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# Mitral annular calcification predicts coronary artery disease in end-stage renal disease patients on hemodialysis

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## Abstract

### Background

Mitral annulus calcification (MAC) is a chronic, degenerative process of the fibrous support structure of the mitral valve. The reported prevalence of MAC is between 8 and 15%, but it significantly increases with age and in patients with multiple cardiovascular risk factors or chronic kidney disease.

### Aim

The aim of this study was to determine whether MAC predicts coronary artery disease in a group of end-stage renal disease patients.

### Patients and Methods

Twenty-three patients with ESRD on hemodialysis referred for coronary angiography were prospectively studied.

### Results

This study included 23 patients, MAC was seen in nine patients (39%). Seven patients had significant coronary artery disease (CAD) (30%). Ten patients had impaired left ventricular function (LVEF <50%) but none had severe impairment (LVEF <30%).

### Conclusion

MAC occurs in a proportion of patients with ESRD and is associated with increased mortality and the presence of significant CAD.

**Keywords:** End stage renal disease, hemodialysis, mitral annulus calcification

## INTRODUCTION

Mitral annular calcification (MAC) is associated with cardiovascular mortality and coronary artery disease in the general population [1,2]. The presence of MAC is a strong risk factor for stroke [3,4] and incident atrial fibrillation [5]. MAC is common in the setting of end-stage renal disease (ESRD) [6–9] and in patients with chronic kidney disease before the onset of ESRD [10]; the significance of MAC in ESRD remains uncertain.

The mitral annulus separates the left atrium from the left ventricle (LV). It has a complex saddle shape that is divided into anterior and posterior portions. The anterior annulus spans the left and right fibrous trigones and is anatomically coupled to the aortic annulus. The posterior annulus encompasses the remainder of the annular perimeter and is composed of a

discontinuous rim of fibrous tissue periodically interrupted by fat [11]. MAC is defined as a chronic degenerative process in the fibrous base of the mitral valve [12–14]. Shurmur *et al.* suggested an association with conduction defects but not mortality in a group of haemodialysis patients [11]. Wang *et al.* suggested that cardiac calcification predicts all-cause and cardiac mortality in long-term peritoneal dialysis patients [7]. Large historical autopsy studies found MAC in ~10% of patients [14,15]. MAC more commonly affects the posterior annulus than the anterior annulus [15,16].

Occasionally, a chest radiograph might show the calcific demarcation of the mitral annulus. MAC is usually C-, J-, U-,

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or O-shaped, with the open part lying at the site of the aortic outflow tract [13] The lateral projection usually demonstrates better mitral calcification because the overlying spine and the main left lower lobe arteries in the poster anterior view may mask its visualization. Fluoroscopy during coronary angiography can also show mitral calcification but is not an accurate modality for the assessment of the extent of MAC.

## PATIENTS AND METHODS

### Population

Twenty-three patients with ESRD on hemodialysis referred to the National Heart Institute over the period between February 2012 and October 2013 for coronary angiography were prospectively studied. Exclusion criteria were age less than 20 years, acute coronary syndrome, severe LV dysfunction, and severe aortic stenosis.

### Risk factors assessment

Routine precatheter assessment for risk factor was done as follows:

- (1) Age.
- (2) Sex.
- (3) Blood pressure.
- (4) Diabetes mellitus.
- (5) Dyslipidemia.
- (6) Blood tests: blood samples were obtained from all patients at the time of echocardiography. Full hematological profile, serum creatinine, fasting cholesterol, fasting glucose, calcium, phosphate, and high-sensitivity C-reactive protein were measured.

### Echocardiography

Two-dimensional measurements were performed as recommended by the American Society of Echocardiography. LV ejection fraction (LVEF) was determined by mortified biplane Simpson's rule. Impaired LV systolic function was defined as an LVEF less than or equal to 50.

The diagnosis of MAC was by M-mode and two-dimensional cross-sectional transthoracic echocardiography. On M-mode echocardiography, the diagnosis was dependent on the presence of an echodense band visualized through one systole and diastole, distinguishable from the posterior mitral valve leaflet and located anterior and parallel to the posterior LV wall [3]. On cross-sectional echocardiography, the diagnosis was made by the presence of an intense echo-producing structure boasted at the junction of the atrioventricular groove and posterior mitral valve leaflet on the parasternal long axis.

Tran's mitral inflow was recorded using pulsed-wave Doppler recordings at the mitral valve leaflet tips in an apical four-chamber view. Peak velocity of early filling (E), of atrial filling (A) and the E/A ratio were measured.

