Naturopathic Primary Care Cardiovascular Disease Risk Reduction Model

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It is a privilege to be able to provide personalized holistic medicine at a time with reliable, efficient assessment tools, well-tested therapeutic programs and a renewed societal acceptance that "prevention is the best medicine". With greater public knowledge of the role for a healthy diet and lifestyle in cardiovascular disease (CVD) risk reduction, naturopathic doctors have been able to position themselves as the developers and managers of detailed patient heart-health wellness plans.

This service of assessing, treating and tracking using well established biomarkers, naturopathic therapies and a foundational holistic approach promotes health span and lifespan while addressing patient desire for a reduction in the use of pharmaceutical interventions and the side effects that accompany them.

This article will outline such a plan to be adapted and used freely with the goal of improving longevity and health span through reduced cardiovascular events and impairments to activities of daily living.

Cardiovascular Disease Risk

Cardiovascular disease (CVD) is the second leading cause of mortality in Canada and cerebrovascular disease is the fourth.[1] These two groups of conditions have held positions similar to these for many years even though prevention tools have been well studied, documented, funded, promoted and thoroughly adopted. Personalized prevention program management may be the missing link in primary and secondary risk reduction.

The term cardiovascular disease refers to ischemic heart disease and/or coronary artery disease.[2] The consequences of this condition include heart attack, heart failure and death. As a group, these conditions account for major suffering amongst our population, needless loss, trauma and disability. It is estimated that 80% of all cardiovascular disease is preventable.[3]

This objective approach to assessment uses tools commonly available to most naturopathic doctors with laboratory access. Naturopathic therapeutics and pharmaceutical prescribing protocols are available for each one of the biomarkers listed. Research for nutraceutical and dietary plan effectiveness through biomarker modulation is growing daily with a focus on CVD and all-cause mortality as endpoints. This review focuses on helpful laboratory biomarkers and is not inclusive of all assessment tools. It is simply a framework to build upon and adapt as necessary.

Naturopathic Approach Principles

While sitting down with a patient at the beginning of this process it is helpful to review our approach. We are able to use naturopathic principles to outline where we are coming from:

- First, do no harm - we will not make the situation worse and will have a procedures/alternatives/risks/questions conference before applying therapeutics.
- Doctor as teacher – through in-office graphics of CVD we can review important mechanisms in disease processes and treatment methodology.
- Prevention - we can quantify risk and take action to modify risk immediately.
- The healing power of nature - natural substances can positively impact biomarkers to reduce risk.
- Identify and treat the cause - we are able to review factors associated with hard and soft plaque including environmental, dietary, genetic and lifestyle mediated.
- Treat the whole person - applying the holistic approach to CVD management is one way we set ourselves apart and go above and beyond for patients. This is a powerful way to improve compliance.

To begin personalization we need to set an objective standard. Assessment and therapeutic cycles of 12 weeks can be useful. Initially we gather information, quantify risk and provide a detailed approach.

Quantify Cardiovascular Disease Risk

This approach to CVD risk reduction starts with our initial visit with a patient. First we must determine if we are attempting primary or secondary risk reduction, review past medical history and family history pertaining to the heart/metabolic syndrome and collect laboratory records from previous medical practitioners.

Our objective approach to CVD risk reduction relies on a risk calculation. A commonly used, easy, quick tool most medical professionals are familiar with is the Framingham Risk Score.[4] Other options include the ASCVD[5] and QRisk.[6] Most of these models require basic inputs including total cholesterol, HDL cholesterol, smoking status, diabetic status, average blood pressure and age.

Most calculators will classify patients into low, intermediate and high-risk categories. A common threshold to use for example could be: Framingham Risk Score (10 year risk of heart attack and stroke) of <10% as low risk, 11-19% intermediate risk and >20% as high risk. Using a risk categorization we can then set goals for biomarkers and subsequent renewed categorization.

We can then do better for our patients and further quantify risk by going beyond basic biomarker assessments and use personalized risk qualification biomarkers as outlined below. For many there is value in the details. For some, depending on financial ability and willingness, the basics could provide adequate information. Finally, if therapeutic routine wouldn't be altered by an unexpected result, further testing might not be warranted.

Advanced Cardiovascular Assessment Tools

Once categorized, the determination for further assessment can be made. Most often further workup is warranted in the intermediate and high-risk classifications. Exceptions are for low risk individuals with a significant family history of CVD. Building a personalized plan in these cases requires personal detail.

