Health Beat

Issue 3

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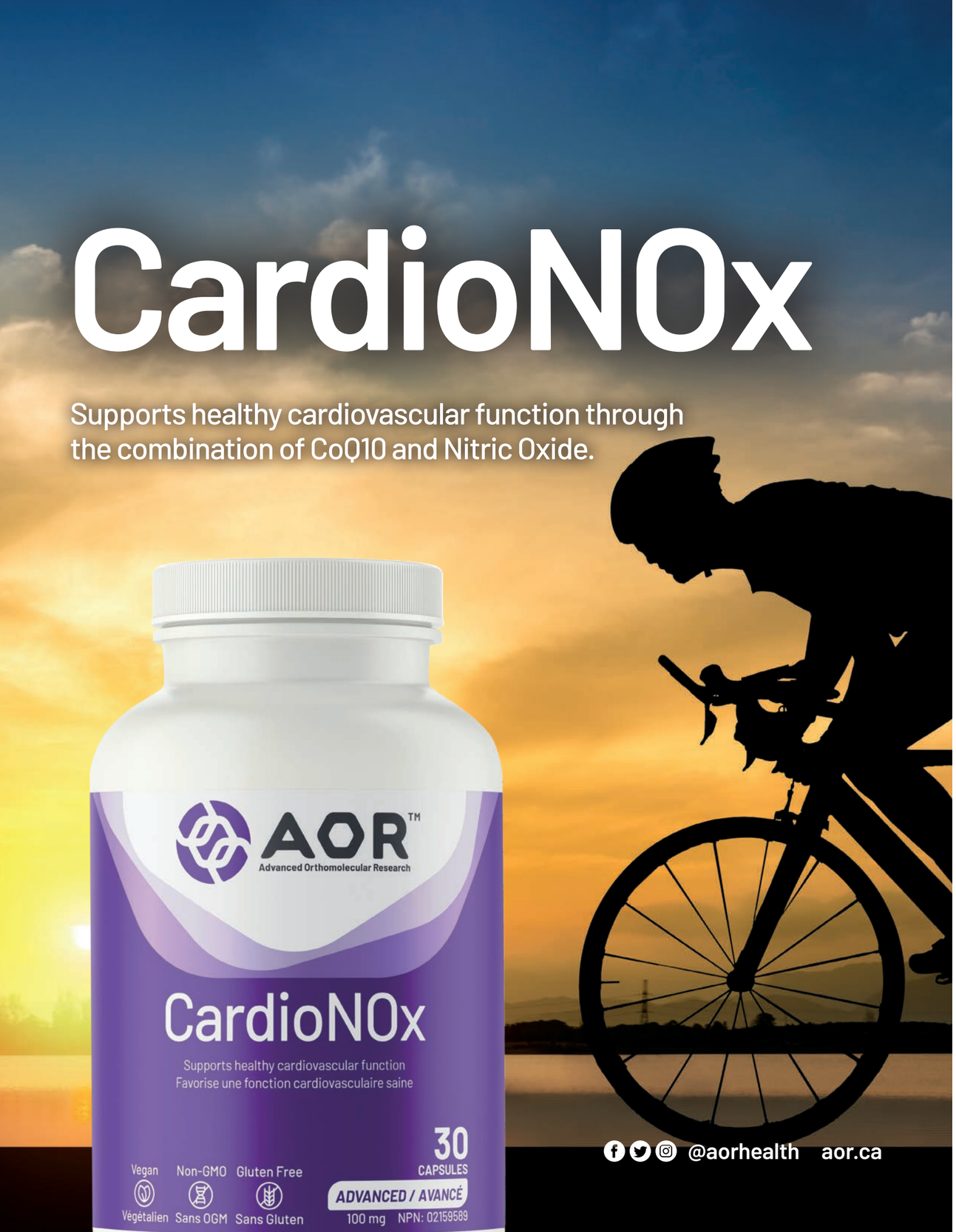
How Weight Lifting Can Help

Cardiovascular Health



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Genetics And Cardiovascular Health

By Dr. Nirat Nibber, ND

Key Terms[1]:

Phenotype: Observable traits or characteristics. How the various genes and environment all interact and are expressed (e.g., height, eye colour, hair colour, etc.).

Genotype: Describes the genetic sequence inherited (as alleles) from our parents (one from each) and may or may not contribute to the phenotypic expression.

Allele: A version or variant of a gene. Every individual inherits two alleles of each gene, when they are the same they are considered homozygous for this gene, while two different alleles are termed heterozygous. Often between heterozygous alleles one may be dominant. [1]

Single Nucleotide Polymorphisms (SNP): These are differences at a single point in the genetic sequence of a gene that can lead to alterations in the genes end product.

Loci: Refers to the location on a chromosome where the gene or genes exist.

Penetrance: A term that defines the probability that a mutation in a disease defining gene will result in the development of that phenotype. [1]

Mendelian Inheritance: This pattern of inheritance is related to single-gene pairs with dominant or recessive characteristics. Consider this the simplest way to inherit a trait from parents.

Complex or polygenic diseases: This disease category relates to the multiple genes that have varying penetrance on disease phenotype and are often understood as genetic modifiers that may or may not contribute to disease.

Advances in medical technology and exploration is boundless. We have learned more about the human body and how it functions in the last century than any other time.

Thanks in large part to the completion of the human genome sequencing project completed in 2003. [1] Completely challenging the simplified understanding of modifiable and nonmodifiable risk factors. The profound impacts on having this information accessible is evident in our advancements in cardiovascular disease prevention, identification and management. In this article we will review the link between genetics and cardiovascular risk.

