Cardio IQ®
Advanced Cardiovascular Testing
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LDL is one of the classes of lipoproteins that transports cholesterol to tissues and organs. Lowering LDL-C levels is a primary focus of the NCEP-ATP III and 2013 ACC/AHA ASCVD Risk and Treatment Guidelines. Elevated LDL-C levels are an independent risk factor for CVD and associated with a 1.6-fold increased risk of CVD events.

**Contributing Factors**

**Genetics/demographics**
- Genetic predisposition

**Lifestyle**
- High consumption of saturated fats
- Overweight or obese
- Sedentary lifestyle

**Illness**
- Nephrotic syndrome
- Hypothyroidism

**Drugs**
- Androgens, progestins, thiazide diuretics, cyclosporines, tacrolimus
- Selective serotonin reuptake inhibitors (SSRIs)
- Atypical antipsychotics

**Treatment Considerations**

**Dietary/lifestyle intervention**
- Cardioprotective diet
- Restricted saturated fat
- Fat weight loss

**Pharmacological intervention**
- Statins
- Nicotinic acid
- Bile acid sequestrants

For informational purposes only, every physician and healthcare practitioner needs to make treatment decisions for their patients based on their clinical evaluation of the patient and the physician's own education and experience.
Low HDL Cholesterol Level

Lipid Disorder

HDL is the major class of lipoproteins that facilitates cholesterol transport from cells, plasma cholesterol esterification, cholesterol transfer to other lipoproteins, and cholesterol transfer to the liver for excretion (reverse cholesterol transport). Low HDL-C levels are a secondary focus of NCEP-ATP III guidelines. Low HDL-C levels are independently associated with a 1.7-fold to 2.4-fold increased risk for CVD.

Contributing Factors

Genetics/demographics
• Genetic predisposition

Lifestyle
• High triglyceride levels
• High consumption of simple carbohydrates
• Overweight or obese
• Sedentary lifestyle
• Smoking

Illness
• Insulin resistance/diabetes mellitus
• Liver, kidney, and thyroid disease

Drugs
• Nonselective beta blockers, androgens, progestins, isotretinoin

Treatment Considerations

Dietary/lifestyle intervention
• Cardioprotective diet
• Fat weight loss
• Regular aerobic exercise
• Smoking cessation
• Omega-3 fish oil

Pharmacological intervention
• Nicotinic acid
• Fibrates
• Thiazolidinediones
• Some statins

Disease intervention
• Correct insulin resistance
• Control diabetes mellitus
**Elevated Triglyceride Level**

**Lipid Disorder**

A triglyceride is an ester derived from glycerol and 3 fatty acids. The major lipid in chylomicrons, VLDLs, and IDLs. Hypertriglyceridemia may increase risk for CVD. Elevated triglyceride levels are a secondary focus of NCEP-ATP III guidelines. Elevated triglyceride levels are a component of the metabolic syndrome and are associated with a 1.7-fold to 4.0-fold increased risk for CVD.

**Contributing Factors**

**Genetics/demographics**
- Genetic predisposition
- Pregnancy and lactation

**Lifestyle**
- High consumption of simple carbohydrates and saturated fats
- Overweight or obese
- Sedentary lifestyle
- Smoking

**Illness**
- Insulin resistance/diabetes mellitus/metabolic syndrome
- Hypothyroidism, renal failure, excess alcohol intake

**Drugs**
- Androgens, estrogens, beta blockers, thiazide diuretics, glucocorticosteroids, cyclosporines, protease inhibitors, tacrolimus, sertraline, isotretinoin, valproate

**Treatment Considerations**

**Dietary/lifestyle intervention**
- Regular aerobic exercise
- Fat weight loss
- Avoid high glycemic foods
- Low simple carbohydrate and saturated fat diet
- Avoid alcohol consumption

