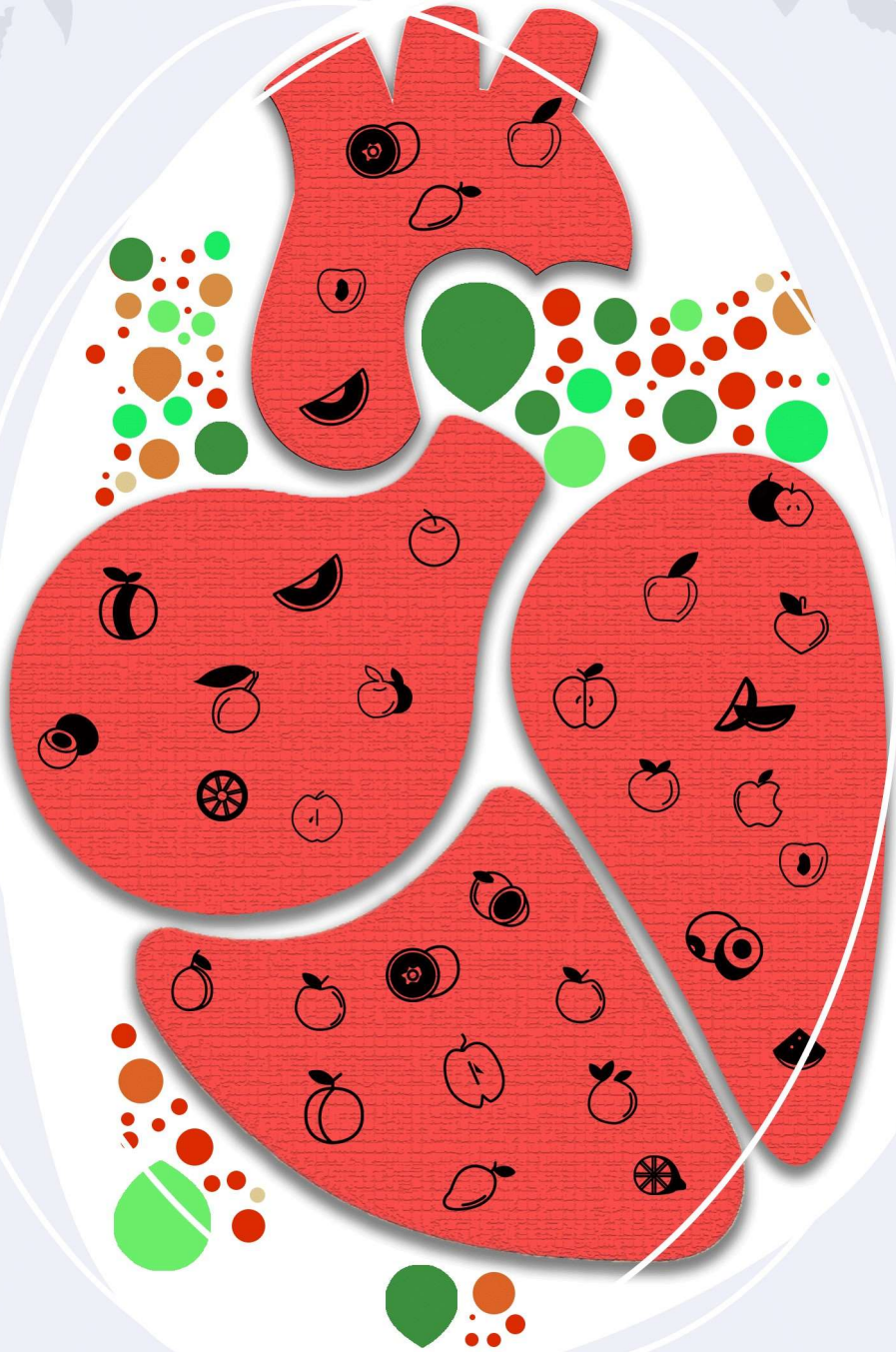

OREGANO

Nutritional Journal of Varastegan Institute for Medical Sciences

Varastegan Institute

SCIENTIFIC ASSOCIATION OF NUTRITION

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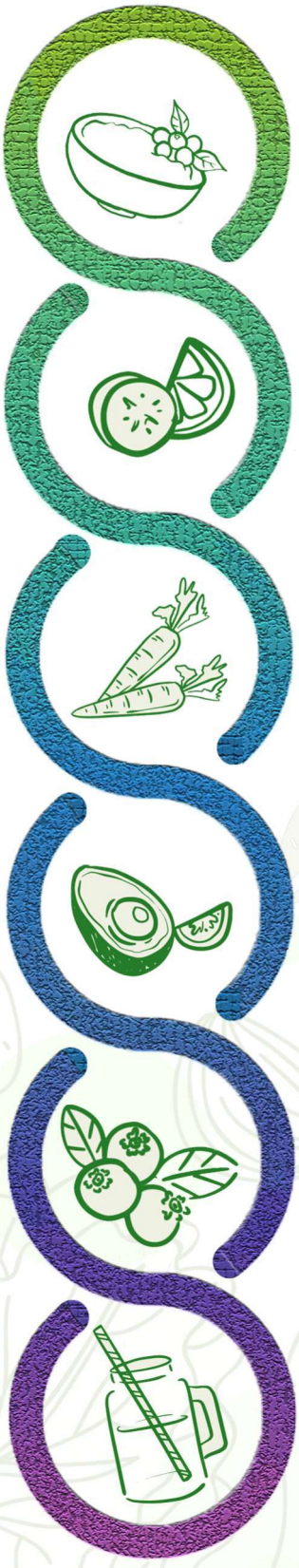

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Director in charge

I am delighted to inform the third edition of Iran's first all-English nutritional journal has published, thanks to the tireless Oregano team endeavor. Firstly, I want to express my gratitude to everyone who participated in this edition, especially the team of our Editorial board which are B.s. students of varastegan institute for medical sciences. Secondly, I would like to thank the designers for their hardworking to develop a new design and also our editors for assisting us in presenting the magazine to you. Finally, I want to convey my heartfelt gratitude to Mr. Babaei who is our editor in chief a great friend and colleague of mine that helps a lot in managing our professional team.

It is clear that the heart plays a significant role as the cause of human love and progress in our lives, that is why we decided to start in our activity with this subject.

Wish you all use this knowledge to the best of your abilities.

Ali Zeyqami

Editor in chief

I'm honoured to be participant as the editor in chief of Oregano journal. But first of all, I want to express my special thanks to all of the authors, editors and designers to this edition. The purpose of our journal is providing reviews of current nutritional informations in the form of a review study.

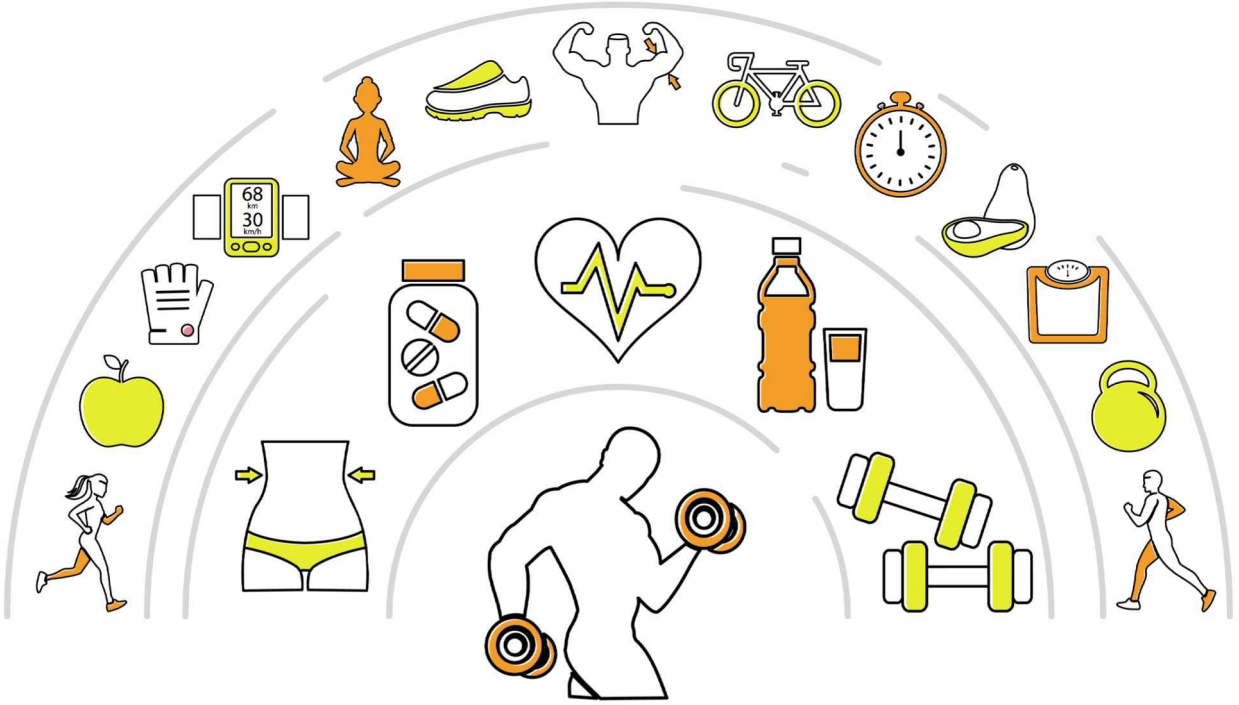
In the third volume of this journal we decided to review the article which is written about heart. Heart which is such an important organ in life, both medically and spiritually!

We checked articles about cases of heart disease and its complications, as well as the effects of nutrients and supplements on the diseases.

I hope you make the most of this volume.

Your sincerely

Arvin Babaei



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The Effect of Vitamin D on Peripheral Arterial Disease

Introduction

Several large epidemiological studies have concluded that vitamin D deficiency is associated with excess mortality (1, 2). It is becoming increasingly clear that vitamin D (Vit D) has much broader range of actions in the human body in addition to its well-known effects on calcium homeostasis and bone metabolism. There is accumulating evidence that Vit D deficiency has important extraskeletal effects, including the cardiovascular system (3, 4).

Several clinical studies have reported a high prevalence of Vit D deficiency in patients with Peripheral Arterial Disease (PAD) (5), coronary artery disease (6) and stroke (7) as well as the association of Vit D deficiency with cardiovascular mortality (2, 8, 9). Furthermore, low Vit D status is related to major cardiovascular risk factors, such as hypertension, obesity and diabetes mellitus (4,10,11). The aforementioned studies suggest that Vit D deficiency promotes atherosclerosis (4,12).

In recent research, inadequate Vit D status has been linked to non-skeletal major disease such as Cardiovascular Disease (CVD) (13). Of particular interest to this review, is the emerging concept of the association of Vit D in cardiovascular health and the contribution of its deficiency towards the development and progression of PAD. While patients with PAD often have a sedentary lifestyle with limited exposure to sunlight.

Age may also be a factor, with the prevalence of PAD being greater in the elderly. Interestingly, the capacity of Ultraviolet (UV) - mediated Vit D synthesis was previously reported to be reduced in aged skin, with an associated reduced expression of the Vit D receptor in aged human muscle (14).

Dietary supplementation of Vit D for some patients may be beneficial towards reducing the risk of CVD/PAD, as well as improving patient outcomes.

Published studies have shown that there is a significant association between Vit D and PAD. Populations with lower Vit D levels are more likely to develop PAD in a graded manner. Higher amputation rates are also observed among patients with PAD and lower Vit D levels. In addition, Vit D deficiency is significantly associated with increased risk of cardiovascular adverse events. This was also observed in the mouse model which low Vit D led to the development of atherosclerosis.

Literature review

A cross-sectional study was conducted in Turkey in 2020 by Mustafa Umut Somuncu, M.D et al. The aim of this study was to investigate the relationship between combination of Vit D and hyperuricemia and CAD levels.

