Physician's Pocket Treatment Guide

Cardio IQ®
Advanced Cardiovascular Testing

Sonora Quest Laboratories™
A Subsidiary of Laboratory Sciences of Arizona

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Elevated LDL Cholesterol Level

Lipid Disorder

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[1]

Lifestyle

- High consumption of saturated fats[1]
- Overweight or obese[1]
- Sedentary lifestyle[2]

Illness

- Nephrotic syndrome,[1] hypothyroidism[1]

Drugs

- Androgens[3], progestins[4], thiazide diuretics[1], cyclosporines[1], tacrolimus[1]
- Selective serotonin reuptake inhibitors[5] (SSRIs)
- Atypical antipsychotics[6]

Treatment Considerations

Dietary/lifestyle intervention

- Cardioprotective diet[2]
- Restricted saturated fat[2]
- Fat weight loss[1]

Pharmacological intervention

- Statins[1]
- Nicotinic acid[1]
- Bile acid sequestrants[1]

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[1]

Lifestyle

- High triglyceride levels[1]
- High consumption of simple carbohydrates[7]
- Overweight or obese[1]
- Sedentary lifestyle[8]
- Smoking[1]

Illness

- Insulin resistance/diabetes mellitus[1]
- Liver,[9] kidney,[10] and thyroid disease[11]

Drugs

- Nonselective beta blockers,[1] androgens,[1] progestins,[3] isotretinoins[3]

Treatment Considerations

Dietary/lifestyle intervention

- Cardioprotective diet[12]
- Fat weight loss[1]
- Regular aerobic exercise[1]
- Smoking cessation[13]
- Omega-3 fish oil[1]

Pharmacological intervention

- Nicotinic acid[1]
- Fibrates[3]
- Thiazolidinediones[3]
- Some statins[1]

Disease intervention

- Correct insulin resistance[1]
- Control diabetes mellitus[1]

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[1]
- Pregnancy and lactation[2]

Lifestyle

- High consumption of simple carbohydrates and saturated fats[2]
- Overweight or obese[1]
- Sedentary lifestyle[2]
- Smoking[2]

Illness

- Insulin resistance/diabetes mellitus/ metabolic syndrome[1]
- Hypothyroidism,[1] renal failure,[14] excess alcohol intake[1]

Drugs

- Androgens,[3] estrogens,[1] beta blockers,*[15] thiazide diuretics,[3] glucocorticosteroids,[3] cyclosporines,[2] protease inhibitors,[3] tacrolimus,[2] sertraline,[16] isotretinoin,[17] valproate[18]

Treatment Considerations

Dietary/lifestyle intervention

- Regular aerobic exercise[1]
- Fat weight loss[1]
- Avoid high glycemic foods[1]
- Low simple carbohydrate and saturated fat diet[1]
- Avoid alcohol consumption[1]

Pharmacological intervention

- Fibrates[1]
- Nicotinic acid[1]
- Omega-3 fish oil[1]
- Thiazolidinediones (pioglitazone but NOT rosiglitazone)[3]
- Some statins[1]

Disease intervention

- Treat triglyceride levels >500 mg/dL to help prevent acute pancreatitis[1]

*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

Lipid Disorder

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.

Contributing Factors

Genetics/demographics

- Genetic predisposition[1]

Lifestyle

- High consumption of saturated fats[1]
- Overweight or obese[1]
- Sedentary lifestyle[1]

Illness

- Nephrotic syndrome,[10]
- Hypothyroidism[1]

Drugs

- Androgens,[3] thiazide diuretics,[19] cyclosporines,[20] tacrolimus[21]
- SSRIs[22]
- Atypical antipsychotics[23]

Treatment Considerations

Dietary/lifestyle intervention

- Cardioprotective diet[24]
- Restricted saturated fat[1]
- Fat weight loss[1]

Pharmacological intervention

- Statins[1]
- Nicotinic acid[1]
- Bile acid sequestrants[1]

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[25]
- High triglyceride and low HDL-C levels[2]

Lifestyle

- High consumption of simple carbohydrates[26]
- Overweight or obese[27]
- Sedentary lifestyle[28]

Illness

- Insulin resistance/diabetes mellitus/ metabolic syndrome[2]

Drugs

- Nonselective beta blockers[29]

Treatment Considerations

Dietary/lifestyle intervention

- Avoid simple carbohydrate diet[26]
- Fat weight loss[2]
- Regular exercise[28]
- Omega-3 fish oil[30]

Pharmacological intervention

- Thiazolidinediones[31]
- Nicotinic acid[32]
- Fibrates[33]
- Statins (minor effect)*[34]

Disease intervention

- Consider evaluation of cardiometabolic function[35]
- Noninvasive imaging[36]
- Additional blood tests[2]
- Identify and correct insulin resistance[2]
- Control diabetes mellitus[2]

*Effect is specific to atorvastatin.

