Canadian Cardiovascular Society
Leadership. Knowledge. Community.

Société canadienne de cardiologie
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1997: CONSENSUS CONFERENCE ON THE EVALUATION AND MANAGEMENT OF CHRONIC ISCHEMIC HEART DISEASE

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1997: CONSENSUS CONFERENCE ON THE EVALUATION AND MANAGEMENT OF CHRONIC ISCHEMIC HEART DISEASE

The purpose of the Canadian Cardiovascular Society (CCS) Consensus on the Evaluation and Management of Chronic Ischemic Heart Disease is to establish an appropriate position for Canadian physicians to choose appropriate diagnostic manoeuvres and treatment for patients with this disorder. The CCS has published consensus positions on acute myocardial infarction (MI), the postinfarction patient and interventional therapy for coronary artery disease (CAD). A consensus will be developed for cardiovascular risk factors. None of these subjects is dealt with in detail in this document. The terms used in this consensus conference are listed in Appendix 1.

Where possible, the weight of evidence based on the scientific quality of clinical trials and the strength of recommendation of the CCS Panel are according to those listed in Appendix 2 (1).

PATHOPHYSIOLOGY OF CHRONIC ISCHEMIC HEART DISEASE

The overwhelming majority of patients with clinically recognizable chronic ischemic heart disease have atherosclerosis of the coronary arteries as the pathological basis. Atherosclerosis is a disease of arterial intima involving monocytes, inflammatory cells, smooth muscle cells, fibrous tissue and variable amounts of extracellular lipid covered on the luminal side by a fibrous cap. These atheromatous plaques produce progressive narrowing of the coronary arteries and ultimately may occlude the vessel gradually or, if the plaque is disrupted, acutely. Less common causes of chronic ischemic heart disease are listed below.

Narrowing and occulusion of vessels results in intermittent or chronic imbalance between myocardial oxygen supply and demand. Fixed coronary lesions produce symptoms as a result

of alteration in oxygen demand. Dynamic coronary lesions produce symptoms by reducing supply without change in demand. The pain of angina is poorly understood but is probably due to the development of tissue acidosis; change in intracellular electrolyte concentration; the release of adenosine and other metabolites; and the production of bradykinin, serotonin and histamine in ischemic myocardium. The pain is transmitted to the brain through afferent autonomic nerve fibres via sympathetic ganglia. Many ischemic episodes are symptomless, while others may produce acute symptoms of heart failure or low cardiac output due to depressed myocardial contractility. Atherosclerosis in coronary arteries is often accompanied by atherosclerosis in other parts of the arterial circulation.

Frame 1

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Pathophysiology of chronic ischemic heart disease

Fixed narrowing of lumen may be caused by

- Atherosclerosis;
- Congenital anomalies;
- Arteritis;
- Emboli;
- Thrombus;
- Kawasaki disease.

Dynamic narrowing of lumen may be caused by

- Vasospasm plus atherosclerosis;
- Platelet thrombus plus atherosclerosis;
- Fibrin thrombus plus atherosclerosis;

- Vasospasm;
- Ventricular hypertrophy;
- Microcirculation flow abnormality (syndrome X).

Inadequate flow reserve may be caused by

- Ventricular hypertrophy;
- Microcirculation flow abnormality (syndrome X).

EPIDEMIOLOGY OF CHRONIC ISCHEMIC HEART DISEASE

Ischemic heart disease is the single most common cause of death in Canada. The incidence increases significantly for both sexes beyond the age of 65 years (Table 1). The frequency and extent of ischemia predict both morbidity and mortality in individual patients, while symptoms alone are relatively poor predictors of morbidity and mortality.

DIAGNOSIS OF CHRONIC ISCHEMIC HEART DISEASE

Diagnosis of chronic ischemic heart disease should begin with a history and physical examination seeking findings of chronic stable angina, complications of myocardial ischemia or anginal equivalents. Very great patient to patient variation may occur in all of these clinical groups, as illustrated below.

Diagnosis of chronic ischemic heart disease

Patient history may reveal

- Chronic stable angina (typical or atypical [diagnosed by defining the character or location], radiating or nonradiating);
- Acute complications (unstable angina, myocardial infarct, sudden death);
- Anginal equivalents (acute left ventricular failure, dyspnea, weakness, flash pulmonary edema, arrhythmia, dizziness, palpitation, syncope, resuscitated sudden death).

The following risk factors for early onset of ischemia should be sought:

- Male;
- Postmenopausal female;
- Family history;
- Tobacco use;
- Hyperlipidemia;
- Hypertension;
- Diabetes mellitus;
- Central obesity;
- Sedentariness;
- Stress;
- Personality type.

The likelihood of symptoms or signs being due to chronic ischemic heart disease is increased by the presence of risk factors for early onset of coronary atherosclerosis or other disorders producing myocardial ischemia. Abnormalities on physical examination may alert the clinician to the likelihood of chronic ischemic heart disease.

Diagnosis of chronic ischemic heart disease: Physical examination

The physician may be alerted to the likelihood of ischemic heart disease by

- Vascular abnormalities including
- hypertension;
- fundal arteriolar sclerosis;
- peripheral arterial abnormalities;
- aortic aneurysm;
- Cardiac abnormalities including
- mitral regurgitation murmur;
- S3 or S4;

- displaced/broadened apex impulse;
- ventricular aneurysm impulse;
- jugular venous distension/hepatojugular reflex.

Risk factors that may be revealed on physical examination include

- Corneal arcus;
- Xanthelasma and xanthomata;
- Obesity.