**Pharmacological intervention**
- Fibrates
- Nicotinic acid
- Omega-3 fish oil
- Thiazolidinediones (pioglitazone but NOT rosiglitazone)
- Some statins

**Disease intervention**
- Treat triglyceride levels >500 mg/dL to help prevent acute pancreatitis

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*Effect on elevating triglyceride levels is limited to newer beta blockers (eg, pindolol, acebutolol, nebivolol, atenolol) and not older beta blockers (eg, propranolol, metoprolol).
Elevated LDL Particle Number

**Contributing Factors**

**Genetics/demographics**
- Genetic predisposition

**Lifestyle**
- High consumption of saturated fats
- Overweight or obese
- Sedentary lifestyle

**Illness**
- Nephrotic syndrome
- Hypothyroidism

**Drugs**
- Androgens, thiazide diuretics, cyclosporines, tacrolimus
- SSRIs
- Atypical antipsychotics

**Treatment Considerations**

**Dietary/lifestyle intervention**
- Cardioprotective diet
- Restricted saturated fat
- Fat weight loss

**Pharmacological intervention**
- Statins
- Nicotinic acid
- Bile acid sequestrants

Ion mobility measures the number of particles in each of the 8 LDL subclasses. These 8 subclasses comprise the LDL particle number. An elevated total LDL particle number is associated with a 1.4-fold increased risk for CVD.
Elevated Small and/or Medium LDL Particle Number

**Lipoprotein Subfraction Disorders**

Ion mobility measures the number of particles in each of the 8 LDL subclasses. Six of these 8 subclasses are small LDL subclass particles. These smaller particles are associated with rapid uptake into the endothelium contributing to accelerated atherosclerosis. There is a 1.3-fold increased risk for CVD associated with the small LDL trait and a 1.4-fold increased risk with the medium LDL trait.

**Contributing Factors**

**Genetics/demographics**
- Genetic predisposition
- High triglyceride and low HDL-C levels

**Lifestyle**
- High consumption of simple carbohydrates
- Overweight or obese
- Sedentary lifestyle

**Illness**
- Insulin resistance/diabetes mellitus/metabolic syndrome

**Drugs**
- Nonselective beta blockers

**Treatment Considerations**

**Dietary/lifestyle intervention**
- Avoid simple carbohydrate diet
- Fat weight loss
- Regular exercise
- Omega-3 fish oil

**Pharmacological intervention**
- Thiazolidinediones
- Nicotinic acid
- Fibrates
- Statins (minor effect)*

**Disease intervention**
- Consider evaluation of cardiometabolic function
- Noninvasive imaging
- Additional blood tests
- Identify and correct insulin resistance
- Control diabetes mellitus

*Effect is specific to atorvastatin.
**Lipoprotein Subfraction Disorders**

Pattern B is described as a predominance of small LDL subclass particles as represented on the Ion Mobility patient result figure. Pattern B represents an atherogenic lipid profile that is associated with a 1.3-fold increased risk for CVD.

**Decreased LDL Peak Size**

Further assessment of pattern includes measurement of peak size. An average size of LDL peak subclass particles measuring less than 218 angstroms, as measured with Ion Mobility, is associated with a 1.35-fold increased risk for CVD.

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### Contributing Factors

**Genetics/demographics**
- Genetic predisposition
- High triglyceride and low HDL-C levels

**Lifestyle**
- High consumption of simple carbohydrates
- Overweight or obese
- Sedentary lifestyle

**Illness**
- Insulin resistance/diabetes mellitus/metabolic syndrome

**Drugs**
- Nonselective beta blockers

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### Treatment Considerations

**Dietary/lifestyle intervention**
- Avoid simple carbohydrate diet
- Fat weight loss
- Regular exercise
- Omega-3 fish oil

**Pharmacological intervention**
- Thiazolidinediones
- Nicotinic acid
- Fibrates
- Statins (minor effect)

**Disease intervention**
- Consider evaluation of cardiometabolic function
- Noninvasive imaging
- Additional blood tests
- Identify and correct insulin resistance
- Control diabetes mellitus
**Decreased Large HDL Level**

### Lipoprotein Subfraction Disorders

Ion Mobility identifies 5 subclasses of HDL, 1 is identified as the large HDL subclass. Decreased levels of the large HDL subclass are associated with a 1.8-fold increased risk for CVD. Large HDL particles are functionally associated with an antioxidant, paraoxanase, which may help protect the arterial wall.

