

## Utility of Echocardiography in the Evaluation of Coronary Artery Disease in Patients with End-Stage Renal Disease

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*Patients with chronic kidney disease (CKD) are at increased risk of cardiovascular events. Echocardiography is an integral part of the evaluation of coronary artery disease. Chronic kidney disease has a predictable and unique effect on the myocardium and the epicardial circulation that may be detected by echocardiography. In particular, dobutamine stress echocardiography has proved to be an invaluable tool in the detection of cardiovascular disease in patients with CKD. Here, we review the usefulness of echocardiography in the detection and evaluation of coronary artery disease in patients with CKD.*

### Key words

Echocardiography, chronic kidney disease, coronary artery disease, dobutamine stress echocardiography

### Introduction

Chronic kidney disease (CKD) is a well-established risk factor for coronary artery disease (1). In 1998, the U.S. National Kidney Foundation Task Force on Cardiovascular Disease in Chronic Renal Disease recommended that patients with CKD be considered to belong to the highest risk group for the development of cardiovascular events (2). As compared with diabetes mellitus, CKD imparts a higher risk of mortality and adverse outcomes in acute coronary syndromes (3).

### Discussion

#### *Syndromes*

The detection of ischemic heart disease in CKD and dialysis patients can be difficult. Diabetes is frequently

associated with CKD (1). Thus, patients with chronic renal failure may often experience silent ischemia.

Patients with CKD commonly develop mitral annular calcification, aortic sclerosis, and calcification of the aortic arch (4). Mitral annular calcification is associated with decreased left ventricular function, treatment with dialysis, and inflammation as characterized by high-sensitivity C-reactive protein (5). Mitral annular calcification is associated with significant coronary artery disease and increased mortality in patients with end-stage renal disease. These patients tend to have increased left ventricular cavity size, poorer systolic function, and higher systolic filling pressures (6).

Pericardial effusion commonly develops in uremia. Uremic pericarditis can present as an acute chest pain syndrome that may be confused clinically with an acute coronary syndrome. Chest pain, fever, leukocytosis, and pericardial friction rub are classic signs of uremic pericarditis. Hypotension during or after ultrafiltration in a dialysis patient with pericardial effusion may indicate a low-pressure tamponade physiology. Dialysis-associated pericardial effusions may present with low blood urea nitrogen and creatinine (7).

Mitral valve regurgitation may also be an indication of ischemic heart disease in patients with CKD. The papillary muscles attached to the posterior leaflets of the mitral valve receive their blood supply from the terminal portion of the posterior descending coronary artery. Posterior ischemia may lead to papillary muscle dysfunction, scarring, and possible rupture. Ischemic regurgitation may be differentiated from other causes of mitral regurgitation such as mitral valve prolapse, infective endocarditis, and congenital causes of mitral regurgitation. Mitral prolapse typically affects the anterior leaflet of the mitral valve and is characterized by a classic

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“parachute” appearance protruding into the left atrium during systole. Infective endocarditis may affect either leaflet and is often associated with vegetations. Congenital defects may include fenestrations within the leaflets that are often associated with other cardiac congenital malformations (8).

#### Detection

Echocardiography is a valuable tool in assessing cardiac structure and function in patients with CKD. Corya was the first to review the echocardiographic findings of ischemic heart disease (9). Regional wall motion abnormalities and myocardial thinning with systole all correlate well with critical narrowing of the coronary lumen. These findings become more evident with the induction of myocardial stress.

Stress testing in patients with CKD is a challenge. Patients with CKD are often unable to exercise because of poor functional capacity. In addition, many patients have baseline ST–T wave changes (that is, left ventricular hypertrophy) that interfere with the interpretation of stress echocardiograms. Compared with other stress modalities, dobutamine stress echocardiography (DSE) in CKD may have increased sensitivity and specificity in patients with hypertension and left bundle branch block (10,11).

