IGF-1 and Cardiovascular and Non-Cardiovascular Mortality Risk in Patients with Chronic Kidney Disease: A Model of “Malnutrition-Inflammation-Atherosclerosis Syndrome”

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See article vol. 29: 000-000

Cardiovascular (CV) and Non-CV Mortality Risk in Chronic Kidney Disease (CKD) and End-Stage Renal Disease (ESRD)

CKD is an independent risk factor for CV diseases (CVDs). Events in patients with CKD included are atherosclerotic CVD such as acute myocardial infarction or stroke, but also non-atherosclerotic events such as sudden cardiac death or fatal arrhythmia. Notably, patients with CKD have a higher risk not only for the incidence of CVD but also for death after CVD events. All-cause mortality and CVD mortality rates increase with progression of the stage of CKD and most dramatically when patients reach ESRD.

Increased mortality in CKD/ESRD is considered to occur from traditional and emerging risk factors in this population. Traditional CV risk factors in CKD/ESRD include older age, male sex, hypertension, high low-density lipoprotein-cholesterol and low high-density lipoprotein-cholesterol, diabetes smoking, physical inactivity, menopause, family history of CVD, and left ventricular hypertrophy. Emerging risk factors include albuminuria, anemia, abnormal calcium/phosphate metabolism, extracellular fluid volume overload electrolyte imbalance, oxidative stress, inflammation (C-reactive protein), malnutrition, thrombogenic factors, and sleep disturbances.

IGF-1 and CV and Non-CV Mortality Risk

In the current study, Nakaya et al. showed that a lower insulin-like growth factor 1 (IGF-1) level is an independent predictor of all-cause mortality, and that it also predicts poor survival after new CVD events and infection in a Japanese cohort of hemodialysis patients. Divided into two steps, they suggested that a lower IGF-1 level can be linked not preferentially to the first step (occurrence of a CVD event), but to the second step (death after the CVD event). In addition, they suggested that a lower serum IGF-1 level serves as a biomarker of frailty in hemodialysis patients.

Sarcopenia is a progressive and generalized skeletal muscle disorder involving the enhanced loss of muscle mass and function, often associated with muscle weakness (dynapenia) and frailty. While primary sarcopenia develops with age, secondary sarcopenia develops independently of age in the milieu of chronic disease such as CKD/ESRD. Sarcopenia, as well as its components, has been frequently shown to be associated with adverse outcomes, including multiple morbidity and all-cause mortality.

The development of sarcopenia in patients with CKD/ESRD is common, and it may occur independently of weight loss, cachexia, or obese sarcopenia via multifactorial mechanisms. Hormonal imbalance is a cause of development of sarcopenia in CKD/ESRD and may be another emerging risk for all-cause and CVD mortality. Hormones that may influence the development of sarcopenia include testosterone, growth hormone and IGF-1, insulin, thyroid hormones, vitamin D, and gherlin, estrogen, cortisol, and dehydroepiandrosterone. As mentioned above, the possible underlying mechanisms for the link between IGF-1 level and mortality in CKD/ESRD may be elucidated (Fig. 1). Previous reports suggested that “malnutrition-inflammation-atherosclerosis syndrome,” “malnutrition-inflammation complex syndrome,” and protein-energy wasting are the factors closely related to the
second step to CV death.

The paper prompted us to consider that IGF-1 and other related molecules can be a biomarker of frailty for all-cause and CVD mortality in patients with CKD/ESRD and also with other chronic diseases.

Conflict of Interest

None.

References