### Contributing Factors

<table>
<thead>
<tr>
<th>Genetics/demographics</th>
<th>Lifestyle</th>
<th>Illness</th>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genetic predisposition$^1$</td>
<td>High consumption of simple carbohydrates$^{48}$</td>
<td>Insulin resistance/diabetes mellitus$^1$</td>
<td>Nonselective beta blockers,$^1$ androgens,$^1$ progestins$^{49}$</td>
</tr>
<tr>
<td>High triglyceride levels$^2$</td>
<td>Overweight or obese$^1$</td>
<td>Liver,$^2$ kidney,$^2$ and thyroid disease$^2$</td>
<td></td>
</tr>
</tbody>
</table>

### Treatment Considerations

<table>
<thead>
<tr>
<th>Dietary/lifestyle intervention</th>
<th>Pharmacological intervention</th>
<th>Disease intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avoid simple dietary carbohydrates$^2$</td>
<td>Nicotinic acid$^1$</td>
<td>Correct insulin resistance$^1$</td>
</tr>
<tr>
<td>Fat weight loss$^2$</td>
<td>Nicotinic acid plus statin$^1$</td>
<td>Control diabetes mellitus$^1$</td>
</tr>
<tr>
<td>Regular exercise$^2$</td>
<td>Statins (minor effect)$^1$</td>
<td></td>
</tr>
<tr>
<td>Smoking cessation$^2$</td>
<td>Fibrates when triglyceride levels are elevated$^1$</td>
<td></td>
</tr>
<tr>
<td>Omega-3 fish oil$^{50}$</td>
<td></td>
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</tr>
</tbody>
</table>

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1. Genetics/demographics
2. Lifestyle
3. Illness
4. Drugs
5. Treatment Considerations
Apolipoprotein Disorders

Apolipoprotein B (ApoB) is a chief structural protein of all non-HDL lipoproteins. The amount of ApoB is considered to correspond to the number of atherogenic particles. Elevated ApoB levels are associated with a 2.0-fold to 2.5-fold increased risk for CVD.

Contributing Factors

Genetics/demographics
• Genetic predisposition

Lifestyle
• High consumption of saturated fats
• Overweight or obese
• Sedentary lifestyle

Illness
• Nephrotic syndrome
• Hypothyroidism

Drugs
• Androgens, progestins, thiazide diuretics, cyclosporines, tacrolimus, atypical antipsychotics

Treatment Considerations

Dietary/lifestyle intervention
• Cardioprotective diet
• Restricted saturated fat
• Fat weight loss

Pharmacological intervention
• Statins
• Nicotinic acid
• Bile acid sequestrants
Elevated Lp(a) Level

**Apolipoprotein Disorders**

Lipoprotein(a) (Lp(a)) is a heterogeneous lipoprotein that shares many properties with LDL, but Lp(a) is metabolically distinct from LDL. It contains a structurally unique protein, apolipoprotein(a), the size of which is genetically determined and highly variable. High plasma Lp(a) concentrations are associated with a 1.5-fold to 5.3-fold increased risk for CVD.

