Underlying Causes of Cardiovascular Inflammation Leading to Degeneration

Brandon Orzech, Dr Darren Koch
Alvernia University, 400 Saint Bernardine St, Reading, PA 19607

Background: Cardiovascular inflammation has led to the rapid degeneration of the cardiovascular system and has a wide variety of underlying causes. There are many factors that were examined in this literature review; all of which greatly increase the risk of cardiovascular inflammation. Factors such as high triglyceride levels, above normal cholesterol levels such as LDL, sugar and obesity, and hypertension and diabetes were all examined through various research studies. All of these factors play an important role in an individual’s health. The main goal of this paper was to see which factor was the underlying cause for cardiovascular inflammation and how can that be prevented. Cardiovascular disease covers a wide variety of different cardiovascular conditions. Cardiovascular disease can refer to heart disease. Heart disease is strongly related to atherosclerosis, which is a condition where plaque builds up in the walls of the arteries. Heart disease accounts for one in every four deaths (CDC, 2019). Another condition that is a form of cardiovascular disease is a heart attack. A heart attack or myocardial infarction, is when blood flow to a part of the heart is blocked by a blood clot. A third condition that is part of cardiovascular diseases is a stroke. A stroke is when a blood vessel that feeds the brain gets blocked by a blood clot. Congestive heart failure refers to the heart not being able to pump blood efficiently. Heart valve problems and arrhythmias also fall under the umbrella of cardiovascular diseases. Many of the different factors that were examined in this literature review play a part in the cause of many of these different types of conditions relating to cardiovascular disease.

High Triglyceride Levels

A triglyceride is an ester that is derived from glycerol and three fatty acids. These triglycerides can build up in the blood and cause a variety of problems in the cardiovascular system. In one study conducted by Sanchez-Inigo et al. found that decreases in mortality from cardiovascular diseases were partially offset by increases in the prevalence of hyperinsulinemia. In regards to the TG index: the product of fasting plasma glucose and TG, has been found to correlate with the rise of insulin resistance known as hyperinsulinemia. Data from 1946 women and 3068 men with a mean age at 55 were observed for a median of 10 years. There were 505 cases of incident CVD, incidence was 6.4% for women and 12.4% for men. There was an increase in the TGIndex for individuals that were smokers, had hypertension, and exhibited sedentary behavior(Sanchez-Inigo, et al., 2016). They found that using the TG index could be used as an indicator of hyperinsulinemia and a indicator of developing a cardiovascular event. In another study done out of Norway by Lindman, et al. found that high triglyceride levels lead to a higher risk of cardiovascular events. They conducted a study with 86,261 participants between 1974-2007, initially aged between 20-50 years old and free of any CVD. A total of 9,528 men died and 5,676 women died of CVDs. After adjustment for CVD risk factors other than HDL cholesterol, the HRs (95% CI) per 1 mmol/L increase in non-fasting triglycerides were 1.16 (1.13–1.20), 1.20 (1.14–1.27), 1.26 (1.19–1.34) and 1.09 (0.96–1.23) for all cause mortality, CVD, HD, and stroke mortality in women (Lindman, et al., 2010). Higher levels of TG were correlated with cardiovascular incidents. The average mortality rate for an individual in this study was 63.4 years. As different studies were reviewed, looking at the levels of triglycerides in the blood did not seem to be the main indicator for cardiovascular diseases. As seen in the study conducted by Sanchez-Inigo et al. high TG levels found to be indicative of hyperinsulinemia, suggesting that hyperinsulinemia could be a major factor for cardiovascular degeneration.

