alongside cardiovascular events and mortality (226 [EL 4; NE]; 228 [EL 2; PCS]; 229 [EL 4; NE]). However, the link between homocysteine levels and cardiovascular event risk is much stronger after disease onset (212 [EL 4; NE]; 226 [EL 4; NE]; 229 [EL 4; NE]; 230 [EL 2; PCS]; 231 [EL 3; CCS]; 232 [EL 2; PCS]; 233 [EL 3; CCS]; 234 [EL 2; PCS]; 235 [EL 2; PCS]). Evaluation of homocysteine levels in individuals with established ASCVD (including ischemia) may help explain the ASCVD etiology (226 [EL 4; NE]). Data from the National Health and Nutrition Examination Survey III (236 [EL 3; SS]) and MESA (237 [EL 3; SS]) have shown that the addition of homocysteine is a powerful tool when used in conjunction with the Framingham Risk Score to identify individuals with ASCVD at high risk who might otherwise be classified as being at intermediate risk.

Elevated homocysteine levels appear to be mediated by deficiencies in folic acid and vitamins B6 and B12 (238 [EL 4; NE]). Although treatment with these supplements lowers plasma homocysteine levels, research to date does not indicate that such therapy reduces ASCVD risk (239 [EL 1; RCT]; 240 [EL 1; RCT]; 241 [EL 1; RCT]; 242 [EL 1; RCT]; 243 [EL 4; NE]). Therefore, homocysteine measurement is not recommended as part of routine screening.

Elevated Uric Acid

Increased serum uric acid levels are linked to insulin resistance syndrome, obesity, dyslipidemia, and hypertension (244 [EL 3; SS]). Data from the First National Health and Nutrition Examination Survey and the National Health and Nutrition Examination Survey 1 Epidemiologic Follow-up Study showed a significant increase in ASCVD mortality among the highest uric acid quartile (>6.99 mg/dL for men and >5.6 mg/dL for women), suggesting that uric acid may be an independent risk factor (244 [EL 3; SS]). However, Framingham research evaluating the impact of uric acid lowering has not shown a positive effect on reducing CV events (245 [EL 2; PCS]). Therefore, available evidence indicates that the role of uric acid in ASCVD risk remains undefined (245 [EL 2; PCS]; 246 [EL 4; NE]).

ASCVD Risk and the Insulin Resistance Syndrome

Individuals who have insulin resistance are at increased risk for developing a cluster of abnormalities known as the insulin resistance syndrome (15 [EL 4; NE]). Although this is sometimes referred to as MetS or dysmetabolic syndrome, the AACE prefers the term *insulin resistance syndrome*, as this more accurately pinpoints the underlying pathophysiology of insulin resistance and compensatory hyperinsulinemia that unites these conditions (15 [EL 4; NE]). The components of the insulin resistance syndrome, outlined in Table 7, include important risk factors for ASCVD. Thus, individuals with the insulin resistance syndrome are at increased risk for developing ASCVD. Likewise, individuals who do not have diabetes but have a diagnosis of ASCVD have a greater prevalence of the insulin resistance syndrome than those without ASCVD (15 [EL 4; NE]). Individuals who are insulin resistant will not necessarily develop all of the abnormalities that comprise the insulin resistance syndrome; however, the identification of even 1 component raises the likelihood of an insulin resistance syndrome diagnosis (15 [EL 4; NE]).

Elevated blood glucose is a late and possibly terminal manifestation of insulin resistance. Before the development of hyperglycemia, diagnosing insulin resistance syndrome may be difficult, with no simple, single clinically measurable test available (15 [EL 4; NE]). However, the components of the insulin resistance syndrome are frequently identifiable. Individuals who exhibit nonhyperglycemic signs of insulin resistance should undergo further assessment, with consideration given to performing a 2-hour, 75-g oral glucose tolerance test (15 [EL 4; NE]).

CKD

Growing evidence suggests that individuals with CKD, who represent a growing population, have increased risk for ASCVD (17 [EL 2; MNRCT]). It appears that the increased risk of ASCVD does not occur only in individuals with end-stage renal disease, but also in those with mild-to-moderate chronic renal dysfunction. These findings led the National Kidney Foundation in 2002 to consider CKD as an ASCVD equivalent (247 [EL 4; NE]).

Chronic Inflammatory Conditions

Individuals with chronic inflammatory conditions such as rheumatoid arthritis, systemic lupus erythematous, and ankylosing spondylitis appear to have an increased risk of ASCVD. In the Nurses' Health Study, individuals who had had rheumatoid arthritis for more than 10 years appeared to have an increased risk for ASCVD compared with individuals without rheumatoid arthritis (relative risk, 3.1; confidence interval [CI], 1.64-5.87) (248 [EL 2; PCS]). Also in the Nurses' Health Study that included 119,332 female nurses, systemic lupus erythematous was eventually diagnosed in 148 women. The age-adjusted relative risk of ASCVD was 2.25 (95% CI, 1.77-4.27), while after adjustment for other traditional risk factors, the hazard ratio (HR) remained greater than 2 for the group of women with systemic lupus erythematous (249 [EL 2; PCS]). Increased prevalence of ASCVD has been also reported in individuals with ankylosing spondylitis (250 [EL 3; CSS]).

Human Immunodeficiency Virus (HIV)

Individuals with HIV appear to have increased risk of ASCVD. It is not well established whether the increased risk for ASCVD is secondary to traditional or nontraditional risk factors, such as changes in body composition (lipoatrophy/lipodystrophy) or inflammation, effect of antiretroviral medications, or direct effects of HIV on the vasculature (251 [EL 4; NE]).