Frame 321

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Chronic ischemic heart disease

A number of noncoronary disorders of the heart may induce myocardial ischemia or mimic the symptoms or signs of ischemia. Many noncardiac diseases must be considered in the differential diagnosis of chronic ischemic heart disease.

Differential diagnosis of chronic ischemic heart disease: Noncoronary cardiac disease

The following cardiac disorders may induce or mimic myocardial ischemia

- Arrhythmia;
- Aortic aneurysm;
- Pericardial disease;
- Aortic dissection;
- Myocarditis;
- Syndrome X;
- Cardiomyopathy;
- Valve disease.

The following noncardiac diseases may mimic chronic ischemic heart disease

- Gastrointestinal disorders including
- esophageal disorders;
- gallbladder disorders;
- peptic ulcers;
- pancreatitis;
- splenic flexure distension;
- acute upper airway aspiration;
- Musculoskeletal disorders including
- thoracic outlet syndrome;
- fibromyalgia;
- herpes zoster;
- chest wall hyperesthesia;
- Pulmonary disorders including
- pulmonary embolus;
- pulmonary hypertension;
- pneumothorax;
- mediastinal emphysema;
- asthma;
- Neuropsychiatric disorders including
- chronic anxiety;
- hypochondriasis.

DIAGNOSTIC TESTING IN CHRONIC ISCHEMIC HEART DISEASE

Noninvasive and invasive testing are performed to confirm or clarify a diagnosis of chronic ischemic heart disease, determine the severity and extent of the disease, and determine prognosis and optimal treatment. Sensitivity and specificity define how effectively a test is able to confirm or rule out a diagnosis. Sensitivity is the percentage of individuals with a disease who have abnormal tests. Specificity is the percentage of individuals without the disease who have a normal test. Specificity may be affected by age, sex, family history, presence of risk

factors for the disease and other variables. These variables differ from test to test. Sensitivity and specificity are inversely related, and false negative and false positive results are expected when arbitrary cut-off points are selected to optimize the diagnostic accuracy of the test.

Bayesian theory, which incorporates the pretest risk of the disease and the sensitivity and specificity of the test, allows one to calculate the post-test probability of disease being present. The diagnostic power of testing is maximal when the pretest probability of disease being present is intermediate (between 30% to 70%). If the pretest risk is very low, a positive test has a high probability of being falsely positive, and if the pretest risk is very high, a negative test result may be falsely negative.

Noninvasive testing

Electrocardiography: The electrocardiogram is of value in diagnosis and follow-up of all patients with known or suspected chronic ischemic heart disease. While a normal electrocardiogram is a basis for follow-up, an intermittent or fixed repolarization abnormality is of diagnostic and sometimes prognostic value.

Ambulatory electrocardiography: Ambulatory 24 h electrocardiogram recording may be useful, for both diagnosis and quantification of myocardial ischemia. It is useful for assessment of clinical stability when exercise testing is not feasible, in detection of silent ischemia during daily activities and in cases where ischemia is suspected at rest. It detects ischemia during activities of daily living. Exercise stress testing is, however, a more efficient way to confirm the diagnosis and accurately quantify individual patient limitation. Holter monitoring for ambulatory detection of ST segment shift is not recommended as a routine screening or diagnostic procedure in patients with known or suspected chronic ischemia.

Noninvasive diagnosis of chronic ischemic heart disease

Electrocardiography

- Is rapid;
- Is readily available;
- Is inexpensive;
- Often provides a diagnosis based on pathological Q waves;
- May time events;
- May reveal associated disorders;
- Is useful during ischemia.

The following are less helpful aspects of electrocardiography:

- Results are often normal;
- It is seldom specific;
- It has low sensitivity;
- Electrocardiographic interpretation may be impossible in patients with left bundle branch block (LBBB), pre-excitation, left ventricular hypertrophy (LVH) or digitalis effect.

Holter monitoring

- Has a sensitivity and specificity equal to that of exercise test;
- Detects silent ischemia;
- Can be used to evaluate therapy;
- Detects ischemia-related arrhythmia.

Exercise testing: Exercise testing is a valuable diagnostic tool for objective confirmation of the presence of myocardial ischemia on exertion, assessment of the extent of myocardial ischemia and documentation of the exercise capacity of the patient. Significant electrocardiographic changes during exercise testing are of value in diagnosis and prognosis, in the presence or absence of symptoms. Electrocardiographic interpretation may be impossible in LBBB and right bundle branch block (RBBB), paced rhythm, LVH, pre-excitation phenomenon or digitalis

effect. The advantages and prognostic value of exercise testing and the determinants of a positive test are described below.

The highest yield is found in populations with an intermediate probability of having the disease. A high rate of false positive tests in females who are premenopausal or on estrogen therapy, up to 50%, makes a negative test valuable, but a positive test is of less diagnostic value because of lower pretest likelihood of disease.

Noninvasive diagnosis of chronic ischemic heart disease *(grade A, classII)*

Exercise testing

- Tests the body's response to graduated dynamic exercise;
- Establishes a diagnosis;
- Assesses functional capacity;
- Provides a rate pressure product that correlates with myocardial VO_2;
- Assesses response to treatment;
- Estimates prognosis;
- Detects hypertension;
- Detects ventricular failure (ischemic).

The exercise test may be interpreted as follows:

- ST segment depression is significant with or without pain.
- ST depression 1.0 mm or greater is abnormal if horizontal or downsloping.
- ST elevation 1.0 mm or greater is abnormal.
- Systolic blood pressure drop greater than
  10 mmHg indicates severe disease.
- Sensitivity and specificity vary with disease severity and pretest probability.
- Prognosis is good with Bruce stage III or more.
- Mortality is greater than 5%/year in patients with a positive test result for Bruce stage I.
- Mortality is less than 1%/year in patients with a negative test result for Bruce stage III.

