

Hazards of Mitral Valve Replacement for Mitral Stenosis Caused by Massive Mitral Annular Calcium With or Without Aortic Valve Replacement for Aortic Stenosis



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Mitral annular calcium (MAC) is common in older adults in the Western World and if extensive may cause mitral stenosis. The purpose of this report is to describe outcomes of 12 patients having mitral valve replacement for mitral stenosis secondary to massive MAC. Operatively excised deposits of calcium removed from the mitral annular area and the accompanying stenotic mitral valves were examined and then the patients' medical records were examined to confirm the diagnosis and the degree of valvular dysfunction. A total of 12 patients with massive MAC causing mitral stenosis and receiving mitral valve replacement with or without aortic valve replacement for aortic stenosis were observed in 2013 to 2015. Of the 12 patients, 7 died from 5 to 44 days (mean 19) after the valve operation and all had "stormy" postoperative courses; one survived 150 days and another, 600 days; the remaining 3 were improved by the operation and are alive 22, 27, and 59 months postoperatively. In conclusion, the high mortality in these patients suggests that mitral valve replacement in the setting of massive MAC be considered with caution. © 2018 Elsevier Inc. All rights reserved. (Am J Cardiol 2019;123:650–657)

Deposits of calcium beneath the posterior mitral leaflet and especially near its attachment to the left atrial and left ventricular junctional regions, so called *mitral annular calcium* (MAC), is relatively common in older patients, especially in women, in patients with chronic renal disease, in those with left ventricular outflow obstruction (aortic stenosis [AS] and hypertrophic cardiomyopathy), and in younger persons with mitral valve prolapse, mucopolysaccharidosis and the Marfan syndrome.^{1–8} In older patients MAC is usually accompanied by calcific deposits in the epicardial coronary arteries and in the aortic valve cusps, producing what has been termed “the senile cardiac calcification syndrome”⁹ (Figure 1). The quantity of calcium in the mitral annular region varies from minimal to massive and when the latter is the case the result may be mitral stenosis (MS), especially in the setting of associated AS.^{10–15} We have encountered through the years many patients who have had aortic valve replacement for AS and who had massive MAC but no operative procedure was carried out on the mitral valve (Figure 2). In recent times in patients with combined AS and massive MAC causing MS there has been a tendency among some surgeons to replace the mitral valve as well as the aortic valve in this scenario.^{16–25} This report describes certain clinical and morphologic findings

in 12 patients with massive MAC causing MS and leading to isolated mitral valve replacement or to combined mitral and aortic valve replacement, the latter for AS.

Methods

Since March 1993, I have examined, described, and submitted the report on all surgical specimens excised from the heart or aorta at Baylor University Medical Center (BUMC). During a recent 3-year period—2013, 2014, and 2015—portions of the mitral valve in 130 patients were submitted to the surgical pathology unit of the department of pathology at BUMC (Figure 3). Of the 130 patients, 58 (45%) had mitral valve repair for pure mitral regurgitation (no element of stenosis), and 73 (56%) had mitral valve replacement. Of the latter 72 patients, 53 (74%) had isolated mitral valve replacement (only the mitral valve was replaced) and 19 (26%) had replacement of both the mitral and aortic valves. Of the 53 patients with isolated mitral valve replacement; 16 (30%) had mitral stenosis resulting from massive MAC in 6 and from rheumatic heart disease in 10. Of the 19 patients having combined mitral and aortic valve replacements, 10 had combined mitral stenosis and aortic stenosis, the result of rheumatic heart disease, and in 6 from massive MAC. This report focuses on the 6 patients having MS and isolated mitral replacement from massive MAC, and on the 4 patients who had both mitral and aortic valve replacement for combined MS resulting from massive MAC and aortic valve stenosis. Additionally, 2 other patients with massive MAC causing MS and associated with AS and operated on at another Dallas hospital also were included in this study.

The medical records in all of the 130 patients were examined.

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Figure 1. Shown here is a radiograph of the heart specimen at autopsy in an 82-year-old woman who died of volvulus of the colon. She never had symptoms of cardiac dysfunction. The amount of calcium in the mitral annular area is enormous. The calcium behind posterior mitral leaflet forms a beautiful “C” and the bar of calcium below the aortic valve is that on the ventricular aspect of anterior leaflet. Calcific deposits also are present in each of the three valve cusps causing some degree of aortic stenosis. Additionally, calcium is present focally in the left circumflex and left anterior descending coronary arteries. (Figure reproduced from Roberts WC, Perloff JK. Mitral valvular disease: A clinicopathologic survey of the conditions causing the mitral valve to function abnormally. *Ann Intern Med* 1972 Dec; 77:939–975.)