What is Cardiovascular Disease (CVD)?

Our cardiovascular (CV) systems are vital, multi-organ systems all designed to transport our blood. Oxygenating tissues, delivering hormones and immune cells, regulating temperature, and so much more. Akin to the complex highways, roadways, side streets and lanes, our circulatory system employs arteries, veins, capillaries and a very large pump to ensure things are flowing. Like any city planner will tell you, the organisation and tight regulation ensures there is smooth flow - no crashes, buildups, breakdowns or blockages. Every individual carries the same framework of their cardiovascular system, however there are important differences in how this system is managed and organised. Regulation of the CV system means we are highly sensitive to the needs of our environment, lifestyle, activity, behaviour, etc. [2] For example, the heart can adjust the force and rate of contractions while blood vessels mange pressure and perfusion based on several signals such as fluid volume, exertion and even our mood. [2]

Cardiovascular disease (CVD) is used to describe the wide array of diseases that arise from a breakdown in these processes. [2] CVD is a significant concern with serious implications on individual quality of life, mortality, stressing communities and health care systems. CVD can be related to the integrity of the heart (how well can you pump), difficulties in peripheral circulation (is blood getting where it needs to go). This group of diseases includes:

- Coronary heart disease (CHD) : a type of heart disease caused by the accumulation of fat in the arteries leading to the hardening. [3] Damage affects the small vessels before they impact larger vessels. This disease has serious repercussions on the health of individuals as it can lead to heart attacks, blood clots and death
- Cerebrovascular disease: those which impact blood flow or blood vessels in the brain[2]
- Peripheral arterial disease: reduced blood flow to limbs[2]
- Congenital heart disease: dysfunctions in the anatomy of the heart or blood vessels from birth[2]

Which can often culminate in major adverse cardiac events (MACE) such as myocardial infarction, stroke, cardiac death, ischemia, pulmonary embolism and deep vein thrombosis. [4]

Redefining CVD Risk

With the stakes this high it's important to understand risk, particularly those that we can modify that will help prevent these events from occurring. Researchers have described these risk factors as either non-modifiable, those which we cannot directly impact through choices we make genetics, age, sex; and those that are modifiable, characterised as seen in Table 1. However, this model of classification may be overly simplistic as geneticists are uncovering multiple causal pathways leading to CVD. Each of which has specific gene to gene and gene to environmental interactions, meaning that having certain genes or single nucleotide polymorphisms (SNP's) isn't enough, they need to be expressed in the right way, with the right circumstances. Meaning that which we previously thought was non-modifiable may be altered with greater targeted insights. Further, some of the risk factors that were considered modifiable may have stronger genetic affinities than previously thought.

Table 1. Modifiable and non-modifiable risk factors for CVD[3,4,6]

Modifiable	Modifiable with Strong Genetic Influence	Non-modifiable
• Lack of exercise • Smoking: both actively smoking and passive smoke inhalation due to disruptions in nitric oxide synthase pathways • Drugs	• Hypertension: chronically elevated high blood pressure • Atherosclerosis: hardening of blood vessels • Hypercholesteremia: high cholesterol specifically LDL cholesterol and low HDL • Vascular disease • Type II Diabetes Mellitus • Abdominal obesity or excess visceral fat accumulation	• Family history • Sex: men >45yo higher risk while post-menopausal women have elevated risk • Age

Historically, risk assessment tools for CVD such as the Framingham cardiovascular risk offered models of risk based on pooled cohort studies. [5] This risk stratification gives patients a score that relates to the likelihood of them experiencing a cardiovascular event in five and 10 years. These percentages are estimates based on epidemiological data. While not exact, they do offer clinicians and patients insight into the risk to help motivate and direct change. Though clinicians see the inclusion of genetic markers in risk stratification as an important next step for more precise risk scoring. [6]

How do you know which genes impact CVD?

As one can imagine this is a complicated web of interactions that is continuously evolving. Currently there are three major types of studies that help unravel this web. [7]

Linkage studies: These large-scale studies enrol families with multiple affected members over different generations to identify inheritance patterns of genes related to CVD using DNA markers throughout the genome.

Association studies: These case-controlled studies compare allele frequencies in disease and control populations to understand the impact of genetic variants to phenotype (or expression). These studies can help define the predisposition to disease, drug response and aging (e.g., Genetic anomalies where homocysteine is dramatically elevated → early death from CVD).

Genome-wide association studies: Similar to association studies above, these studies are more specifically related to investigating single nucleotide polymorphisms (SNPs) across the genome helping us identify specific regions and the impact on CVD risks.

Let's investigate some of the "modifiable" risk factors with genetic modifiers.

Hypertension: Blood pressure is a measurement of how hard your heart is working to pump blood out to the body. It calculates the volume of blood leaving your heart (cardiac output) by the resistance it faces when it leaves (peripheral resistance). There are natural fluctuations in blood pressure which are normal. [6] Genetic variations in the blood pressure regulatory mechanisms such as the renin angiotensin system (ACE and AT1R8) influencing blood pressure variations, may explain why some of us are sensitive to these fluctuations and why we may stay elevated while others can recover.

Hypercholesteremia: High total cholesterol, triglycerides, LDL and trans fats, combined with low HDL is linked to increased risk of cardiovascular events. Cholesterol can build up due to increased production, increased consumption or decreased excretion. Researchers identified 95 loci associated with regulation of at least one of: LDL, HDL and triglycerides.[8] However, they found that each individual variant had only a modest effect (25% of the genetic variance) meaning that, while genetic input is important the consumption and external factors are much more pronounced. [8] While familial hypercholesterolemia is inherited through mendelian inheritance with one single genetic mutation resulting in high penetrance of the disease. [8]

Specific Examples and Gene Marker Table

- Please note this is not a comprehensive list. Rather a collection of key modifiable markers that may be seen on common genetic tests.