Echocardiography: Echocardiography is very useful in identifying and quantifying the consequences of chronic ischemic heart disease, MI or chronic ischemic cardiomyopathy. In the absence of ischemia, previous MI or its complications, or hypertension as a risk factor, resting echocardiography may be normal and should not be routine. Echocardiography gives information about cardiac anatomy and pathology in addition to the myocardial component.

Stress echocardiography: Stress echocardiography can be carried out during or following exercise or with pharmacological provocation of myocardial ischemia. Ischemia produces wall motion changes identified and quantified by echocardiography. The diagnostic determinants of myocardial ischemia identified with stress echocardiography and the indications for stress echocardiography are listed below. Stress echocardiography has diagnostic value similar to that of stress nuclear myocardial perfusion imaging or stress radionuclide angiography.

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Chronic ischemic heart disease

Noninvasive diagnosis of chronic ischemic heart disease *(grade A, class II)*

Resting echocardiography

- Is very useful in confirming an old myocardial infarct when history or electrocardiogram is not diagnostic;
- Rules out transmural infarction by detection of normal left ventricular function;
- Is very useful in detecting and quantifying left ventricular aneurysm, papillary muscle dysfunction, ventricular septal defect, left ventricular thrombus, mural scar, systolic or diastolic dysfunction, or associated valvular or congenital abnormalities.

Stress echocardiography

- Detects change in wall motion in response to increased workload stress induced by treadmill exercise or cycle ergometer exercise, atrial pacing, pharmacological stress, dipyridamole or adenosine (lower sensitivity), and arbutamine or dobutamine (higher sensitivity);

- Has a sensitivity of 89%, specificity of 80% and positive predictive value of 87%.

The following are indicators of ischemia:

- Failure of segment(s) to become hyperdynamic;
- New or worsened wall motion abnormality;
- Typical pain or ST changes;
- Greater than 10 mmHg drop in blood pressure (with exercise or dobutamine).

The following are indications for stress echocardiography:

- Suspected false positive or negative standard stress test;
- Abnormalities on resting electrocardiogram including
- ST or T wave abnormality;
- LBBB, RBBB or LVH;
- pre-excitation;
- digitalis.
- Pharmacological stress for patient unable to exercise.

Radionuclide myocardial perfusion imaging: Where exercise stress testing or 24 h ambulatory electrocardiographic recording has left doubt about the diagnosis or more detailed and accurate definition of the extent of myocardial ischemia is needed, radionuclide perfusion imaging provides all the information available from the less expensive procedures as well as a highly reliable definition of the distribution and severity of ischemic disease. The sensitivity and specificity of single photon imaging with sestamibi or tetrafosmin along with attenuation correction, gated images and simultaneous acquisition of ejection fraction (EF) are 91% and 90%, respectively. These techniques have largely replaced planar imaging. Although exercise testing is a common mode of inducing myocardial hyperemia, supplementary or complementary pharmacological methods such as intravenous dipyridamole, dobutamine,

arbutamine or adenosine have similar sensitivity and specificity. Radionuclide myocardial perfusion imaging is particularly useful in individuals who cannot exercise, in whom myocardial ischemia is induced pharmacologically. It is also extremely useful in premenopausal women in whom the exercise stress test is thought to be falsely positive. The sensitivity and specificity of perfusion imaging, abnormalities that indicate extensive ischemia and a poorer prognosis, and important indications for this valuable procedure are listed below.

There is no indication for routine myocardial perfusion imaging in patients with known coronary CAD unless the clinical diagnosis of change of degree of ischemia has been made.

Noninvasive diagnosis of chronic ischemic heart disease ***(grade A, class II)***

Radionuclide myocardial perfusion imaging

- Uses thallium-201 or sestamibi single photon emission computed tomography imaging (sensitivity 91%, specificity 90%);
- Is useful because high risk images are
- multiple reversible defects;
- large perfusion defects;
- increased lung uptake indicating low cardiac output or elevated left ventricular end-diastolic pressure;
- transient left ventricular dilation postexercise;

 Uses quantitative planar thallium-201 or sestamibi scintigraphy (sensitivity 80%, specificity 80%), largely replaced with single photon emission computed tomography imaging.

The following are indications for radionuclide myocardial perfusion imaging (exercise or pharmacological stress):

- Suspected false positive or negative exercise test;
- LBBB, RBBB, LVH, digitalis, pre-excitation, pacemaker;
- Women with positive exercise test and low or intermediate probability of coronary disease;

- Inability to exercise;
- Prognosis of known coronary disease;
- Detection of postpercutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass graft (CABG) stenosis;
- Determination of myocardial viability;
- Risk evaluation in noncardiac surgery patients;
- Assessment of functional significance of coronary stenosis.

Radionuclide angiography: Radionuclide angiography at rest gives important information about complications of ischemic heart disease, including ventricular dilation, segmental wall motion abnormality and depressed EF. When coupled with exercise, important information about ischemia-induced wall motion abnormality or depression of global left ventricular EF is obtained, which is useful for diagnosis and prognosis. Radionuclide angiography may be the best noninvasive procedure for measurement of EF at rest or on exercise. EF normally rises in men during exercise but often does not rise in women whose rise in cardiac output is due to cardiac dilation.