“Massive MAC” was defined by the presence of a huge quantity of calcium underlying the posterior mitral leaflet forming a circle C and extending across all or nearly all of the ventricular aspect of the anterior mitral leaflet to “close” the “C” forming a circle O. Examples of massive MAC forming a circle O are shown in [Figures 1 and 2](#).

The present study includes all patients having mitral valve replacement for massive MAC encountered at BUMC during the 3-year period (2013 to 2015). Several other patients having mitral valve replacement for mitral valve prolapse causing mitral regurgitation had small focal deposits of calcium behind posterior mitral leaflet but in no patients were the deposits behind mitral leaflet large and in none did calcium extend across the ventricular aspect of anterior mitral leaflet.

Results

Pertinent clinical and morphologic data in these 12 patients were sought and the findings are summarized in [Table 1](#). The 12 patients ranged in age from 25 to 82 years (median 59); 8 were women and 4 were men. Six patients had isolated mitral valve replacement and 6 had combined mitral and aortic valve replacement.

Preoperatively, the peak systolic pulmonary pressures ranged from 50 to 117 mm Hg (average 79); the pulmonary artery wedge-left ventricular mean diastolic gradients at rest ranged from 6 to 23 mm Hg (average 11) and the peak systolic left ventricular to systemic artery peak pressure gradients ranged from 20 to 28 mm Hg. Four patients had considerable coronary arterial narrowing by angiogram, 3 of whom had coronary bypass performed. Preoperatively,

8 patients had atrial fibrillation, 1 had complete heart block, and 1 had right bundle branch block. Six patients had diabetes mellitus. The body mass index (11 patients) ranged from 21 to 52 kg/m² including 8 patients (73%) in whom the value was ≥ 30 kg/m². The 12 patients were operated on by 5 different surgeons.

Of the 12 patients, 7 died from 5 to 44 days after valve replacement, 1 at 150 days and 1 other at 600 days after the valve replacement. The remaining 3 were improved by the operation and are alive 22, 27, and 59 months after the valve operation. The operatively-excised mitral specimens ranged in weight from 1.92 to 7.20 g. The operatively excised aortic valves (3 patients) weighed 0.49, 1.20, and 2.95 g, respectively.

Several of the operatively excised mitral and aortic specimens are illustrated in [Figures 4 to 8](#). Autopsies were performed in 2 patients: in each considerable quantities of calcium remained in the mitral annular area. Periannular mitral disruptions were present in each of the 2 autopsied patients.

Discussion

It is apparent from study of these hitherto described 12 patients that mitral valve replacement in the setting of massive MAC is hazardous. Nine of the 12 patients have died, 7 within 45 days of the operation and 2 others 150 and 600 days, respectively, postoperatively. The postoperative courses in the 7 early deaths were complicated by stroke; excessive bleeding (requiring return to the operating room); parabasililar mitral regurgitation; long periods of intubation, and usually evidence of inadequate cardiac output (“multiorgan failure”).

In the early days of cardiac valve replacement (1960s and 1970s), combined mitral and aortic valve replacement was a frequent procedure and was usually because of rheumatic heart disease, most commonly resulting in stenosis of both valves, occasionally causing pure regurgitation of both valves, and rarely producing 1 stenotic and 1 purely regurgitant valve. Today in the Western World, rheumatic heart disease, of course, is far less frequent than in the past, and now both isolated MS and that combined with AS may commonly be the result of massive MAC. Replacement of both left-sided cardiac valves at the same operation is a formidable operation, especially when both valves are stenotic.²⁶ In this latter setting, usually the left ventricular free wall is thickened, the left ventricular cavity is not dilated, and the ascending aorta is not dilated. When the mitral dysfunction is caused by massive MAC the operation is even more formidable. At least in the patients with combined rheumatic MS and AS the patients are usually relatively young, and the mitral annulus is not calcified. In the patients with MAC of sufficient quantity to obstruct the mitral orifice, the patients are usually in the older age group.

