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Vitamin D Is a Prognostic Marker in Heart Failure, Study Finds

Science Daily (Sep. 5, 2010) — Survival rates in heart failure patients with reduced levels of vitamin D are lower than in patients with normal levels. This is the finding of a major study carried out at University Medical Center, Groningen, Netherlands, according to a presentation at the European Society of Cardiology's Congress 2010 in Stockholm.

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Results also suggest that low levels of vitamin D are associated with activation of the Renin Angiotensin System (RAS -- a pivotal regulatory system in heart failure) and an altered cytokine profile.

Vitamin D is produced by the skin when it is exposed to the natural Ultra Violet-B (UV-B) radiation from the sun. Low levels have long been known as the underlying mechanism of rickets however, in recent years, new studies have provided novel insight into the multiple vitamin's functions. It has been proved that most tissues and cells have a vitamin D receptor, and there is strong evidence that its presence plays a part in reducing the risk factor profiles of several chronic illnesses, such as common cancers, autoimmune diseases, kidney diseases, chronic infectious diseases, hypertension and apparently also heart failure.

"By showing that vitamin D is an independent predictor, we hoped to prove that it is a contributory factor to, rather than peripheral to, the development and prognosis of heart failure," said Ms. Licette Liu of the University Medical Center, Groningen. "With this new information, we then hope to provide better insight into the pathophysiology of heart failure."

Experiments with mice lacking the vitamin D receptor have shown typical signs of heart failure, while small-scale clinical studies have shown that low levels are a consistent factor amongst human heart failure patients. "There are several potential reasons for low vitamin D levels in heart failure patients, including the fact that they are often bedridden or house-bound due to their clinical symptoms" Ms. Liu explains. "This would lead to a serious deficiency, because 80-90 percent of vitamin D is obtained by UV-B radiation. Another factor is that the capacity of the skin to produce vitamin D declines with age, and as heart failure has a high incidence among elderly people, it is not entirely surprising to measure low levels. Furthermore, severe heart failure is associated with impaired renal function due to decreased blood supply. This may be responsible for a reduced synthesis of the active form of vitamin D, since the final step of conversion takes place in the kidneys. All of these factors may add to vitamin D deficiency in heart failure patients."

Observations in animal studies suggest that vitamin D is a negative regulator of the RAS, which is responsible for volume and blood pressure homeostasis and is a pivotal regulatory system in heart failure. Low levels may activate the RAS, which in turn may contribute to the development and progression of heart failure. There is also growing evidence that overproduction of several pro-inflammatory cytokines (and underproduction of anti-inflammatory cytokines) plays an important role in heart failure. Several studies have shown that vitamin D alters the cytokine profile and may therefore contribute to the inflammatory processes in heart failure.

In the current study, vitamin D concentration was assessed in plasma samples from 548 heart failure patients, using data supplied by the Coordinating study evaluating Outcomes of Advising and Counseling in Heart failure (COACH). Results showed that vitamin D concentration is associated with the prognosis of heart failure. Patients with lower concentrations had a higher

risk of death or required re-hospitalization, whereas patients with higher concentrations had lower survival risks for these endpoints. Further, significant correlations between vitamin D, and Plasma Renin Activity and C-Reactive Protein were found. These correlations suggest that the association between vitamin D and the prognosis in heart failure may be explained by activation of the RAS and an altered cytokine profile.

This is the first study in a large cohort of patients recruited due to hospitalisation for heart failure, in which the role of vitamin D has been determined, along with the roles of plasma renin activity and cytokines. Previous reports involved smaller study cohorts, and did not determine either plasma renin activity or cytokines, or they included patients who were referred routinely for coronary angiography at baseline.

The major limitation of this observational study was that bystander and indirect effects of variables could not be discounted. Therefore, a prospective randomised intervention study is necessary to investigate the effect of vitamin D on the RAS, cytokines profile and, finally, on the prognosis in heart failure patients. Ms. Liu concludes, "This study provides compelling evidence that a high vitamin D status is associated with improved survival in heart failure patients. Until an intervention study has been designed and completed, it seems that we should advise patients with heart failure to maintain appropriate vitamin D levels by taking supplements, by eating oily fish or eggs, or simply by exposure to sunlight."