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iREVIEWS

STATE-OF-THE-ART PAPERS

Defining the Natural History of Uremic Cardiomyopathy in Chronic Kidney Disease

CME

The Role of Cardiovascular Magnetic Resonance

Nicola C. Edwards, PhD, William E. Moody, MBChB, Colin D. Chue, MBChB, Charles J. Ferro, MD, Jonathan N. Townend, MD, Richard P. Steeds, MA, MD

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CME Objective for This Article: After reading this article the reader should understand: 1) the prevalence and clinical importance of cardiovascular disease across all stages of chronic kidney disease (1 to 5); 2) the role and limitations of different imaging modalities to characterize the various phenotypes of uremic cardiomyopathy; and 3) the application of recent advances on echo and cardiac magnetic resonance which provide additional insight into the causes and consequences of myocardial disease in chronic kidney disease.

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From the Birmingham Cardio-Renal Group, University of Birmingham and Queen Elizabeth Hospital Birmingham, Birmingham, United Kingdom. Dr. Chue has received an unrestricted educational grant, as well as lecture and advisory board fees, from Genzyme Corporation. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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Defining the Natural History of Uremic Cardiomyopathy in Chronic Kidney Disease

The Role of Cardiovascular Magnetic Resonance

ABSTRACT

Chronic kidney disease (CKD) is an under-recognized, highly prevalent cardiovascular (CV) risk factor affecting 1 in 7 adults. Large epidemiological studies have clearly established a graded association between the severity of CKD and CV event rates. Although patients with end-stage renal disease who are undergoing dialysis are at greatest CV risk, the disease process is evident in the early stages of CKD with glomerular filtration rates as high as 75 ml/min/1.73 m^2. Indeed, these patients are at least 6 times more likely to die of CV disease than to reach end-stage CKD. Thus, the major impact of CKD on the population and the healthcare budget is not that of providing renal replacement therapy but the cost of death and disability from premature CV disease.

Although end-stage CKD is characterized by a clustering of conventional atherosclerotic risk factors, it has little association with CV event rates. This is reflected in disproportionate levels of sudden cardiac death, heart failure, and stroke, rather than myocardial infarction. Thus it appears that *nonatherosclerotic processes*, including left ventricular hypertrophy and fibrosis, account for most of the excess CV risk. Over the past decade, the use of cardiac magnetic resonance in CKD has brought about an improved understanding of the adverse CV changes collectively known as uremic cardiomyopathy. The unique ability of cardiac magnetic resonance to provide a comprehensive noninvasive examination of cardiac structure and function, arterial function, myocardial tissue characterization (T_1 mapping and inversion recovery imaging), and myocardial metabolic function (spectroscopy) is ideally suited to characterize the phenotype of CV disease in CKD and to provide insight into the mechanisms leading to uremic cardiomyopathy. Concerns relating to an association between gadolinium contrast agents and nephrogenic systemic fibrosis in dialysis recipients have led to the use of lower doses and lower-risk gadolinium agents that appear to minimize this risk. (J Am Coll Cardiol Img 2014;7:703–14) © 2014 by the American College of Cardiology Foundation.

The term chronic kidney disease (CKD) encompasses all renal disease states from the earliest stages through to end-stage renal disease (ESRD) requiring renal replacement therapy (**Table 1**). Although the cardiovascular risk of patients with ESRD is extreme, the major burden lies in early-stage CKD, which is highly prevalent. Early-stage CKD affects 10% to 16% of adults in developed nations with a prevalence that is increasing rapidly as the population ages and as rates of obesity, diabetes, and hypertension continue to rise (1). Although most of the original studies examining cardiovascular disease in CKD focused on patients with ESRD, more recent large studies have demonstrated that cardiovascular risk increases very early in the natural history of CKD, probably at a glomerular filtration rate (GFR) level of approximately 75 ml/min/1.73 m^2 when serum creatinine may still be within the normal range (2). The risk of cardiovascular death in early-stage CKD far exceeds the risk of progressing to dialysis; therefore, treatment should be focused at least as much on reducing this risk as on reducing the rate of progression of renal disease.

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Epidemiological studies suggest that most cardiovascular deaths that occur in ESRD are attributable to sudden cardiac death, arrhythmia, or congestive heart failure, and relatively few deaths result from coronary artery disease and myocardial infarction (3). Although traditional cardiovascular risk factors are more common in patients with CKD, these fail to account for the elevated risk. This finding suggests that the mechanistic processes driving cardiovascular disease in CKD may differ from those in the general population (**Table 2**). Nonatheromatous processes such as arteriosclerosis, arterial stiffening, and abnormalities of cardiac structure appear to predominate and could explain why standard cardiovascular disease–modifying drugs such as statins have failed to have the same impact on cardiovascular mortality in CKD as they do in the general population (4). Thus, detection of these