Patients were grouped according to the presence of hyperuricemia (>7 mg/dL) and Vit D deficiency (<20 ng/mL). This study showed that the hyperuricemia and Vit D deficiency group, had 4 times greater chance of severe CAD than the control group (15).

K.M. van de Luijtgaarden et al. conducted a clinical trial in 2012 in Netherlands. The aim of this study was to evaluate the status of Vit D in patients with obstructive or aneurysmal arterial disease in relation to clinical disease risk profiles and atherosclerotic disease markers. They included 490 patients with symptomatic PAD (n ¼ 254) or aortic aneurysm (n ¼ 236). Risk factors for heart disease and comorbidities were assessed by the Carotid Intima-Media Thickness test (CIMT), high-sensitivity C-Reactive Protein (hs-CRP) and serum Vit D. In general, 45% of patients suffered from moderate or severe Vit D deficiency. The prevalence of Vit D deficiency was similar in patients with PAD and arterial aneurysms. Low levels of Vit D were also associated with congestive heart failure and CVD (16).

A review study conducted by Chua et al. in 2011 in Hong Kong aimed to check Vit D as a contributory factors in the development of PAD and published studies have shown that there is a significant association between Vit D and PAD also populations with lower Vit D levels are more likely to develop PAD in a graded manner. In addition, Vit D deficiency is significantly associated with increased risk of cardiovascular adverse event (17).

In 2019, Smriti Murali Krishna conducted a review study. The Experimental studies have shown that optimal levels of Vit D have beneficial effects on heart and blood vessels. However, high concentrations of Vit D are promoting vascular calcification and arterial stiffness. Observations from various clinical studies suggest that Vit D deficiency is also associated with an increased risk of PAD (18).

Discussion

We can summarize the findings of our study as follows:

(a) Among myocardial infarction (MI) patients, 44.0% had isolated Vit D deficiency, 11.3% had isolated hyperuricemia and 16.5% had both hyperuricemia and Vit D deficiency; (b) Patients with higher levels of serumuric acid (SUA) and low levels of 25- hydroxyvitamin D (25-OHD) had significantly severe CAD quantified by the number of diseased vessels, Gensini score and SYNTAX score; (c) After adjustment for potential confounders, the presence of hyperuricemia or Vit D deficiency was an independent predictor of severe CAD.

In addition, we found an additive effect of the existence of both Vit D deficiency and hyperuricemia on severity of coronary artery disease in MI patients.

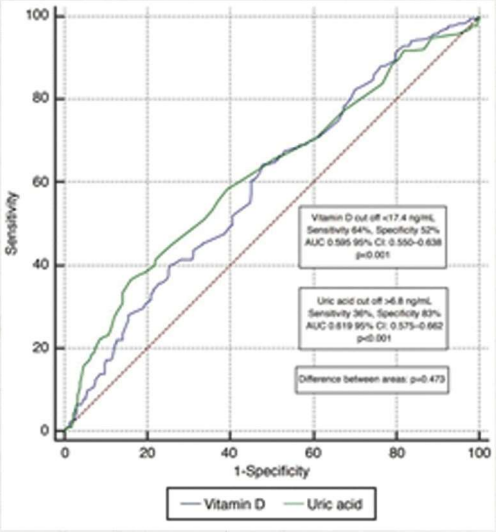
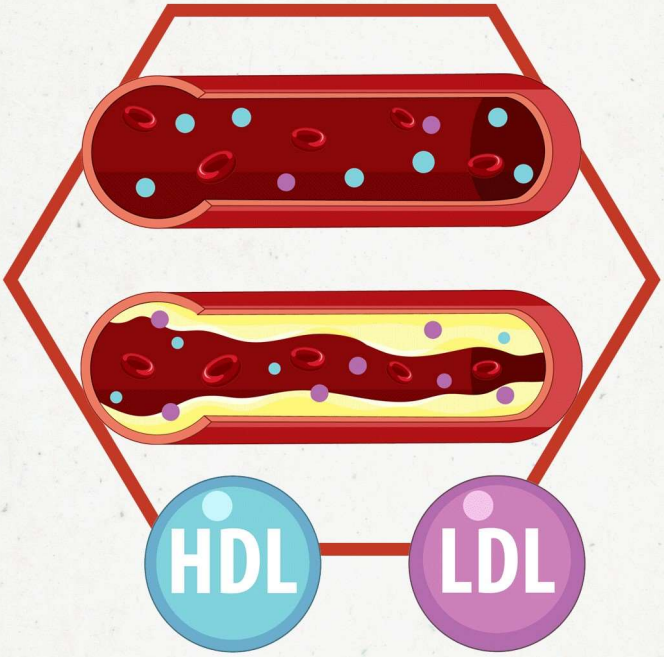


Figure 1: Receiver operating characteristic (ROC) curve showing the distinguishing ability of the 25-hydroxyvitamin D and serum uric acid levels for the severity of coronary artery disease (4).



The effects of these mechanisms on clinical outcome have been investigated many times. It was reported in a large prospective study that Vit D deficiency was related to the risk of MI (19). In the Framingham Heart Study, low-level 25-OHD levels were shown to partially enhance cardiovascular events (4).

In our study, clinical response to treatment for Vit D deficiency and hyperuricemia was not evaluated. The data from our study indicate that a low level of 25-OHD and a high level of SUA were associated with the severity of CAD, which was determined using different angiographic scoring systems and the number of diseased vessels in MI patients.

Considering this finding, it could be speculated that Vit D supplementation and treatment of hyperuricemia by changing eating habits (low purine diet and low alcohol intake) or drug use may reduce the severity of CAD, especially in the presence of the combination of these 2 pathologies. In addition, a treatment for Vit D deficiency and hyperuricemia may be more effective in individuals with risk factors such as older age, male gender, hyperlipidemia, diabetes mellitus, family history of CAD, which were seen to be associated with the severity of CAD in our study (20).

There are several limitations to this review. Firstly, most of the studies included were population-based, cross-sectional or longitudinal studies. Only associations, not causal relationships, could be established between Vit D and PAD.

Although most studies concluded that Vit D deficiency was a potential risk factor of PAD, it was also sensible to think that Vit D deficiency could be a complication of PAD as a result of impaired mobility and subsequent lack of sunlight exposure.

Secondly, there was a lack of information about certain aspects in these studies, including the geographical location of residence, seasonal variations during which blood samples were obtained and measurement of parathyroid hormone which were significant confounding variables.

Thirdly, these studies were targeted to western populations. The associations between Vit D

and PAD in Asians or other ethnic populations, such as those of Arabic descent, remain unclear. Currently, there is still no level one evidence or any randomized-controlled trials studying whether Vit D supplementation is useful in reducing the rate or the risk of developing PAD, so a systematic review or meta-analysis of randomized controlled trials is not yet possible.

Conclusion

We found a synergistic effect on hyperuricemia and Vit D deficiency on the severity of CAD that was quantified using different angiographic scoring systems and the number of diseased vessels. Emerging studies are also showing that there is an association between low Vit D levels and PAD.

Future studies should focus on various ethnic populations and investigate whether Vit D should be recommended for prevention of PAD and if so, what is the dosage. Only randomized controlled trials will be able to provide the answers.

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The Efficacy of Resveratrol on Cardiac Function after Myocardial Infarction

Introduction

Myocardial Infarction (MI), also known as a heart attack, is one of the most common causes of cardiovascular morbidity and mortality in the world (1).

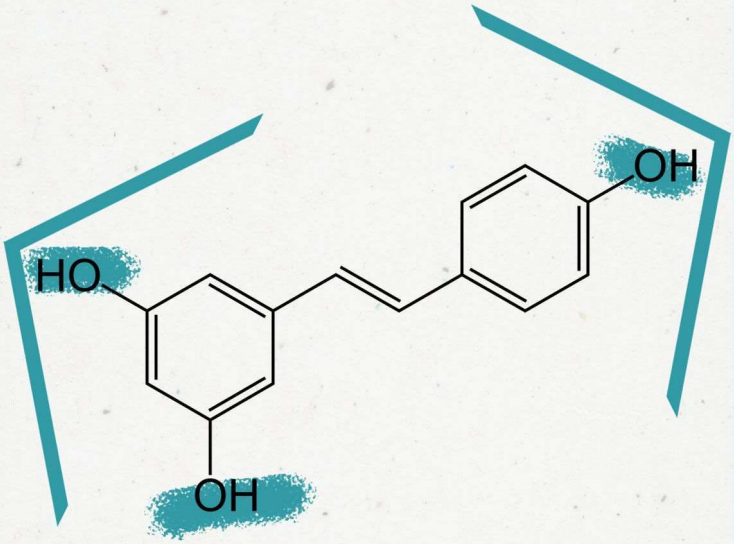
Alarmingly, Cardiovascular Disease (CVD) is expected to increase substantially due to increases in the rates of metabolic syndrome and obesity (2). 85% of all CVD deaths are due to heart attacks and strokes (3). Approximately 45,000 MI occur every day across the globe (1). The mortality rate due to MI has been reported as 85 per 100,000 in the Islamic Republic of Iran (4).

MI is caused by acute and persistent coronary ischemia and hypoxia, which can be complicated by arrhythmia, shock or heart failure (5).

Post MI remodeling is the term used to define the changes in cardiac musculature after sustaining an ischemic injury. These changes decrease myocardial function and ultimately lead to heart failure (6). We know that in many cases, after the ischemic injury in myocardium, adverse post-MI remodeling occurs, leading to poor long-term outcomes (7).

Resveratrol is a phenolic phytochemical derived from grapes. It is a bioactive substance that is physiologically cardioprotective, along with a broad spectrum of antioxidant, anti-aging effects (8). We also know resveratrol as a therapeutic drug to prevent adverse post-MI remodeling (6).

In the past two decades, many preclinical and some pilot clinical studies have reported that resveratrol has anti-inflammatory and vascular protective effects in different experimental models (9). The main focus is on the effects of resveratrol in the cardiovascular system and it's potential for therapeutic use in preventing long-term cardiovascular morbidity and mortality (6).



The main discussion of this review study is going to be the viability of resveratrol as a supplement for the prevention of oxidative damage in the heart post-MI and preventing cardiomyocyte aging and senescence.

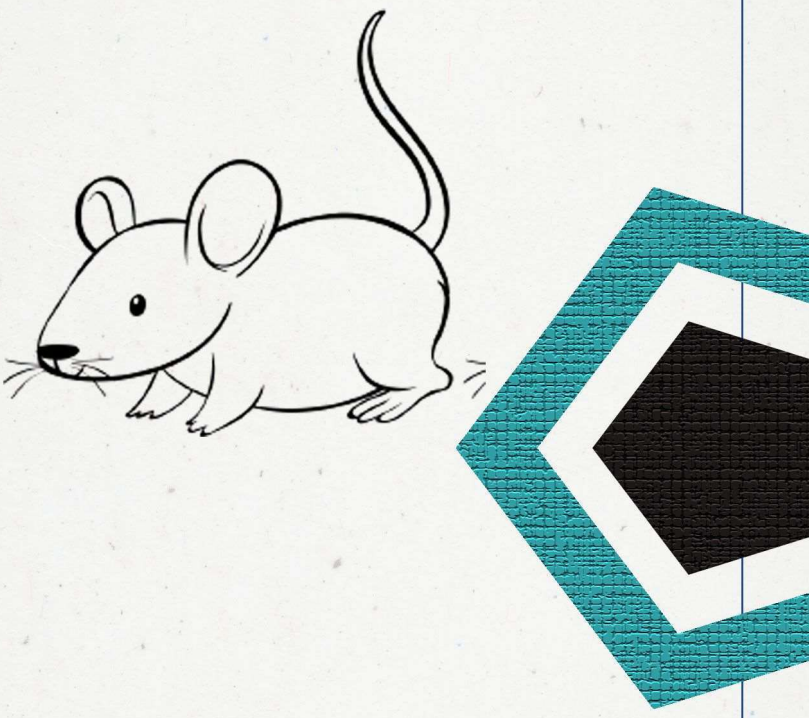
Literature review

Gutlapalli et al. has been studied on the effects of resveratrol on telomeres and post MI remodeling as a review in 2020.The main focus is on the effects of resveratrol in the cardiovascular system and it's potential for therapeutic use in preventing long-term cardiovascular morbidity and mortality. The result showed that resveratrol has been generally proven to be cardio-protective and vasculo-protective, it can be an effective therapeutic drug to counteract adverse myocardial remodeling following MI or any other form of cardiac injury (6).