Pattern B Phenotype/Decreased LDL Peak Size

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 .

Contributing Factors

Genetics/demographics

- Genetic predisposition[37]
- High triglyceride and low HDL-C levels[2]

Lifestyle

- High consumption of simple carbohydrates[38]
- Overweight or obese[39]
- Sedentary lifestyle[2]

Illness

- Insulin resistance/diabetes mellitus/ metabolic syndrome[40]

Drugs

- Nonselective beta blockers[29]

Treatment Considerations

Dietary/lifestyle intervention

- Avoid simple carbohydrate diet[26]
- Fat weight loss[26]
- Regular exercise[41]
- Omega-3 fish oil[30]

Pharmacological intervention

- Thiazolidinediones[42]
- Nicotinic acid[43]
- Fibrates[44]
- Statins (minor effect)

Disease intervention

- Consider evaluation of cardiometabolic function[45]
- Noninvasive imaging[46]
- Additional blood tests[47]
- Identify and correct insulin resistance[26]
- Control diabetes mellitus[26]

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

Genetics/demographics

- Genetic predisposition[1]
- High triglyceride levels[2]

Lifestyle

- High consumption of simple carbohydrates[48]
- Overweight or obese[1]
- Sedentary lifestyle[2]
- Smoking[1]

Illness

- Insulin resistance/diabetes mellitus[1]
- Liver,[2] kidney,[2] and thyroid disease[2]

Drugs

- Nonselective beta blockers,[1] androgens,[1] progestins[49]

Treatment Considerations

Dietary/lifestyle intervention

- Avoid simple dietary carbohydrates[2]
- Fat weight loss[2]
- Regular exercise[2]
- Smoking cessation[2]
- Omega-3 fish oil[50]

Pharmacological intervention

- Nicotinic acid[1]
- Nicotinic acid plus statin[1]
- Statins (minor effect)[1]
- Fibrates when triglyceride levels are elevated[1]

Disease intervention

- Correct insulin resistance[1]
- Control diabetes mellitus[1]

Elevated ApoB Level

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[2]

Lifestyle

- High consumption of saturated fats[51]
- Overweight or obese[52]
- Sedentary lifestyle[53]

Illness

- Nephrotic syndrome[54]
- Hypothyroidism[55]

Drugs

- Androgens,[56] progestins,[57] thiazide diuretics,[58] cyclosporines,[59] tacrolimus,[60] atypical antipsychotics[61]

Treatment Considerations

Dietary/lifestyle intervention

- Cardioprotective diet[62]
- Restricted saturated fat[51]
- Fat weight loss[2]

Pharmacological intervention

- Statins[59]
- Nicotinic acid[63]
- Bile acid sequestrants[1]

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[2]
- Menopausal loss of estrogen may increase Lp(a) levels by 20% to 30%[64]

Illness

- Chronic renal failure[65]
- Nephrotic syndrome[66]
- Hypothyroidism[67]
- Diabetic nephropathy[68]

Treatment Considerations

Pharmacological intervention

- Nicotinic acid[69]
- Niaspan 2000 mg per day decreases Lp(a) levels by ~24%[2]
- IR Niacin 3000 mg per day decreases Lp(a) levels by ~36%[2]
- Fibrates (limited effect)[70]
- Mipomersen[2]
- PCSK9 inhibition[2]
- Anacetrapib[2]

Disease intervention

- Consider evaluation of cardiometabolic function[2]
- Noninvasive imaging[71]
- Additional blood tests[2]
- Consider that some statins may elevate Lp(a) levels in some patients[71]
- Aggressively treat all associated atherogenic conditions[2]
- LDL or Lp(a) apheresis in some extreme cases of resistance to Lp(a)-lowering drugs[70]

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[2]
- Sex (women often have higher levels)[72]

Lifestyle

- Tobacco use[2]
- Overweight[2]
- Increasing age[2]
- Sedentary lifestyle[2]

Illness

- Insulin resistance/diabetes mellitus[73]
- Hypertension[74]
- Postmenopausal state[75]
- Acute/chronic inflammation[72]

