participants taking other therapies, such as statins, antiplatelet agents, beta-blockers, and drugs that influence the renin-angiotensin axis. As discussed by Rizos et al.,[144] demonstrating benefits with a low dosage of EPA + DHA (median intake of 1.0 g/day omega-3 acid ethyl esters) when added to these cardioprotective therapies may not be possible.

Mechanisms for ASCVD benefits of long-chain omega-3 fatty acids

Long-chain omega-3 fatty acids may influence ASCVD event risk through a number of mechanisms, including altering susceptibility to ventricular arrhythmia, lowering heart rate and blood pressure, and reducing platelet activation and inflammation.[126] The dose-response characteristics for these various effects have not been fully explored, and the relative importance of these mechanisms in different population subgroups may vary. At higher levels of intake, omega-3 fatty acids lower levels of TG and VLDL-C.

Heart failure

Nestel et al.[146] noted that there may be a benefit for use of omega-3 fatty acid supplements as an adjunct to heart failure therapy. Results of the Gruppo Italiano per lo Studio della Sopravvivenza (GISSI)-Prevenzione Trial[147] showed that there was a substantially larger benefit for sudden cardiac death reductions with EPA and DHA supplementation in patients with ejection fractions <40% compared with those >50% (58% reduction vs 11% reduction, $P = .0003$). In the GISSI-Heart Failure Trial, patients with functional Class II to IV heart failure who were randomized to 1 g/day of EPA and DHA ethyl esters for 3.9 years had an absolute 9% reduction in mortality or hospital admission ($P = .04$). In a subsequent review, Marchioli and Levantesi[148] reported that in 100 heart failure patients, treatment with 1 g/day omega-3 fatty acid supplements was associated with prevention of 1.8 deaths and 1.7 cardiovascular hospitalizations. Moreover, in the GISSI-Heart Failure Trial, baseline plasma phospholipid EPA levels were inversely related to total mortality.[149] The National Heart Foundation of Australia concluded that there is modest support for 1 g/day of omega-3 PUFA in addition to standard therapy for patients with heart failure.[146]

ALA

In a systematic review and meta-analysis of 27 studies, Pan et al.[150] reported an inverse association between ALA intake and total CVD risk. They found a 14% higher incidence in total events in the lowest vs highest tertile of dietary ALA intake and biomarker levels (combined). In the dietary ALA studies, there was a 10% reduction in risk when comparing those with the highest vs those with the lowest tertiles of intake. Each 1 g/day increment of ALA intake is associated with a 10% lower risk of CHD death. This epidemiologic evidence needs to be corroborated with clinical studies that evaluate the effects of ALA on primary prevention of CVD events. The 2010 DGA recommendation for ALA intake was 0.6 to 1.2% of energy, which may lower CVD risk; however, evidence was insufficient to warrant a greater intake.[19]

Dietary considerations for management of hypertriglyceridemia

Part 1 of the NLA Recommendations for Patient-Centered Management of Dyslipidemia endorses non-HDL-C and LDL-C as targets of therapy.[1] Currently, TG is not a specific target for therapy except when levels are ≥500 mg/dL. When the TG concentration is ≥500 mg/dL—and especially if ≥1000 mg/dL—reducing risk of pancreatitis by lowering of TG to <500 mg/dL becomes the primary goal of therapy. For patients with hypertriglyceridemia who have borderline high to high TG (range: 150 to 499 mg/dL), the primary objective of therapy is to reduce risk for an ASCVD event by lowering levels of atherogenic cholesterol (non-HDL-C and LDL-C). The predominant lipoprotein transporter of TG in the blood is VLDL, and the circulating level of TG is highly correlated with VLDL-C, a component of non-HDL-C (non-HDL-C is mainly comprised of LDL-C and VLDL-C).

Non-dietary secondary causes of hypertriglyceridemia, such as medications and disease conditions, including uncontrolled diabetes, hypothyroidism, and renal disease, should be identified and treated where applicable (Refer to Part 1 of the NLA recommendations[1]). Elevated TG (and VLDL-C) reflect multifactorial metabolic imbalances derived from the interaction of genetic and environmental factors and are highly responsive to lifestyle practices.[151–154]

The 2011 AHA Scientific Statement on TG and CVD[152] provides a comprehensive review of the epidemiology, pathophysiology, etiology, special populations and treatment for hypertriglyceridemia, and proposes a practical algorithm for screening and management of elevated TG levels (Fig. 1 adapted[152]). This evidence-based analysis yielded the following conclusion on nutrition and TG management:

> Overall, optimization of nutrition–related practices can result in a marked triglyceride-lowering effect that ranges between 20% and 50%. These practices include weight loss, reducing simple carbohydrates at the expense of increasing dietary fiber, eliminating industrial-produced trans fatty acids, restricting fructose and saturated fatty acids, implementing a Mediterranean-style diet, and consuming marine derived omega-3 PUFA. Dietary practices or factors that are associated with elevated triglycerides levels include excess body weight, especially visceral adiposity; simple carbohydrates, including added sugars and fructose; a high glycemic load; and alcohol.

The NLA has provided practical information for physicians to give patients regarding approaches to reduce TG (Supplemental Figure 1).[155]