High Cholesterol Levels

There is good cholesterol, known as HDL or high density lipoprotein, and there is bad cholesterol, known as LDL or low density lipoprotein. In one study, there was evidence that says the dietary cholesterol that individuals intake on a daily basis plays an integral role in increasing the risk of atherosclerotic cardiovascular disease. In a study that analyzed forty different studies, in 17 of the trials that were examined, dietary cholesterol statistically increased both serum cholesterol levels and low density lipoprotein levels. Serum cholesterol levels in participants there was an average net change of 11.2 mg/dL and for low density lipoprotein there was an average net change of 6.7 mg/dL (Berger et al., 2015). Although there was an increase in serum cholesterol levels and low density lipoprotein levels, there was found to be no correlation between increased cholesterol levels and cardiovascular disease. Ischemic strokes, or hemorrhagic strokes. Within all of these studies that were examined there were a total of 361,923 participants, making these studies fairly reliable and accurate. In another study that was conducted found that an enigmatic lipoprotein called lipoprotein(a) or Lpa is responsible for pro-atherogenic and pro-thrombotic effects. In the vascular wall, oxidized LDLs trigger both directly and indirectly a detrimental sequence of pro-inflammatory events leading to atherosclerosis. On entrance and possible trapping within the arterial intima, triglyceride-rich lipoprotein degradation by lipoprotein lipase liberates free fatty acids, causing local inflammation, (Mao et al., 2013). Lpa has also been linked to induce endothelial injury with impairment of endothelial homeostasis. Increased levels of Lpa reduces the migration of ECs. ECs are what is known as endothelial progenitor cells. They play an important part in the regeneration of the endothelial lining and blood vessel walls. When there is tissue injury, the ability of increased Lpa levels to inhibit the migration of ECs has shown to have a direct impact on the various repair mechanisms.

Obesity and Diabetes

In a study published in the New England Journal of Medicine, it puts hyperinsulinemia and diabetes as a vast contributor to cardiovascular degeneration. A study was conducted where blood samples were collected from 2103 obese individuals and 3240 non-obese; in Quebec City, Canada, who were 45 to 76 years of age and who did not have ischemic heart disease. After excluding men with diabetes, they compared fasting plasma insulin and lipoprotein concentrations at baseline in 91 higher plasma levels of LdL, and subjects with this allele had a higher mortality with a relative risk of 2.95 over a 5-year follow-up (Stephens, J., Humphries, S., 2003).

Genetic Influences

An individual’s genes have been linked to an increase in cholesterol levels and an increased risk for a number of CVDs. There have also been studies that have shown a correlation between atherosclerosis and genetics. In one study, blood samples were taken from 230 adults admitted for elective coronary angiography. It was found that a total of 130 had significant (>50%) stenosis in at least one main coronary artery branch and 100 had not. There were significant differences in the genotype group and were analyzed. Interleukin-6 is an important pro-inflammatory cytokine. Several variations in the promoter region of the IL-6 gene on chromosome 7 have been identified and the -174G/C polymorphism has been found through this study to be an association with atherosclerosis and coronary artery disease. The CC genotype of the IL-6 -174 polymorphism was more frequent in the group with significant stenosis (Berg et al., 2008). The concenation of IL-6 is about 35% higher in atherosclerosis plaque than in the normal intima (Berger et al., 2008).

In a second study there was also found to be a genetic link to cardiovascular diseases. IL-6 was found again in this study to play an important role in atherosclerosis and coronary artery disease. A common G/C polymorphism is located 174 base pairs upstream from the start of the transcription site for the gene IL-6. The role of the –174C/G polymorphism in determining the pathogenesis of aneurysmal disease has previously been explored in studies in the UK Small Aneurysmal Trial. The results showed an association between the–174G allele, higher plasma levels of IL-6, and subjects with this allele had a higher mortality with a relative risk of 2.95 over a 5-year follow-up (Stephens, J., Humphries, S., 2003).

Conclusion:

There are various components such as triglycerides, cholesterol, obesity, genetics, and hyperinsulinemia that contribute to cardiovascular inflammation that lead to degeneration. Hyperinsulinemia and diabetes play an integral role in the deterioration of the cardiovascular system. Obesity typically precedes type 2 diabetes and is a leading health concern in this country. The role that genetics play is still a fairly new area of research and is being investigated further. It is known that there is genetic predisposition that can make an individual susceptible to having higher cholesterol, even when maintaining a healthy weight and diet. The research into this area of cardiovascular degeneration is only at the toe of the iceberg and many new studies and advancements are being made in the fight against cardiovascular diseases.

Acknowledgements:

This work was supported by Alvernia University and in collaboration with Dr. Darren Koch.