

Society Guidelines

Canadian Cardiovascular Society Guidelines for the Diagnosis and Management of Stable Ischemic Heart Disease

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ABSTRACT

This overview provides a guideline for the management of stable ischemic heart disease. It represents the work of a primary and secondary panel of participants from across Canada who achieved consensus on behalf of the Canadian Cardiovascular Society. The suggestions and recommendations are intended to be of relevance to primary care and specialist physicians with an emphasis on rational

RÉSUMÉ

Cette vue d'ensemble offre des recommandations sur la prise en charge de la cardiopathie ischémique stable. Elle représente le travail d'un panel principal et d'un panel secondaire de participants de l'ensemble du Canada qui ont atteint un consensus au nom de la Société canadienne de cardiologie. Les suggestions et les recommandations doivent avoir rapport avec les soins primaires et les médecins

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The disclosure information of the authors and reviewers is available from the CCS on their guidelines library at www.ccs.ca.

This statement was developed following a thorough consideration of medical literature and the best available evidence and clinical experience. It represents the consensus of a Canadian panel comprised of multidisciplinary experts on this topic with a mandate to formulate disease-specific

recommendations. These recommendations are aimed to provide a reasonable and practical approach to care for specialists and allied health professionals obliged with the duty of bestowing optimal care to patients and families, and can be subject to change as scientific knowledge and technology advance and as practice patterns evolve. The statement is not intended to be a substitute for physicians using their individual judgment in managing clinical care in consultation with the patient, with appropriate regard to all the individual circumstances of the patient, diagnostic and treatment options available and available resources. Adherence to these recommendations will not necessarily produce successful outcomes in every case.

deployment of diagnostic tests, expedited implementation of long- and short-term medical therapy, timely consideration of revascularization, and practical follow-up measures.

In 2008, cardiovascular (CV) disease accounted for 29% of all deaths in Canada. Of these, 54% were due to ischemic heart disease.¹ Such an effect warrants careful attention to the appropriate diagnosis and management of stable ischemic heart disease (SIHD) to optimize outcomes and resource utilization. The Canadian Cardiovascular Society (CCS) last updated guidelines for SIHD in 2000.² Many advances in care have since occurred and guidelines from other societies updated.^{3,4} The purpose of this article is to promote evidence-based practice by providing SIHD recommendations of relevance in the Canadian context. The project was undertaken by primary and secondary panels of physicians who achieved a final consensus document. All recommendations use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) convention, which provides a descriptor of the strength of the recommendation and the quality of evidence.⁵ In the case of diagnostic testing, evidence evaluation considered bias, consistency, and precision of study results but with a major emphasis on readily available methods in community practices. This article does not focus on aspects of cardiac care covered by other CCS guidelines,⁶⁻¹⁴ but supports the access to specialty care and expertise framework of the CCS¹⁵ and the Choosing Wisely campaign.¹⁶ The main focus is on adult patients with suspected or known SIHD, covering 4 fundamental processes: establishing diagnosis and prognosis, initiating medical treatment, consideration of revascularization, and provision of appropriate follow-up (Fig. 1).

I. Establishing Diagnosis and Prognosis

In patients with symptoms suggestive of SIHD, the probability of having obstructive coronary artery disease (CAD) is primarily obtained using a thorough history. Classically, angina is described as a dull retrosternal discomfort/ache/heaviness that might or might not radiate to the jaw, neck, shoulders or arms, is provoked by exertion or emotional stress, and is relieved within 5 minutes of rest or nitroglycerine use.² However, nonclassical symptoms are common, particularly among diabetic patients, and even response to nitroglycerine might be misleading.¹⁷⁻¹⁹ Accordingly, the context is important and all risk factors should also be considered (Table 1). Although the physical examination has low sensitivity for the detection of CAD, abnormalities such as gallops, bruits or absent pulses, or obvious chest wall problems might alter the probability of underlying disease. A normal electrocardiogram (ECG) does not exclude the diagnosis, but an abnormal resting ECG increases the probability and might influence the choice of diagnostic tests. Routine laboratory tests should be obtained to determine the presence and severity of factors that might influence angina, choice of tests, or implementation of therapy (Tables 2 and 3).^{3,20} It is also important to evaluate non-CV comorbidities and quality of

spécialistes tout en insistant sur l'utilisation rationnelle des examens diagnostiques, la mise en œuvre rapide d'un traitement médical à court et à long terme, la prise en considération en temps opportun de la revascularisation et les mesures concrètes de suivi.

life issues because these might substantially influence appropriateness of diagnostic and treatment choices.

RECOMMENDATION

1. We recommend that a focused history and physical examination be obtained to elucidate symptoms, cardiac risk factors, medical history, and signs of CV disease or other aetiologies of symptoms (Strong Recommendation, High-Quality Evidence).
2. We recommend that CV comorbidities of heart failure, valvular heart disease, cerebrovascular and peripheral vascular disease, and renal disease should be fully documented (Strong Recommendation, High-Quality Evidence).
3. We suggest that initial assessment be supplemented by routine testing that includes hemoglobin, full cholesterol panel, fasting glucose, hemoglobin A1c, renal function tests, liver function tests, thyroid function tests, and a 12-lead ECG (Conditional Recommendation, Moderate-Quality Evidence).