Specific Marker	Role in Cardiovascular Health
MLXIPL gene[9]	Involved in the activation of triglyceride synthesis. At least one genetic variant is associated with an elevated risk of having higher than ideal triglyceride levels.
LPL gene[10]	Encodes lipoprotein lipase, an enzyme that helps to break down the fat (triglycerides) travelling through our blood as well as promotes the uptake of lipoproteins into cells.
CLOCK gene[1]	The CLOCK gene is involved in the regulation of our body's circadian rhythm, which can affect our ability to synthesize and break down fats properly. Circadian rhythm dysfunction is associated with an increased risk of type 2 diabetes, obesity, and cardiovascular disease.
FADS2 gene[2]	Encodes a portion of the D6D enzyme which converts between different types of fatty acids, including the conversion of ALA into EPA/DHA.
IL6 gene[3]	Encodes interleukin-6, a protein involved in the generation of inflammation. Variants in IL-6 are also associated with increased risk of certain metabolism-related disorders, specifically obesity and metabolic syndrome, in response to omega 3 fatty acid intake. Certain variants can lead to an increased risk of obesity when you don't consume adequate omega 3 fatty acids.
Endothelial nitric oxide synthase (eNOS)[7]	eNOS Glu298Asp polymorphism made a statistically significant contribution to predicting blood pressure response to diuretics
APOE family[4]	Genes involved in the lipid metabolism.
A functional mutation in one of three genes: NCCT, NKCC2 or ROMK[8]	Is associated with clinically significant alterations in blood pressure.
SERPINE[6]	Encodes fibrinolytic proteins (PAI-1) which activates pathways to breakdown blood clots.
Angiotensin-converting enzyme (ACE) gene[5]	Regulated blood pressure and fluid balance which can impact exercise endurance.
Methylenetetrahydrofolate reductase (MTHFR[6])	MTHFR C677T variant modestly affects how your body processes folate which is normally used to reduce homocysteine levels.

Pharmacogenetics

In addition to the study of the genes responsible for elevated CVD risk we can also use genetic insights to predict the response of commonly used cardiovascular drugs on different patient populations. This can be related to metabolic and detoxification capacity of individuals. For example, the FDA adjusted warfarin dosing recommendations dependent on patients' genetic variants in CYP2C9 and VKORC1, which can affect antiplatelet efficacy. [8] Many other drugs are being reassessed using similar logic and we will likely see advancements in drug prescriptions and dosage adjustments based on genetic insights.[7]

Future Directions in Genetic Testing for CVD

It is important to reiterate that we are still within the infancy of our understanding on this amazing and complex topic. So much more is yet to be discovered and there is a lot that can still change. Physicians strive to contextualise the genetic information with environmental and lifestyle risks, framing the genetic data as a sort of blueprint.

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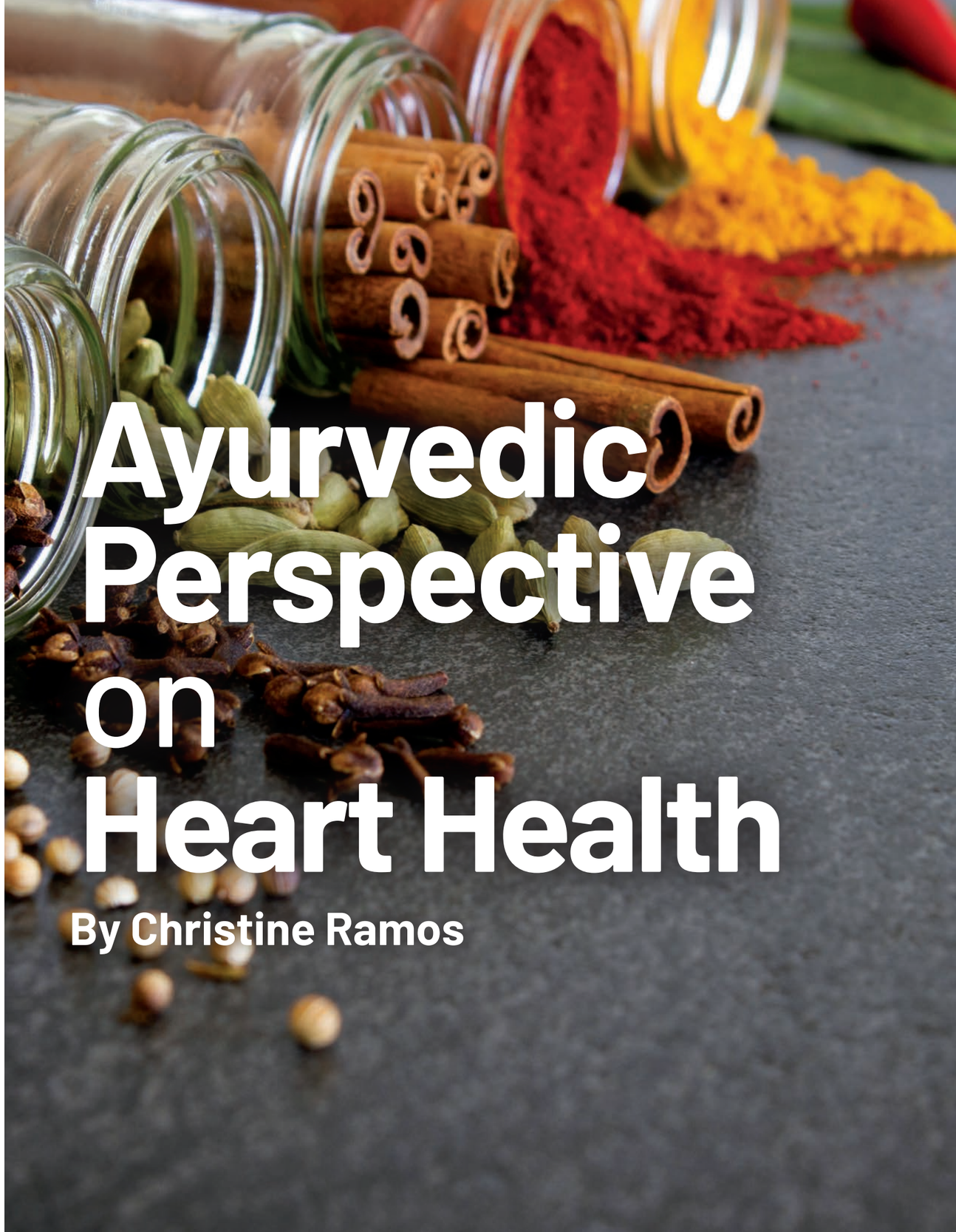