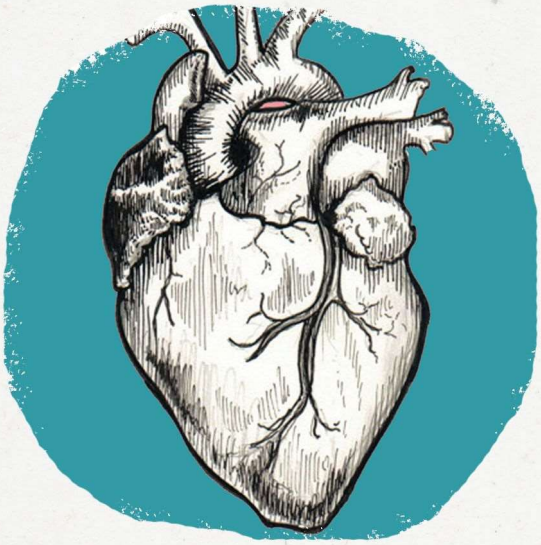
An interventional animal study of Jiang et al. was conducted in 2021 in China that aimed to investigat the protective effects of resveratrol on cardiac function in a rat model of Acute Myocardial Infarction (AMI) and the related underlying mechanisms. In this study a total of 40 male rats were randomly divided into 4 groups: .1)The Sham group: underwent sham operation; .2) The Sham-RES group: underwent sham operation and received RES (50 mg/kg/day) supplementation; .3) The AMI group: underwent AMI induction; .4) The AMI-RES group: underwent AMI induction and received resveratrol (50 mg/kg/day) supplementation. The result showed that resveratrol supplementation decreased the inflammatory cytokine levels, improved the cardiac function and ameliorated atrial interstitial fibrosis in the rats with AMI (10).

An experimental study in 2021 by Mei et al. in China investigated that resveratrol can reduce myocardial cell apoptosis after MI by regulating the Protein Kinase R-like endoplasmic reticulum stress pathway. It can also improve myocardial remodeling and cardiac function in rats and can provide a new target for clinical treatment of MI. The successfully modeled rats were divided into model group and resveratrol group and normal rats were selected as control group and sham operation group. Rats in the resveratrol group were intraperitoneally injected with resveratrol (8 mg/kg/d) and the other three groups were intraperitoneally injected with dimethyl sulfoxide (0.5 ml/kg) for 4 weeks. The levels of Left Ventricular End Diastolic diameter (LVEDD) and Left Ventricular End systolic Diameter (LVESD) in the model group were significantly higher than those in the control group and the levels of Left Ventricular Ejection Fraction (LVEF) and Left Ventricular Fractional Shortening(LVFS) were significantly lower than those in the control group ($p<0.01$) (2).

Raj et al. conducted a review in 2021 to demonstrate the efficacy of resveratrol as a new therapeutic agent for the management of atherosclerosis, MI and Heart Failure (HF). This comprehensive review concludes that current



evidence from pre-clinical studies strongly support the role of resveratrol as a very promising bioactive molecule with a wide range of cardioprotective action in the context of ischemic heart disease and HF (5).



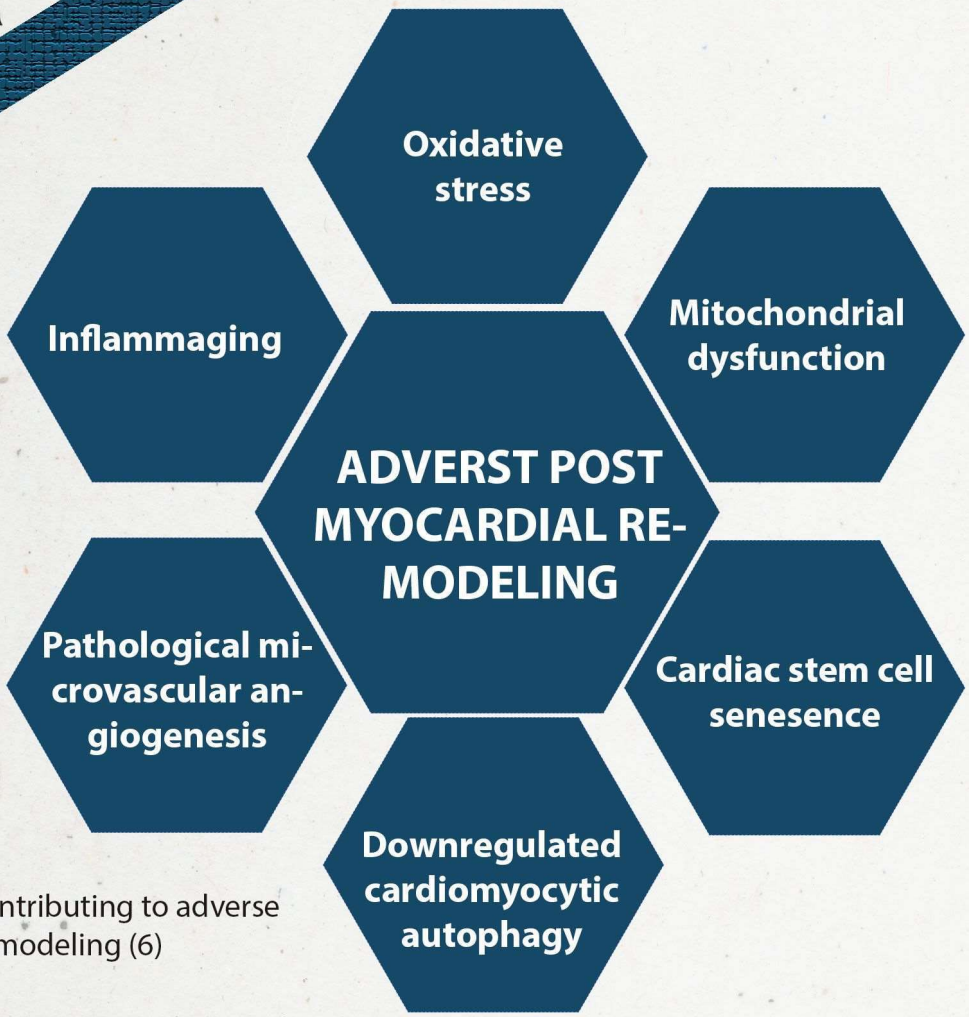


Figure 1: Factors contributing to adverse post-myocardial remodeling (6)

Discussion

MI originally caused injury by reducing the blood supply to the tissues, and then further triggered an extensive inflammatory response that occurs during organ reperfusion. It is well known that resveratrol exerts multiple health-beneficial effects by regulating a variety of key molecules (11,12).

A previous study has reported that treatments with low doses of resveratrol (2.5 mg/kg/day) or perindopril (2.5 mg/kg/day) for 8 weeks were equally effective in significantly alleviating adverse cardiac remodeling and improving contractile dysfunction in rats with AMI (13). Moreover, resveratrol (50 mg/kg/day) has been shown to partially reverse MI-induced remodeling (left ventricular dilation) in heart by enhancing the autophagy-activating AMP-kinase pathway and significantly improve cardiac function (14). These above studies provide a strong rationale to hypothesize that resveratrol treatment may ameliorate the progression of adverse cardiac remodeling following MI.

These inconsistent results regarding the effects of resveratrol treatment on cardiac remodeling following MI may be due to the differences in the dose administered and/or the intervention procedures with resveratrol.

Conclusion

Current evidence strongly supports the role of resveratrol as a very promising bioactive molecule with a wide range of cardioprotective action, but further research should be conducted to increase our current understanding of resveratrol, especially large-scale clinical trials.

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The Effect of Selenium Deficiency on Heart Failure

Introduction

Heart Failure (HF) is a clinical syndrome and its signs include dyspnea, orthopnea, tachycardia, elevated jugular venous pressure and pulmonary congestion. HF is defined as the inability of the heart to meet the needs of the blood and peripheral tissues to meet their metabolic needs. It is caused by a structural or functional abnormality of the heart that leads to a decrease in cardiac output. HF can be mostly due to an underlying myocardial disease. High levels of oxidative stress markers and inflammatory cytokines may indicate the severity of acute heart (1, 2).

HF in the modern world is considered as an epidemic that affects approximately 1% to 2% of the adult population. The prevalence of CHF increases with age (2).

Risk factors of HF include several medical states, and are enough to cause cardiac dysfunction; mostly a combination of them occurs in patients with heart failure. Hypercholesteremia, obstructive sleep apnea, drug abuse and excessive alcohol consumption, connective tissue disorders (systemic lupus erythematosus, sarcoidosis and amyloidosis), congenital heart defects, family history, smoking, obesity, viral infections, arrhythmias are found strongly associated with higher risk of HF (2).

HF can result in pulmonary congestion, dyspnea, orthopnea, bendopnea, paroxysmal nocturnal dyspnea, cardiac asthma, cheynestokes respiration, anemia, cardiac cachexia, renal failure and cerebral symptoms (2).

Medical management of HF involves treatment of volume overload for symptom relief and disease modification to reduce mortality which includes pharmacological and non-pharmacological treatments (3).

Selenium (Se) is an essential micronutrient necessary for different kinds of biological functions in animals, including redox hemostasis, inflammation, thyroid hormone metabolism, respiratory capacity of mitochondria in the myocardium and cardiovascular function. Which performs these functions through selenoproteins in the form of the amino acid selenocysteine (Sec) (4). Decreased Se levels deprives the cell of its ability to synthesize enzymatically active selenoproteins (5). Rich sources of Se include Nuts (and Brazil nuts in particular), red meat, seafood and grains (6).

Severe Se deficiency in humans is associated with Keshan disease, an endemic dilated

cardiomyopathy, which has been restricted to areas with very low levels of Se in the soil and therefore in food (5). Although the disease is treated with selenium supplementation, this could indicate a possible role for Se in cardiovascular function.

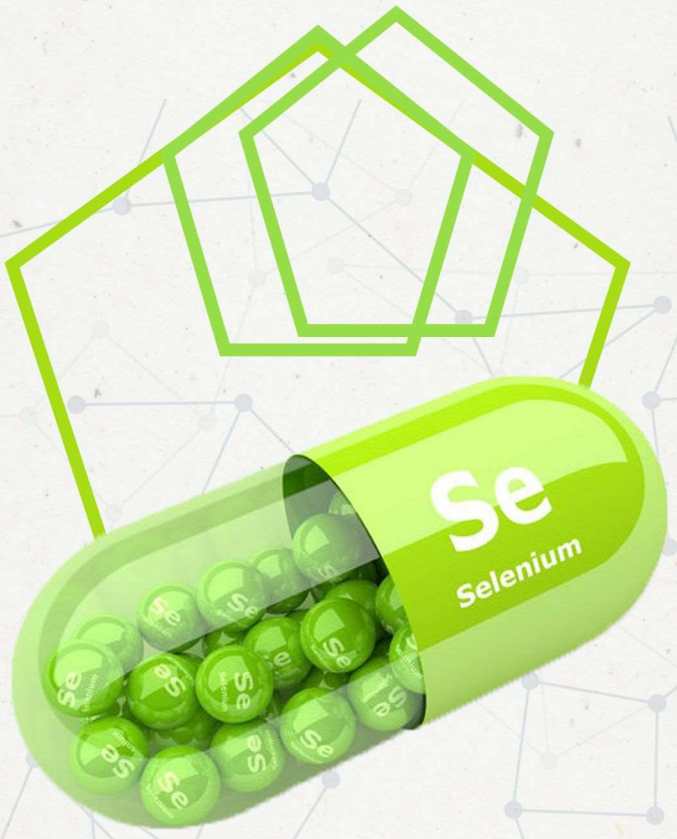
This study aims to investigate the relationship between Se deficiency and HF.