Using noninvasive diagnostic and prognostic testing

Bayesian theory supports the premise that diagnostic testing has less effect on final diagnosis when pretest probability is at the extreme (eg, < 10%-15% or > 85%-90%). For example, a patient with a very high pretest probability of CAD

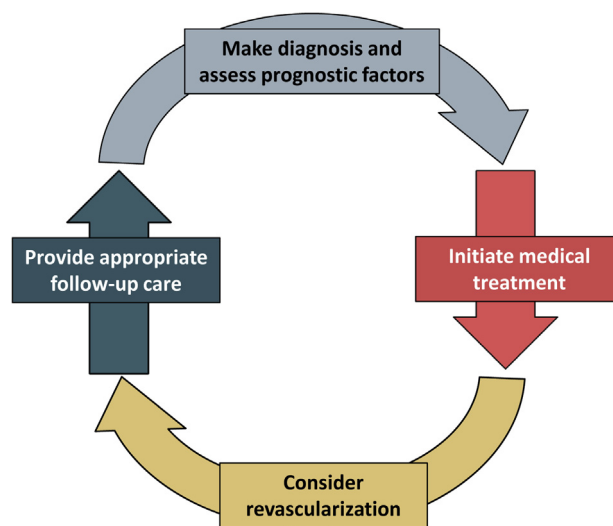


Figure 1. Diagnosis and management of patients with stable ischemic heart disease.

still has an intermediate to high posttest probability despite a negative or normal test result (likely false negative). Conversely, patients with a low pretest probability of CAD will still have a low to intermediate posttest probability despite a positive test result (which might be a false positive result). Thus, testing is generally considered to be inappropriate for diagnostic purposes in patients with a very low or very high pretest probability for CAD. However, recent evidence suggests that original values for pretest probability for obstructive CAD might be overestimated and alternative risk estimation algorithms have been proposed, some of which take into account underlying risk factors beyond age, sex, and number of angina characteristics.^{3,22-29}

Literal adherence to the pretest probabilities as shown for example in Figure 2 is not appropriate.^{22,29} For example, Figure 2 would imply that only men ≥ 50 years of age with typical angina can be confidently diagnosed clinically. Testing in this group will identify high-risk features affecting management decisions and dictating the pace at which the next steps are taken. Additionally, noninvasive testing would not normally be recommended for women < 60 or men < 40 years of age with only 1 classical feature of angina given a low pretest probability of CAD. However, other features, especially in women (eg, abnormal baseline ECG, diabetes, smoking, hyperlipidemia, hypertension, chronic kidney disease) would prompt a need for noninvasive testing.²⁵⁻²⁷ Finally, the intermediate risk group is an extremely broad group of patients. Thus, most patients ≥ 30 years of age with any classical features of angina might warrant noninvasive testing, not only for diagnostic reasons but also for prognostic purposes (Fig. 3).

RECOMMENDATION

1. We suggest that adults ≥ 30 years of age with 2 or 3 anginal criteria should undergo testing for diagnostic (and prognostic) purposes (Conditional Recommendation, Moderate-Quality Evidence).
2. We suggest that men ≥ 40 and women ≥ 60 years of age with 1 of 3 anginal features should undergo noninvasive testing for diagnostic (and prognostic) purposes (Conditional Recommendation, Moderate-Quality Evidence).
3. We suggest that men < 40 and women < 60 years of age with 1 of 3 anginal features have a low pretest likelihood of CAD but should undergo noninvasive diagnostic testing if other features indicative of CV risk are present (Conditional Recommendation, Low-Quality Evidence).

The diagnosis of underlying CAD can be established by detection of provoked myocardial ischemia (reflected by abnormal ECG changes, new regional wall motion abnormalities, or perfusion deficits) or underlying left ventricular wall motion abnormalities at rest or with stress, especially when associated with perfusion defects, or by detection of anatomical coronary artery stenoses.^{30,31} Advances in cardiac imaging using magnetic resonance and positron emission

Table 1. Cardiac risk factors

Modifiable	Nonmodifiable
Tobacco use/smoking history	Age
Dyslipidemia	Sex
Diabetes	Family history of premature established CV disease
Hypertension	Ethnic origin
Chronic kidney disease	
Physical inactivity	
Diet	
Obesity or metabolic syndrome	
Depression	

CV, cardiovascular.