This is where the holistic approach to case management can be most obviously applied. The cardiovascular system is influenced and interacts with all other organ systems. The rationale behind the holistic approach is easy to justify using epidemiologic studies and biochemical pathway instruction. Our role is to optimize the body's ability to heal through supportive, non-invasive intervention when possible. For example, observational studies have shown that both low levels of serum testosterone and high levels of serum testosterone have been associated with increased CVD risk.[7] Taking this biomarker into the normal range through lifestyle improvements, dietary recommendations and herbal prescribing could provide a beneficial vasodilatory effect, positive cardiac and skeletal muscle strength and improved insulin sensitivity.[7] This is the kind of detail personalized risk management we can facilitate. If our therapeutic approach provides the time and resources for such detailed analysis we have a duty to provide it.

The following list and review provides a series of testing options to further quantify and qualify risk. This tool kit takes intermediate and high-risk individuals and allows us to qualify them with one or multiple tendencies. Is this picture an inflammatory one, hormone imbalance, nutrient deficiency or excess, genetic, exposure mediated, autoimmune, etc? It also informs us to what we should be tracking long term and what other conditions could be concomitant.

Finally, we can act in a way that is objective, holistic, evidence-based and rational. If CVD is the "silent killer", prevention of CVD requires as much detail as possible. This process is the gamification of biomarker management. We can use our toolkit to improve these biomarkers and thus decrease risk.

Biomarkers of Consideration

As previously described a consult begins with a review of lipids (LDLc, HDLc and triglycerides), HbA1C, fasting plasma glucose and blood pressure. Before moving forward there can be value in providing the triglyceride:HDL ratio as a high number has been associated with insulin resistance and cardio/cerebrovascular disease.[8] Next a determination for appropriate laboratory workup can guide requisition choices. Here are a few examples of categories for testing:

Inflammatory:

- CRP - c-reactive protein - a nonspecific, acute-phase reactant protein commonly used to diagnose bacterial infections and inflammatory disorders. CRP is made in the liver and produced in response to antigen-immune complexes, bacteria, fungi and trauma. As a complement activator CRP plays an important role in promoting an immune response to foreign invaders. We are interested in this molecule for its ability to induce genetic expression of genes required for adhesion of monocytes and the recruitment of intracellular molecules such as E-selectin and monocyte chemoattractant protein-1 (MCP-1) in atherogenic plaques.[9] It is elevated in inflamed plaques and thus is a helpful tool in CVD assessment.

- LP-PLA2 - lipoprotein associated phospholipase A2 - an enzyme involved in the hydrolysis of oxidized LDL within the intima used to determine the inflammatory activity of an atherogenic process. This measure is highly predictive of coronary artery disease mortality indicating it is of highest importance in determining severity of illness.[10] The benefit of adding LP-PLA2 to a risk stratification program is that it is predictive independent of CRP and elevation confirms a doubled event risk.[10]

- Fibrinogen - another acute-phase reactant, fibrinogen is elevated at times of inflammation and tissue necrosis. Its role is as part of the clotting cascade as it is converted to fibrin by thrombin during coagulation. Fibrinogen is helpful as a screening tool to assess increased thrombotic risk.[11]

- Myeloperoxidase - a heme peroxidase responsible for the formation of reactive oxygen species within atherosclerotic lesions and is now known as a role player in both promotion and propagation of atherosclerosis through lipid peroxidation.[12] This enzyme is a predictor of cardiovascular risk independent of Framingham score or CRP.[12]

Metabolic:

- Fasting Insulin and HOMA-IR - the acronym HOMA-IR stands for Homeostatic Model Assessment of Insulin Resistance and is a simple method for estimating insulin sensitivity and pancreatic function. This tool requires a fasting insulin and fasting glucose test and is determined using a calculation found online.[13] In non-obese, non-diabetic patients this measure can help predict risk of CVD thus making it a great tool for prevention and longevity workups in a healthy population.[14]

- OGTT - oral glucose tolerance test - achieving an OGTT with insulin measurements can provide detailed insight into insulin sensitivity and beta cell function. This test adds another metabolic tool to our toolkit for non-diabetics looking to predict their CVD risk. If they do not reach pretest glucose levels after the 2 hour mark of the OGTT they are at higher risk of mortality from cardiovascular disease and all-cause mortality.[15] Compared with fasting glucose this test better predicts coronary heart disease and ischemic stroke.[16]

- TSH - thyroid stimulating hormone - the holistic approach to CVD risk assessment allows us to look at all organ systems. It is important to note with patients how thyroid function impacts the cardiovascular system. In hypothyroidism cardiac output is reduced, arterial stiffness is increased, diastolic blood pressure increases and pulse pressure narrows resulting in sodium sensitive diastolic hypertension.[17] When evaluating Framingham score for hypothyroid patients it is important to note decreased hepatic clearance of LDLc as well as elevations of CRP and homocysteine.[17] Untreated hyperthyroidism is a risk factor for left ventricular hypertrophy, atrial fibrillation and heart failure.[17]

Toxicity:

- Cadmium - well-controlled epidemiologic studies show a correlation between chronic cadmium exposure and CVD.[18] Blood and urine assessments can determine body burden. Cadmium is found in cigarette smoke, air pollution and in certain foods.