The Tiron E. David group^{16,18} in Toronto has written extensively on methods and results for replacing and/or repairing the mitral valve in the setting of “extensive” MAC. In one of their reports the operative mortality was 6.2 times that occurring in patients having mitral valve

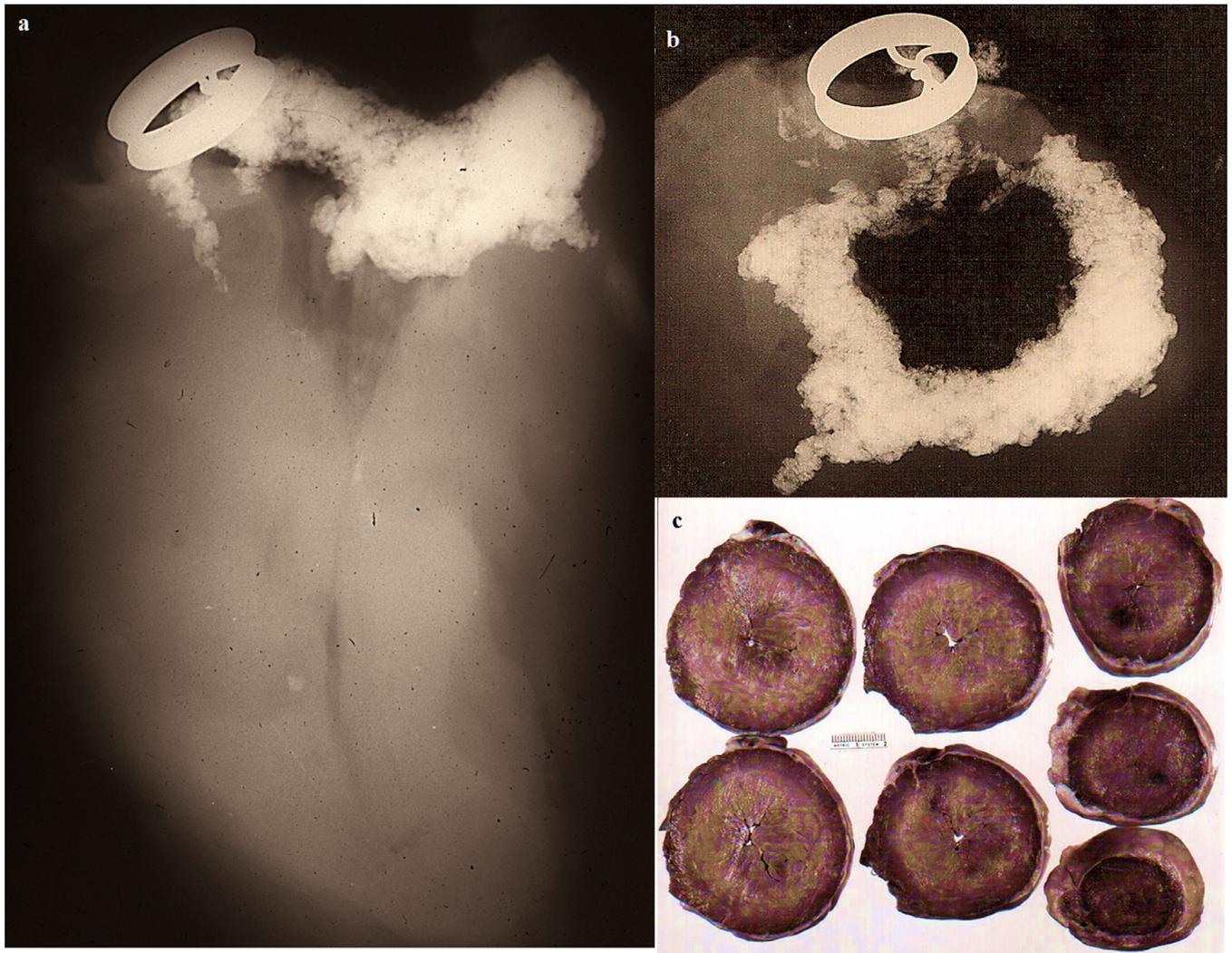


Figure 2. Shown here in *a*, *b*, and *c* views are radiographs of the heart at necropsy. There is massive mitral annular calcium which forms nearly a “C” as shown in *b*. The aortic valve was replaced with a Bjork-Shailey prosthesis. No replacement of the mitral valve was attempted even though the mitral orifice was stenotic. *c* shows transverse sections of the left ventricle to illustrate its small cavity. Death occurs in peak systole, so the left ventricular cavity would be larger during ventricular diastole.