Ayurvedic Perspective on Heart Health

By Christine Ramos

What is Ayurveda?

Ayurveda is a holistic system of medicine that has been practiced for over 5,000 years. Ayurvedic medicine focuses on improving overall health rather than treating disease states, taking a preventative rather than reactive approach to maintaining optimal wellness. When the body, mind and consciousness are harmoniously working as one, then there is "health". But, when the balance of any of these is disturbed, the disease process begins.

Taking a whole picture view of the impact that stress, diet, lifestyle, mindset, movement (or lack thereof) and rest have on one's health, especially one's heart, Ayurveda provides effective strategies to prevent the onset of heart disease.

Heart Health Stats

Heart disease is the second leading cause of death in Canada[1], behind cancer. According to the Public Health Agency of Canada, one in 12 Canadians over the age of 20 live with diagnosed heart disease, that's 2.4 million Canadians. In the United States, the Center of Disease Control and Prevention shows heart disease as the leading cause of death, with one person dying every 36 seconds due to cardiovascular disease.[2] The numbers are staggering and clearly, the fast-paced, fast-food, fast-fix lifestyle that is characteristic of North American living takes a heavy toll on our hardworking hearts.

Heart Health: An Ayurvedic Perspective

Rather than reducing the heart to a circulatory pump, in Ayurveda the heart is the storehouse of energy and consciousness, a critically important physical and energic hub. It is the seat of prana (life energy, life force) and the seat of ojas (that substance which maintains life, the essence of vitality and immunity). Heart health depends on the delicate balance of the doshas (vata, pitta and kapha), agni (biological fire or solar energy) and soma (lunar energy).

The Doshas

Ayurvedic medicine holds that the world is composed of five basic elements: ether (space), water, air, fire and earth. These elements when combined, compose the three life forces or doshas: vata (air + space), kapha (water + earth) and pitta (fire + water). Vata governs movement in the body, mental and physiological. Pitta governs metabolism and digestion, impacting the body's ability to absorb and assimilate nutrients from food. Kapha governs structure in the body, holding cells, forming fat, bone and sinew. Vata, kapha, and pitta act as basic constituents and protective barriers for the body. When they are out of balance, the disease process begins. As an example, pitta imbalances can manifest as red, irritated skin or hot flashes (both fiery and not fun conditions).

It is thought that everyone inherits their very own mix of the three doshas at birth. This means that a person can be primarily one dosha, a combo of any two or a mix of all three. One's health is dependant on balancing the doshas throughout one's lifetime. And while, one's basic constitution or prakruti (one's nature, creativity, or first creation) remains unaltered (as it is genetically determined), changes in one's bodily functions can occur to respond to changes in the external environment. A basic principle of healing in Ayurveda holds that one may create balance in the internal forces working in the individual by altering diet and habits of living to counteract changes in the external environment.[3]

The Doshas and the Heart

All three doshas are said to dwell in part in the heart. Meaning that the condition of each dosha can affect our heart health but also that whatever is happening in the heart can affect vata, pitta and kapha throughout the body. Interestingly, one clinical study analyzed the association of constitutional type with cardiovascular risk factors. 300 patients over 25 years old were studied. They were assessed to determine their dosha type and their biochemical parameters, inflammatory markers and insulin resistance were also measured. The study found that half of the cardiovascular disease patients possess a vata-kapha constitution type. The study also found a correlation among kapha types and future risk of cardiovascular disease.[4]

Agni, Ama and Health

Agni is our bodies digestive fire and an integral part of the body's pitta system. It is the biological fire that governs metabolism and is subtly related to vata because bodily air enkindles bodily fire. Within every tissue and cell, agni is present and necessary for tissue nutrition and immune function. When agni is impaired, proper metabolism is affected, thus food components are undigested and unabsorbed. These accumulate and form what is called ama, the enemy which clogs the intestines, blood vessels and capillaries. Ama creates contraction, clogging and stagnation within the body, reducing the immune mechanisms of tissues and ultimately leading to disease.

Preventing Heart Disease with Ayurveda

Needless stress to the body and the mind, poor diet, lifestyle choices and repressed emotions or emotional outbursts, can all contribute to compromised heart health in Ayurveda. As such, making simple changes can result in beneficial results, not strictly for those with metabolic syndrome but anyone with a heart.