**Contributing Factors**

**Genetics/demographics**
- Genetic predisposition
- Menopausal loss of estrogen may increase Lp(a) levels by 20% to 30%

**Illness**
- Chronic renal failure
- Nephrotic syndrome
- Hypothyroidism
- Diabetic nephropathy

**Treatment Considerations**

**Pharmacological intervention**
- Nicotinic acid
- Niaspan 2000 mg per day decreases Lp(a) levels by ~24%
- IR Niacin 3000 mg per day decreases Lp(a) levels by ~36%
- Fibrates (limited effect)
- Mipomersen
- PCSK9 inhibition
- Anacetrapib

**Disease intervention**
- Consider evaluation of cardiometabolic function
- Noninvasive imaging
- Additional blood tests
- Consider that some statins may elevate Lp(a) levels in some patients
- Aggressively treat all associated atherogenic conditions
- LDL or Lp(a) apheresis in some extreme cases of resistance to Lp(a)-lowering drugs
Elevated Fibrinogen Level

Inflammatory Disorders

Fibrinogen is a plasma glycoprotein that can be transformed into a fibrin clot in response to vascular or tissue injury. The combination of elevated fibrinogen level with other CVD risk factors produces an additive risk and can substantially increase disease potential. There are 2 fibrinogen assays available: one measures clotting, the other antigen level. Elevated fibrinogen is associated with inflammation and a 1.4-fold to 2.5-fold increased risk for CVD.

Contributing Factors

Genetics/demographics
- Genetic predisposition
- Sex (women often have higher levels)

Lifestyle
- Tobacco use
- Overweight
- Increasing age
- Sedentary lifestyle

Illness
- Insulin resistance/diabetes mellitus
- Hypertension
- Postmenopausal state
- Acute/chronic inflammation

Drugs
- Oral contraceptives
- Gemfibrozil

Treatment Considerations

Dietary/lifestyle intervention
- Fat weight loss
- Increase physical activity
- Smoking cessation

Pharmacological intervention
- Nicotinic acid
- Fibrates: fenofibrate may reduce whereas gemfibrozil may elevate

Disease intervention
- Consider evaluation of cardiometabolic function
- Noninvasive imaging
- Additional blood tests
- Control hypertension
- Control diabetes mellitus
Elevated hs-CRP Level

**Inflammatory Disorders**

CRP is a plasma protein produced by the liver in response to systemic inflammation. The high sensitivity CRP (hs-CRP) test accurately determines CRP levels in the low range of 1-10 mg/L. Elevated hs-CRP levels correlate with the presence of the metabolic syndrome, insulin resistance, endothelial dysfunction, and impaired fibrinolysis. hs-CRP can discern the low levels of inflammation associated with a 1.5-fold to 2.0-fold increased risk for CVD.

**Contributing Factors**

- **Lifestyle**
  - Obese²
  - Stress²
  - Smoking²
  - Adiposity in women²

- **Illness**
  - Systemic inflammation²
  - Insulin resistance/diabetes mellitus/metabolic syndrome²

- **Drugs**
  - Hormone-replacement therapy, contraceptive⁸⁰

**Treatment Considerations**

- **Dietary/lifestyle intervention**
  - Cardioprotective diet²
  - Fat weight loss²

- **Pharmacological intervention**
  - Statins²
  - Statins plus ezetimibe⁸¹
  - Fibrates⁸²
  - Nicotinic acid⁸³

- **Disease intervention**
  - Consider evaluation of cardiometabolic function²
  - Noninvasive imaging⁸⁴
  - Additional blood tests²
Elevated Lp-PLA$_2$ Level

**Inflammatory Disorders**

The Lp-PLA$_2$ test [94218(X)] measures the activity of an enzyme that plays a causal role in the vascular inflammatory process. This test measures the disease activity within the arterial wall under the calcified cap of an atherosclerotic plaque; such activity indicates a potential thinning of the cap and thus a potential for plaque rupture. Elevated Lp-PLA$_2$ activity levels have been associated with a 2-fold increased risk for developing coronary heart disease (CHD) at 7 years independent of non-HDL cholesterol levels. Also, elevated Lp-PLA$_2$ activity levels indicate a 2-fold increased risk of having a CHD event (MI, coronary revascularization or CHD-related death) at 5 years. In some studies, tests that measured Lp-PLA$_2$ activity (such as the one offered by Quest Diagnostics), as compared with Lp-PLA$_2$ mass levels, had a higher predictive value for cardiovascular events.