procedures at their institution without MAC. Early postoperative complications in their 54 MAC patients included re-exploration for bleeding (9%), permanent heart block requiring a pacemaker (20%), reoperation later related to valve complications (7%), late postoperative thromboembolic events (9%), and late major hemorrhagic complications (5%). Their series of 54 patients having mitral operations—combined with aortic valve replacement for AS in 23 (43%)—appear to be the best from anywhere in the setting of extensive MAC. Possibly, most of their patients had smaller quantities of MAC than the patients described herein. In 31 (57%) of their 54 patients the MAC was located only behind the posterior mitral leaflet and did not extend across the ventricular aspect of anterior mitral leaflet as it did in the 12 patients described herein. These investigators emphasize the difficulty of the operation and state the following:

“Extensive calcification of the mitral annulus may present a formidable surgical challenge during mitral valve surgery. The patient is at risk from such potentially fatal complications as intractable hemorrhage, atrioventricular disruption, and ventricular rupture. . . . Although we recommend removal of the calcium bar, this is a major undertaking and should not be considered lightly. . . .”

Another unemphasized difficulty of mitral replacement in the setting of massive MAC and associated AS is the lack of dilatation of the left ventricular cavity in most of these patients including all 12 described herein.²⁶ Shown in Figure 2 is the heart of a 70-year-old woman who died shortly after replacement of a severely stenotic congenitally bicuspid aortic valve (peak transvalvular gradient = 153 mm Hg). A 15-mm Hg mean diastolic pressure gradient was present between left atrium

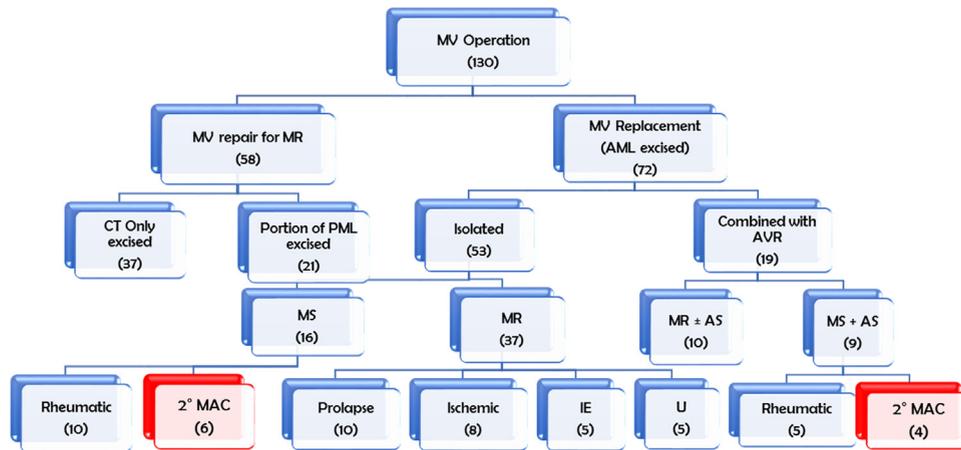


Figure 3. Reason for mitral valve operations at Baylor University Medical Center at Dallas during the 3 years: 2013, 2014, and 2015. Abbreviations: AML = anterior mitral leaflet; AS = aortic stenosis; AVR = aortic valve replacement; CT = chordae tendineae; IE = infective endocarditis; MAC = mitral annular calcium; MR = mitral regurgitation; MV = mitral valve; PML = posterior mitral leaflet; U = unknown.



Figure 4. Case #1, Table 1. Portions of the posterior and anterior leaflets of the mitral valve and fragments of calcium excised from the mitral annular region. Calcium extends across the ventricular aspect of the anterior mitral leaflet.

and left ventricle. The mitral valve, however, was not replaced. The reason for showing these photos is to emphasize the small size of the left ventricular cavity in the setting of combined MS and AS. The small sized ventricular cavity makes it especially difficult to insert a prosthesis or a bioprosthesis in the mitral position in addition to the difficulty in excising the massive MAC in this scenario.

There has been recent interest in transcatheter mitral valve implantation in patients with MS caused by MAC.^{27,28} Sud and colleagues²⁷ reviewed 10 previously-reported case studies of patients having transcatheter mitral valve implantation and 44 patients in a global registry having the percutaneous procedure. In the individual case studies, no deaths were reported. In the series of 44 patients, the 1-year all-cause mortality was 36%. The transvalvular gradients were reduced in most

patients although nonfatal complications were frequent. Guerrero and associates²⁸ updated the MAC Global Registry multicenter data to include 106 patients followed >1 year. One and 12-month all-cause mortality was 25% and 54%, respectively. Of the 77 patients who were alive 30 days after the procedure, 49 (64%) were alive at 1 year. The mean transmitral pressure gradient by echocardiogram, available in 34 patients, at 1 year was 6 ± 2 mm Hg. Examination of hearts with massive MAC causing MS as shown in Figures 1 and 2 suggest why both the surgical and the percutaneous approach for treatment of MS secondary to massive MAC is fraught with difficulty.