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Noninvasive diagnosis of chronic ischemic heart disease *(grade A, class II)*

Radionuclide angiography (rest and exercise)

- Determines left and right ventricular EF;
- Determines regional wall motion;
- Determines normally greater than 5% increase in EF on exercise;
- Determines falling EF on exercise, which denotes poor prognosis;
- Determines right ventricular dilation due to increased pulmonary artery pressure.

Positron emission tomography: The fundamentals of positron emission tomography are outlined below. It remains expensive and is unavailable in the majority of Canadian centres. Positron emission tomography is the gold standard of noninvasive tests in its ability to detect the metabolic consequences of myocardial ischemia and to discriminate between viability of myocardium and abnormalities of coronary flow.

Noninvasive diagnosis of chronic ischemic heart disease ***(grade A, class II)***

Positron emission tomography

- Detects viable myocardium with F-18-fluorodeoxyglucose;
- Uses rubidium-82, nitrogen-13 ammonia and 15O-labelled water as flow tracers;
- Is highly accurate in detecting functional significance of coronary disease;
- Is expensive and of limited availability.

Selective coronary angiography and left heart catheterization: No other procedure gives as much and as accurate information about coronary artery anatomy and pathology and the extent of myocardial damage or other structural abnormalities resulting from complications of chronic ischemic heart disease as selective coronary angiography and left heart catheterization. Full evaluation of high risk patients ultimately requires cardiac catheterization and coronary angiography.

Major indications for cardiac catheterization and coronary angiography are to confirm the diagnosis, determine the extent of coronary disease and decide upon angioplasty or bypass surgery as a supplement or alternative to medical therapy. It is less frequently required to diagnose and determine the extent of complications of chronic ischemic heart disease, such as structural cardiac changes, that may require surgical intervention. Finally, unusual individual circumstances, as outlined below, may require catheterization information to resolve important issues for the patient, such as ruling out atherosclerotic coronary disease in atypical pain.

The newly emerging technique of intravascular ultrasound, which shows fine details of vessel anatomy and pathology, is being evaluated for determining the adequacy of ancillary procedures to coronary angioplasty, such as stenting, and for detecting and assessing left

main lesions. The reader is referred to the 1995 CCS Consensus on Indications for and Access to Revascularization (2) for further detail.

Indications for invasive testing ***(grade B, class III)*** *are*

- Angina inadequately controlled by medical therapy;
- High risk determined by noninvasive test results such as
- exercise test five or fewer metabolic equivalents (METS);
- exercise heart rate 120 beats/min or less not due to drugs;
- flat blood pressure response, systolic blood pressure less than 130 mmHg or drop greater than
  10 mmHg;
- flat or downsloping ST depression greater than 1.0 mmHg at heart rate less than 120 beats/min or five METS, or greater than 2 mmHg or lasting longer than 6 mins in multiple leads;
- ST elevation in noninfarct leads without Q wave;
- ventricular tachycardia;
- Stress myocardial perfusion scintigraphy reveals
- abnormal perfusion in multiple regions or redistribution;
- large perfusion defect anterior wall, septum and apex;
- perfusion defect with increased lung uptake with normal resting left ventricle;
- cardiac enlargement with exercise;
- Exercise radionuclide angiogram or stress echocardiogram reveals
- greater than 10% fall in EF;
- resting EF less than 50% due to CAD with poorly controlled angina.

Contraindications for invasive testing (relative) ***(grade B, class III)****are*

- Anemia (hemoglobin less than 80 g/L);
- Uncontrolled systemic hypertension;

- Severe contrast reaction;
- Uncontrolled blood sugar;
- Severe arterial hypoxemia;
- Anticoagulation or bleeding disorders;
- Recent stroke;
- Untreated renal failure;
- Uncontrolled fever or infection;
- Uncooperative patient.

MEDICAL THERAPY OF CHRONIC ISCHEMIC HEART DISEASE

Risk factors for chronic ischemic heart disease

The major risk factors for coronary disease should be sought in all individuals to maximize the benefits of prevention. Twenty per cent to 25% of deaths in Canada annually are due to ischemic heart disease. The number of people 65 years or older, those most at risk, will nearly double over the next 25 years. Twenty per cent of Canadians have two or more modifiable risk factors for ischemic heart disease. Table 2 outlines some of the risk factors and the estimated potential risk reduction achievable if they are modified as a primary or secondary preventive manoeuvre.

Cessation of smoking produces the greatest immediate impact of all risk factors. The importance of early recognition and appropriate dietary, exercise and pharmacological therapy for hyperlipidemia is now widely accepted. Control of systemic hypertension has less impact on the manifestation of chronic ischemic heart disease but has great benefit overall in reducing the incidence of stroke, large artery aneurysm and dissection, and heart or renal failure. Vascular and renal disease are extremely common problems in all types of diabetes. Appropriate control of blood glucose levels and maintenance of normal body weight in diabetics have significant benefits to a number of organ systems other than the heart. Whether MI and unstable angina frequency are reduced in patients with chronic ischemic heart disease who are diabetics is less certain. Homocysteinemia is emerging as a possible important risk

factor that can be modified by pharmacological therapy in families that have premature coronary disease in the absence of the usual risk factors and in elderly patients with inadequate dietary folate. The weight of evidence of risk factor reduction for prevention or treatment of chronic ischemic heart disease is significant.