tomography are rapid and exciting but not generally available outside of academic practice settings. Therefore, although commonly available tests are emphasized, local expertise and access to specialized tests should be considered when making these choices. The diagnostic accuracy of noninvasive tests varies (Table 4). When selecting the best initial test for a specific patient, clinicians must also consider patient characteristics, potential contraindications to testing, limitations of each modality, local availability, and local expertise (Fig. 4). Monitored exercise provides the most information concerning exercise capacity, patient symptoms, CV function, and hemodynamic response during usual forms of activity. It is also of greatest relevance to patient perception of disease. These factors are also of prognostic importance. With this in mind, treadmill exercise testing with a 12-lead ECG and blood pressure monitoring is a useful option for suspected SIHD because of its simplicity, low cost, and widespread availability. Patients must be able to exercise and to adequately augment their heart rate (85% of their target heart rate), and must not have ECG abnormalities limiting interpretation of ST segments (ST-depression ≥ 0.10 mV, digoxin use, pre-excitation/Wolff-Parkinson-White syndrome, complete left bundle branch block [LBBB], ventricular paced rhythm). A symptom- or sign-limited test should be performed, ideally without the influence of anti-ischemic drugs to obtain maximal diagnostic information. In patients who cannot exercise to an adequate workload, pharmacological testing with vasodilator perfusion imaging or dobutamine echocardiography should be considered. In the presence of LBBB or ventricular paced rhythm, vasodilator perfusion imaging is an appropriate option recognizing that absence of abnormalities is reassuring, reversible perfusion abnormalities confined to the septum might represent false positive results and defects elsewhere likely represent ischemia. Anatomical imaging for diagnostic purposes is an appropriate alternative when LBBB or paced ventricular rhythm is present.

Computed tomography (CT) can be used to detect coronary calcium or to generate a coronary angiogram. Although the presence of calcium identifies atherosclerosis, correlation with the degree of luminal narrowing is poor. Even with severe calcification, luminal stenosis might not be present, and, conversely, the absence of calcium does not rule out coronary artery stenoses in symptomatic individuals. Thus, if CT is used to evaluate suspected ischemic symptoms, cardiac CT angiography (CCTA) is preferred over calcium scoring. CCTA has a very high negative predictive value for obstructive CAD and is most appropriate for individuals who have a

Table 2. Alternative diagnoses to angina for patients with chest pain

Cardiovascular	Pulmonary	Gastrointestinal	Chest wall	Neurological	Psychiatric
Aortic dissection	Pulmonary embolism	Esophagitis	Costochondritis	Cervical disease	Anxiety disorders
Congestive heart failure	Pneumothorax	Esophageal spasm	Fibrositis	Herpes zoster	Hyperventilation
Pericarditis	Pleuritis	Biliary colic:	Fibromyalgia		Panic disorder
Syndrome X (microvascular disease)	Primary pulmonary hypertension	- Cholecystitis - Cholelithiasis - Cholangitis	Rib fracture		Affective disorders (eg, depression)
		Peptic ulcer disease	Sternoclavicular arthritis		Somatiform disorders
		Pancreatitis			Thought disorders (ie, fixed delusions)

Data from Fihn et al.³ and Gibbons et al.²¹

pretest probability in the lower ranges of the intermediate risk category for CAD. Patients with very high risk features requiring definitive assessment are likely to require invasive angiography and should not undergo CCTA. CCTA should also be avoided in patients with arrhythmia, significant renal dysfunction, or contrast media allergies.

Invasive coronary angiography is the benchmark investigation for establishing the presence of CAD causing luminal compromise but not for detection of early atheroma. Although radiation and contrast media concerns need to be considered within any clinical scenario, it remains the preferred diagnostic tool for patients who have a high pretest likelihood of CAD, high-risk features on previous noninvasive testing, persistent or uncontrolled symptoms, or impaired quality of life despite optimal medical treatment (see section II), life threatening arrhythmias, or who have survived sudden cardiac arrest.³⁵ However, it should not be offered to patients who do not wish to consider revascularization, or who are not candidates for revascularization because of significant non-CV comorbidities and non-CV quality of life issues.

As indicated already, noninvasive diagnostic tests also provide prognostic information. This is determined by the fundamental triad of ischemic burden, anatomical burden of

CAD, and left ventricular function, with baseline left ventricular ejection fraction generally providing the strongest prognostic information (Fig. 5).³⁶⁻⁴⁰ There are no routine, noninvasive tests that currently provide all three elements.^{41,42} Detection of ischemia provides a rationale for use of medications and consideration of revascularization, which should be limited to anatomically significant lesions associated with larger ischemic burden or lesion-specific measures of impaired flow.^{43,44} Left ventricular ejection fraction and anatomical extent of CAD retain value as measures of residual risk even in treated patients.³⁶⁻⁴⁰ Thus, the clinician should strive to assess all 3 elements within the limits of local expertise and availability of tests. This principle is also important when the initial test result is equivocal or highly discordant with clinical assessment. In this case, a second test can be chosen that assesses one of the 3 elements on which diagnosis and prognosis can be based that has not yet been assessed (eg, follow a nondiagnostic functional test with an anatomical test). Finally, in highly specialized centres with expertise and access to cardiac positron emission tomography, magnetic resonance imaging or CT perfusion scanning, these modalities might be considered a complement or alternative to the more routine testing already described. Accordingly, in Figure 4, reasonable options for an initial noninvasive test in routine practice are described. Finally, for any modality involving radiation it is important to keep in mind the relative radiation dosages and to ensure that the laboratory is using appropriate radiation reduction methods.⁴⁵