### Coronary angiography

Coronary angiography was performed in all patients. Coronary artery stenosis severity of each epicardial artery was assessed

**Table 1: Patient characteristics**

Age (years)	40±15
Sex	18 males:5 female
Serum creatinine (µmol/l)	11±267
Serum hemoglobin (g/l)	9±1.2
Cholesterol (µmol/l)	200±1.07
Hs-CRP (µmol/l)	82.8
NYHA class [n (%)]	
0	13 (58)
1	5 (21)
2	5 (21)
Diabetes	10 (43)
Hypertension	21 (92)
Systolic blood pressure (mmHg)	151±15
Diastolic blood pressure (mmHg)	88±14
Raised cholesterol [n (%)]	13 (56)
Smoker [n (%)]	9 (39)
Significant CAD at angiography [n (%)]	7 (30)
MAC [n (%)]	9 (39)

CAD, coronary artery disease; Hs-CRP, high-sensitivity C-reactive protein; MAC, mitral annulus calcification; NYHA, New York Heart Association.

visually and graded as follows: normal, mild (<50 luminal narrowing); moderate (50–70% luminal narrowing), and severe (>70% luminal narrowing). Significant coronary artery disease was defined as a severe stenosis in one or more coronary arteries.

## RESULTS

This study included 23 patients, 18 men and five women; the mean age was 40 ± 15 years; the patient characteristics are shown in Tables 1 and 2:

- (1) MAC was seen in nine patients (39%).
- (2) Seven patients had significant coronary artery disease (CAD) (30%).
- (3) 10 patients had impaired left ventricular function (LVEF <50%) but none had severe impairment (LVEF <30%).

## DISCUSSION

In this study, we have demonstrated that MAC predicts cardiovascular morbidity in an unselected group of renal patients. The results support previous studies suggesting that MAC predicts mortality in the general population [2]; Patients on long-term dialysis [7] and patients with chronic kidney disease [10] Unique to this study in ESRD was the fact that all patients had coronary angiography. The results differ from the study by Shurmer *et al.*, who concluded an association between MAC and conduction defects but not mortality in 66 dialysis patients with a 12-month follow-up. MAC was also associated with larger LV cavity size, impaired LV systolic function, and significant CAD. Patients with MAC had higher serum high-sensitivity C-reactive protein calcium and phosphate concentrations, but the total

**Table 2: Difference in patients with and without mitral annulus calcification**

	MAC (n=9, 39%)	No MAC (n=14, 6%)	P
Age (years)	40±15	41±10	0.005
Creatinine (mg)	10.9±2.69	580±243	0.04
Estimated glomerular filtration rate (ml/min)	12±7	16±5	0.08
Diabetic patient [n (%)]	10 (45)	8 (34)	0.03
Systolic blood pressure (mmHg)	156±18	154±16	0.37
Diastolic blood pressure (mmHg)	82±10	84±12	0.41
Number with significant CAD [n (%)]	5 (55)	2 (15)	<0.001
Hemoglobin (g/l)	9.6	9.8	0.64
Cholesterol (mg)	220±1.6	180	0.12
Calcium (mg %)	9.3±15	8.2±2	0.002
Phosphate (mg %)	3.5±0.38	2.5±0.34	0.002
LVESD (cm)	3.2±0.9	2.6±0.7	0.004
LVEDD (cm)	5.2±0.9	4.6±1.0	0.05
LVFS (%)	33±11	40±8	0.03
LVEF (%)	6±15	72±12	0.02
Left atrium (cm)	4.6±2.1	4.1±2.6	0.001
Mitral E/A ratio	13.5±6.8	9.7±4.1	0.02

CAD, coronary artery disease; LVEF, left ventricular ejection fraction; LVEDD, left ventricular end-diastolic dimension; LVESD, left ventricular end-systolic dimension; LVFS, left ventricular fractional shortening; MAC, mitral annulus calcification.

cholesterol was similar to those without MAC. MAC is a fibrous; degenerative calcification of the mitral valve ring. In the general population, it is associated with endocarditis, CAD, stroke, atrial fibrillation, and heart failure [3,5]. In a prospective study of 1197 Framingham Heart Study patients, MAC was associated with cardiovascular disease and cardiovascular mortality [2]. MAC occurred in 14% of these patients. This study, in which 39% of patients had MAC, supports previous reports suggesting a much higher prevalence of MAC in ESRD [6,7], the likely reasons include age, male sex, diabetes, and length of time on dialysis. Indeed, in our study, MAC was associated with impaired LV systolic function, left atrial dilatation, and higher incidence of CAD in these patients.

The observed higher cardiac morbidity of ESRD patients with MAC is in part due to the association with CAD and cardiac structural abnormalities. This study has demonstrated that MAC predicts CAD, cardiac structural changes, and morbidity in an unselected group of patients with renal disease and who are on hemodialysis.

## CONCLUSION

MAC occurs in a proportion of patients with ESRD and is associated with increased mortality and the presence of significant CAD. These patients have increased LV cavity size, and poorer LV systolic function; there is also an association with diabetes and high calcium and phosphate.

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## Conflicts of interest

There are no conflicts of interest.

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