The following modifications are recommended to reduce the risk of ischemic heart disease:

- Abstinence from smoking ***(grade A, class I)***;
- Moderate exercise 30 to 60 mins, three to four times weekly ***(grade B, class II)***;
- American Heart Association step II diet to ideal weight ***(grade B, class II)***;
- Therapy to reduce blood pressure to less than 140/90 mmHg ***(grade A, class I)***;
- Lowering low density lipoprotein cholesterol to less than 2.6 mmol/L with hepatic hydroxy- methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor ***(grade A, class II)***;
- Drug therapy to lower triglyceride levels and raise high density lipoprotein cholesterol level ***(grade C, class III)***.

Nitrate therapy

Nitroglycerin in various forms (Table 3) is used in virtually all patients with symptomatic ischemic heart disease. Sublingual nitroglycerin is highly effective in shortening or terminating episodes of angina on exertion or at rest. It is highly effective if used prophylactically before activities that the patient has learned may bring on angina. Intermediate- and long-acting nitrates are also effective forms of antianginal therapy, although there is no evidence that they alter long term mortality. Intermediate- and long-acting preparations are only effective if used intermittently to allow resolution of nitrate tolerance, which develops within 24 h of maintaining a high, constant blood nitrate level. The indications for nitrate therapy are outlined below.

Frame 913

Chronic ischemic heart disease

Nitrate therapy in chronic ischemic heart disease

- Patients with angina should use sublingual tablets or spray for pain and prophylaxis *(grade A, class I)*.
- Nitrospray is as effective as tablets *(grade B class I)*.
- Nitrate preparations used to produce therapeutic blood levels for 24 h are ineffective due to tolerance *(grade A, class I)*.
- Standard preparations of isosorbide dinitrate should be given three times daily with a 14 h free period to prevent tolerance.
- Standard preparations of isosorbide-5-mononitrate except Imdur (Astra Pharma Inc) should be given eccentrically 7 h apart twice daily *(grade A class I)*.
- Sustained release preparations of nitroglycerin should be given once daily or twice daily with 6 h between doses *(grade C, class II)*.
- Controlled release isosorbide-5-mononitrate is given 30 to 120 mg once daily *(grade A, class I)*.
- Transdermal patches are given once daily and removed for 12 h *(grade A, class I)*.

Beta-blockers

Beta-adrenergic blockers, with or without concomitant nitrate therapy (Table 4), are the drugs of choice for postinfarction angina and are extremely useful in chronic stable angina and angina in patients with systemic hypertension. Early and late after MI, beta-blockers reduce morbidity and mortality in all patient groups. Beta-blockers are used cautiously in the management of both systolic and diastolic dysfunction heart failure. Cardioselective beta-blockers can be used cautiously in patients with chronic obstructive pulmonary disease in most instances. Beta-blockers may mask the symptoms of hypoglycemia in diabetics, but most diabetics with coronary disease are able to take them safely. The evidence in support of beta-blockers in chronic ischemic heart disease is outlined below.

Beta-blockers in chronic ischemic heart disease

Beta-blockers

- Reduce mortality postinfarction ***(grade A class I)***;
- Reduce morbidity and mortality in hypertensive patients ***(grade A, class I)***;
- Reduce angina frequency ***(grade A, class I)***;
- Are contraindicated in asthmatics ***(grade E, class III)***;
- May induce MI or destabilization when they are withdrawn abruptly ***(grade D, class III)***.

When prescribing beta-blockers the physician should

- Aim for a heart rate of less than 60 beats/min at rest and less than 100 beats/min on exercise;
- Optimize dosage of individual agents before using combination therapy.

Calcium channel blocking agents

Calcium channel blockers are a valuable form of therapy for the management of symptomatic chronic ischemic heart disease. They are particularly valuable in patients who are intolerant to nitrate or cannot take beta-blocker therapy. Calcium channel blocking agents can be used to treat angina in patients with hypertension. The short-acting dihydropyridine calcium blockers may worsen angina, and increase morbidity and mortality in patients with angina and hypertension or following MI if used in the absence of beta-blocker therapy. Verapamil or diltiazem may be used in patients with coronary disease who have diastolic dysfunction heart failure in the absence of systolic dysfunction. Long-acting dihydropyridine agents are safe in cardiomyopathy and ischemic heart disease.

Frame 911

Calcium blockers in chronic ischemic heart disease

- All calcium blockers except short-acting dihydropyridines are safe and effective in treating stable angina ***(grade A, class I)***.
- Long-acting calcium blockers may be used in hypertensive patients with angina ***(grade B class II)***.
- Calcium blockers are potentially harmful postinfarction when congestive heart failure (CHF) or known left ventricular dysfunction is present ***(grade E, class I)***.
- Rate-reducing calcium blockers can be used in the absence of left ventricular dysfunction post-MI ***(grade B, class I)***.
- Third-generation dihydropyridines can be used safely to treat angina in patients with CHF ***(grade A, class I)***.
- Short-acting dihydropyridines are dangerous in patients with CHF ***(grade E, class I)***.

Antiplatelet agents

Antiplatelet drugs are unequivocally beneficial during and following unstable angina and acute MI. There is evidence supporting their benefit in patients with stable angina. Acetylsalicylic acid (ASA) is the antiplatelet drug of choice. In the small proportion of patients intolerant to ASA, ticlopidine or clopidogrel may be an alternative.

Antiplatelet drugs in chronic ischemic heart disease

- Antiplatelet therapy has a key role in all patients with coronary disease. ASA is the drug of choice because of efficacy ***(grade A, class I)***.
- Ticlopidine may be an appropriate alternative to ASA ***(grade A, class II)***.
- Clopidogrel may soon be available and has fewer side effects than ticlopidine and greater efficacy than ASA ***(grade A, class I)***.