**Contributing Factors**

**Genetics/demographics**
- Increasing age in both sexes
- Increased carotid intima-media thickness

**Lifestyle**
- Tobacco use
- Sedentary lifestyle

**Illness**
- Metabolic syndrome
- Elevated blood glucose level
- Hypertension

**Treatment Considerations**

**Dietary/lifestyle intervention**
- Omega-3 fish oil supplements
- Diet high in Omega-3 fatty acids

**Pharmacological intervention**
- Statins
- Fenofibrate
- Nicotinic acid plus statins
- Ezetimibe
- Combination of statin with other suggested drugs results in further Lp-PLA$_2$ reduction
- Antihypertensive therapy for optimal BP control

**Disease intervention**
- Consider evaluation of cardiometabolic function
- Noninvasive imaging
- Additional blood tests

*In April 2016, the US Food and Drug Administration withdrew the indication of extended-release niacin and delayed-release fenofibrate when used in combination with a statin.
Inflammatory Disorders

Myeloperoxidase (MPO) is a vascular-specific inflammatory enzyme released by the leukocytes into the bloodstream in response to vulnerable plaque, erosions, or fissures in the endothelium of the arterial wall. MPO is involved in (1) lipid peroxidation converting LDL to an atherogenic form and HDL to a dysfunctional form, (2) destabilization and rupture of atherosclerosis plaque, and (3) vasoconstriction and endothelial dysfunction.

Elevated MPO level is an independent risk factor for CVD and is associated with a 2.0-fold increased risk for CVD events. MPO levels increase with clinical severity of known CAD.

Contributing Factors

Genetics/demographics
- Increasing age

Lifestyle
- Overweight or obese
- Tobacco use
- Extreme athletes (marathon runners) seen after strenuous exercise

Illness
- Hypertension
- Vascular damage
- Vasculitis
- Autoimmune disorders
- Chronic inflammatory disease (rheumatoid arthritis, lupus)
- Chronic lymphocytic leukemia
- Bone marrow dyscrasias

Treatment Considerations

Dietary/lifestyle intervention
- Fat weight loss
- Regular exercise
- Smoking cessation
- Cardioprotective diet

Pharmacological intervention
- Statins

Disease intervention
- Antiplatelet therapy
- Antihypertensive therapy for optimal BP control
- Additional blood test (NT-proBNP)
- Noninvasive imaging
Elevated Insulin Level

**Metabolic Disorders**

Insulin is a polypeptide produced by specialized beta cells of the islets of Langerhans in the body and tail of the pancreas. An elevated fasting insulin level is associated with a 3.2-fold increased risk for CVD events.

**Contributing Factors**

**Genetics/demographics**
- Genetic predisposition
- Elderly people

**Lifestyle**
- Obese
- Visceral adiposity
- Sedentary lifestyle
- High carbohydrate diet
- Stress

**Illness**
- Menopausal drop in estrogen
- Chronic inflammation with elevated inflammatory markers
- Illnesses such as:
  - Polycystic ovarian syndrome
  - Cushing’s disease
  - Hemochromatosis, insulinoma
  - Insulin resistance/diabetes
  - Diabetes mellitus/metabolic syndrome

**Drugs**
- Rifampin, progesterone, antiretrovirals, corticosteroids
- Elevations may be caused by postprandial blood sample or exogenous administration of insulin

**Treatment Considerations**

**Dietary/lifestyle intervention**
- Fat restricted, cardioprotective diet
- Limit simple carbohydrates, utilize high-fiber sources
- Fat weight loss
- Regular exercise

**Disease intervention**
- Recommended pharmacologic methods of meeting insulin requirements or regulating insulin sensitivity
Elevated Homocysteine Level

Metabolic Disorders
Homocysteine is a metabolic by-product of methionine metabolism. An elevated homocysteine level increases oxidative stress, may cause endothelial dysfunction and vascular injury, and enhances thrombogenicity. Patients with elevated homocysteine levels have a 1.5-fold increased risk for CVD events.

