Even mild elevations in blood pressure can increase risk. In individuals aged 40 to 70 years with a blood pressure starting at 115/75 mm Hg, ASCVD risk doubles with each increase of 20 mm Hg in systolic blood pressure or 10 mm Hg in diastolic blood pressure (16 [EL 4; NE]). Blood pressure-lowering therapy has been associated with significant decreases in the incidence rates of MI (20-25%), CVA (35-40%), and heart failure (>50%) (16 [EL 4; NE]); however, hypertension may remain an ASCVD risk factor even when normalized with treatment (123 [EL 4; NE]; 124 [EL 2; PCS]; 125 [EL 3; SS]; 126 [EL 2; PCS]). A thorough evaluation of blood pressure, either through 24-hour or home blood pressure monitoring, provides the most accurate results and may be warranted for certain individuals (16 [EL 4; NE]; 28 [EL 4; NE]; 83 [EL 2; PCS]; 127 [EL 2; PCS]).

Cigarette Smoking

Cigarette smoking is a powerful risk factor, especially for MI, peripheral artery disease, and CVA. Smoking accelerates coronary plaque development and may lead to plaque rupture; it is particularly dangerous in individuals with advanced coronary atherosclerosis (14 [EL 4; NE]). The risk of ASCVD mortality for individuals who smoke cigarettes is about double that of lifetime nonsmokers. However, within 1 year of smoking cessation, this risk is reduced by about 50%, and continues to decline with time (128 [EL 4; NE]).

One possible explanation for the ASCVD risk associated with cigarette smoking may be related to its effect on HDL-C. Numerous studies have shown that smoking has a substantial, negative effect on HDL-C levels and the LDL-C to HDL-C ratio. Smoking also appears to have a negative effect on postprandial lipids, including TG (129 [EL 3; SS]; 130 [EL 2; NRCT]; 131 [EL 3; SS]; 132 [EL 2; PCS]; 133 [EL 2; NRCT]; 134 [EL 3; SS]). However, smoking cessation significantly increases HDL-C, with improvements noted as early as 30 days (135 [EL 2; MNRCT]).

Obesity and Overweight

Approximately two-thirds of the adults in the U.S. have overweight (body mass index [BMI] 25 to 29.9 kg/m^2) or obesity (BMI ≥30 kg/m^2) (136 [EL 4; NE]; 137 [EL 3; SS]). It is well documented that individuals who have overweight also have a high prevalence of risk factors such as hypertension, T2DM, and dyslipidemia (138 [EL 2; PCS]; 139 [EL 2; PCS]). In particular, excess visceral or intra-abdominal fat increases and independently predicts ASCVD risk (18 [EL 2; PCS]; 136 [EL 4; NE]; 140 [EL 2; SS]; 142 [EL 2; PCS]). Elevated intra-abdominal fat is highly and independently correlated with insulin resistance (142 [EL 3; CSS]; 143 [EL 3; CSS]) and is also associated with prothrombotic/pro-inflammatory states; increased TG, total cholesterol, LDL-C, small dense LDL-C and apo B; and decreased HDL-C (10 [EL 4; NE]; 142 [EL 3; CSS]; 143 [EL 3; CSS]).

Intra-abdominal obesity is one of the most reliable markers of the insulin resistance syndrome (143 [EL 3; CSS]). Existing U.S. guidelines indicate that a waist circumference greater than 102 cm (40 in) in men or greater than 88 cm (35 in) in women is considered "categorical abdominal obesity" (10 [EL 4, NE]). However, other organizations have adopted a more stringent definition. For example, the International Diabetes Federation defines abdominal obesity as ≥94 cm (≥37 in) for men and ≥80 cm (≥31.5 in) for women; for Asians and Central/South Americans the cutoffs are ≥90 cm (≥35 in) for men and ≥80 cm (≥31.5 in) for women (144 [EL 4, NE]).

LDL Particle Number

The genetically influenced small, dense LDL-C particle is believed to be especially atherogenic, perhaps due in part to its oxidative susceptibility (145 [EL 4; NE]; 146 [EL 4; NE]; 147 [EL 3; CSS]; 148 [EL 4; NE]; 149 [EL 4; NE]; 150 [EL 4; NE]). Several studies point to increased ASCVD risk associated with small, dense LDL-C (151 [EL 2; RCCS]; 152 [EL 3; SS]; 153 [EL 1; RCT]). In addition, evidence from the Framingham Offspring Cohort indicates that primary consideration should be given to measuring and adjusting risk based on particle number (measured directly or as apo B). Specifically, researchers found that compared with LDL-C or non-HDL-C assessments, LDL particle number was a more sensitive indicator of ASCVD risk (20 [EL 3; SS]). The Cardiovascular Health Study and MESA both demonstrated that although LDL-C and LDL particle size are associated with atherogenicity, LDL particle number is a more potent measure of ASCVD risk than either of these 2 measures (154 [EL 2; PCS]; 155 [EL 3; CSS]).

Small, Dense LDL

Small, dense LDL-C is found in 50% of men with ASCVD and is also referred to as LDL pattern B (61 [EL 4; NE]). This pattern is often observed in individuals with elevated TG and low HDL-C, a combination known as the dyslipidemic triad, as well as in individuals with T2DM, the insulin resistance syndrome, and/or chronic anovulation or PCOS (150 [EL 4; NE]; 156 [EL 3; CSS]; 157 [EL 2; CSS]; 158 [EL 2; PCS]; 159 [EL 3; CSS]). Elevated non-HDL-C (i.e., total serum cholesterol – HDL-C) and apo B levels are also clinical markers for the presence of small, dense LDL (80 [EL 4; NE]). Approximately 25% of individuals with small, dense LDL particles inherit this abnormality and do not have hypertriglyceridemia. Measurement of apo B will identify these individuals (156 [EL 3; CSS]). Elevated non-HDL-C (i.e., total serum cholesterol – HDL-C) and apo B levels are also clinical markers for the presence of small, dense LDL (80 [EL 4; NE]).