Drugs

- Oral contraceptives,[75] gemfibrozil[76]

Treatment Considerations

Dietary/lifestyle intervention

- Fat weight loss[77]
- Increase physical activity[77]
- Smoking cessation[2]

Pharmacological intervention

- Nicotinic acid[78]
- Fibrates: fenofibrate may reduce whereas gemfibrozil may elevate[70]

Disease intervention

- Consider evaluation of cardiometabolic function[2]
- Noninvasive imaging[2]
- Additional blood tests[2]
- Control hypertension[74]
- Control diabetes mellitus[73]

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 dysfuntion, 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

- Obese[2]
- Stress[79]
- Smoking[2]
- Adiposity in women[2]

Illness

- Systemic inflammation[2]
- Insulin resistance/diabetes mellitus/ metabolic syndrome[2]

Drugs

- Hormone-replacement therapy,[80] contraceptives[80]

Treatment Considerations

Dietary/lifestyle intervention

- Cardioprotective diet[2]
- Fat weight loss[2]

Pharmacological intervention

- Statins[2]
- Statins plus ezetimibe[81]
- Fibrates[82]
- Nicotinic acid[83]

Disease intervention

- Consider evaluation of cardiometabolic function[2]
- Noninvasive imaging[84]
- Additional blood tests[2]

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[85]
- Increased carotid intima-media thickness[86]

Lifestyle

- Tobacco use[87]
- Sedentary lifestyle[88]

Illness

- Metabolic syndrome[89]
- Elevated blood glucose level[70]
- Hypertension[87]

Treatment Considerations

Dietary/lifestyle intervention

- Omega-3 fish oil supplements[90]
- Diet high in Omega-3 fatty acids[90]

Pharmacological intervention

- Statins[70]
- Fenofibrate*[70]
- Nicotinic acid plus statins*[91]
- Ezetimibe[92]
- Combination of statin with other suggested drugs results in further Lp-PLA$_2$ reduction[93]
- Antihypertensive therapy for optimal BP control[94]

Disease intervention

- Consider evaluation of cardiometabolic function[2]
- Noninvasive imaging[95]
- Additional blood tests[2]

*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.

Elevated Myeloperoxidase (MPO) Level

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[96]

Lifestyle

- Overweight or obese[97]
- Tobacco use[98]
- Extreme athletes (marathon runners) seen after strenuous exercise[99]

Illness

- Hypertension[100]
- Vascular damage[101]
- Vasculitis[102]
- Autoimmune disorders[103]
- Chronic inflammatory disease[104] (rheumatoid arthritis,[104] lupus[105])
- Chronic lymphocytic leukemia[106]
- Bone marrow dyscrasias[107]

Treatment Considerations

Dietary/lifestyle intervention

- Fat weight loss[108]
- Regular exercise[109]
- Smoking cessation[98]
- Cardioprotective diet[110]

Pharmacological intervention

- Statins[111]

Disease intervention

- Antiplatelet therapy[112]
- Antihypertensive therapy for optimal BP control[100]
- Additional blood test (NT-proBNP)[113]
- Noninvasive imaging[114]

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[2]
- Elderly people[115]

Lifestyle

- Obese[116]
- Visceral adiposity[117]
- Sedentary lifestyle[118]
- High carbohydrate diet[26]
- Stress[119]

Illness

- Menopausal drop in estrogen[120]
- Chronic inflammation with elevated inflammatory markers[121]
- Illnesses such as:
  - Polycystic ovarian syndrome[2]
  - Cushing's disease[122]
  - Hemochromatosis, insulinoma[123]
  - Insulin resistance/diabetes[124]
  - Diabetes mellitus/metabolic syndrome[1]

Drugs

- Rifampin,[125] progesterone,[126] antiretrovirals,[127] corticosteroids[128]
- Elevations may be caused by postprandial blood sample or exogenous administration of insulin[129]

Treatment Considerations

Dietary/lifestyle intervention

- Fat restricted, cardioprotective diet[130]
- Limit simple carbohydrates, utilize high-fiber sources[131]
- Fat weight loss[132]
- Regular exercise[133]

Disease intervention

- Recommended pharmacologic methods of meeting insulin requirements or regulating insulin sensitivity[2]

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[3]

Lifestyle

- Deficiencies of vitamins folic acid, B6, and B12[1]
- Excess alcohol,[134] caffeine,[135] or nicotine[136]
- Diet low in greens, high in meats[137]