Indications for DSE include detection of significant coronary artery disease, evaluation of myocardial viability, and cardiac risk stratification in patients who are unable to exercise or who have a contraindication to vasodilator forms of stress testing. Contraindications to stress echocardiography include recent myocardial infarction, unstable angina, significant aortic stenosis or obstructive cardiomyopathy, atrial tachyarrhythmias with uncontrolled ventricular response, uncontrolled hypertension, thoracic aortic aneurysm, and left bundle branch block (12).

Dobutamine stress echocardiography is performed in a monitored setting by a nurse, echocardiographer, and supervising physician. Resting echocardiographic images are obtained and stored for later comparison with stress images. Dobutamine is infused continuously, and the dose is increased incrementally every 3–5 minutes. This infusion results in a gradual and usually well-tolerated increase in heart rate and contractility. Low-dose images are obtained and stored. Atropine is used in patients with a blunted heart-rate response. After reaching an age-based target heart rate, stress images are obtained before cessation of

the infusion. Recovery images are obtained after the heart rate has returned to baseline. These images are displayed on a screen split into quadrants and are then compared side-by-side by an experienced cardiologist and evaluated for new left ventricular wall motion abnormalities indicative of ischemia revealed by the varying stages of stress (13).

Marwick *et al.* were the first to demonstrate the prognostic value of DSE in the presence of CKD (14). They followed 193 consecutive CKD patients (serum creatinine above 2.5 mg/dL) who had undergone DSE over a period of  $38 \pm 14$  months. Stress echocardiography was performed to detect coronary artery disease in patients with chest pain or prior myocardial infarction, or in preparation for dialysis or renal transplantation. The study concluded that patients with ischemia noted on baseline scans experienced a high rate of ischemic events at 24 months. Ischemia at baseline echo was not an independent predictor of adverse clinical events after 24 months.

Rakhit *et al.* used dobutamine stress echo combined with three cardiac-event risk models to optimize risk stratification in patients with CKD. The Framingham, Brisbane, and Portland risk scores were applied to 224 patients with CKD who underwent DSE. Lower diastolic blood pressure, ischemia with reduced left ventricular function, and angina during the test were independent predictors of cardiac events (15). Use of these clinical risk scores combined with DSE improved the predictive power of DSE alone.

More recently, studies have attempted to refine and further characterize the relationship between ischemia diagnosed with DSE and CKD. Bergeron *et al.* evaluated 485 patients over a period of  $2.3 \pm 1.8$  years. Chronic kidney disease was defined as serum creatinine above 3.0 mg/dL or as dialysis dependence. They observed that the percentage of ischemic myocardial segments on DSE was an independent predictor of mortality and cardiac events. Patients with more than 25% ischemic segments experienced the lowest survival over the study period (16).

The largest study to date was published by Karagiannis *et al.* in 2008. Over a period of 8 years, they followed 2292 patients with CKD who had undergone DSE for detection of coronary artery disease. Patients who were dialysis-dependent with more than four ischemic segments on DSE experienced nearly 80% mortality over the trial period. In addition, those authors found that the “warranty period” of a normal

DSE in patients with moderate renal dysfunction was approximately 15 months, with a 10% risk for hard cardiac events and cardiac deaths. They concluded that the “warranty period” of normal DSE depended more on the severity of renal dysfunction than on the number of abnormal myocardial segments (17).

Transesophageal echocardiography (TEE) has also been used predict cardiovascular risk. Leskinen *et al.* used TEE to detect aortic plaque in patients with CKD. Their study included 118 patients who were followed over  $3.4 \pm 0.8$  years. Patients with no aortic atherosclerotic plaque were unlikely to have coronary artery disease (sensitivity: 73%; specificity: 90%). The positive predictive value of aortic atherosclerotic plaque for the presence of coronary artery disease was 95%. In addition, the size of the aortic plaque seemed to correlate with the severity of the coronary artery disease (18).

### Summary

Echocardiography remains an important tool in the evaluation of ischemic heart disease in CKD. In particular, DSE is highly sensitive and specific for the detection of ischemia. It also predicts outcome in patients with CKD.

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