Speak Your Truth

Repressed emotions create dosha imbalances in the mind and affect the body. The idea that our issues are in our tissues, is very real in Ayurveda and western studies confirm the correlation between stress, anxiety[5] and depression[6] with increased cardiovascular disease or even death. Repressing emotions is also linked to decreased immune system function. That said, be honest with what you feel and allow yourself to process emotions, rather than trying to fast-fix the situation by distraction, burying feelings or indulging in toxins. Better yet, learn how to mediate to mitigate stress in the first place.

Soothe Stress with Meditation

Developing a meditation practice helps tap into the subtle channels of the mind and may even re-pattern our habituated responses to challenging situations. Meditation is really exercising the ability to recognize that our thoughts are just thoughts, and we don't need to create endless narratives around them but instead, can choose to focus on the present moment – one breath at a time. Mindfulness can improve heart health by improving our emotional and mental well-being, while supporting the flow of prana to encourage proper digestion of food, thoughts, and emotions. This helps to balance the doshas and also allows us to recognize past patterns that no longer serve us.

Eat Well and Mindfully

Fast food is not a fast fix for nutrition. It's just fast food. The most critical step that can be taken to improve heart health is to eat a heart-healthy diet. Eating more fresh fruits and vegetables, incorporating heart healing spices like turmeric, cinnamon and black pepper can help pack an antioxidant punch in your lunch, breakfast or dinner. Choose light foods over rich, deep fried, and oily (kapha-type) foods. Also, eat when you eat, which is to say, don't eat and watch TV, work, or have some other thing on the go. Eating mindfully allows you to appreciate the flavours and the nourishment (or lack thereof) that your body is receiving.

Exercise

Pain does not mean gain, it means pain. Regular activity is more important than strenuous activity. Studies have shown a consistent inverse association between physical activity/fitness and the incidence of heart disease and general risk factors. It has also been determined that regular, moderately intense activity, such as brisk walking for 30 to 60 minutes daily, is sufficient to reduce cardiovascular risk factors. Research suggests that everyone, especially those with cardiovascular risks, should exercise daily. Ayurveda also states that exercise improves circulation, keeps the joints healthy, preserves bone and muscle strength, preserves coordination, cures depression, detoxifies the tissues, maintains a firm yet flexible body and is a daily lifestyle measure that is integral to health maintenance.

Sleep

Ayurveda considers sleep just as important as diet in maintaining health. Numerous research studies have linked sleep deprivation to high blood pressure[7], cardiovascular disease[8] and a plethora of non-pleasant conditions. Practice calming activities before bed. Avoid distractions and stimulants, put on comfy pj's, maintain a temperature that's comfortable and try to sleep by 10 p.m. Early to bed, early to rise – it's the Ayurvedic way.

Herbals that Help the Heart

Ayurveda offers many different herbal medicines which can play a role in treating and preventing different aspects of cardiovascular disease. These include Arjuna, Tulsi (Holy Basil), Ginger, Turmeric, Amalaki, Ashwagandha and Saffron.

Our hearts circulate our life force to deliver oxygen and nutrients to our cells, in addition to processing the joys and heartbreaks that our beautiful lives bestow on us. Keeping them happy by tending to our mind, body and spirit, allows us to heal and ultimately safeguard the very organ that keeps the rest of our body functioning. May your heart be healthy and full of joy always!

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Cytokines That Support Cardiovascular Health

By Krista Powell

What are Cytokines?

Cytokines are small protein molecules that play a key role in cell signaling, that is, they act as cellular messengers, with different cytokines providing different messages to cells about how they should act or react in various situations. Cytokines are produced by cells of the nervous system and by cells of the immune system, especially macrophages which are specialised cells involved in the detection and destruction of bacteria. Cytokines act by binding to surface receptors on other cells, where they initiate a specific response. They may also be inhibitory and reduce the production of proteins or other cytokines. In this way, the interplay of different cytokines is involved in the regulation and progression of various cellular responses in the body, including the inflammatory response.

Cytokines that play key roles in the inflammatory process are often referred to as inflammatory cytokines. Cytokines can be further broken down into three general categories: chemokines, interleukins and lymphokines. Chemokines are chemicals that attract cells to other cells or a certain area. For example, chemokines are responsible for attracting the major innate immune cells from the blood stream to damaged areas as part of the inflammatory response. Interleukins include a broad range of signaling molecules involved in the immune response. Many interleukins play a very important role in the mediation of inflammation in the body. Finally, lymphokines are produced by cells called lymphocytes, and are generally involved in the body's immune response.

How are Cytokines Involved in Cardiovascular Health?

While all cytokines affect the body in a variety of positive and negative ways, chemokines and interleukins are vital to maintaining a healthy heart.[1] Chemokines have an important role in directing the migration of blood cells to target tissues.[2] They also regulate the inflammatory recruitment of classical monocytes, one of the largest types of white blood cells, during a cardiac event like a heart attack or the hardening of the arteries.[3]

Interleukins have pro-inflammatory and anti-inflammatory properties. The primary functions of interleukins are to modulate growth, differentiation and activation during inflammatory and immune responses. Interleukins consist of a large group of proteins that can elicit many reactions in cells and tissues by binding to high-affinity receptors in cell surfaces. While many Interleukins can have an effect on the heart indirectly, interleukins (IL) 19 and 24 have a direct impact.