One of the reviewers of this manuscript asked why the results of the present study were so much worse than those described by Ng and colleagues²⁰ in 2000. Study of the Na report suggests that their 37 patients had far less mitral annular calcium than the patients described herein. None of Ng's

Table 1
Pertinent findings in the 12 patients with massive mitral annular calcium and mitral valve replacement for mitral stenosis with or without aortic valve replacement for aortic stenosis

Case	Age (years)	Sex	MS	MVR	Mitral valve weight (g)	Substitute mitral valve (mm)	AS	AVR	Aortic valve weight (g)	Substitute aortic valve (mm)	CKD	Narrowed coronary arteries	AF	BMI (Kg/m ²)	DM	Interval VR → D (days)
1	39	F	+	+	6.0	SJM (25)	0	0	-	-	+(H)	0	0	21	0	8
2	52	F	+	+	3.9	Bioprosthesis (29)	0	0	-	-	0	0	0	40	+	Alive †
3	58	M	+	+	3.2	Bioprosthesis (27)	0	0	-	-	+(RT)	+	0	30	+	Alive ‡
4	61	F	+	+	1.5	SJM (33)	0	0	-	-	0	0	+	38	0	Alive ¶
5	62	F	+	+	5.7	SJM (27)	0	0	-	-	0	0	0	28	0	5
6	76	M	+	+	1.9	Bicor (29)	0	0	-	-	0	+	+	36	+	44
7	40	M	+	+	3.3	O ₂ -X (25)	+	+	3.0	Carbomedius (21)	+(P)	0	+	34	0	600
8	42	F	+	+	1.9	SJM (27)	+	+	-	SJM (21)	+(H)	0	+	-	0	150
9	71	F	+	+	-	St. Jude Epic (-)	+	+	-	Magna Ease (21)	0	+	+	31	+	32
10	74	F	+	+	7.2	ATS Mech (24)	+	+	1.2	ATS Mech (20)	+	0	+	36	+	12
11	76	F	+	+	4.7	Bicor (25)	+	+	0.5	CE (19)	+	0	0	52	+	25
12	82	M	+	+	-	Edwards Magna (27)	+	+	-	-	0	+	+	-	0	11

Abbreviations: AF = atrial fibrillation; AS = aortic stenosis; AVR = aortic valve replacement; BMI = body mass index; CABG = coronary artery bypass grafting; CKD = chronic kidney disease; D = death; DM = diabetes mellitus; F = female; H = hemodialysis initiated months or years before MVR; LV = left ventricle; M = male; MS = mitral stenosis; MVR = mitral valve replacement; P = peritoneal dialysis; RT = renal transplant earlier; VR = valve replacement.

* BAV;
 † AVR 22 months before excision of the bioprosthesis in the aortic valve position and replacement of the MV;
 ‡ Alive 36 months postoperatively. Improved, less breathlessness, twenty pounds less (250→230);
 § Alive 59 months postoperatively. Much improved. Little breathlessness;
 ¶ Alive 27 months postoperatively. Greatly improved. Nearly no breathlessness. Thirty pounds weight loss (240→210).