Contributing Factors

Genetics/demographics
• Genetic predisposition

Lifestyle
• Deficiencies of vitamins folic acid, B6, and B12
• Excess alcohol, caffeine, or nicotine
• Diet low in greens, high in meats

Illness
• Renal insufficiency/failure, pernicious anemia, megaloblastic anemia, hypothyroidism

Drugs
• Nicotinic acid (dose dependent), fenofibates, sulfonamides, metformin, anticonvulsants, methotrexate, theophylline, cyclosporine

Treatment Considerations

Dietary/lifestyle intervention
• Diet high in green leafy vegetables
• Traditional treatment has been folic acid, B6, and B12 vitamins

Disease intervention
• Identify and treat any underlying abnormality such as renal insufficiency/pernicious anemia
• Initiating treatment of elevated homocysteine continues to be controversial in reducing risk for CVD events versus increased risk for other conditions
Omega-3 & -6 Fatty Acids

The 3 major omega-3 fatty acids are eicosapentaenoic acid (EPA), docosahexaenoic acid (DHA), and alpha-linolenic acid. Omega-6 fatty acids are proinflammatory and prothrombotic. The major omega-6 fatty acid is arachidonic acid (AA).

The omega-3 index (EPA and DHA expressed as a percentage of phospholipid fatty acids) is an indicator of risk for sudden cardiac death and nonfatal cardiovascular events and helps measure response over time to recommended therapy target. The EPA/AA ratio is a marker of cardiovascular risk, with higher ratios being associated with lower cardiac risk.

Contributing Factors

Genetics/demographics
- Genetic polymorphisms in the Fatty acid desaturase (FAD) genes

Lifestyle
- Low dietary consumption of omega-3 fatty acids
- High dietary consumption of omega-6 fatty acids
- Dietary deficiency of omega-3 fatty acids

Treatment Considerations

Dietary/lifestyle intervention
- Two primary omega-3 fatty acids are EPA and DHA. Dietary sources are:
  - Fish oil
  - Fatty fish
- ALA, 1 of the 3 major omega-3 fatty acids, is found in plant-based foods. It is converted to EPA and DHA after being ingested.
**Metabolic Disorders**

Vitamin D and its metabolites are hormones and hormone precursors. A deficiency of 25-hydroxyvitamin D is associated with development of atherosclerosis and increased risk for cardiovascular events. Decreased vitamin D level is associated with a 1.8-fold increased risk for cardiovascular mortality and a 1.6-fold to 5.0-fold increased risk for CVD events.

**Contributing Factors**

<table>
<thead>
<tr>
<th>Genetics/demographics</th>
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<tbody>
<tr>
<td>• Elderly and newborns¹</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Lifestyle</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Inadequate sun exposure¹:</td>
</tr>
<tr>
<td>• People with more skin pigment are at higher risk for vitamin D deficiency¹</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Obesity¹</td>
</tr>
<tr>
<td>• Malabsorption³</td>
</tr>
<tr>
<td>• Renal disease²</td>
</tr>
<tr>
<td>• Liver disease¹⁴⁶</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Corticosteroids,¹⁴⁷ anticonvulsants,¹ antirejection medications,¹⁴⁸ HIV medications¹⁴⁸</td>
</tr>
</tbody>
</table>

**Dietary/lifestyle intervention**

- Vitamin D supplementation³

**Disease intervention**

- Initial loading therapy:
  - 50,000 IU vitamin D₂ weekly for 2 months³
- Maintenance therapy:
  - 50,000 IU vitamin D₂ once or twice monthly³
  - 2000-4000 IU vitamin D₃ daily and/or appropriate sun exposure and/or high vitamin D diet (eg, salmon, tuna fish, shiitake mushrooms)³