Anticoagulants in chronic ischemic heart disease

- There are no data supporting a benefit of oral anticoagulants in stable angina ***(grade C, class II)***.
- Low molecular weight heparin and ASA are superior to heparin and ASA in unstable angina ***(grade A, class I)***.
- Heparin and ASA are recommended in unstable angina ***(grade A, class I)***.
- Warfarin or ASA is recommended postmyocardial infarct ***(grade A, class I)***.

Angiotensin-converting enzyme inhibitors

Angiotensin-converting enzyme (ACE) inhibitors have been shown to reduce morbidity and mortality in patients with low EF or CHF following MI and are effective antihypertensive drugs for patients with chronic ischemic heart disease. As illustrated below, there is, as yet, insufficient evidence in the absence of moderate to severe left ventricular dysfunction to support the use of ACE inhibitors in stable chronic ischemic heart disease without MI or hypertension. In patients with diabetes and CAD, ACE inhibitors reduce the development of renal insufficiency. The role of angiotensin-1 (AT1) receptor blockers is less clear except in patients who are intolerant to ACE inhibitors, where they may be valuable antihypertensives, or in treating chronic heart failure.

ACE inhibitors

- Are indicated in chronic ischemic heart disease with moderate to severe left ventricular dysfunction ***(grade A, class I)***;
- Cannot be recommended in uncomplicated chronic ischemic heart disease ***(grade C, class III).***

AT_1-receptor blockers

- Beyond their use in hypertension or heart failure there is no evidence to recommend these agents in chronic ischemic disease ***(grade C, class III).***

A number of agents that have been or are being studied or are otherwise used in a nonprescription manner in the treatment of chronic ischemic heart disease are listed below. Of these, antioxidant vitamin therapy, potassium channel activator therapy, the Mediterranean diet, neovascularizing therapy and temperate use of alcohol show some promise. Chelation therapy represents the other side of the spectrum, with no evidence whatsoever of benefit and significant potential risk.

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Investigational and unproven therapy in chronic ischemic heart disease

- **Zatebradine:** Zatebradine is not effective in stable angina ***(grade E, class I)***.
- **Nicorandil (available and commonly used in Europe):** Nicorandil is an ATP-sensitive potassium channel activator that is as effective as current antianginal therapy in angina control ***(grade B, class I)***.
- **Antioxidants:** Antioxidant vitamin therapy requires further evaluation and cannot be currently recommended ***(grade C, class I)***.
- **Fish oils:** Dietary or supplementary fish oils cannot be recommended ***(grade C, class I)***.
- **Mediterranean diet:** A low saturated fat, high fibre diet with wine confers relative cardioprotection ***(grade B, class I)***.
- **Garlic:** Garlic contains vitamins and antioxidants, and has been claimed to lower lipids and blood pressure and have antiplatelet and fibrinolytic properties with no current proof of harm or benefit ***(grade C, class II)***.
- **Neovascularizing therapy:** Vascular endothelial growth factor and fibroblast growth factor show promise in research studies.
- **Chelation:** There is no evidence of benefit and may cause renal tubular necrosis, arrhythmia, hypocalcemia, marrow depression, bleeding, hypotension or allergic reaction ***(grade E, class III)***.

- **Ethanol:** Light ethanol use raises high density lipoprotein cholesterol II and III, increases fibrinolysis, and decreases platelet aggregation and insulin resistance. Light use is not deleterious and may be beneficial ***(grade C, class II)***.
- **Neural stimulation/acupuncture:** Spinal cord stimulation and transcutaneous nerve stimulation relieve angina and diminish ischemia. Acupuncture is not superior to sham procedure. It may be helpful and is not harmful ***(grade B, class II)***.
- **Stress management/behaviour modification:** Individual and group stress management reduce psychological distress, blood pressure, heart rate, cardiac morbidity and mortality in meta-analyses of randomized controlled trials ***(grade B, class I)***.
- **Self-medication:** Effects of nonprescription therapy are probably placebo mediated. It may help individuals and is generally harmless but expensive ***(grade C, class III)***.

Estrogen therapy in women with chronic ischemic heart disease

Premenopausal women with CAD who are using estrogen in oral contraceptives should use low dose estrogen and should not smoke. Estrogen replacement with or without progestin therapy is being actively investigated as a means of reducing morbidity and mortality in postmenopausal women. Although estrogen therapy is of great potential value as preventive therapy, clinical trials evidence is insufficient to support this form of therapy strongly.

Estrogen therapy in women with chronic ischemic heart disease ***(grade C, class II)***

- Oral contraceptives with low dose estrogen (less than 36 µg) are safe for women with CAD.
- Postmenopausal women with or at high risk for coronary disease should consider estrogen replacement with progestin to prevent MI. Unopposed estrogen can be used if the woman has had a hysterectomy.

- Estrogen should be considered in postmenopausal women with symptomatic coronary disease to improve survival and reduce angina.
- Estrogen may reduce angina in patients with syndrome X (angina with normal coronary arteries).

A very detailed series of recommendations regarding revascularization therapy for various stages and complications of ischemic heart disease is available in the CCS Consensus paper of 1995 (2). The reader is referred to this publication for details of this form of therapy. The roles of PTCA, with or without stents, and coronary bypass surgery for patients with chronic ischemic heart disease and for the management of complications of chronic ischemic heart disease are outlined below.

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Revascularization for chronic ischemic heart disease

- CABG improves survival for left main, two-vessel disease with proximal left anterior descending artery, and three-vessel disease with ischemic left ventricular dysfunction ***(grade A, class I)***.
- Left internal mammary artery graft and
  possible right internal mammary artery graft improve prognosis and duration of grafts
  (grade A, class II).
- Prognostic benefit of this procedure in elderly women and possibly men is unconfirmed.
- CABG and PTCA are excellent for symptom control in failed medical therapy.
- Laser angioplasty is not widely used.
- Directional and rotational atherectomy are used for specific anatomical problems.