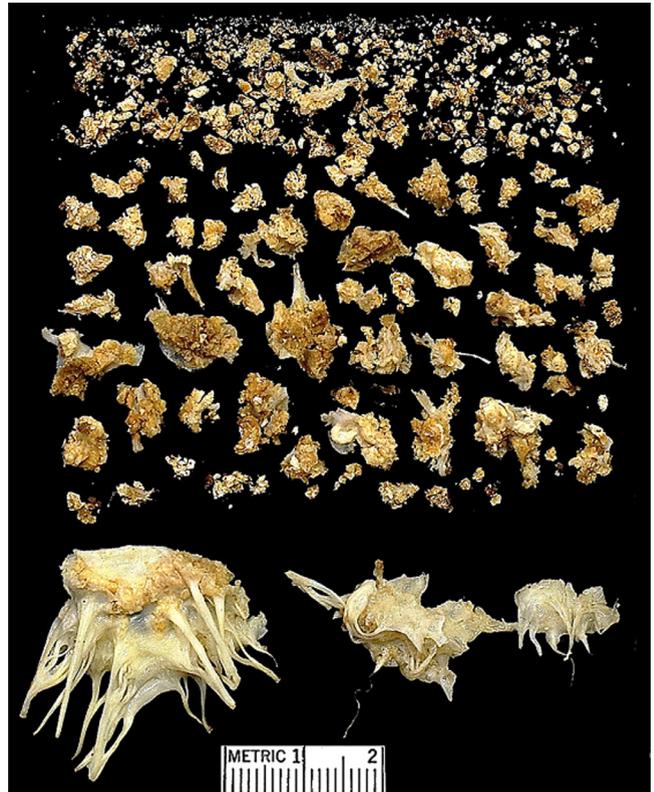


Figure 5. Case 5, Table 1. Shown here are large deposits of calcium excised from the mitral annular region and the anterior mitral leaflet with a bar of calcium across its ventricular aspect and two fragments of posterior leaflet. The quantity of calcium in the mitral annular area was obviously enormous.

patients had mitral stenosis, only mitral regurgitation and it is likely that much heavier deposits of calcium are required to obstruct the mitral orifice by annular calcium than to produce only regurgitation. It is unlikely that the annular calcium behind posterior leaflet extended across the ventricular surface of anterior mitral leaflet in Ng's patients as it did in the patients described herein. Indeed Ng et al wrote: "Five patients were excluded from (their) study due to severe calcification of nearly the entire annulus..." None of Ng's patients had associated aortic stenosis, a feature in half of the patients in the present study and something that tends to make the left ventricular cavity smaller and probably the mitral orifice smaller. Finally, none of Ng's patients had mitral valve replacement as did all the patients in the present study.

The mechanism of development of MAC and its commonly associated AS is not entirely clear but most likely is a consequence of atherosclerosis, although that word would have to be redefined to include MAC and AS under that heading. Most young people living in the Western World have yellow deposits on the undersurface of the posterior mitral leaflet and fewer such deposits on the ventricular surface of anterior mitral leaflet. Additionally, similar deposits occur on the aortic aspects of the aortic valve cusps, whether its structure is tricuspid or bicuspid. In later life the lipid deposits may transform into calcific deposits, and, depending on the quantity of those deposits in the 2 valves, may or may not