IL-19 can induce angiogenesis in ischemic tissue, where the blood flow and thereby oxygen has been reduced to the point where it causes damage. Angiogenesis is the formation of new blood vessels. This process involves the migration, growth, and differentiation of endothelial cells, which line the inside wall of blood vessels. This process is controlled by chemical signals in the body like the activation of interleukins. The formation of new blood vessels can help to repair the damaged tissue.

IL 24 is made up of immune cells, mostly T and B cells. Among other functions, it protects against bacterial infections and cardiovascular diseases. It does this by reducing the quantity of reactive oxygen species (ROS) in the cells, thus decreasing cellular oxidative damage and improving cellular survival rate.[4]

Why is this so Important for the Heart?

Inflammation is your body's response to infection or injury. While it serves a purpose and promotes healing in the short term, chronic inflammation negatively affects many areas of the body and is a cause of many major diseases, including heart disease. Inflammation in and around the heart causes damage and can lead to serious health problems.

There are three main types of heart inflammation: endocarditis, myocarditis, and pericarditis. Endocarditis is inflammation of the inner lining of the heart's chambers and valves. Myocarditis is inflammation of the heart muscle. Pericarditis is inflammation of the tissue that forms a sac around the heart. If the chemokines and interleukins that regulate inflammatory and immune responses aren't functioning properly, it can lead to viral or bacterial infections which may cause inflammation and damage the heart.

What are some of the warning signs that this may be happening in the body? Depending on the type and severity of the heart inflammation, the symptoms may look different. They could include swelling in the feet, ankles, legs and hands, chest pain or pressure, shortness of breath or heart palpitations. Whether it's inflammation of the lining of the heart or valves, the heart muscle, or the tissue surrounding the heart, treatment may include medicine, or possibly surgery to treat the condition or complications like an arrhythmia (irregular heartbeat) or heart failure. There are also preclinical studies that are researching the possibility of targeting chemokines into therapeutic strategies for cardiovascular disease.[3] While this type of treatment may still be years away, it does introduce an interesting and exciting new option.

Conclusion

While cytokines like chemokines and interleukins may be small molecules, they can have a huge impact on the health of the heart. By limiting inflammation and modulating the immune response in a diverse range of actions, some cytokines can offer protection for the heart and reduce the risk of severe outcomes from cardiac events.

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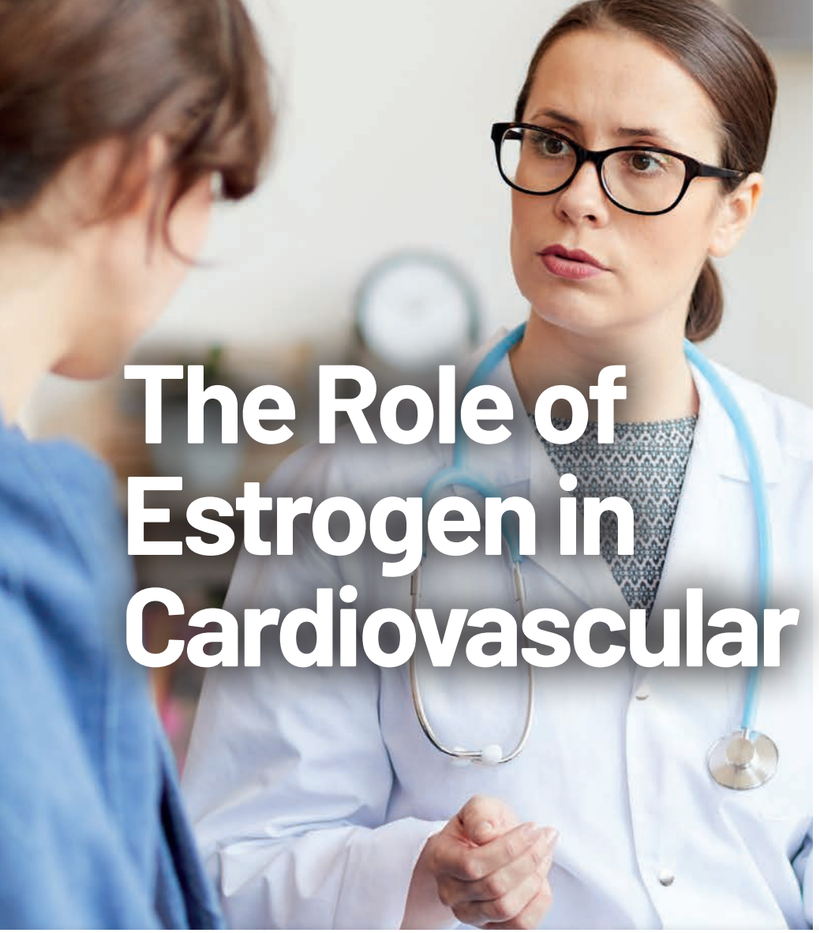

The Role of Estrogen in Cardiovascular Disease Risk

By
Dr. Sarah Zadek ND

When estrogen levels decline in perimenopause and menopause, women may begin to experience hot flashes and night sweats among other common issues such as insomnia, depression, weight gain and decreased bone density. But estrogen also plays a major role in protecting women against cardiovascular disease. This was first demonstrated by the finding that men were experiencing heart attacks and chronic cardiac chest pain 10 years earlier than women. In fact, most cardiac events in women occur after natural or medically induced menopause.[1]
Estrogen and its receptors are found all over the body and conduct a number of different actions. We actually have three different types of estrogens with different binding strengths:

- Estrone (E1): Weaker than E2, it's found in higher concentrations post-menopause
- Estradiol (E2): Secreted by the ovaries, this is the dominant form of estrogen before menopause and the strongest
- Estriol (E3): Produced by the placenta during pregnancy, this is a short-acting and low-potency estrogen

Estradiol (E2) is the prominent estrogen that exerts cardioprotective effects. E2 has multiple actions that protect arteries from thickening and hardening, as well as preventing clot formation and stroke risk.[1] In addition to its antiplatelet and antioxidant effects, it actually prevents a key step in the formation of artery plaque, or atherosclerosis: It can inhibit certain white blood cells, called monocytes, from sticking to the inside of blood vessels - the "vascular epithelium."