Table 3. Conditions that provoke or exacerbate ischemia

Increased oxygen demand	Decreased oxygen supply
Noncardiac	
Hyper/hypothermia	Anemia
Hyperthyroidism	Hypoxemia/high altitude
Sympathomimetic toxicity (eg, cocaine use)	Pneumonia
Hypertension	Asthma
Anxiety	Chronic obstructive pulmonary disease
High cardiac output states (eg, arteriovenous fistulae)	Pulmonary hypertension
	Interstitial pulmonary fibrosis
	Obstructive sleep apnea
	Sickle cell disease
	Sympathomimetic toxicity (eg, cocaine use, pheochromocytoma)
	Hyperviscosity (polycythemia, leukemia, thrombocytosis, hypergammaglobulinemia)
Cardiac	
Left ventricular hypertrophy	Aortic stenosis
Aortic stenosis	Hypertrophic cardiomyopathy
Hypertrophic cardiomyopathy	Obstructive coronary artery disease
Dilated cardiomyopathy	Microvascular disease
Tachycardia (ventricular, supraventricular)	Coronary spasm

Data from Fihn et al.³ and Gibbons et al.²¹

Age, Years	Chest Pain Criteria					
	1. Substernal chest discomfort with characteristic quality and duration					
	2. Provoked by exertion or emotional stress					
	3. Relieved promptly by rest or nitroglycerin					
	Nonanginal Chest Pain 1 of 3 Criteria		Atypical Angina 2 of 3 Criteria		Typical Angina 3 of 3 Criteria	
	Male	Female	Male	Female	Male	Female
30 – 39	4%	2%	34%	12%	76%	26%
40 – 49	13%	3%	51%	22%	87%	55%
50 – 59	20%	7%	65%	33%	93%	73%
60 – 69	27%	14%	72%	51%	94%	86%

Figure 2. Pretest likelihood of CAD detected using invasive angiography in symptomatic patients according to age and sex (combined Diamond Forrester and CASS Data). A low pretest risk of CAD was considered < 10% (green) and a high pretest risk was considered > 90% (red). All others were at intermediate risk (yellow). CAD, coronary artery disease; CASS, Coronary Artery Surgery Study. Data from Diamond and Forrester²² and Weiner et al.²⁹

RECOMMENDATION

1. We suggest that exercise testing, if possible, is preferred because it is more strongly perceived by patients as relevant to their activities than pharmacologic testing and provides assessment of functional capacity (Conditional Recommendation, Low-Quality Evidence).
2. We suggest that patients with an interpretable rest ECG who are able to exercise should have an exercise ECG test (ideally free of anti-ischemic drugs) (Conditional Recommendation, Low-Quality Evidence).
3. We suggest that the initial test in patients able to exercise, with a rest ECG that precludes ST segment interpretation, should be exercise myocardial perfusion imaging or exercise echocardiography (Conditional Recommendation, Moderate-Quality Evidence).
4. We suggest that the initial test in patients without LBBB or paced rhythm who cannot exercise be vasodilator stress myocardial perfusion imaging or dobutamine echocardiography (Conditional Recommendation, Moderate Quality Evidence).
5. We recommend that the initial test in patients with LBBB or ventricular paced rhythm should be either vasodilator stress myocardial perfusion imaging or CCTA (Strong Recommendation, High-Quality Evidence).
6. We recommend that a noninvasive assessment of rest left ventricular function be obtained in all patients with suspected SIHD (Strong Recommendation, High-Quality Evidence).
7. We suggest that patients with initially equivocal or non-diagnostic test results or a strong discrepancy between clinical impression and test results be considered for further testing using a complementary, noninvasive modality (Conditional Recommendation, Low-Quality Evidence).
8. We suggest that CCTA not be used in patients who are believed likely to warrant invasive angiography on the basis of high risk symptom pattern, high pretest probability of CAD, severe risk factors, or important reasons to minimize exposure to radiation or contrast material (Conditional Recommendation, Low-Quality Evidence).
9. We suggest that invasive coronary angiography be obtained in patients with SIHD who have a high pre-test likelihood of CAD, high-risk features on previous noninvasive testing, survived sudden cardiac arrest, or who have life-threatening arrhythmias (Conditional Recommendation, Moderate-Quality Evidence).

II. Initiation of Medical Treatment in Patients With Established CAD

Therapy for SIHD involves a combination of approaches to improve quality of life by minimizing or abolishing symptoms, and to improve prognosis by preventing myocardial infarction (MI) and premature death. Medical management can be implemented more expeditiously in most settings than can the steps required in anticipation of possible revascularization. However, expeditious revascularization therapy might be considered in parallel based on prognostic features of the diagnostic tests as discussed in section III.

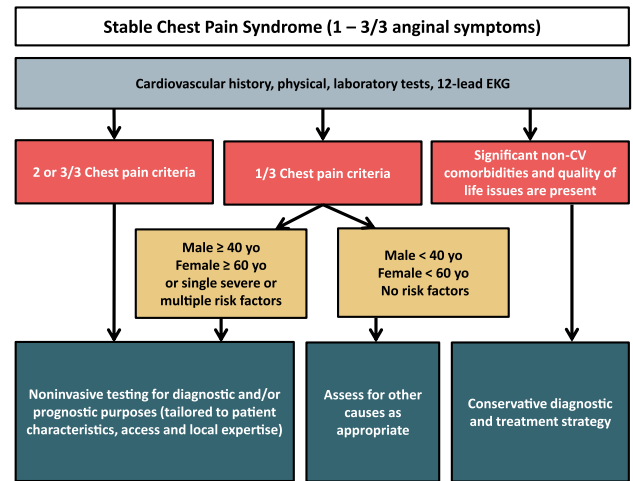


Figure 3. Use of noninvasive testing for diagnostic and prognostic purposes in patients with classical anginal chest pain symptoms suggestive of SIHD. CV, cardiovascular; ECG, electrocardiogram; SIHD, stable ischemic heart disease; yo, years old.