- Lead - in 2018 The Lancet Public Health published a study quantifying the contribution of lead exposure to CVD risk. Their conclusion was that even low level environmental lead exposure is an important marker for CVD risk and promoting its avoidance should be addressed at a public health level.[19] The mechanism of impact for lead is multifold and includes its ability to promote oxidative stress, limit nitric oxide availability, impair nitric oxide signaling, augment adrenergic activity, increase endothelin production, alter the renin-angiotensin system, raise vasoconstrictor prostaglandins, lower vasodilator prostaglandins, promote inflammation, disturb vascular smooth muscle Ca2+ signaling, diminish endothelium-dependent vasorelaxation, and modify the vascular response to vasoactive agonists.[20]

Lipid/Vascular microenvironment:

- APOB100 - as a protein constituent of both low-density lipoprotein and very low-density lipoprotein (VLDL) APOB100 is a recognition signal for cellular binding and internalization of LDL particles.[21] There is one APOB100 per LDL particle and therefore it is a highly accurate, less expensive proxy for the LDL particle measurement. The fatty streak phase of atherosclerosis is initiated by APOB containing LDL and VLDL particles. This assay is of highest use in the setting of high triglycerides to further determine the extent of LDLc suppression required.[22]

- APOA1 - this protein constituent lives in the high-density lipoprotein (HDL) molecule and therefore is involved in the cycle of HDL redistribution of cholesterol to the liver for recycling. APOA1 helps to quantify HDL capacity and can be compared to APOB100 using the ratio APOB/APOA1 providing a superior predictor of cardiovascular events compared with simple HDLc and LDLc management.[23]

- Oxidized LDL - although long studied, the measure of oxidized LDL in clinical practice is relatively new. As a key stimulus for inflammatory and immunologic mechanisms leading to endothelial dysfunction, foam cell formation and induction of platelet adhesion and aggregation this assay could provide added detail to a clinical workup beyond that of LDLc.[24]

- Lp(a) - a separate lipoprotein similar to LDL but with increased prothrombotic and anti-fibrinolytic effects and the ability to accelerate atherogenesis through intimal deposition of Lp(a) cholesterol.[25] This measure is an independent risk factor for cardiovascular event risk and elevation is mostly genetically determined.[26]

- PULS - the Protein Unstable Lesion Signature is a group of tests estimating traces of proteins leaking from inflamed vessel plaque in an attempt to determine the severity of atherosclerosis and plaque rupture potential. The PULS protein biomarkers include HDL, HbA1C, Fas ligand, HGF, Eotaxin, CTACK, MCP-3, IL-16 and sFas.[27] The test provides a personalized 5-year diagnosis and prognosis of unstable cardiac lesion and rupture risk as well as a calculated "Heart Age" comparing their risk score relative to their age and gender group.

Nutritional:

- Homocysteine - as an intermediate in the metabolism of methionine, homocysteine should not remain in circulation long. When it does it acts as a diagnostic tool given its label as an independent risk factor for ischemic heart disease, cerebrovascular disease and peripheral arterial disease. Mechanistically, homocysteine is damaging to endothelium, promotes low-density lipoprotein deposition and increased vascular smooth muscle growth. It is known as a risk factor for stroke, dementia and Alzheimer's disease. The two main causes of homocysteine elevation are genetic risk and B12, B6 and folate deficiency.

- Omega 3 Index - the assessment of omega 3, 6 and 9 is now widely available via a simple blood test. The omega 3 index has been validated as a risk marker for CVD mortality with the risk reduction in the highest levels of omega 3 index achieving greater prevention than those with the lowest concentrations of CRP.[28] Intervention trials show omega 3 supplementation reduces risk of sudden cardiac death and can be helpful in secondary prevention of CVD.[28] This assay's sensitivity to diet allows further determination for omega 3 requirements.

- Vitamin D3 - deficiency in this vitamin has been linked to the following cardiovascular outcomes; congestive heart failure, impaired systolic and diastolic function, myocardial infarction, peripheral vascular disease, abdominal aortic aneurysm in older men, nonvalvular atrial fibrillation and hypertension.[29] Low levels of vitamin D3 trigger increased renin and angiotensin II synthesis, inhibition of the pathways necessary for intracellular glucose transporter, thus the development of insulin resistance, and calcium homeostasis disruption impacting smooth muscle calcification and proliferation.[29]

Hormonal:

