confidence in managing stables patients with INOCA.

| Medication                           | Not very confident | Neutral | Somewhat confident | Very confident |
|--------------------------------------|--------------------|---------|--------------------|----------------|
| Statins                              | 53%                | 70%     | 73%                | 71%            |
| Aspirin                              | 53%                | 50%     | 75%                | 74%            |
| Calcium channel blockers             | 53%                | 70%     | 58%                | 66%            |
| Nitrates                             | 50%                | 50%     | 58%                | 71%            |
| Beta blockers, or alpha/beta blockers| 40%                | 50%     | 54%                | 65%            |
| Ranolazine                           | 27%                | 25%     | 22%                | 35%            |
| ACEi/ARBs                            | 7%                 | 30%     | 25%                | 35%            |
| Cardiac rehabilitation               | 0%                 | 25%     | 31%                | 26%            |
| Antplatelets (Plavix or Ticagrelor)  | 7%                 | 10%     | 14%                | 26%            |
| L-arginine                           | 0%                 | 0%      | 2%                 | 3%             |
| Ivabradine                           | 0%                 | 0%      | 2%                 | 3%             |
| Enhanced External Counter Pulsation (ECP) | 0%           | 0%      | 2%                 | 0%             |
| Oral anticoagulation (i.e., warfarin or direct-oral anticoagulants) | 0% | 0% | 0% | 0% |
| Diuretics                            | 0%                 | 0%      | 0%                 | 0%             |
| Hormone therapy                      | 0%                 | 0%      | 0%                 | 0%             |
| Other                                | 0%                 | 5%      | 0%                 | 0%             |

N-Size: n=15, n=20, n=59, n=31

Heat Map Legend

Less used → More used
Figure S5. Follow-Up Timeframe with INOCA Patients After Initial Evaluation/Diagnosis. Results reported by tenure level (early, mid, late career) and by number of INOCA patients seen in practice.
Figure S6. Frequency of Referral to Other Colleagues or Centers for INOCA Patients. Results reported by tenure level (early, mid, late career) and by number of INOCA patients seen in practice.
Figure S7. Cardiologist Reported Common Characteristics and/or Risk Factors of INOCA Patients.
Figure S8. Ways to Improve Clinical Management of INOCA Patients.