When a diagnosis of CAD is made, expeditious medical treatment optimization is a priority. Some drugs primarily improve prognosis by affecting underlying mechanisms of atherothrombosis, plaque stabilization, reduction of rate of progression, and neurohumoral activation. The need to use these agents perpetually requires emphasis when counselling patients, particularly if and when interventional therapy is provided. However, other drugs used primarily for relief of symptoms might be modulated throughout the course of follow-up and can often be diminished or eliminated over time.

The fundamental pharmacological therapy of SIHD consists of antiplatelet therapy, statins, angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers, and anti-ischemic drugs including β -blockers.^{2-4,11,13,46-60} Other medications for optimal management of risk factors or for optimization of heart failure symptoms are presented in other guidelines.^{9,12,13,61}

β -blockers are often preferred for chronic management of angina largely because of the association of benefit in the

Table 4. Summary estimates of pooled sensitivity and specificity (with 95% confidence intervals) for noninvasive cardiac tests for the diagnosis of coronary artery disease

Technology	Sensitivity	Specificity
Exercise treadmill	0.68 (0.23-1.0)	0.77 (0.17-1.0)
Attenuation-corrected SPECT	0.86 (0.81-0.91)	0.82 (0.75-0.89)
Gated SPECT	0.84 (0.79-0.88)	0.78 (0.71-0.85)
Traditional SPECT	0.86 (0.84-0.88)	0.71 (0.67-0.76)
Contrast stress echocardiography (wall motion)	0.84 (0.79-0.90)	0.80 (0.73-0.87)
Exercise or pharmacologic stress echocardiography	0.79 (0.77-0.82)	0.84 (0.82-0.86)
Cardiac computed tomographic angiography	0.96 (0.94-0.98)	0.82 (0.73-0.90)
Positron emission tomography	0.90 (0.88-0.92)	0.88 (0.85-0.91)
Cardiac MRI (perfusion)	0.91 (0.88-0.94)	0.81 (0.75-0.87)

MRI, magnetic resonance imaging; SPECT, single photon emission computed tomography.

Data from Gianrossi et al.,³² Medical Advisory Secretariat,³³ and McArdle et al.³⁴

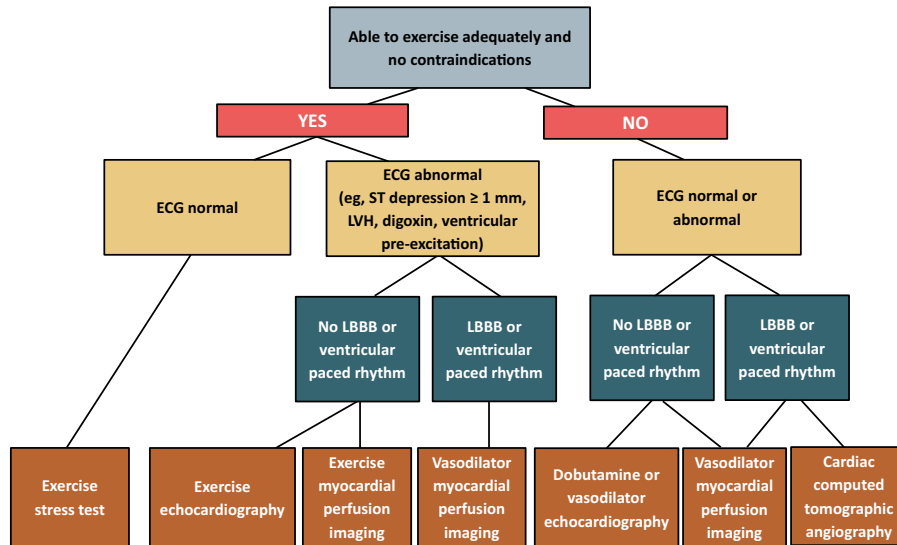


Figure 4. Guidance for selection of an initial noninvasive test for diagnosing suspected CAD in routine practice settings. Testing options may be modified where expertise and access to positron emission tomography, magnetic resonance imaging, or CT perfusion scanning exists. Patients expected to be able to augment heart rate to 85% of predicted maximum would be ideal candidates for stress ECG or stress imaging, but exercise stress should be avoided in the presence of symptomatic or known significant aortic stenosis or pulmonary hypertension (vasodilator stress or cardiac computed tomographic angiography are preferred in these circumstances). Exercise testing is also contraindicated in patients with acute myocardial infarction (within 2 days), unstable angina pectoris, uncontrolled arrhythmias causing symptoms of hemodynamic compromise, uncontrolled symptomatic heart failure, active endocarditis or acute myocarditis or pericarditis, suspected aortic dissection, suspected acute pulmonary or systemic embolism, and noncardiac disorders that might be aggravated with exercise. Concomitant use of atropine with dobutamine stress is contraindicated in patients with glaucoma. Dobutamine should not be used in patients with ventricular arrhythmias, recent myocardial infarction, unstable angina, significant aortic outflow obstruction, aortic dissection, or severe hypertension. Vasodilator stress should not be used in patients with known renal artery stenosis, hypotension, high-degree AV block, sick sinus syndrome, severe bronchospasm, or oral use of dipyridamole. Patients with atrial fibrillation are not ideal candidates for coronary imaging using cardiac computed tomographic angiography (special gating or retrospective imaging will be required). AV, atrioventricular; CAD, coronary artery disease; CT, computed tomography; ECG, electrocardiogram; LBBB, left bundle branch block; LVH, left ventricular hypertrophy.