Literature review

Niels Boomer conducted a prospective observational cohort study in 2019 in Netherlands. Selenium deficiency can lead to myocardial dysfunction. Therefore, this study was performed to evaluate selenium deficiency, its symptoms and consequences in patients with HF. They cultured human cardiomyocytes in the absence of selenium and evaluated mitochondrial function and oxidative stress. This study showed that selenium deficiency can cause mitochondrial dysfunction and oxidative phosphorylation, elevated levels of intracellular reactive oxygen species, increases mortality and death due to HF (5).

A study in 2018 by Z. Asemi in Iran aimed to evaluate the effects of Se supplementation on metabolic profiles in patients with Congestive Heart Failure (CHF). The use of 12 weeks Se supplementation led to significant reductions in serum insulin, homoeostatic model of assessment for insulin resistance and high-sensitivity C-reactive protein. In addition, Se supplementation also improved lipid profile and caused elevation in plasma total antioxidant capacity and total glutathione levels. Overall, According to the study Se supplementation for 12 weeks to patients with CHF had beneficial effects on insulin metabolism and some markers of cardio-metabolic risk (4).

In 2022, Ali A. Al-Mubarak et al. done a prospective observational cohort of 5973 subjects in Netherlands to elucidate the relationship between serum Se levels and the risk of mortality and new-onset HF in the general adult population. Serum Se was measured and mean Se concentration was 84.6 (±19.5) µg/L. Mean age was 53.6 (±12.1) years and 3103 subjects (52%) were female. Median follow-up was 8.4 years. Se levels associated positively with female sex, higher total cholesterol and glucose concentrations, and associated negatively with incidence of anemia, iron deficiency, current smoking, increased C-reactive protein levels, and higher body mass index. Univariate analysis on all subjects showed no association of continuous Se concentrations, per 10 µg/L increase, with the composite endpoint. However, significant interaction with smoking status was observed. In non-smoking subjects (n=4288), continuous Se concentrations were independently associated with reduced mortality risk, lower risk of new-onset HF, as well as reduced risk of the composite endpoint. In smoking subjects, no associations were found (1).



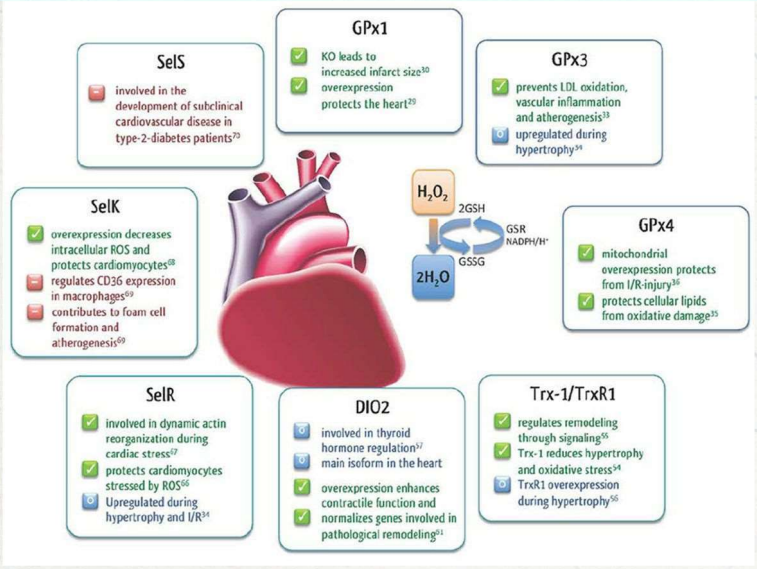


Figure1: Roles of selenoproteins in the heart (8).

Briana K. Shimada et al. done a review study in 2021 to find the relationship between Se and cardiovascular health. They searched 25 keywords in PubMed (NLM) for references. Due to the results, it is still unknown whether Se supplementation can be useful as a nutritional supplement for patients with Cardiovascular Disease (CVD) (7).

Discussion

The role of Se in cardiovascular function has been studied since more than fifty years ago and Se is now known as a participated factor in different cardiovascular disorders, including HF (7). Se is incorporated into the polypeptide chain as component of the amino acid Sec so proteins including Sec in their polypeptide chain are called selenoproteins. There are 25 so-called selenoproteins in the human body (6), some of which play a role in cardiovascular function through different mechanisms (5). Selenoproteins act as antioxidants, regulators of oxidative stress, controllers of calcium flux. They may also play a role in mediation of thyroid hormones and immune cell migration, contributing to atherogenesis (1). Given the role of selenoproteins in different body systems, each of them can affect cardiovascular function in some way, it is not surprising that Se deficiency is a risk factor for CVD and HF (7). Therefore, Se supplementation can be effective in reducing the risk of HF by improving the lipid profile and reducing insulin resistance (4).

Conclusion

Research into the role of Se in HF has shown a link between Se deficiency and HF. It can increase mortality and mitochondrial dysfunction and metabolic syndrome. High levels of Se can reduce death to some extent.

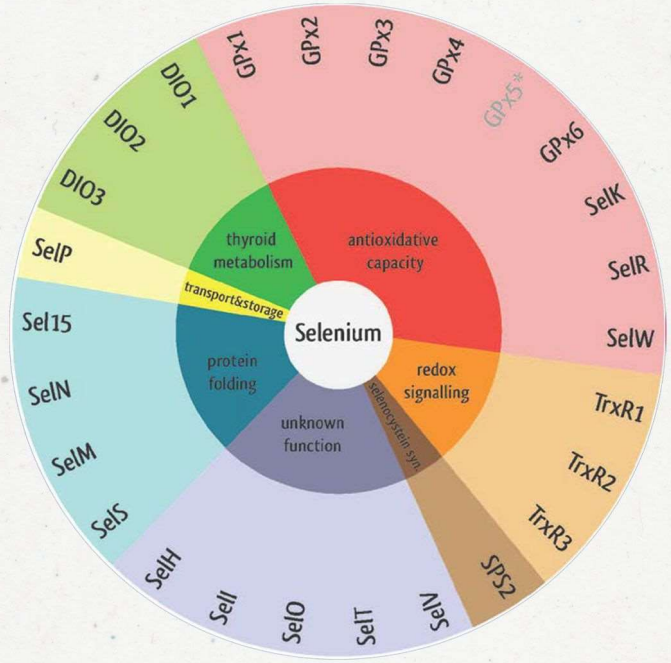


Figure 2: Classes of selenoproteins and their putative functions (8).

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Association of Potassium and Heart Failure

Introduction

Potassium (K) is the most abundant cation in humans and is essential for normal cellular function. Alterations in K regulation can lead to neuromuscular, gastrointestinal and cardiac abnormalities. Dyskalemia (i.e., hypokalemia and hyperkalemia) in heart failure (HF) is common because of HF itself, related comorbidities, and medications. Dyskalemia has important prognostic implications.

Hypokalemia is associated with excess morbidity and mortality in HF. The lower the K levels, the higher the risk, starting at K levels below approximately 4.0 mmol/l, with a steep risk increment with K levels <3.5 mmol/l. Hyperkalemia (>5.5 mmol/l) has also been associated with increased risk of adverse events; however, this association is prone to reverse causation bias as stopping Renin Angiotensin Aldosterone System Inhibitor therapy (RAASi) in the advent of hyperkalemia likely contributes the observed risk. In this state-of-the-art review, practical and easy to implement strategies to deal with both hypokalemia and hyperkalemia are provided as well as guidance for the use of potassium-binders (1).

The prognostic value of long-term K monitoring and dynamics in HF has not been characterized completely. We sought to determine the association between serum K values collected at follow-up with all-cause mortality in a prospective and consecutive cohort of patients discharged from a previous acute HF admission (2).

HF is a common clinical syndrome characterized by a reduction in cardiac output and/or increase in intra cardiac pressures at rest or during exercise, which is strongly associated to reduced functional capacity, poor quality of life and cardiac events including cardiovascular death and hospitalization rates.

In this study, we aimed to assess the impact of K levels on the prognosis of an ambulatory chronic and symptomatic HF cohort (3).

HF represents a global pandemic affecting up to 37.7 million people worldwide, with a prevalence of approximately 1–2% of the adult population in developed countries, rising to more than 10% among people older than 70 years of age. Dyskalemia (hypo- and hyperkalemia) is common in HF, linked to underlying pathophysiological processes, pharmacological treatments and concomitant comorbidities. Hypokalemia is defined as serum K <3.5 mmol/L, and hyperkalemia as serum potassium >5 mmol/L. Both hypo- and hyperkalemia have been associated with a poor outcome in patients with HF. However, it is not clear if this association is causal.

We therefore examined the available literature and implemented the Bradford Hill criteria for causation in order to reach conclusions regarding this relation. Subsequently, we reviewed the benefits of RAASi therapy up titration in patients with HFrEF and examined the role of hyperkalemia as a limiting factor for their optimal use. Finally, we propose a practical guide on the clinical management of K imbalance in patients with HF (4).

Literature review

A study was done by João Pedro Ferreira et al. in 2020 While literature is emerging with epidemiology, pathophysiology, outcomes and acute management of moderate to severe hyperkalemia, practical guidance on chronic management and guideline derived comorbidity optimization in a broader group of patients with dyskalemia is not well described. This paper aims to provide such a review. Dyskalemia can be life-threatening if not corrected, either directly or indirectly by impact provision of optimal medical therapy (1).

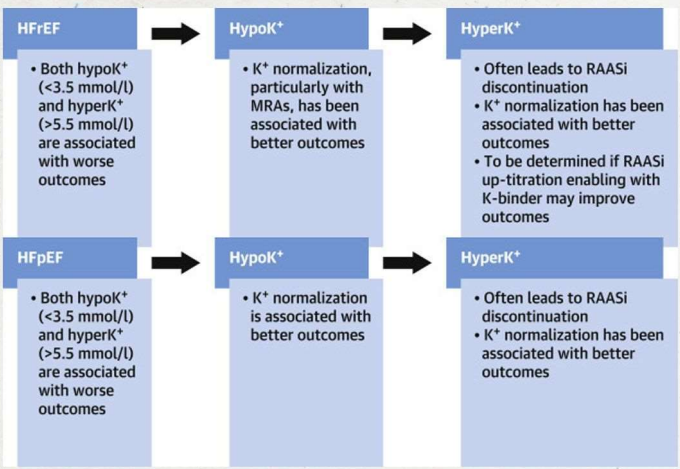

Figure 1: Outcome Associations Dyskalemia in HFrEF and HFpEF (1)

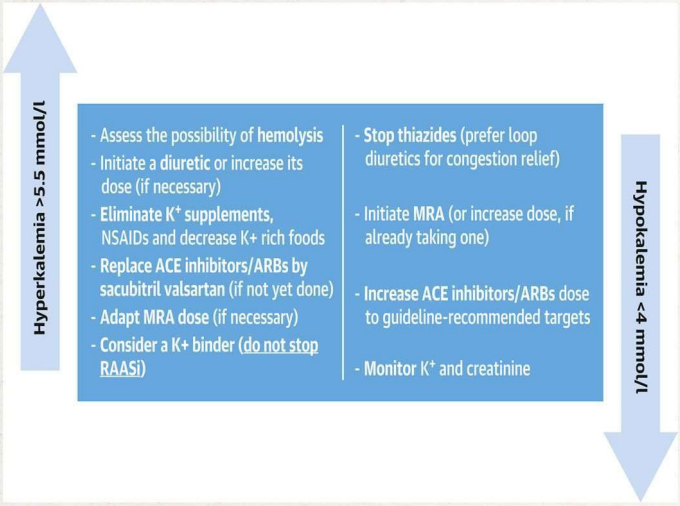

Figure 2: Management of Hyperkalemia and Hypokalemia (1).