These plaques are particularly dangerous as they cause disruptions in blood flow and can restrict blood flow. Blood vessels become narrow and hardened, and blood pressure increases. That pressure can then dislodge plaques and clots into circulation, but a plaque or clot can be much larger than a small artery or capillary and if it gets stuck, can cause a stroke, heart attack, or pulmonary embolism, depending on its location. We call these occurrences venous thromboembolism (VTE).

Estrogen receptors located within vessel epithelium and heart muscle tissue act to protect against the development of atherosclerosis and cardiovascular disease (CVD).

The most common estrogen receptors (ER) are α-ER, found in the uterus and ovary, and ß-ER, found in bone tissue, the kidneys, lungs and vascular endothelial cells. A third ER called GPR30 (G protein-coupled estrogen receptor) is found specifically in heart muscle cells. This allows estrogen to protect both major components of the cardiovascular system: heart tissue and blood vessels.

When estrogen binds to ß-ERs it activates pathways that decrease blood pressure and vascular resistance. When it binds to GPR30 receptors in the heart it alters genetic expression, resulting in antioxidant protection, enhanced cellular energy production, and decreased tissue fibrosis. It also prevents abnormal enlarging of the heart.[2]

Can I Take Estrogen to Decrease My Cardiovascular (CV) Risk?

Pre-menopausal, cycling, women produce relatively vast amounts of estrogen, however at some point this will decline and/or cease completely. Women can either undergo natural (including premature) or surgical menopause which leads to an estrogen deficiency, removing the cardiovascular protection. Many women also tend to notice menopausal symptoms when estrogen levels decline and this leads many to seek therapeutic options.

Hormone replacement therapy (HRT) is commonly used in both natural and surgical menopause as a means of reducing symptoms while also conferring cardiovascular protection long-term. In particular, estrogen replacement therapy (ERT) can prevent the early development of atherosclerosis and hypertension.

A few major studies have been monitoring the outcomes of short and long-term HRT use. The Nurses' Health Study (NHS) is one of the largest ongoing observational studies of women. They reported that women who received HRT had a significantly decreased risk of major coronary disease and overall decreased risk of CVD.[1]

Another study, the Women's Health Initiative (WHI) found a significant cardioprotective effect when given to women aged 50 to 54 years, with a 40% decreased risk compared to those given placebo.[1] However, they also disclosed results that made many patients afraid to continue their HRT: There was a large increase in VTE occurrence during the study, and it had to be stopped early. When researchers looked into why CVD risk and occurrence increased, they found it had to do with the timing of HRT.

Women who were experiencing VTEs had started HRT 10 years or more after menopause. This means 10 years without ovarian estrogens and without the same cardio-protection. So in this time, especially with certain genetic predispositions and diet and lifestyle choices, these women were already developing atherosclerosis and hypertension before the HRT.

The Heart and Estrogen/Progestin Replacement Study (HERS) found increased risks as well, though with different circumstances compared with the WHI. The HERS found that women were having increased CV events, especially VTE, during their first year of HRT. Due to the high risk of this study it was also stopped early. The HERS was different in that all women started the study with an active clinical CVD, including a history of heart attack and/or chronic cardiac chest pain. Therefore their risk of VTE was already increased.

Once a plaque has formed, estrogen cannot remove it or reduce its size. Therefore timing is everything! This explains the high rate of VTE in both the WHI and the HERS.

Both these studies taught us when HRT is not appropriate. Estrogen can confer major cardioprotective effects but there is a point in time where HRT may actually increase the incidence of a CV event. This seems to be 10 years or more post-menopause, and in pre-existing CVD. Starting HRT closer to menopause - and in cases of surgical menopause, immediately - will decrease risk of developing CVD.

So in 2016 another study put this to the test and divided women into two groups and gave them E2 alone or in combination with bioidentical progesterone, or placebo:[3]

<6 years post-menopause
>10 years post-menopause

After about five years, researchers noticed that women who were closer to menopause onset had better protective effects against vascular thickening compared to those who were in menopause for longer. More so, these older women had vessel thickening regardless of if they were given E2, placebo, or progesterone, and regardless if they were on a cholesterol-lowering medication. Researchers also found that in women given E2, their levels of LDL cholesterol were also significantly lower (with greater amounts of HDL, "good" cholesterol), compared to placebo.

Decreasing CV Risk Early

Estrogen seems to provide the most amount of CV protection before the development of vessel damage, plaques and hypertension. Decreasing this risk depends on each person's genetic predisposition, diet and lifestyle.

We all have certain versions of genes that affect our health and risk of disease. These can include genes involved in heart function, blood pressure, metabolism, and hormone function (including estrogens).

Meanwhile our diet and lifestyle choices also influence the risks of atherosclerosis, CVD and metabolic disease. These include diets high in fried foods, trans fats and animal saturated fats, and low in omega 3 fatty acids found in salmon, anchovies and sardines. A sedentary lifestyle is another risk factor, especially compared to individuals that participate in regular exercise.

