Peer-Reviewed Papers Demonstrate the Benefit and Value of **MI-HEART CERAMIDES**

Coronary artery disease (CAD) is the most common type of heart disease in the U.S. and the main cause of heart attack. More than 26.6 million adults (11.3%) have been diagnosed with CAD. In 2010, there were 12.4 million physician visits with heart disease (excluding ischemic) as a primary diagnosis.

With so many confirmed/suspected CAD patients being seen at physician offices, it is difficult to know which among them are at the greatest risk and need intervention. Risk conferred by plasma ceramides is independent of LDL cholesterol, HDL cholesterol, C-reactive protein, LDL particles, HDL particles, and Lp-PLA2 (concentration and activity).

These typical markers may not be enough to measure the risk of future cardiac episodes:

- **LDL-C**: Up to 72% of people who have heart attacks have LDL-C levels below 130 mg/dL.
- **LDL-P/ApoB**: Good markers, but all measure the same pathway and only predict the likelihood of coronary artery atherosclerosis.
- **Lp(a)**: Provides important information, but is genetically determined, and only 15% of people express pathological concentrations of Lp(a).
- Furthermore, 19.4% cardiovascular events occur in the absence of traditional risk factors.

**A BETTER TOOL FOR PREDICTING CV RISK**

Ceramides are complex lipids that play a central role in cell membrane integrity, cellular stress response, inflammatory signaling, and apoptosis. Plasma ceramides are predictors of adverse cardiovascular events resulting from unstable atherosclerotic plaque. Risk conferred by ceramides is independent of traditional biomarkers including age, sex, smoking status, and history of CAD.

Plasma ceramides predict adverse cardiovascular events:

- Within 1 year among patients with established coronary artery disease.
- Within 3 to 5 years for patients with suspected CAD and/or chronic heart failure.
The following peer-reviewed publications highlight the clinical value of ceramides.

**Ceramide remodeling and risk of cardiovascular events and mortality**

**Publication/Authors:**  
*J Am Heart Assoc.* 2018 May 3.  
Peterson LR, Xanthakis, V, Duncan MS, et. al.

**Key Point:**  
- Plasma ceramide concentrations are predictive for incident coronary heart disease, heart failure, and cardiovascular mortality in the Framingham Heart Study. Addition of ceramides to a base model, including standard risk factors, significantly improved the C-statistic.

**Plasma ceramides, Mediterranean diet, and incident cardiovascular disease in the PREDIMED trial (prevención con dieta Mediterránea)**

**Publication/Authors:**  
*Circulation.* 2017 May 23.  
Wang DD, Toledo E, Hruby A, et. al.

**Key Points:**  
- This study documented a novel positive association between baseline plasma ceramide concentrations and incidental CVD. In addition, a Mediterranean dietary intervention may mitigate potentially deleterious effects of elevated plasma ceramide concentrations on CVD.

**Plasma ceramides predict cardiovascular death in patients with stable coronary artery disease and acute coronary syndromes beyond LDL cholesterol**

**Publication/Authors:**  
*Eur Heart J.* 2016 Jul 1.  

**Key Point:**  
- Distinct plasma ceramide ratios are significant predictors of CV death in patients with stable CAD and ACS over and above currently used lipid markers. This may improve the identification of high-risk patients in need of more aggressive therapeutic interventions.
The following peer-reviewed publications highlight the clinical value of ceramides.

**Circulating ceramides predict cardiovascular outcomes in the population-based FINRISK 2002 cohort**

**Publication/Authors:**

**Key Points:**
- Distinct serum ceramides are associated with the risk of incident MACE in suspected healthy individuals. These results should encourage more detailed analyses of ceramides in cardiovascular pathobiology and suggest new biomarkers of MACE risk.

**Molecular lipids identify cardiovascular risk and are efficiently lowered by simvastatin and PCSK9 deficiency**

**Publication/Authors:**

**Key Points:**
- These data suggest that distinct ceramides associate significantly with CAD outcome independently of traditional risk factors. The mechanism of lowering lipids is important.
Additional ceramides peer-reviewed publication summary

2019

2018


2017


2016


2015


2014


2013