A study was conducted by Julio Núñez et al. in 2018. Serum K was measured at every physician-patient encounter, including hospital admissions and ambulatory settings. The study sample included 2164 patients with a total of 16116 K observations. Either modeled continuously or categorically, serum K levels during long-term monitoring were independently associated with mortality in patients with HF. Likewise, persistence of abnormal K levels was linked to a higher risk of death in comparison with patients who maintained or returned to normal values (2).

A cohort study by Camila Cristiane Toledo et al. aimed to investigate the prognostic role of K levels on a cohort of patients with symptomatic chronic HF. Patients with symptomatic chronic HF were identified at the referral to 6 min walking test (6MWT) and were prospectively followed up for cardiovascular events. K levels were independently associated with worse outcomes in patients with chronic symptomatic HF (3).

Dimitrios Sfairopoulos et al. in 2020 In order to investigate Both hypo- and hyperkalemia have been associated with a poor outcome in HF, we implemented the Bradford Hill criteria for causation examining the available literature. Of note, hypokalemia and low-normal K levels (serum K <4.0 mmol/L) appear

to be associated with adverse clinical outcomes in HF in a cause-and-effect manner. Conversely, a cause-and-effect relationship between hyperkalemia (serum K >5.0 mmol/L) and adverse clinical outcomes in HF appears unlikely. We also examined the benefits of RAASi therapy up titration in patients with HF and reduced ejection fraction. In fact, hyperkalemia often limits RAASi use, thereby negating or mitigating their clinical benefits. Finally, serum K levels in HF should be maintained within the range of 4.0–5.0 mmol/L and although the correction of hyperkalemia does not appear to improve clinical outcomes per se, it may enable the optimal titration of RAASi, offering indirect clinical benefit (4).

Discussion

Studies in various studies, have shown that changes in blood K levels patients with chronic and symptomatic HF disease, as well as inpatients or outpatients, especially increases, increase the risk of mortality in humans and correct and keep it at normal level has direct and indirect clinical benefits.

Conclusion

Dyskalemia can be life-threatening if not corrected, either directly or indirectly by impact provision of optimal medical therapy.

Even though the correction of hyperkalemia does not appear to improve clinical outcomes per se, it may enable the optimal titration of RAASi and thus offer indirect clinical benefit.

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Association of Vitamin D and Risk of Atrial Fibrillation

Introduction

Atrial Fibrillation (AF) is the most common heart rhythm disturbance. AF can result in thromboembolic stroke, congestive heart failure (HF), impaired quality of life and other adverse consequences. Postoperative Atrial Fibrillation (POAF) is associated with increased morbidity, mortality and longer hospital stay; it is also associated with a two-to-three-fold increase in postoperative stroke. Ageing, obesity, hypertension (HT), prior AF and HF are found strongly associated with higher risk of POAF (1).

Vitamin D (Vit D) is a fat-soluble vitamin. It is produced under the skin on exposure to ultraviolet sunlight and metabolized in liver and kidney. studies have demonstrated that Vit D is associated with cardiovascular diseases such as coronary artery disease, myocardial infarction, cardiomyopathy and HF. Vit D has various cardiovascular pleiotropic effects by activating its nuclear receptor in cardiomyocytes and vascular endothelial cells and by regulating the renin-angiotensin aldosterone system (RAAS), adiposity and energy expenditure. There is inconsistent data about the association between Vit D and POAF (3).

POAF incidence was significantly higher in patients with Vit D deficiency or insufficiency than in patients with normal Vit D level in previous studies moreover, several new research articles reported higher serum 25-OHD is associated with new-onset AF after Coronary Artery Bypass Grafting (CABG) surgery. To date, results from several observational studies have suggested that patients with Vit D deficiency were approximately twice as likely to have AF than patients with normal levels (> 30 ng/ml) (1).

Therefore, we performed a comprehensive study to evaluate the shape of the dose-re sponse relation between circulating 25-OHD concentration and the risk of AF and post-op eration AF (POAF) after CABG (4).

Literature review

A prospective cohort by Selen Öztürk et al. in 2020 in Turkish which aimed to investigate the possible relationship between AF after cardiac surgery and preoperative Vit D levels in the light of literature data. The results showed we concluded that low preoperative Vit D levels were associated with the development of AF after cardiac surgery (2).

A study by Xiao Liu et al. conducted in 2019 in the China. The purpose of this study was to perform a comprehensive meta-analysis to evaluate the shape of the dose-response relation between circulating 25-OHD concentration and the risk of AF and POAF after CABG. The results of this study showed that our dose-response meta-analysis suggested serum vit D deficiency was associated with an increased risk of AF in the general population and POAF in patients after CABG (8).

In a randomised, blinded clinical trial study, Levent Cerit et al. in 2018 in Cyprus examined the relationship between preoperative vit D supplementation and the development of POAF. Finally preoperative vit D supplementation was found to be significantly preventive to the occurrence of POAF in patients with vit D deficiency while it was not found to be preventive to the occurrence of POAF in those with vit D insufficiency (6).

Discussion

The two different mechanisms are considered between vit D deficiency and the risk of AF. The first mechanism is associated with the RAAS. Some studies showed that vit D could inhibit the RAAS. Also, there's a significant association between lower 25-OHD levels with higher Angiotensin II (Ang II) concentration.

Clinical researches showed that the blockade of Ang II has been shown to have beneficial effects on electrical remodeling in human atrial tissue. on the other hand, RAAS inhibition might reduce the risk of AF. Therefore, low vit D level might increase the AF risk (3, 5, 6).

Another possible mechanism is the association between inflammatory markers and the risk of AF. Measuring the levels of inflammatory markers such as CRP, IL-6, IL-8 and IL-10 can work as positive predictors for AF. An elevated C-reactive protein (CRP) level are associated with AF. Also, low vit D level could increase the synthesis of CRP (3, 7, 8).

Conclusion

Our studies show conflicting results regarding the role of vit D in preventing AF. Therefore, more research is needed to obtain more definitive results.

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The Effect of DASH Diet on Blood Pressure

Introduction

Hypertension is the leading cause of chronic diseases and premature death worldwide (1). Raised blood pressure (BP) levels resulted in increasing the exposure of lifestyle risk factors including unhealthy diet (high sodium and low potassium intake) and lack of physical activity. Recently researches demonstrate that different dietary patterns such as the Dietary Approaches to Stop Hypertension (DASH) diet, are correlated with BP reduction (2).

For the reduction of BP, the contemporary hypertension management guidelines advocate as a crucial part of ongoing treatment and the adoption of life-style modifications, which include a wholesome weight-reduction plan, independently of the underlying antihypertensive drug treatment (3, 4).

At the primary DASH clinical trial, which was a controlled feeding trial, tested the consequences of three different diets on BP stages. The "combination" weight-reduction plan, which was rich in fruits, vegetables and low-fat dairy products, presently named the "DASH" diet, decreased systolic BP (SBP) and diastolic BP (DBP) compared with both the control and fruits and vegetables diets (5). Due to the fact then, different clinical trials have advised that the DASH diet alone or in combination with other way of life changes, consisting of sodium limit, weight reduction or exercising is useful for BP reduction (6).

In the present review we aimed to check out the effect of the DASH diet on the BP reduction.

Literature review

In the randomized clinical trial study by Hashemi R, et al. in 2018, 80 patients with type 2 diabetes and prehypertension in the age range of 18-65 years were examined. Evaluating the effect of DASH diet on BP and prehypertension in patients with type 2 diabetes was the aim of this study. As a result, Following the DASH diet in patients with prehypertension has beneficial effects in improving SBP (P-value=0.003) and can be effective to prevent the development of hypertension (7).

Tiong XT, et al. examined cross-sectional associations between DASH diet and cardiometabolic risk factors among 1837 Malaysian and 2898 Philippines participants in a multi-national cohort. The 5-units increase in total DASH score was significantly and inversely associated with SBP (-1.41, SE: 0.40), DBP (-1.09, SE: 0.28). This study demonstrate differential associations of DASH diet and dietary components with cardio-metabolic risk factors by country suggest the need for country specific tailoring of dietary interventions to improve cardiometabolic risk profiles (8).

In the prospective study in 2019 in Iran Ghorabi S, et al. investigated the association of adherence to the DASH diet with metabolic syndrome (MetS) and its components. This cross-sectional study on 396 Iranian adults dis-

covered that adherence to DASH become inversely related to odds of MetS and some of its components which include elevated BP (OR: 0.12, 95% CI: 0.05 e0.29, low serum HDL-C and high serum triglyceride) (9).

In 2019 Crystal CC, et al. was accomplish a research which involved 3135 black Americans enrolled in the Jackson heart study (2000–2004) with diet and office BP records. They compared the affiliation of dash accordance to BP and widespread hypertension among blacks with/without Chronic Kidney Disease (CKD). CKD status modified the affiliation of the DASH score with SBP and DBP (DBP; P-value interactions were 0.06 and <0.01). As the result, despite low dash scores ordinary, higher DASH accordance become associated with lower BP among Black Americans with CKD (10).

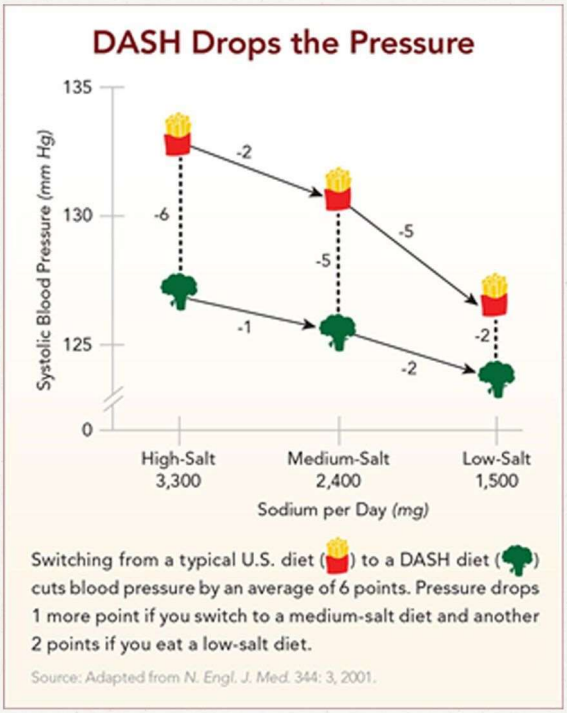


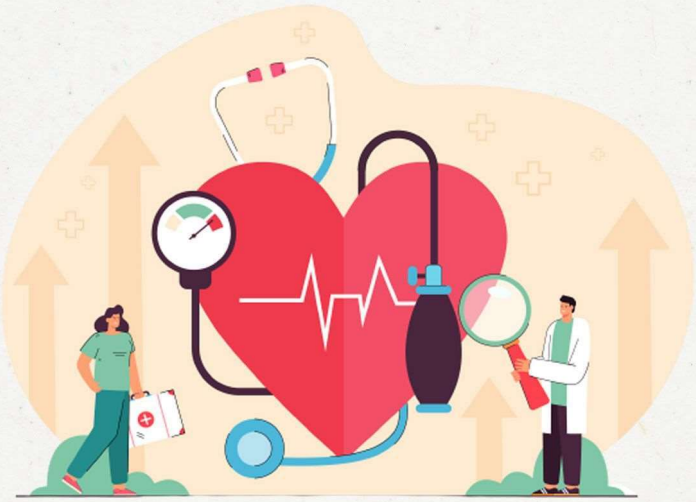
Figure1: Effect of DASH diet on BP

Discussion

In recent studies, what is obtained is the effect of DASH diet on overweight or obesity in adolescent patients. What encourages people to follow this diet: reducing consumption Energy is without reducing the number of meals. The recipe of the diet is water, not eating candy and sweets, high-fiber foods, low-fat dairy, fish and red meat. Oilseeds give us the feeling of satiety due to fiber and protein (11). Also, studies have shown that this diet is beneficial for adolescents and helps them control their weight and growth. This diet can help prevent cardiovascular disease and control BP by more effective performance mechanism of renin-angiotensin and reducing cholesterol concentration (12).