Risk Factors for Atherosclerosis:

- High blood pressure
- Smoking
- Obesity
- High LDL cholesterol and triglycerides
- Sedentary or low-active lifestyle
- Insulin resistance and diabetes
- Inflammatory conditions

Each of these areas should be addressed as early as possible for the most benefit, both as we age, and for those who will want to use estrogen replacement therapy in menopause.

Conclusions

In post-menopausal women, the incidence of CVD events is inversely associated with E2 levels.[2] The results and observations from large-scale long-term studies show that estrogen, particularly E2, provides multiple cardioprotective actions, and that in the event of estrogen deficiency or decline, ERT can provide continued CV protection. However, timing is everything and it seems that a soft cut-off time for starting HRT is about six years post-menopause. In women undergoing premature or surgical menopause, HRT should start as early as possible.
In the presence of CV risk factors such as hypertension, abnormal cholesterol profile and metabolic syndrome, women should be carefully evaluated for clotting disorders and sub-clinical CVD before starting HRT. This is why early diet and lifestyle modifications are so important; once CVD starts developing, it may be too late to gain the benefits of E2 therapy.
The protective effects of ERT have been shown in treatment periods longer than five years and therefore treatment may continue for decades or indefinitely, assuming regular medical follow-ups.

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Weight Lifting to Support Cardiovascular Health

By Jennifer Marion, ND (inactive)

Cardiovascular disease is the leading cause of death in North America and is estimated to cause one third of deaths globally.

The economic impact is 330 billion dollars per year and by 2035 it is estimated to reach 749 billion dollars. Half of the adult population in North America has high blood pressure, defined as 130/80 mmHg. These are alarming statistics. The good news is that we do have some control over this destiny. First line therapy for preventing cardiovascular disease is a healthy diet and exercise.

Traditionally, the type of exercise that has been studied for cardiovascular health has been aerobic exercise. This seems intuitive because this is the type of exercise that gets your heart rate up and can leave you breathless, hence conditioning your lungs, heart and blood vessels. Recently, there has been more discussion and research into the possible benefits of strength training or weightlifting either alone or in conjunction with aerobic exercise for cardiovascular disease prevention and treatment. Aerobic and resistance training each provide their own benefits to cardiovascular health.

Aerobic exercise is well documented in terms of benefiting cardio-metabolic markers, blood pressure, glycemic control, hypercholesterolemia and endothelial function. Anyone who has ever had such issues has likely been told by their doctor to start an aerobic exercise regime. Resistance training has historically been left out of these discussions.

Resistance training is defined as muscle work against an external load. This type of exercise may be an easier, long-term lifestyle change that can be incorporated by those with limited space, time or mobility. With the growing evidence that resistance training may be as beneficial as aerobic training for cardiovascular health, this should certainly be considered. Resistance training is understood as being important for building and maintaining skeletal muscle and strength, which is important for aging; however, until recently, little has been understood about the impact of resistance training on cardiovascular health.

Hypertension is the number one risk for mortality in terms of cardiovascular disease. It is also one of the most modifiable factors. Recent review and meta-analysis have shown that aerobic and resistance training can both lower systolic and diastolic blood pressure by 3-4mmHg. This may sound like a small reduction, but this amount has been shown to reduce cardiac morbidity by 5%, stroke by 8-14% and all-cause mortality by 4%. In a 2019 study, 69 hypertensive adults were assigned to either aerobic, resistance training or a combination of both for 60 minutes a day, three times a week. All groups followed The Dietary Approaches to Stopping Hypertension or DASH diet. It was found that the combination group showed a reduction of peripheral and central diastolic blood pressure of 4mmHg. A reduction in resting heart rate in both the aerobic and combination group was also found. This study found that combination training provided the most significant benefit for blood pressure.

In a review with meta-analysis published in the British Journal of Sports Medicine, resistance training was found to have a positive effect on both systolic and diastolic blood pressure. Reductions in blood pressure were like those seen in aerobic exercise interventions. The review suggests that resistance training could be an effective non-pharmacological approach to the prevention and treatment of hypertension. This review also found that resistance training alone had a positive effect on cardiopulmonary fitness which is the capacity of the circulatory and respiratory systems to supply oxygen to muscles, what people often refer to when they are discussing being in or out of shape. This review also found that resistance training helped with endothelial dysfunction, which contributes to hypertension.

Endothelial dysfunction refers to non-obstructive coronary artery disease. There is nothing blocking the coronary arteries, but they become more constricted and have difficulty dilating. A deterioration of flow mediated dilation of 1% is associated with a 13% increased risk of a cardiovascular event. To paint an even clearer picture, a reduction of 0.62% of endothelial function is associated with an increase of 20mmHg in systolic blood pressure. Endothelial dysfunction is linked to a reduction in nitric oxide which can be improved through exercise. Resistance training leads to improvements in nitric oxide metabolism because of muscular contractions, resting heart rate and blood pressure changes during training, ultimately leading to an improvement in flow mediated dilation. In one study it was found that resistance training increased flow mediated dilation by 4% and the combination of resistance and aerobic training improved it by 6.8%. If we consider that 1% has such a significant impact, these changes should result in significant clinical reductions of cardiovascular risk.

Further to the improvements discussed above, resistance training has also been shown to improve many blood biomarkers associated with cardiovascular risk. In a meta-analysis involving patients with type 2 diabetes, supervised resistance training compared to other forms of exercise, was found to show the most improvement on cholesterol and triglyceride levels, and a combined program yielded the best result for weight loss.

Resistance training has been shown to improve physical function, fat mass, lipid profiles, cardiovascular health, endothelial function, blood pressure and insulin resistance and should be part of an exercise prescription for the prevention and treatment of cardiovascular disease.

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