setting of previous MI, low ejection fraction, or heart failure. In the absence of these, angina can be treated with either a β -blocker or calcium channel blocker depending on symptom relief and tolerability. In cases of suboptimal symptom relief, consideration should be given to switching to the other therapy, combining β -blockers with preferably a long-acting calcium channel blocker (preferably a dihydropyridine), or

adding long-acting nitrates.^{3,62,63} Caution is warranted when combining a β -blocker with nondihydropyridine calcium channel blockers (eg, verapamil or diltiazem) because of the potential development of severe bradycardia, atrioventricular block, or excessive fatigue. In patients who might not tolerate even cardioselective β -blockers or who have contraindications to β -blockade (eg, asthma, severe Raynaud phenomenon), calcium channel blockers and long-acting nitrates become the recommended initial options for angina relief. Sublingual nitroglycerin can be used intermittently for exertional angina or prophylactically when certain activities are known to elicit angina. It should be noted that other antianginal medications not yet available in Canada might warrant modification of these recommendations in the future (eg, ivabradine, ranolazine). Finally, some methods for improving angina or exercise tolerance remain controversial and are not recommended at this time (eg, chelation therapy, allopurinol, magnesium supplementation, coenzyme Q10, suxiao jiu xin wan and shenshao tablets, testosterone).³ Although a recent National Institutes of Health-sponsored trial⁶⁴ comparing ethylenediaminetetraacetic (EDTA)-based chelation vs placebo infusion in post-MI patients demonstrated a significant reduction in recurrent vascular events, all previous studies on this topic in patients with SIHD have been negative.³ Failure to achieve elimination or an acceptable level of symptoms and/or an acceptable quality of life after optimal implementation of recommended medications warrants consideration of revascularization rather than these controversial antianginal therapies.

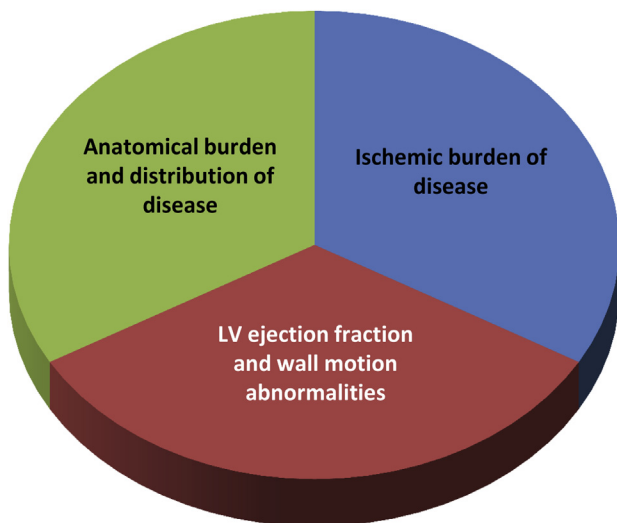


Figure 5. Fundamental prognostic factors for assessing stable ischemic heart disease. LV, left ventricular.

All SIHD patients should receive information and therapeutic interventions focused on ameliorating and eliminating unhealthy behaviours such as smoking, physical inactivity, and poor nutrition with recommendations available in other Canadian guidelines.^{14,61,65} These also address the specifics of individual risk factor management (eg, hypertension, diabetes, dyslipidemia, smoking cessation).^{11-13,61} In the absence of high-risk noninvasive test features warranting early consideration of revascularization (Table 5), the practitioner should strive to expeditiously initiate and optimally titrate all warranted medications. Based on access to care criteria within Canada, it is suggested that patients suspected of having SIHD should have noninvasive diagnostic testing within 2 weeks of initial assessment, specialist assessment within a further 6 weeks, and, if necessary, cardiac catheterization within another 6 weeks.¹⁵ This period of roughly 12-16 weeks should be adequate to aggressively institute and titrate all indicated medications, determine adequacy of symptom relief and quality of life, and identify patients who might warrant consideration of revascularization. Many patients treated in this fashion will achieve quality of life and symptom resolution equivalent to that afforded by early revascularization, with equivalent long-term outcomes.⁶⁶⁻⁶⁹