- Minimally invasive procedures are under evaluation ***(grade B, class III)***.

The following surgeries may be performed for complications of chronic ischemic heart disease:

- Aortic valve replacement plus CABG for aortic stenosis;
- Mitral valve repair or replacement for acute papillary muscle dysfunction or rupture;
- Repair of acute interventricular septal rupture;
- Resection of discrete left ventricular aneurysm;
- Resection of left ventricular pseudoaneurysm;
- Orthoptic transplant for ischemic cardiomyopathy ***(grade B, class III)***;
- Left ventricular remodelling procedure for ischemic cardiomyopathy (experimental).

Exercise training in chronic ischemic heart disease

The benefit of regular exercise on overall well-being and general physical fitness has long been recognized. Exercise, along with medical or surgical therapy, has been shown to reduce the frequency of angina and improve the lifestyle of patients with chronic ischemic heart disease. More recently, the benefit of regular exercise in reducing overall morbidity and mortality in patients with chronic ischemic heart disease has been shown.

Exercise training in chronic ischemic heart disease

- Regular exercise training reduces angina and promotes well-being ***(grade A, class I)***.
- Regular physical exercise lowers the risk of a cardiac event ***(grade B, class II)***.
- Regular exercise in patients with known coronary disease reduces morbidity and mortality postinfarction ***(grade B, class II)***.

The complex patient with chronic ischemic heart disease

Many patients with chronic ischemic heart disease have associated disorders that alter overall function, and modify morbidity and mortality of CAD. Systemic hypertension, diabetes mellitus, chronic pulmonary disease and heart failure are common associated disorders that may require modification of investigations and therapy of the coronary disease. The impact of associated disease in the complex patient with CAD is outlined below.

Left ventricular dysfunction and chronic ischemic heart disease *(grade B, class I)*

- There is a common association between the two diseases.
- Either disease may precede the other.
- Destabilization of either may worsen the other.
- Patients with left ventricular dysfunction have high risk of recurrent ischemic events.
- Revascularization is indicated if anatomically feasible.
- Aggressive failure therapy is essential (especially ACE inhibitor).
- Physicians should beware of lowering coronary perfusion pressure.
- Nitrates are indicated for both diseases to relieve symptoms.
- Beta-blockers (carvedilol) are indicated for both diseases to relieve symptoms.
- Calcium blockers, except for amlodipine or felodipine, are contraindicated.

Diabetes mellitus and chronic ischemic heart disease *(grade B, class III)*

- Diseases have common association and risk factors.
- Diabetics have an adverse prognosis compared with nondiabetics.
- Type I diabetes is a weak relative contraindication for beta-blocker.
- Beta-blockers are especially indicated in type II diabetic postinfarct patients.
- CABG is superior to PTCA graft for first revascularization if triple vessel disease is present.

Systemic arterial hypertension and chronic ischemic heart disease *(grade A, class I)*

- Diseases have common association and risk factors.
- Patients with systemic arterial hypertension have an adverse prognosis compared with normotensives.
- Control of both arterial hypertension and chronic ischemic heart disease is essential.
- Beta-blockers are first-line therapy.
- Calcium blocker with rate limitation without beta-blockers is appropriate.
- Beta-blocker plus dihydropyridines is appropriate therapy.
- Dihydropyridines (except amlodipine or felodipine) are contraindicated postinfarction.
- Rate-limiting calcium blockers can be used postinfarction if EF is greater than 40%.
- ACE inhibitors are effective, especially postinfarction with left ventricular dysfunction.

Beta-blockers are absolutely contraindicated in asthma (grade E, class II).

Nitrates are effective.

Rate-limiting or second-generation calcium blockers are effective.

Beta-blockers may be used with caution in patients with chronic obstructive pulmonary disease.

Chronic ischemic heart disease

Personal, social and occupational factors in the patient with chronic ischemic heart disease

Employability: The presence or complications of CAD may have a major impact on the type of work suitable for the patient. A careful analysis of the demands of employment and the work environment is essential to allow the physician to counsel the patient appropriately about employment. Some occupations require special skills such as operating an airplane or vehicle, and the physician needs to understand the limitations imposed by coronary disease or varying severity on the ability of the patient to perform these activities and thereby remain employed. The major factors surrounding the issue of employment are detailed below.

Employability of patients with chronic ischemic heart disease

- Both exercise capacity of the patient and energy demands of the work must be known.
- Most occupations do not increase morbidity or mortality, and return to or continued work should be encouraged.
- Severe left ventricular dysfunction, ischemia or arrhythmia should be optimally treated before return to work.
- Peak exercise workload should exceed peak energy requirement of workplace by 20% or more, and patient should be able to maintain a sustained workload.
- Chronic ischemic heart disease may preclude occupations posing a risk to society.

Driving with chronic ischemic heart disease

- Patients with CCS class IV angina should not drive.
- Driving should await revascularization of greater than 50% left main stenosis for commercial and greater than 70% left main stenosis for private drivers.
- Drivers with angina should be stabilized on therapy, and commercial drivers should be in CCS class I angina.

Aircraft pilots with chronic ischemic heart disease

- Chest pain precludes piloting unless coronary disease is ruled out by testing.
- Pilots may fly six months postinfarct if exercise test is greater than 85% normal, the patient is off drugs and EF is greater than 50% at rest with no drop greater than 5% with exercise.
- Major modifiable risk factors must be controlled.