Conclusion

In conclusion, our results indicated that training nutrition based on DASH diet can be considered as a useful strategy to improve SBP and control high BP among hypertensive patients, odds of metabolic syndrome, CKD and type 2 diabetes.



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The Effect of Omega-3 Fatty Acids on Cardiovascular Diseases

Introduction

At a global level, 7 of the 10 leading causes of death in 2019 were non-communicable diseases (NCD). These seven causes accounted for 44% of all deaths or 80% of the top 10. However, all NCDs together accounted for 74% of deaths globally in 2019 (1).

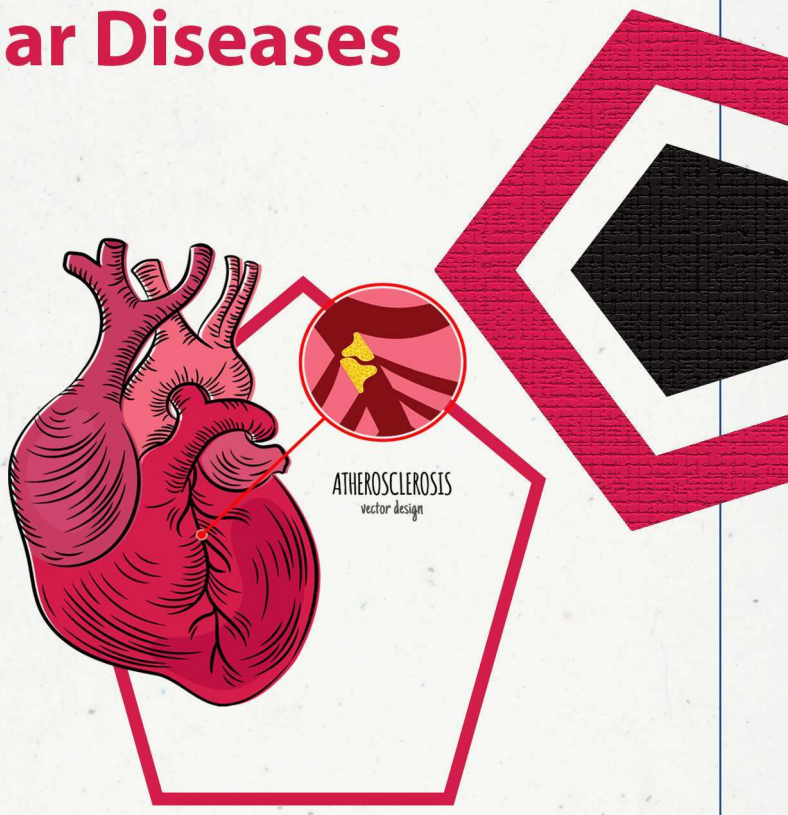
NCDs are like Cardiovascular Disease (CVD), cancer and chronic respiratory diseases. CVD can be defined as all abnormalities in the heart and blood vessels. Types of CVD include hypertension, coronary heart disease (CHD), stroke, rheumatic heart disease, heart failure and others (2). Two factors cause CVD. The first factor is modifiable risk factors, including hypertension, dyslipidemia, physical activity, smoking, obesity, diet, stress and alcohol consumption. The second factor is non-modifiable risk factors, including a history of CVD in the previous family, gender, and age. The most common risk factor for CHD patients is smoking, and the least one is hyperlipidemia (3).

Observational studies in Western and Asian populations have reported that regular consumption of fish that contains Omega-3 Fatty Acids (Ω-3FAs) once or twice a week is associated with lower risks of death from CHD (4).

These marine-derived Ω-3FAs include eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) found in fish and other seafood (5).

Subsequently, several large trials have reported conflicting results on the associations of supplementation with Ω-3FA, supplements in contrast with placebo or untreated controls on fatal and nonfatal vascular events (6).

Ω-3FAs like EPA reduce Inflammation, Low-Density Lipoprotein Cholesterol (LDL-C) oxidation and endothelial dysfunction (7). In particular, the Randomized Reduction of Cardiovascular Events with EPA Intervention Trial (REDUCE-IT) showed that icosapent ethyl,



which is the ethyl ester form of the Ω-3FA EPA, induced a significant reduction in cardiovascular events. Notably, EPA serves as a substrate for the formation of the specialized pro-resolving mediator resolvin E1 (RvE1), which stimulates the resolution of Inflammation. RvE1 reduces atherosclerosis and intimal hyperplasia using its specific receptor ERV1/ChemR23. The decreased levels of proinflammatory and proatherosclerotic leukotrienes by Ω-3FA may further contribute to a beneficial inflammatory balance. Consequently, the Rv/leukotriene ratio is emerging as a marker of non-resolving vascular inflammation. Recent experimental studies have shown that the anti-inflammatory and pro-resolving effects of lipid mediators derived from Ω-3FAs inhibit atherosclerosis independently of cholesterol and triglyceride levels (8).

This review aims to investigate the effect of Ω-3FAs on CVDs.

Literature review

Theingi Aung et al. In 2018, a study aimed at conducting a meta-analysis of all major trials that correlated Ω-3FA, supplements with the risk of fatal and nonfatal CHD and major vascular accidents in the study population as a whole and predetermined subgroups. They concluded that Ω-3FAs had no significant association with lethal or nonfatal CVD or any major vascular event. There is no current support for the use of such supplements in people with a history of CHD (5).

In 2019, a systematic review and meta-analysis of the effects of Ω-3FAs on inflammatory biomarkers and lipid profiles in diabetic and cardiovascular patients with the aim of investigating the effect of Ω-3FAs on 12 inflammatory biomarkers LDL, HDL, TG cholesterol, HbA1c, Apo AI, Apo AII, Apo B, CRP, TNF-α, fasting glucose and blood sugar in diabetic and cardiovascular patients by Zuhair S. NATO et al. concluded that Ω-3FAs may be associated with lower inflammatory biomarkers in diabetic and cardiovascular patients. Physicians should be aware of these potential benefits. However, it is recommended that patients consult a physician before consuming Ω-3s (9).

An article on the association of Ω-3FA, levels with long-chain erythrocytes with mortality and CVD by Harris et al. written in 2018, showed that a higher Ω-3, index was associated with a reduced risk of CVD and mortality from all causes (8).

Discussion

The ultimate target of any inflammatory process is to clear the insults and leukocytes from lesions and resolve and restore tissue homeostasis (10). The restoration of tissue homeostasis always begins with inflammatory lipid mediators (e.g., leukotrienes). The concept of inflammation resolution depends primarily on the active class switch in the mediators from classical prostaglandins and leukotrienes to promising newer immunoresolvents molecules (11).

Endogenous immunoresolvent lipid mediator molecules (e.g., resolvins, protectins, lipoxins and maresins) are produced during the inflammation resolution phase and have anti-inflammatory and pro-resolving functions, which have promising findings that may treat several human diseases (12). Although lipoxins are derived from different sources than others (arachidonic acid in contrast with dietary fatty acids, primarily fish oil), they all can help inhibit neutrophil recruitment, promote tissue regeneration, the lymphatic removal of phagocytes and attenuate proinflammatory gene expression (13).

Some studies have introduced Ω-3FAs to decrease levels of Fasting Plasma Glucose (FPG), improve lipid profiles inflammatory mediators and reduce insulin resistance (14). However, low dosages of Ω-3FAs may have limited effects on insulin resistance, inflammatory markers and lipid profiles among HIV patients and other certain populations (15)

These molecules' precise mechanisms of action in diabetic or CVD patients are not yet clear. However, Ω-3FAs may affect insulin metabolism and lipid profiles in the following four ways: reducing LDL/ cholesterol synthesis, enhancing lipid profiles and receptor activity in the liver (e.g., affecting LDL receptors, increasing LDL/cholesterol catabolism), improving insulin function and glucose tolerance and increasing the expression of AMP-activated protein kinase (AMPK) (16).

Several hypotheses have been proposed to explain the Ω-3 effect, including elevated adiponectin levels, the inhibition of proinflammatory cytokines, and nuclear factor-kB (NF-κB) protein expression. These molecules can have anti-diabetic properties because of improved insulin metabolism and the anti-atherosclerotic and anti-inflammatory effects attributable to the resolution of inflammation, as mentioned previously (17).

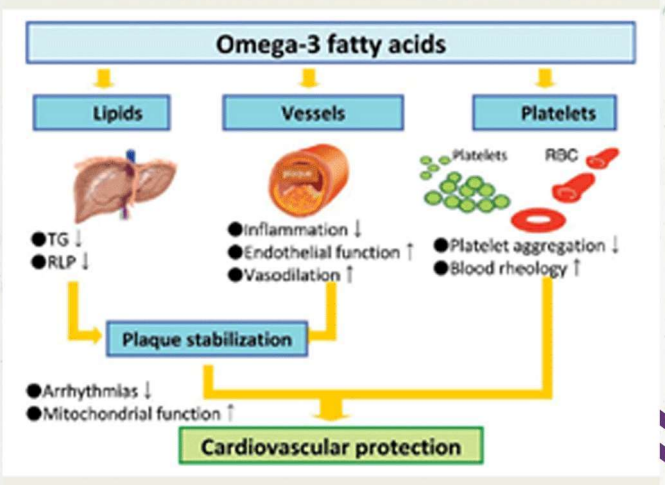


Figure 1: Beneficial Effects of Ω-3FAs. (TG, triglycerides; RLP, remnant lipoproteins;

As a consequence, the reduced proinflammatory mediators on the one hand and the increased production of anti-inflammatory molecules, such as adiponectin, on the other, will improve insulin resistance (12).

Moreover, high dietary intake of Ω-3FAs may be associated with low inflammation and endothelial function in patients with hypercholesterolemia (18), although Ω-3FAs' effects on those with CVD are unclear. However, Ω-3 intake may change the HDL cholesterol subfraction composition and absolute size. Ω-3FA, also lower triglycerides by reducing the hepatic secretion of VLDL cholesterol. Further, it may decrease triglycerides and increase LDL cholesterol in patients with hypertriglyceridemia. Our study has shown that LDL level increases and triglyceride level reductions. However, this mechanism remains unclear and some studies have shown neutral effects (19).

Thies et al. suggested that another way in which Ω-3FAs might act on CVD patients is by stabilizing advanced atherosclerotic plaques and reducing their anti-inflammatory effects thereby (20). Few studies have examined Ω-3FAs' effects on TNF-α levels and the results are inconsistent (21). However, this study showed that Ω-3FAs improved TNF-α levels.

Some research shows that Ω-3FA, supplementation had no significant effect on fatal CHD or any other CVD subtypes. Ω-3FA, supplementation had no association with the risk of major vascular events, all-cause mortality, sudden cardiac death or revascularization (22).

Related to analyzes, mechanisms that may explain the associations between higher RBC n-3 PUFA and improved longevity and reduced CVD risk are not clearly understood, but there are beneficial effects of these FA, on a variety of cardivascular risk factors. These include reductions in serum triglyceride levels, blood pressure, platelet aggregation, heart rate, susceptibility to ventricular fibrillation (in some settings), inflammatory markers and plaque vulnerability along with improvements in endothelial function (23).

Conclusion

Clinical and basic research data indicate that EPA and DHA, which have distinct effects on membrane structure, lipid dynamics and rates of membrane lipid oxidation have a beneficial role as an add-on to statin therapy in slowing the development and progression of atherosclerotic disease.