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¹ From Reference

² From Reference

³ From Reference

⁴ From Reference

⁵ From Reference

⁶ From Reference

⁷ From Reference

⁸ From Reference

⁹ From Reference
Heart Failure Contributing Factors

NT-proBNP is an endogenously produced neurohormone secreted from the cardiac ventricular myocytes in response to cardiac stress. As a sensitive marker for cardiac dysfunction, elevated NT-proBNP levels provide aid in diagnosis of heart failure (HF) and assessment of response to therapy, prediction of chronic HF progression (which is associated with a 1.9-fold to 2.9-fold* increased risk for CVD events) and incidence of CVD death or HF after ACS, which carries a 2.4-fold to 6.6-fold* increased risk for CVD.

Illness

Cardiac and Pulmonary
- Medical conditions that may be associated with myocardial stress
- Systemic hypertension
- HF of any etiology
- Left or right ventricular hypertrophy
- Diastolic dysfunction
- Myocardial infarction
- Acute coronary syndrome
- Cardiac arrhythmias, especially atrial fibrillation
- Cardiomyopathy
- Myocarditis, possibly endocarditis
- COPD
- Pulmonary embolism

Other
- Sepsis
- Diabetes mellitus
- Renal disease

Pharmacological intervention
- Dependent on etiology, consider:
  - Preload medications: nitrates, diuretics
  - Rate-control medications: beta blockers
  - Afterload medications: ACE inhibitors, ARBs, alpha blockers, calcium channel blockers, direct vasodilators
  - Cardiac pacing

Disease intervention
- Complete evaluation of cardiometabolic function to exclude causes of cardiac dysfunction
- Echocardiography
- Other noninvasive imaging
- Additional blood tests

*Risk for HF progression is substantially increased in patients when both NT-proBNP and ST2 levels are elevated.
Heart Failure

ST2 is an interleukin-1 family receptor that is expressed in cardiomyocytes. There are 2 isoforms: transmembrane-bound ST2 and soluble, ie, circulating, ST2 (sST2). The sST2 biomarker binds and removes interleukin(IL)-33 from the circulation, thus eliminating the protective effect that IL-33 provides to the cardiac muscle.

Patients with HF who have elevated sST2 levels >35 ng/mL have a worse prognosis, and are at increased risk for HF progression, rehospitalization, need for heart transplantation, and death. sST2 level is not affected by confounding factors as is BNP/NT-proBNP. Measuring both sST2 and NT-proBNP levels can help improve the risk stratification of patients with chronic HF.*

Contributing Factors

Illness

Cardiac and Pulmonary
- Systemic hypertension
- Ventricular hypertrophy
- Diastolic dysfunction
- Myocardial infarction / Acute coronary syndrome
- Cardiomyopathy
- Pulmonary embolism

Other
- Diabetes mellitus
- Renal disease

Treatment Considerations

Pharmacological intervention
- Dependent on etiology, consider:
  - Diuretics
  - Beta blockers
  - ACE inhibitors
  - Angiotensin Receptor Blockers
  - Direct vasodilators

Disease intervention
- Complete evaluation of cardiometabolic function:
  - Electrolytes/renal function/CK-MB
- Echocardiography
- Additional blood tests:
  - NT-proBNP

*Risk for HF progression is substantially increased in patients when both NT-proBNP and ST2 levels are elevated.
References


27. Iacobellis G. Obesity and Cardiovascular Disease: Oxford University Press. 2009.


References


144. Simopoulos AP. Dietary omega-3 fatty acid deficiency and high fructose intake in the development of metabolic syndrome, brain metabolic abnormalities, and non-alcoholic fatty liver disease. Nutrients. 2013;5:2901-2923.