Chronic management for the patient with SIHD to improve prognosis

RECOMMENDATION

1. We recommend that all patients receive 81 mg of acetylsalicylic acid daily indefinitely, unless contraindicated (Strong Recommendation, High-Quality Evidence).
2. We recommend that clopidogrel 75 mg daily be used in acetylsalicylic acid-intolerant individuals (Strong Recommendation, High-Quality Evidence).
3. We suggest that dual antiplatelet therapy should not be used in routine management of SIHD or beyond the time period required as a result of stenting (Conditional Recommendation, Moderate-Quality Evidence).
4. We recommend that all patients receive a statin in accordance with CCS 2012 Dyslipidemia Guidelines (Strong Recommendation, High-Quality Evidence).
5. We recommend that all patients with SIHD who also have hypertension, diabetes, a left ventricular ejection fraction of < 40%, or chronic kidney disease should receive an ACE inhibitor, unless contraindicated (Strong Recommendation, High-Quality Evidence).
6. We recommend that it is also reasonable to consider treatment with an ACE inhibitor in all patients with SIHD (Strong Recommendation, High-Quality Evidence).
7. We recommend that angiotensin receptor blockers should be used for patients who are intolerant of ACE inhibitors (Strong Recommendation, High-Quality Evidence).
8. We recommend that β -blocker therapy be used in all patients with SIHD and left ventricular systolic dysfunction (ejection fraction < 40%) with or without heart failure, unless contraindicated, and continued indefinitely (Strong Recommendation, High-Quality Evidence).

Chronic management of anginal symptoms

RECOMMENDATION

1. We suggest that β -blockers be considered for first-line therapy for chronic stable angina if the patient has had an MI, or has reduced ejection fraction or heart failure, with the dose titrated to reach a target resting heart rate of 55-60 beats per minute (Conditional Recommendation, Moderate-Quality Evidence).
2. We suggest that β -blockers or long-acting calcium channel blockers be used for chronic stable angina in uncomplicated patients (Conditional recommendation/Moderate-Quality Evidence).
3. We suggest the addition of a long-acting nitrate when initial treatment with a β -blocker and/or a long-acting calcium channel blocker is not tolerated or contraindicated or does not lead to adequate symptom control (Conditional Recommendation, Moderate-Quality Evidence).
4. We recommend avoiding nondihydropyridine calcium channel blockers in combination with β -blockers if there is risk of atrioventricular block or excessive bradycardia (Strong Recommendation, High-Quality Evidence).
5. We suggest that chelation therapy, allopurinol, magnesium supplementation, coenzyme Q10, suxiao jiu xin wan or shenshao tablets, and testosterone should not be used to attempt to improve angina or exercise tolerance (Conditional Recommendation, Moderate-Quality Evidence).
6. We recommend that implementation and optimization of medical therapy should be achieved within 12-16 weeks of an initial evaluation suggesting presence of SIHD without high-risk features during which adequacy of symptom control and quality of life can be assessed before consideration of revascularization therapy (Strong Recommendation, High-Quality Evidence).

III. Consideration of Revascularization Therapy

Revascularization therapy is also indicated to improve symptoms or quality of life and/or to reduce the risk of MI and premature death. There is no controversy regarding the need to explore revascularization in SIHD patients with inadequate symptom relief, suboptimal quality of life, or emergence of acute chest pain syndromes while using medical therapy. However, because of the success of available medical therapy, and new forms of medical and revascularization therapies, categorical statements about interventions solely for improvement of prognosis remain somewhat controversial and are the subject of ongoing trials. Revascularization can be considered early when high-risk features are identified in noninvasive test results although even this common practice is under current investigation.^{21,70} Patients with high-risk features (Table 5) warrant expedited follow-up and specialist consultation. Invasive angiography is appropriate and a prerequisite for selecting the best revascularization option, even as optimization of medical therapy takes place. Because

noninvasive functional testing might still represent a false positive result and revascularization would not be warranted in patients without critical or multivessel disease.^{21,71-73} CCTA is sometimes used before proceeding to invasive angiography although this practice remains controversial.

The choice between coronary artery bypass grafting and percutaneous coronary intervention can be complicated because the decision must consider comorbidities such as diabetes, extent of atherosclerosis, and many technical issues including but not limited to location of stenosis with respect to side branches and bifurcations, and whether arterial vs venous conduits are feasible^{23,44,66,71-133} (a more technical CCS guideline on multivessel revascularization is in process). There are also some clinical circumstances pertaining to lifestyle and occupation (eg, drivers, pilots, train engineers, athletes). In many situations, decision-making by a "heart team" consisting of cardiologists and cardiac surgeons taking into account all of these factors, including patient preferences, technical advances in revascularization, and local practice nuances should be used.

RECOMMENDATION

1. We recommend that coronary angiography be considered early in patients who are identified to have high-risk noninvasive test features (Strong Recommendation, High-Quality Evidence).
2. We recommend that patients who develop medically refractory symptoms or inadequate CV quality of life while using medical therapy should undergo elective coronary angiography in anticipation of possible revascularization procedures (Strong Recommendation, High-Quality Evidence).