Illness

- Renal insufficiency/failure,[138] pernicious anemia,[139] megaloblastic anemia;[140] hypothyroidism[2]

Drugs

- Nicotinic acid (dose dependent);[141] fenofibrates,[141] sulfonamides,[141] metformin,[141] anticonvulsants,[141] methotrexate,[141] theophylline,[141] cyclosporine[142]

Treatment Considerations

Dietary/lifestyle intervention

- Diet high in green leafy vegetables[137]
- Traditional treatment has been folic acid, B6, and B12 vitamins[2]

Disease intervention

- Identify and treat any underlying abnormality such as renal insufficiency/pernicious anemia[2]
- Initiating treatment of elevated homocysteine continues to be controversial in reducing risk for CVD events versus increased risk for other conditions[2]

Abnormal Omega-3 & -6 Index/Abnormal EPA/AA Ratio

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[143]

Lifestyle

- Low dietary consumption of omega-3 fatty acids[144]
- High dietary consumption of omega-6 fatty acids[144]
- Dietary deficiency of omega-3 fatty acids[145]

Treatment Considerations

Dietary/lifestyle intervention

- Two primary omega-3 fatty acids are EPA and DHA. Dietary sources are:
  - Fish oil[2]
  - Fatty fish[2]
- 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[2]

Decreased Vitamin D, 25 Hydroxy, LC/MS/MS

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

Genetics/demographics

- Elderly and newborns[1]

Lifestyle

- Inadequate sun exposure[1]:
  - People with more skin pigment are at higher risk for vitamin D deficiency[1]

Illness

- Obesity[1]
- Malabsorption[3]
- Renal disease[2]
- Liver disease[146]

Drugs

- Corticosteroids,[147] anticonvulsants,[1] antirejection medications,[148] HIV medications[148]

Treatment Considerations

Dietary/lifestyle intervention

- Vitamin D supplementation[3]

Disease intervention

- Initial loading therapy:
  - 50,000 IU vitamin D_2 weekly for 2 months[3]
- Maintenance therapy:
  - 50,000 IU vitamin D_2 once or twice monthly[3]
  - 2000-4000 IU vitamin D_3 daily and/or appropriate sun exposure and/or high vitamin D diet (eg, salmon, tuna fish, shiitake mushrooms)[3]

Elevated NT-proBNP Level

Heart Failure

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.

Contributing Factors

Illness

Cardic and Pulmonary

- Medical conditions that may be associated with myocardial stress[149]
- Systemic hypertension[150]
- HF of any etiology[2]
- Left or right ventricular hypertrophy[151]
- Diastolic dysfunction[152]
- Myocardial infarction[153]
- Acute coronary syndrome[154]
- Cardiac arrhythmias, especially atrial fibrilation[155]
- Cardiomyopathy[155]
- Myocarditis, possibly endocarditis[155]
- COPD[156]
- Pulmonary embolism[157]

Other

- Sepsis[158]
- Diabetes mellitus[159]
- Renal disease[160]

Treatment Considerations

Pharmacological intervention

- Dependent on etiology, consider:
  - Preload medications: nitrates,[161] diuretics[162]
  - Rate-control medications: beta blockers[163]
  - Afterload medications: ACE inhibitors,[164] ARBs,[70] alpha blockers,[70] calcium channel blockers,[165] direct vasodilators[166]
  - Cardiac pacing[167]

Disease intervention

- Complete evaluation of cardiometabolic function to exclude causes of cardiac dysfunction[2]
- Echocardiography[168]
- Other noninvasive imaging[2]
- Additional blood tests[2]

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

Elevated Soluble ST2 Level

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

Cardic and Pulmonary

- Systemic hypertension[169]
- Ventricular hypertrophy[170]
- Diastolic dysfunction[171]
- Myocardial infarction / Acute coronary syndrome[172]
- Cardiomyopathy[173]
- Pulmonary embolism[174]

Other

- Diabetes mellitus[175]
- Renal disease[176]

Treatment Considerations

Pharmacological intervention

- Dependent on etiology, consider:
  - Diuretics[177]
  - Beta blockers[178]
  - ACE inhibitors[179]
  - Angiotensin Receptor Blockers[180]
  - Direct vasodilators[181]

Disease intervention

- Complete evaluation of cardiometabolic function:
  - Electrolytes/renal function/ CK-MB[2]
- Echocardiography[177]
- Additional blood tests:
  - NT-proBNP[182]

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

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