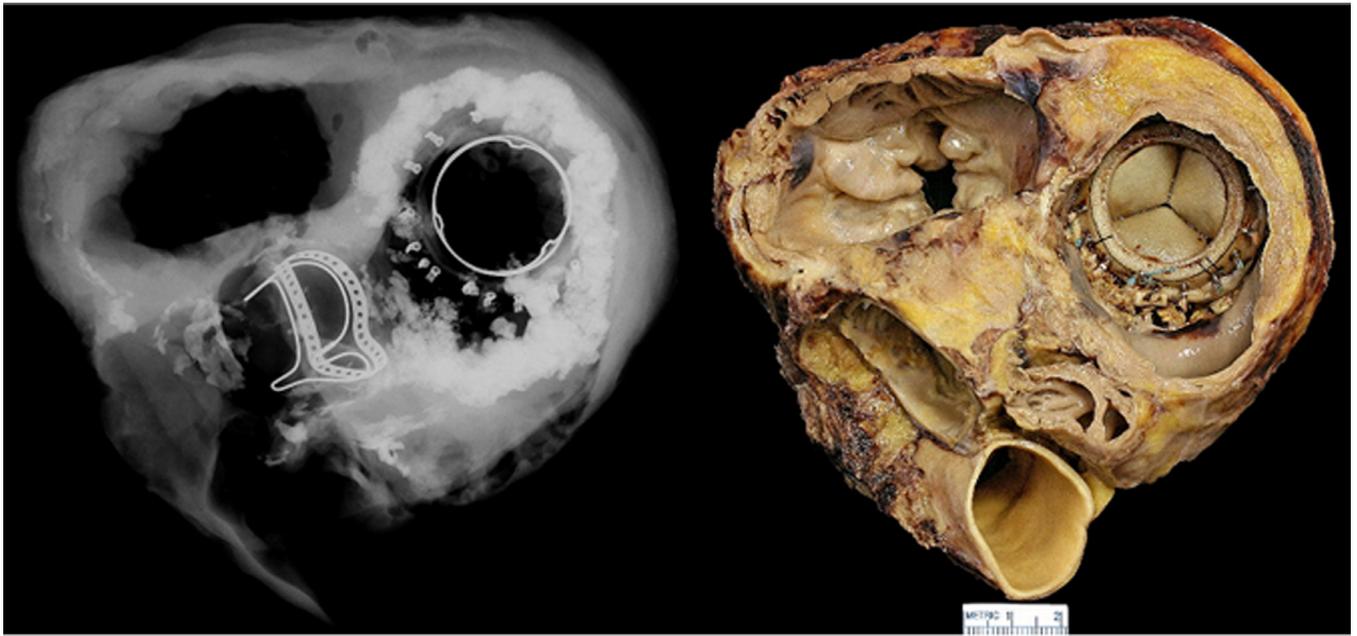


Figure 6. Case #9, Table 1. Shown here is a radiograph of the heart specimen at necropsy on the *left* and the actual specimen shown on the *right*. Both the mitral and aortic valves were replaced because of stenosis. A large amount of calcium was removed from the mitral annular region at operation but there is still a great deal of calcium left in that area. The more anterolateral portion of the mitral annulus had a communication between the cloth ring and the annulus so there was a para-annular leak. Heavy calcific deposits are also seen in the epicardial coronary arteries.



Figure 7. Case 10, Table 1. Shown here are huge calcific fragments excised from the mitral annular region (*left*), the operatively excised aortic valve cusps containing calcific fragments (*top right*), and the ventricular aspect of anterior mitral leaflet (*bottom right*). About half of the anterior leaflet has a bar of calcium extending across its ventricular aspect.

lead to symptoms of cardiac dysfunction. Because “atherosclerosis” preferentially affects the systemic arteries, associated coronary narrowing in these patients is common.

In conclusion, performing mitral valve replacement in the setting of *massive* MAC is both difficult and hazardous, even more so when the aortic valve is also stenotic.



Figure 8. Case 11, Table 1. Shown here is both the operatively excised mitral valve and the 3-cuspid aortic valve plus the numerous calcific fragments excised from the mitral annular region. These fragments together weighed 4.72 g. Of course, not all the calcium in the mitral annular region was excised.

Disclosures

The author has no conflict of interests to disclose.