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References

1. Melamed ML, Astor B, Michos ED, Hostetter TH, Powe NR, Muntner P. 25-Hydroxyvitamin D Levels, Race, and the Progression of Kidney Disease. J Am Soc Nephrol [Internet]. 2009 Dec 1 [cited 2022 May 13];20(12):2631. Available from: /pmc/articles/PMC2794237/
2. Dobnig H, Pilz S, Scharnagl H, Renner W, Seelhorst U, Wellnitz B, et al. Independent association of low serum 25-hydroxyvitamin d and 1,25-dihydroxyvitamin d levels with all-cause and cardiovascular mortality. Arch Intern Med [Internet]. 2008 Jun 23 [cited 2022 May 13];168(12):1340–9. Available from: https://pubmed.ncbi.nlm.nih.gov/18574092/
3. Rosen CJ. Clinical practice. Vitamin D insufficiency. N Engl J Med [Internet]. 2011 Jan 20 [cited 2022 May 13];364(3):248–54. Available from: https://pubmed.ncbi.nlm.nih.gov/21247315/
4. Wang TJ, Pencina MJ, Booth SL, Jacques PF, Ingelsson E, Lanier K, et al. Vitamin D deficiency and risk of cardiovascular disease. Circulation [Internet]. 2008 Jan 29 [cited 2022 May 13];117(4):503–11. Available from: https://pubmed.ncbi.nlm.nih.gov/18180395/
5. Melamed ML, Muntner P, Michos ED, Uribarri J, Weber C, Sharma J, et al. Serum 25-hydroxyvitamin D levels and the prevalence of peripheral arterial disease: results from NHANES 2001 to 2004. Arterioscler Thromb Vasc Biol [Internet]. 2008 Jun 1 [cited 2022 May 13];28(6):1179–85. Available from: https://pubmed.ncbi.nlm.nih.gov/18417640/
6. Zittermann A, Koerfer R. Vitamin D in the prevention and treatment of coronary heart disease. Curr Opin Clin Nutr Metab Care [Internet]. 2008 Nov [cited 2022 May 13];11(6):752–7. Available from: https://pubmed.ncbi.nlm.nih.gov/18827580/
7. Pilz S, Dobnig H, Fischer JE, Wellnitz B, Seelhorst U, Boehm BO, et al. Low vitamin d levels predict stroke in patients referred to coronary angiography. Stroke [Internet]. 2008 Sep 1 [cited 2022 May 13];39(9):2611–3. Available from: https://pubmed.ncbi.nlm.nih.gov/18635847/
8. Pilz S, Dobnig H, Nijpels G, Heine RJ, Stehouwer CDA, Snijder MB, et al. Vitamin D and mortality in older men and women. Clin Endocrinol (Oxf) [Internet]. 2009 Nov 1 [cited 2022 May 13];71(5):666–72. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/j.1365-2265.2009.03548.x
9. Ginde AA, Scragg R, Schwartz RS, Camargo CA. Prospective study of serum 25-hydroxyvitamin D level, cardiovascular disease mortality, and all-cause mortality in older U.S. adults. J Am Geriatr Soc [Internet]. 2009 Sep [cited 2022 May 13];57(9):1595–603. Available from: https://pubmed.ncbi.nlm.nih.gov/19549021/
10. Pittas AG, Lau J, Hu FB, Dawson-Hughes B. The role of vitamin D and calcium in type 2 diabetes. A systematic review and meta-analysis. J Clin Endocrinol Metab [Internet]. 2007 [cited 2022 May 13];92(6):2017–29. Available from: https://pubmed.ncbi.nlm.nih.gov/17389701/
11. Witham MD, Nadir MA, Struthers AD. Effect of vitamin D on blood pressure: a systematic review and meta-analysis. J Hypertens [Internet]. 2009 [cited 2022 May 13];27(10):1948–54. Available from: https://pubmed.ncbi.nlm.nih.gov/19587609/
12. Norman PE, Powell JT. Vitamin D, shedding light on the development of disease in peripheral arteries. Arterioscler Thromb Vasc Biol [Internet]. 2005 Jan [cited 2022 May 13];25(1):39–46. Available from: https://pubmed.ncbi.nlm.nih.gov/15499037/
13. Wang L, Ma J, Manson JE, Buring JE, Gaziano JM, Sesso HD. A prospective study of plasma vitamin D metabolites, vitamin D receptor gene polymorphisms, and risk of hypertension in men. Eur J Nutr [Internet]. 2013 Oct [cited 2022 May 13];52(7):1771–9. Available from: https://pubmed.ncbi.nlm.nih.gov/23262750/
14. Girgis CM, Clifton-Bligh RJ, Turner N, Lau SL, Gunton JE. Effects of vitamin D in skeletal muscle: falls, strength, athletic performance and insulin sensitivity. Clin Endocrinol (Oxf) [Internet]. 2014 Feb [cited 2022 May 13];80(2):169–81. Available from: https://pubmed.ncbi.nlm.nih.gov/24256495/
15. Somuncu MU, Serbest NG, Akgül F, Çakır MO, Akgün T, Tatar FP, et al. The relationship between a combination of vitamin D deficiency and hyperuricemia and the severity of coronary artery disease in myocardial infarction patients. Turk Kardiyol Dern Ars [Internet]. 2020 [cited 2022 May 13];48(1):10–9. Available from: https://pubmed.ncbi.nlm.nih.gov/31974328/
16. Van De Luijtgaarden KM, Voûte MT, Hoeks SE, Bakker EJ, Chonchol M, Stolker RJ, et al. Vitamin D deficiency may be an independent risk factor for arterial disease. Eur J Vasc Endovasc Surg [Internet]. 2012 Sep [cited 2022 May 13];44(3):301–6. Available from: https://pubmed.ncbi.nlm.nih.gov/22841360/
17. Chua GT, Chan YC, Cheng SW. Vitamin D status and peripheral arterial disease: evidence so far. Vasc Health Risk Manag [Internet]. 2011 [cited 2022 May 13];7(1):671–5. Available from: https://pubmed.ncbi.nlm.nih.gov/22140318/
18. Krishna SM. Vitamin D as A Protector of Arterial Health: Potential Role in Peripheral Arterial Disease Formation. Int J Mol Sci [Internet]. 2019 Oct 1 [cited 2022 May 13];20(19). Available from: https://pubmed.ncbi.nlm.nih.gov/31623356/
19. Chowdhury R, Kunutsor S, Vitezova A, Oliver-Williams C, Chowdhury S, Kiefte-De-Jong JC, et al. Vitamin D and risk of cause specific death: systematic review and meta-analysis of observational cohort and randomised intervention studies. BMJ [Internet]. 2014 Apr 1 [cited 2022 May 13];348. Available from: https://www.bmj.com/content/348/bmj.g1903
20. Manson JE, Allison MA, Carr JJ, Langer RD, Cochrane BB, Hendrix SL, et al. Calcium/vitamin D supplementation and coronary artery calcification in the Women's Health Initiative. Menopause [Internet]. 2010 Jul [cited 2022 May 13];17(4):683–91. Available from: https://pubmed.ncbi.nlm.nih.gov/20551849/

The Efficacy of Resveratrol on Cardiac Function after Myocardial Infarction

1. Feigin V. Global, regional, and National Incidence, prevalence, and years lived with disability for 310 acute and chronic diseases and injuries, 1990-2015: a systematic analysis for the global burden of disease study 2015. The Lancet. 2016;388(10053):1545-602.
2. Mei C, Liu W, Sun P. Resveratrol Inhibits Myocardial Apoptosis by Regulating the Protein Kinase R-like Endoplasmic Reticulum Kinase Endoplasmic Reticulum Stress Pathway and Improves Myocardial Remodeling and Cardiac Function after MI. Indian Journal of Pharmaceutical Sciences. 2021;83(2):387-92.
3. https://www.who.int/health-topics/cardiovascular-diseases#tab=tab_1. Accessed 11 May 2022
4. Ahmadi A, Soori H, Mehrabi Y, Etemad K, Samavat T, Khaledifar A. Incidence of acute
MI in Islamic Republic of Iran: a study using national registry data in 2012. Eastern Mediterranean health journal = La revue de sante de la Mediterranee orientale = al-Majallah al-sihhiyah li-sharq al-mutawassit. 2015;21(1):5-12.
5. Raj P, Thandapilly SJ, Wigle J, Zieroth S, Netticadan T. A Comprehensive Analysis of the Efficacy of Resveratrol in Atherosclerotic CVD, MI and Heart Failure. Molecules (Basel, Switzerland). 2021;26(21).
6. Gutlapalli SD, Kondapaneni V, Toulassi IA, Poudel S, Zeb M, Choudhari J, et al. The effects of resveratrol on telomeres and post MI remodeling. Cureus. 2020;12(11).
7. Idikio HA. Postmyocardial Infarct Remodeling and Heart Failure: Potential Contributions from Pro- and Antiaging Factors. Cardiology Research and Practice. 2011;2011:836806.
8. Malhotra A, Bath S, Elbarbry F. An Organ System Approach to Explore the Antioxidative, Anti-Inflammatory, and Cytoprotective Actions of Resveratrol. Oxidative Medicine and Cellular Longevity. 2015;2015:803971.
9. Ren X, Chen L, Xie J, Zhang Z, Dong G, Liang J, et al. Resveratrol Ameliorates Mitochondrial Elongation via Drp1/Parkin/PINK1
Signaling in Senescent-Like Cardiomyocytes. Oxidative Medicine and Cellular Longevity. 2017;2017:4175353.
10. Jiang J, Gu X, Wang H, Ding S. Resveratrol improves cardiac function and left ventricular fibrosis after MI in rats by inhibiting NLRP3 inflammasome activity and the TGF-β1/SMAD2 signaling pathway. PeerJ. 2021;9:e11501.
11. Bonnefont-Rousselot D. Resveratrol and CVD acuteNutrients. 2016;8(5):250.
12. Zordoky BN, Robertson IM, Dyck JR. Preclinical and clinical evidence for the role of resveratrol in the treatment of CVD. Biochimica et biophysica acta. 2015;1852(6):1155-77.
13. Sung MM, Dyck JR. Therapeutic potential of resveratrol in heart failure. Annals of the New York Academy of Sciences. 2015;1348(1):32-45.
14. Kanamori H, Takemura G, Goto K, Tsujimoto A, Ogino A, Takeyama T, et al. Resveratrol reverses remodeling in hearts with large, old MI through enhanced autophagy-activating AMP kinase pathway. The American journal of pathology. 2013;182(3):701-13.

The Effect of Selenium Deficiency on Heart Failure

1. Al-Mubarak AA, Grote Beverborg N, Suthahar N, Gansevoort RT, Bakker SJ, Touw DJ, et al. High selenium levels associate with reduced risk of mortality and new-onset heart failure: data from PREVEND. European journal of heart failure. 2022;24(2):299-307.
2. Tanai E, Frantz S. Pathophysiology of heart failure. Comprehensive physiology. 2011;6(1):187-214.
3. Liu SS, Monti J, Kargbo HM, Athar MW, Parakh K. Frontiers of therapy for patients with heart failure. The American journal of medicine. 2013;126(1):6-12. e6.
4. Raygan F, Behnejad M, Ostadmohammadi V, Bahmani F, Mansournia MA, Karamali F, et al. Selenium supplementation lowers insulin resistance and markers of cardio-metabolic risk in patients with congestive heart failure: a randomised, double-blind, placebo-controlled trial. British Journal of Nutrition. 2018;120(1):33-40.
5. Bomer N, Grote Beverborg N, Hoes MF, Streng KW, Vermeer M, Dokter MM, et al. Selenium and outcome in heart failure. European journal of heart failure. 2020;22(8):1415-23.
6. Al-Mubarak AA, van der Meer P, Bomer N. Selenium, selenoproteins, and heart failure: Current knowledge and future perspective. Current heart failure reports. 2021;18(3):122-31.
7. Shimada BK, Alfulaij N, Seale LA. The impact of selenium deficiency on cardiovascular function. International Journal of Molecular Sciences. 2021;22(19):10713.
8. Benstoem C, Goetzenich A, Kraemer S, Borosch S, Manzanares W, Hardy G, et al. Selenium and its supplementation in cardiovascular disease--what do we know? Nutrients. 2015;7(5):3094-118.