- Cortisol - elevated hair cortisol is associated with increased incidence of CVD, poorer recovery and treatment outcomes.[30] Excess cortisol over time can induce hypertension, hyperinsulinemia, hyperglycemia, truncal obesity, insulin resistance and dyslipidemia.[31] The impact of cortisol on the cardiovascular system seems to be mainly mediated through its inhibition of nitric oxide therefore promoting vasoconstriction.[31]

- DHEA - an adrenal prohormone that declines with age. Low levels of DHEA-S have been associated with CVD mortality in postmenopausal women and all-cause mortality, CVD and ischemic heart disease in men independent of other CVD risk factors.[32]

- Testosterone - with a favorable role as a direct vasodilator of coronary arteries and through easing peripheral vascular resistance, adequate testosterone levels have proven useful in cardiovascular risk management. Low levels of this hormone have shown to increase CVD risk and controversy remains with hyper-physiologic levels through exogenous testosterone use as a potential for worsening CVD risk is possible. With its impact on the blood vessels and potential for improving insulin sensitivity, exerting a positive effect on cardiac and

skeletal muscle maintaining normal testosterone levels has proven essential on a holistic risk management plan.[7]

- Estrogen - a decline in estrogen during menopause is associated with increased CVD risk although hormone replacement therapy has shown an increased stroke risk in certain populations and is not considered a solution to this deficiency for the purpose of CVD risk reduction.[33]

- Melatonin - circadian rhythm optimization is important for managing CVD risk and the main hormone involved in this process is melatonin. Low levels of melatonin are associated with increased CVD risk, hypertension and heart failure. Likelihood of adverse cardiac events, including myocardial infarction, sudden cardiac death and cardiac arrhythmias increases in the early morning, when circulating melatonin levels are lowest.[34]

Genetics:

- 9p21 - also known as the "Heart Attack Gene" this gene risk variant confers a 40% increased risk of coronary artery disease when a patient has two copies.[35]

- APOE4 - commonly known as the "Alzheimer's Gene" this gene risk variant predisposes patients to hypercholesterolemia and increased CVD risk.[35]

- APOC3 - the unfavorable variant of this gene predisposes patients to hypertriglyceridemia and increased CVD risk.

Imaging tools:

Finally, to quantify and qualify risk even further, cardiac imaging can be done using ultrasound, X-ray, MRI and/or CT. Common names for these assessments include echocardiogram, ECG, angiogram and coronary calcium scan. The goal here is to pinpoint inflamed plaque for assessment and to determine the value of invasive treatments such as stenting.

Therapeutic options:

We have made it. We have been able to take a patient from low, intermediate or high risk to a personalized medicine track with an ability to focus on one or more categories of overall wellness. This is when we access our therapeutic toolkit.

A well-rounded approach to CVD risk reduction might include fasting, hydrotherapy, exercise, sleep support, stress reduction and/or nutrition therapy with personalized dietary modifications and meal planning. Advanced treatments directed at biomarker manipulation through the use of nutraceuticals, herbal remedies and low dose pharmaceuticals give us the ability to offer evidence-based protocols to address single physiologic mechanisms. We have the ability to spend time, teach and promote optimal metabolism, nutrient status, organ function, stress response, circadian rhythm management, hormone synthesis, inflammation reduction, and so on. This is our core strength.

Tracking, Treating & Re-assessing Cardiovascular Disease Risk

The "silent killer" becomes very loud when you have the amount of detail outlined above. It can be overwhelming if improperly presented. As an approach it is the opposite of simply addressing high LDLc with a statin drug. It is to say yes, we have an inflamed plaque issue brewing in the cardiovascular system. The environmental factors, external and internal, that brought us to this situation can be clearly defined through our test results.

Is there a genetic influence? Is diet impacting metabolic function? Are we seeing an increase in inflammation and oxidative stress because of a lack of one nutrient such as omega 3 or an increase in immune activity such as in rheumatoid arthritis (and accompanying high c-reactive protein)?

Map the outcomes and apply your toolkit. Common follow up times are 12 and 24 weeks to reassess and refine. After biomarker improvement is met, a new Framingham score can be presented outlining an updated 10-year CVD risk.

Happier and healthier years with family and friends are possible with a balanced approach providing this level of personalized care. As leaders in preventative medicine we are primed for this role.

About the Author

Dr. David Duizer is the co-founder of DAMYHealth.com, co-developer of The Healthy Rebel App and the Medical Director at the Finlandia Health Center in Vancouver, BC where he practices full time. His clinical focus is chronic disease management and integrative cancer care. He completed his Bachelor of Science in Chemistry and Psychology as part of the Regular Officer Training Program (ROTP) at the Royal Military College of Canada in 2008 and graduated from the Boucher Institute of Naturopathic Medicine (BINM) as a Doctor in Naturopathic Medicine in 2014. Dr. Duizer is currently serving a second term as a Director on the Board of Governors at BINM.

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