Insurability in chronic ischemic heart disease: Patients with chronic ischemic heart disease may require special counselling regarding eligibility for life insurance, disability insurance, or private or travel medical insurance. Life insurance can usually be purchased, albeit at a higher premium. Increasing age and severity of disease increase the cost of all of these types of insurance.

Insurability of patients with chronic ischemic heart disease

- Life insurance can usually be purchased at a higher premium.
- Disability insurance may be difficult to purchase, benefit periods will be shortened, waiting period may be longer and premiums high.
- Travel medical insurance can be purchased at a higher premium or deductible when the clinical state has been stable for an extended time.

Chronic ischemic heart disease in the elderly: With a growing number of elderly individuals in Canada, the prevalence and burden of chronic ischemic heart disease are increasing and can be expected to increase in the future. Age is not a contraindication to any of the investigations or treatments heretofore discussed. With the exception of the treatment of hypertension, stopping smoking and overall maintenance of good health, there is very little clinical trials evidence upon which to base decisions in managing the elderly patient with coronary disease. In the very elderly, the benefit to risk ratio of invasive therapy such as angioplasty or bypass surgery narrows considerably. The reader is referred to the 1995 CCS Consensus on Indications for and Access to Revascularization for further detail (2).

Cost effectiveness of therapy in chronic ischemic heart disease: In the presence of limited resources for medical care, the physician and patient should be interested in choosing the most cost effective diagnostic procedure and therapy. Nine cost effective investigations or treatments that the physician can use in a patient with chronic ischemic heart disease are listed below, and the costs of different types and preparations of antianginal medications are compared.

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The following cost effective interventions may be used in chronic ischemic heart disease:

- All diagnostic approaches to the diagnosis of ischemic heart disease in patiens with atypical angina;
- Exercise testing for asymptomatic individuals at high risk of ischemic heart disease;
- All strategies for risk stratification and selection for revascularization;
- ASA in patients with or at high risk of ischemic heart disease;
- Beta-blocker following MI;
- Beta-blocker in hypertension;
- HMG-CoA reductase inhibitors in secondary prevention;
- Revascularization in high risk groups;
- Stopping tobacco use.

Relative costs of medication used to treat patients with ischemic heart disease

- Generic drugs tend to be significantly cheaper than name-brand products.
- Special formulations (slow release, long-acting, etc) reduce complexity of dosing and often narrow the cost difference between name-brand and generic products.

- Long-acting nitrates are much more expensive than short-acting nitrates taken three times daily.
- Nitrates are less expensive than beta-blockers.
- Beta-blockers are much less expensive than calcium blockers.

PREOPERATIVE ASSESSMENT FOR NONCARDIAC SURGERY

The patient with CAD may be at significant risk of cardiac morbidity or mortality when undergoing noncardiac surgery. The interaction between the severity of the coronary disease and the type of surgery must be evaluated by the clinician, and investigation and treatment modified accordingly.

Preoperative assessment for noncardiac surgery

Patients with uncomplicated CAD with the following characteristics are at low risk when undergoing noncardiac surgery:

- No previous MI;
- No left ventricular dysfunction;
- No diabetes;
- No arrhythmias;
- Exercise capacity greater than 5 METS.

Patients with complicated CAD with the following characteristics are at intermediate risk when undergoing noncardiac surgery:

- Age greater than 70 years;
- Prior MI (three to six months);
- Left ventricular dysfunction;
- Diabetes;
- Ventricular or supraventricular arrhythmia;
- Less than 5 METS exercise capacity.

CAD patients with the following characteristics are at high risk when undergoing noncardiac surgery:

- Prior MI less than three months earlier;
- CCS class III to IV angina;
- Decompensated CHF.

Low risk surgeries include

- Ophthalmologic surgery;
- Minor head-neck surgery;
- Transurethral prostatic resection;
- Day surgery.

Intermediate risk surgeries include

- Intra-abdominal surgery;
- Intrathoracic surgery;
- Major orthopedic surgery;
- Carotid endarterectomy surgery;
- Major head-neck surgery.

High risk surgeries include

- Aortic surgery;
- Major vascular surgery.

Recommendations for preoperative assessment for noncardiac surgery

- Beta-blockers given pre- and postnoncardiac surgery can reduce overall mortality, and low risk patients should be further evaluated only for high risk operations ***(grade B, class III)***.
- Intermediate risk patients are appropriate candidates for better stratification of cardiac ischemic risks by noninvasive tests ***(grade B class III)***.
- High risk patients should undergo invasive testing and revascularization procedures whenever possible before noncardiac surgery ***(grade B class III)***.
- Beta-blockers given pre- and postnoncardiac surgery can reduce overall mortality and combined cardiovascular outcomes by 50% for as long as two years after surgery ***(grade B, class I)***.

CONCLUSIONS

The purpose of this CCS consensus document is to assist the physician in choosing optimal investigation and therapy for the patient with chronic ischemic heart disease on the basis of evidence derived from basic science research and appropriately designed clinical trials. Phenomenal advances in the management of CAD have occurred over the past three decades, and a great deal of research is continuing in all of the areas discussed in this brief document. The recommendations of the Consensus Panel are generally applicable to all patients with coronary disease. The interindividual variability of patients with disease still requires the physician to make judgements and value decisions in areas in which there is insufficient evidence to allow a broad consensus. It is this variability that maintains the need for the well-trained, skilled and experienced physician to appropriately manage the very large segment of our population afflicted with this disease.

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