- Korn D, DeSanctis RW, Sell S. Massive calcification of the mitral annulus. A clinicopathological study of fourteen cases. *N Engl J Med* 1962;267:900–908.
- Roberts WC, Shirani J. Comparison of cardiac findings at necropsy in octogenarians, nonagenarians, and centenarians. *Am J Cardiol* 1998;82:627–631.
- Roberts WC, Taylor MA, Shirani J. Cardiac findings at necropsy in patients with chronic kidney disease maintained on chronic hemodialysis. *Medicine* 2012;91:165–178.
- Roberts WC, Vowels TJ, Filardo G, Ko JM, Mathur RP, Shirani J. Natural history of unoperated aortic stenosis during a 50-year period of cardiac valve replacement. *Am J Cardiol* 2013;112:541–553.
- Motamed HE, Roberts WC. Frequency and significance of mitral annular calcium in hypertrophic cardiomyopathy: analysis of 200 necropsy patients. *Am J Cardiol* 1987;60:877–884.
- Roberts WC, McIntosh CL, Wallace RB. Mechanisms of severe mitral regurgitation in mitral valve prolapse determined from analysis of operatively excised valves. *Am Heart J* 1987;113:1316–1323.
- Renteria VG, Ferrans VJ, Roberts WC. The heart in the Hurler Syndrome: gross, histologic and ultrastructural observations in five necropsy cases. *Am J Cardiol* 1976;38:487–501.
- Roberts WC. Morphologic aspects of cardiac valve dysfunction. *Am Heart J* 1992;123:1610–1632.
- Roberts WC. The senile cardiac calcification syndrome. *Am J Cardiol* 1986;58:572–574.
- Roberts WC, Waller BF. Mitral valve “annular” calcium forming a complete circle of “O” configuration: clinical and necropsy observations. *Am Heart J* 1981;101:619–621.
- Theleman KP, Grayburn PA, Roberts WC. Mitral “annular” calcium forming a complete circle “O” causing mitral stenosis in association with a stenotic congenitally bicuspid aortic valve and severe coronary artery disease. *Am J Geriatr Cardiol* 2006;15:58–61.
- Hammer WJ, Roberts WC, deLeon AC Jr. “Mitral stenosis” secondary to combined “massive” mitral annular calcific deposits and small, hypertrophied left ventricles: hemodynamic documentation in four patients. *Am J Med* 1978;64:371–376.
- Ramirez J, Flowers NC. Severe mitral stenosis secondary to massive calcification of the mitral annulus with unusual echocardiographic manifestations. *Clin Cardiol* 1980;3:284–287.
- Osterberger LE, Goldstein S, Khaja F, Lakier JB. Functional mitral stenosis in patients with massive mitral annular calcification. *Circulation* 1981;64:472–476.
- Pressman GS, Agarwal A, Braitman LE, Muddassir SM. Mitral annular calcium causing mitral stenosis. *Am J Cardiol* 2010;105:389–391.
- David TE, Feindel CM, Armstrong S, Sun Z. Reconstruction of the mitral annulus: a ten-year experience. *J Thorac Cardiovasc Surg* 1995;110:1323–1332.
- Carpenter AF, Pellerin M, Fuzellier JF, Relland JYM. Extensive calcification of the mitral valve annulus: pathology and surgical management. *J Thorac Cardiovasc Surg* 1996;111:718–729.
- David TE, Kuo J, Armstrong S. Aortic and mitral valve replacement with reconstruction of the intervalvular fibrous body. *J Thorac Cardiovasc Surg* 1997;114:766–772.
- Lin PY, Kan CD, Luo CY, Yang YJ. Mitral valve replacement in the presence of massive posterior annular calcification. *J Card Surg* 1999;14:266–269.
- Ng CK, Punzengruber C, Pachinger O, Nesser J, Auer H, Franke H, Hartl P. Valve repair in mitral regurgitation complicated by severe annulus calcification. *Ann Thorac Surg* 2000;70:53–58.
- Fasol R, Mahdjoobian K, Joubert-Hubner E. Mitral repair in patients with severely calcified annulus: feasibility, surgery and results. *J Heart Valve Dis* 2002;11:153–159.
- Feindel CM, Tufail Z, David TE, Ivanov J, Armstrong S. Mitral valve surgery in patients with extensive calcification of the mitral annulus. *J Thorac Cardiovasc Surg* 2003;126:777–782.
- DiStefano S, Lopez J, Flórez S, Rey J, Arevalo A, San Román A. Building a new annulus: a technique for mitral valve replacement in heavily calcified annulus. *Ann Thorac Surg* 2009;87:1625–1627.
- Atoui R, Lash V, Mohammadi S, Cecere R. Intra-atrial implantation of a mitral valve prosthesis in a heavily calcified mitral annulus. *Eur J Cardiothorac Surg* 2009;36:776–768.
- Nomura A, Fukuda I, Daitoku K, Fukui K. Enucleation of calcium core and in-situ valve replacement for massive posterior mitral annular calcification. *Interact Cardiovasc Thorac Surg* 2011;12:652–654.
- Roberts WC, Sullivan MF. Clinical and necropsy observations early after simultaneous replacement of the mitral and aortic valves. *Am J Cardiol* 1986;58:1067–1084.
- Sud K, Agarwal S, Parashar A, Raza MQ, Patel K, Min D, Rodriguez LL, Krishnaswamy A, Mick SL, Gillinov AM, Tuzcu M, Kapadia SR. Degenerative mitral stenosis: unmet need for percutaneous interventions. *Circulation* 2016;133:1594–1604.
- Guerrero M, Urena M, Himbert D, Wang DD4, Eleid M5, Kodali S, George I, Chakravarty T, Mathur M, Holzhey D, Pershad A, Fang HK, O’Hair D, Jones N, Mahadevan VS, Dumonteil N, Rodés-Cabau J, Piazza N, Ferrari E, Ciaburri D, Nejari M, DeLago A, Sorajja P, Zahr

F, Rajagopal V, Whisenant B, Shah PB, Sinning JM, Witkowski A, Eltchaninoff H, Dvir D, Martin B, Attizzani GF, Gaia D, Nunes NSV, Fassa AA, Kerendi F, Pavlides G, Iyer V, Kaddissi G, Witzke C, Wudel J, Mishkel, Raybuck B, Wang C, Waksman R, Palacios I, Crib-

ier A, Webb J, Bapat V, Reisman M, Makkar R, Leon M, Rihal C, Vahanian A, O'Neill W, Feldman T. 1-year outcomes of transcatheter mitral valve replacement in patients with severe mitral annular calcification. *J Am Coll Cardiol* 2018;71:1841–1853.