Association of Potassium and Heart Failure

1. Ferreira JP, Butler J, Rossignol P, Pitt B, Anker SD, Kosiborod M, et al. Abnormalities of Potassium in Heart Failure: JACC State-of-the-Art Review. Vol. 75, Journal of the American College of Cardiology. 2020.
2. Núñez J, Bayés-Genís A, Zannad F, Rossignol P, Núñez E, Bodí V, et al. Long-Term Potassium Monitoring and Dynamics in Heart Failure and Risk of Mortality. Circulation. 2018;137(13).
3. Toledo CC, Vellosa Schwartzmann P, Miguel Silva L, da Silva Ferreira G, Bianchini Cardoso F, Citelli Ribeiro V, et al. Serum potassium levels provide prognostic information in symptomatic heart failure beyond traditional clinical variables. ESC Hear Fail. 2021;8(3).
4. Sfairopoulos D, Arseniou A, Korantzopoulos P. Serum potassium and heart failure: association, causation, and clinical implications. Vol. 26, Heart Failure Reviews. 2021.

Association of vitamin D and risk of atrial fibrillation

(1). Öztürk S, Öztürk İ. Atrial fibrillation after cardiac surgery and preoperative Vit D levels: A systematic review and meta-analysis. Turkish Journal of Thoracic and Cardiovascular Surgery. 2020 Jan;28(1):101.
(2). Albert CM, Cook NR, Pester J, Moorthy MV, Ridge C, Danik JS, Gencer B, Siddiqi HK, Ng C, Gibson H, Mora S. Effect of marine omega-3 fatty acid and Vit D supplementation on incident atrial fibrillation: a randomized clinical trial. JAMA. 2021 Mar 16;325(11):1061-73.
(3). Liu X, Wang W, Tan Z, Zhu X, Liu M, Wan R, Hong K. The relationship between Vit D and risk of atrial fibrillation: a dose-response analysis of observational studies. Nutrition journal. 2019 Dec;18(1):1-0.
(4). Cerit L, Özcem B, Cerit Z, Duygu H. Preventive effect of preoperative Vit D supplementation on POAF. Brazilian journal of cardiovascular surgery. 2018 Jul;33:347-52.
(5). Forman JP, Williams JS, Fisher ND. Plasma 25-hydroxyvitamin D and regulation of the renin-angiotensin system in humans. Hypertension. 2010 May 1;55(5):1283-8.
(6). Schneider MP, Hua TA, Böhm M, Wachtell K, Kjeldsen SE, Schmieder

RE. Prevention of atrial fibrillation by renin-angiotensin system inhibition: a meta-analysis. Journal of the American College of Cardiology. 2010 May 25;55(21):2299-307.
(7). Kruit A, Zanen P. The association between Vit D and C-reactive protein levels in patients with inflammatory and non-inflammatory diseases. Clinical biochemistry. 2016 May 1;49(7-8):534-7.
(8). Weymann A, Popov AF, Sabashnikov A, Ali-Hasan-Al-Saegh S, Ryazanov M, Tse G, Mirhosseini SJ, Liu T, Lotfaliani M, Sedaghat M, Baker WL. Baseline and postoperative levels of C-reactive protein and interleukins as inflammatory predictors of atrial fibrillation following cardiac surgery: a systematic review and meta-analysis. Kardiologia Polska (Polish Heart Journal). 2018;76(2):440-51

The Effect of Dash Diet on Blood Pressure

1. WHO. Global Health Observatory (GHO) data: raised blood pressure: situation and trends [Internet]. Geneva: WHO; [cited 4 February, 2016]. Available from: http://www.who.int/gho/ncd/risk_factors/ blood_pressure_prevalence_text/en/.
2. Savica V, Bellinghieri G, Kopple JD. The effect of nutrition on blood pressure. Annu Rev Nutr 2010;30:365–401.
3. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, Clement DL, Coca A, de Simone G, Dominiczak A, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension. Eur Heart J 2018;39:3021–104.
4. Whelton PK, Carey RM, Aronow WS, Casey DE, Jr, Collins KJ, Dennison Himmelfarb C, DePalma SM, Gidding S, Jamerson KA, Jones DW, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol 2018;71:2199–269.
5. Appel LJ. The effects of dietary factors on blood pressure. Cardiol Clin 2017;35:197–212.
6. Chiavaroli L, Viguiliouk E, Nishi SK, Blanco Mejia S, Rahelic D, ´ Kahleová H, Salas-Salvadó J, Kendall CW, Sievenpiper JL. DASH dietary pattern and cardiometabolic outcomes: an umbrella review of systematic reviews and meta-analyses. Nutrients 2019;11:338.
7. Hashemi R, Rahimlou M, Baghdadian S, Manafi M. Investigating the effect of DASH diet on blood pressure of patients with type 2 diabetes and prehypertension: Randomized clinical trial. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019 Jan 1;13(1):1-4.
8. Tiong XT, Shahirah AN, Pun VC, Wong KY, Fong AY, Sy RG, Castillo-Carandang NT, Nang EE, Woodward M, van Dam RM, Tai ES. The association of the dietary approach to stop hypertension (DASH) diet with blood pressure, glucose and lipid profiles in Malaysian and Philippines populations. Nutrition, Metabolism and Cardiovascular Diseases. 2018 Aug 1;28(8):856-63.
9. Ghorabi S, Salari-Moghaddam A, Daneshzad E, Sadeghi O, Azadbakht L, Djafarian K. Association between the DASH diet and metabolic syndrome components in Iranian adults. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019 May 1;13(3):1699-704.
10.Tyson CC, Davenport CA, Lin PH, Scialla JJ, Hall R, Diamantidis CJ, Lunyera J, Bhavsar N, Rebholz CM, Pendergast J, Boulware LE. DASH diet and blood pressure among black Americans with and without CKD: the Jackson Heart Study. American journal of hypertension. 2019 Sep 24;32(10):975-82.
11. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, de Ferranti SD, Dionne JM, Falkner B, Flinn SK, Gidding SS. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics. 2017 Sep 1;140(3).
12. Lari A, Sohouli MH, Fatahi S, Cerqueira HS, Santos HO, Pourrajab B, Rezaei M, Saneie S, Rahideh ST. The effects of the Dietary Approaches to Stop Hypertension (DASH) diet on metabolic risk factors in patients with chronic disease: A systematic review and meta-analysis of randomized controlled trials. Nutrition, Metabolism and Cardiovascular Diseases. 2021 Sep 22;31(10):2766-78.

1. WHO. The top 10 causes of death. 2020 [cited 2020 9 December 2020]; Available from: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.
2. WHO. Cardiovascular diseases. 2021 11 June 2021]; Available from: https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds).
3. Sandi, M.R., et al., The description of modifiable risk factors in coronary heart disease at dr. Soetomo regional public hospital. Jurnal Berkala Epidemiologi, 2019. 7(2): p. 85-93.
4. Zheng, J., et al., Fish consumption and CHD mortality: an updated meta-analysis of seventeen cohort studies. Public health nutrition, 2012. 15(4): p. 725-737.
5. Aung, T., et al., Associations of omega-3 fatty acid supplement use with cardiovascular disease risks: meta-analysis of 10 trials involving 77 917 individuals. JAMA cardiology, 2018. 3(3): p. 225-233.
6. Bonds, D.E., et al., Effect of long-chain ω-3 fatty acids and lutein+ zeaxanthin supplements on cardiovascular outcomes: results of the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. JAMA internal medicine, 2014. 174(5): p. 763-771.
7. Preston Mason, R., New insights into mechanisms of action for omega-3 fatty acids in atherothrombotic cardiovascular disease. Current atherosclerosis reports, 2019. 21(1): p. 1-11.
8. Bäck, M. and G.K. Hansson, Omega-3 fatty acids, cardiovascular risk, and the resolution of inflammation. The FASEB journal, 2019. 33(2): p. 1536-1539.
9. Natto, Z.S., et al., Omega-3 fatty acids effects on inflammatory biomarkers and lipid profiles among diabetic and cardiovascular disease patients: a systematic review and meta-analysis. Scientific reports, 2019. 9(1): p. 1-10.
10. Van Dyke, T.E. and K.S. Kornman, Inflammation and factors that may regulate inflammatory response. Journal of periodontology, 2008. 79: p. 1503-1507.
11. Freire, M.O. and T.E. Van Dyke, Natural resolution of inflammation. Periodontology 2000, 2013. 63(1): p. 149-164.
12. Bellenger, J., et al., High pancreatic n-3 fatty acids prevent STZ-induced diabetes in fat-1 mice: inflammatory pathway inhibition. Diabetes, 2011. 60(4): p. 1090-1099.
13. Krishnamoorthy, S., et al., Resolvin D1 receptor stereoselectivity and regulation of inflammation and proresolving microRNAs. The American journal of pathology, 2012. 180(5): p. 2018-2027.
14. Samimi, M., et al., Effects of omega-3 fatty acid supplementation on insulin metabolism and lipid profiles in gestational diabetes: Randomized, double-blind, placebo-controlled trial. Clinical Nutrition, 2015. 34(3): p. 388-393.
15. Oliveira, J.M., et al., Effects of fish oil on lipid profile and other metabolic outcomes in HIV-infected patients on antiretroviral therapy: a randomized placebo-controlled trial. International journal of STD & AIDS, 2014. 25(2): p. 96-104.
16. Higuchi, T., et al., Levels of plasma insulin, leptin and adiponectin, and activities of key enzymes in carbohydrate metabolism in skeletal muscle and liver in fasted ICR mice fed dietary n-3 polyunsaturated fatty acids. The Journal of nutritional biochemistry, 2008. 19(9): p. 577-586.
17. Kondo, K., et al., Effects of a fish-based diet on the serum adiponectin concentration in young, non-obese, healthy Japanese subjects. Journal of atherosclerosis and thrombosis, 2010: p. 1003170207-1003170207.
18. Nestel, P.J., Fish oil and cardiovascular disease: lipids and arterial function. The American journal of clinical nutrition, 2000. 71(1): p. 228S-231S.
19. Davidson, M.H., et al., Efficacy and tolerability of adding prescription omega-3 fatty acids 4 g/d to simvastatin 40 mg/d in hypertriglyceridemic patients: an 8-week, randomized, double-blind, placebo-controlled study. Clinical therapeutics, 2007. 29(7): p. 1354-1367.
20. Thies, F., et al., Association of n-3 polyunsaturated fatty acids with stability of atherosclerotic plaques: a randomised controlled trial. The Lancet, 2003. 361(9356): p. 477-485.
21. Mori, T.A. and L.J. Beilin, Omega-3 fatty acids and inflammation. Current atherosclerosis reports, 2004. 6(6): p. 461-467.
22. Balk, E.M. and A.H. Lichtenstein, Omega-3 fatty acids and cardiovascular disease: summary of the 2016 Agency of Healthcare Research and Quality Evidence Review. Nutrients, 2017. 9(8): p. 865.
23. Pase, M.P., N.A. Grima, and J. Sarris, Do long-chain n-3 fatty acids reduce arterial stiffness? A meta-analysis of randomised controlled trials. British Journal of Nutrition, 2011. 106(7): p. 974-980.
24. Kromhout, D., et al., Fish oil and omega-3 fatty acids in cardiovascular disease: do they really work? European heart journal, 2012. 33 4: p. 436-43.

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