IV. Provision of Appropriate Clinical Follow-up

The most appropriate clinical follow-up in patients with SIHD is difficult to clearly define because of the paucity of robust research. However, there is a need for regular communication between primary care practitioners and specialists expert in the provision of chronic disease care for such patients.³ Follow-up visits should include a focused history, physical examination, and clinically appropriate laboratory testing, with an emphasis on ensuring optimal risk factor control. The history should include an assessment for any changes in symptoms of angina or heart failure, adherence to prescribed medications and any side effects, addition of new medications, appropriate nutrition, weight optimization, smoking cessation where appropriate, and onset of any new disease conditions. On physical examination, clinicians should focus on resting heart rate and blood pressure, signs of heart failure or arrhythmia, and new or worsening vascular bruits or murmurs, and status of the abdominal aorta.

Laboratory investigations should include assessment of metabolic fitness (serum lipids, glucose, complete blood count, renal function) and a resting ECG. Annual ECG testing might be appropriate even in the absence of symptoms or change in status to ensure that a recent comparator ECG is available should symptoms change. New resting ECG repolarization abnormalities have been shown to predict CV events.

Table 5. High-risk features of noninvasive test results associated with > 3% annual rate of death or MI

Exercise treadmill
• ≥ 2 mm of ST-segment depression at low (< 5 metabolic equivalents) workload or persisting into recovery • Exercise-induced ST segment elevation • Exercise-induced VT/VF • Failure to increase systolic blood pressure to > 120 mm Hg or sustained decrease > 10 mm Hg during exercise
Myocardial perfusion imaging
• Severe resting LV dysfunction (LVEF $\leq 35\%$) not readily explained by noncoronary causes • Resting perfusion abnormalities $\geq 10\%$ of the myocardium in patients without previous history or evidence of MI • Severe stress-induced LV dysfunction (peak exercise LVEF < 45% or decrease in LVEF with stress $\geq 10\%$) • Stress-induced perfusion abnormalities encumbering $\geq 10\%$ myocardium or stress segmental scores indicating multiple vascular territories with abnormalities • Stress-induced LV dilation • Increased lung uptake
Stress echocardiography
• Inducible wall motion abnormality involving > 2 segments or 2 coronary beds • Wall motion abnormality developing at low dose of dobutamine (≤ 10 $\mu\text{g/kg/min}$) or at a low heart rate (< 120 beats per minute)
Coronary computed tomographic angiography
• Multivessel obstructive CAD or left main stenosis on CCTA

CAD, coronary artery disease; CCTA, cardiac computed tomography angiography; LV, left ventricular; LVEF, left ventricular ejection fraction; MI, myocardial infarction; VF, ventricular fibrillation; VT, ventricular tachycardia. Data from Fihn et al.³

Patients with a change in symptom status or functional capacity might benefit from testing using the outlined general approach for test selection, to investigate potential progression of CAD, or possible stent or graft stenosis. Comparisons are easier if the noninvasive test chosen previously is chosen again but only if still appropriate. Because most of the therapy in follow-up is based on management of residual or new ischemia and functional status, exercise tests that demonstrate ischemia are preferable if feasible.

The principles for considering revascularization are similar to the principles already described but are affected by the type and extent of medical and revascularization therapies already used.

Exercise-based cardiac rehabilitation is effective in reducing total and CV mortality and hospital admissions in patients with a recent MI, and has been shown to have utility after revascularization.^{14,134-142} Its utility in patients with chronic stable angina is less well documented. Outside of such programs, optimal use of prognostic testing in the absence of symptoms is difficult to frame because of a lack of definitive data. Repeat testing to assess left ventricular function or to document provoked ischemia is not generally indicated in the absence of symptoms. However, it might be considered if the initial presentation was atypical; if revascularization was not performed or is known to be suboptimal or incomplete; if a patient undergoes strenuous tasks at work, during hobbies, or unsupervised exercise programs; if a patient has an unexplained but angina-free deterioration in exercise capacity; or if the patient's employment status warrants testing (eg, commercial driving).¹⁶ Testing might rarely be indicated if non-CV surgery is being considered in patients free of angina or symptoms of heart failure.^{3,4,143}

RECOMMENDATION

1. We suggest that a resting ECG be acquired with a change in symptom status or in the setting of annual routine clinical follow-up (Conditional Recommendation, Low-Quality Evidence).
2. We suggest that patients with SIHD who have not previously participated be referred to a comprehensive cardiac rehabilitation program (Conditional Recommendation, Moderate-Quality Evidence).
3. We suggest that asymptomatic patients with SIHD, with the approval of their physician, should accumulate 150 minutes of moderate to vigorous physical activity per week, preferably in bouts of 10 minutes or more, with additional exercise providing additional benefits (Conditional Recommendation, Moderate-Quality Evidence).
4. We suggest that patients whose symptoms are not controlled with use of optimal medical therapy should be re-evaluated as per the sections on diagnosis and revascularization (Conditional Recommendation, Low-Quality Evidence).
5. We suggest that routine use of exercise stress testing (excluding formal cardiac rehabilitation programs) or exercise/pharmacological stress cardiac imaging in asymptomatic patients with SIHD should be avoided (Conditional Recommendation, Moderate-Quality Evidence).

Summary

SIHD is common, requires expeditious diagnosis, implementation of medical therapies, correction of CV risk factors, timely consideration of revascularization options, and appropriate follow-up. This Canadian perspective provides a practical approach applicable in most practice settings for optimization of longevity and quality of life, with ample regard for rational resource utilization.

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