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ORIGINAL RESEARCH

Transcatheter Repair of Tricuspid Regurgitation with the MitraClip Device and the Observed Rate of Post Procedure Acute Kidney Injury: A Single Center Experience

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Introduction

The MitraClip system was first approved by the US food and Drug administration (FDA) in 2013 for mitral valve repair.[1] This approach is indicated for the repair of the mitral valve in patients with severe and symptomatic mitral insufficiency who are not surgical candidates.[1,2] Aside from the operative risks to the mitral valve associated with traditional open-heart surgery, increased risk of acute kidney injury (AKI) has long been known post cardiac surgery. In one series, 37% of patients experienced post cardiac surgery-associated acute kidney injury (CS-AKI) after mitral valve repair.[3] This rate is higher than post coronary artery bypass (CABG) surgery where 13-20% of patients experience CS-AKI post operatively.[4,5] Tricuspid repair is sometimes medically necessary in cases of tricuspid valvular incompetence associated with right heart failure. The surgical approach with mechanical or bio-prosthetic valves is high risk with a propensity for early and late morbidity and mortality.[6] With optimization of peri-operative conditions, these procedures can be performed relatively safely despite a reported complication rate of nearly 20-30%.[4,5]

The high risks of operative management of valvular disorders in general as well as the inherent high risk of this patient population makes transcatheter options an attractive alternative for managing patients with tricuspid regurgitation. This approach has risks from arterial injury from the puncture site, embolic events, and acute kidney injury from iodinated contrast if needed.[4-7] It is important to note that tricuspid repair approach is usually venous rather than arterial given the need to access the right heart, and as such can be performed solely under fluoroscopy with echocardiography guidance without iodinated contrast in most cases.[6] Prior studies evaluating the risk of AKI and contrast induced nephropathy (CIN), about 38.7% of patients who underwent percutaneous repair of the mitral valve suffered AKI comparable to rates of CS-AKI seen in surgical repair.[3]

Transcatheter approach to mitral valve and aortic valve repair is more established, as transcatheter tricuspid valve repair is a relatively new technique.[8] In our center we are exploring the off-label adaptation of the MitraClip system. We report our experience with seven patients, and while overall valve function improved and survival was excellent, a significant rate of AKI was observed comparable to level reported for MitraClip transcatheter mitral valve repair. We defined AKI as the rise in serum creatinine by at least 0.5mg/L after intervention,[9] and according to this definition 33% of patients without end stage renal disease (ESRD) were noted to have AKI post percutaneous tricuspid valve repair. The renal injury was attributable to renal hemodynamic changes since no iodinated contrast was used during the procedures.

Methods

A search was done regarding the number of patients on whom a transcatheter tricuspid repair was performed in 04/2016-04/2017. A total of seven patients and seven repairs were identified, with renal function data abstracted. The study was reviewed by the UCLA Institutional Review Board (IRB) committee #1 IRB # 17-001845.

Results

In the first year using off-label MitraClip repair of tricuspid valve regurgitation, seven patients were identified at Ronald Reagan Medical Center. These include four patients with varying stages of chronic kidney disease (CKD) not on dialysis, two patients with normal renal function, and one patient with ESRD on dialysis. A brief synopsis of the seven cases will be presented below, along with a tabular synopsis in Table 1, and a graphical trend of the patient's renal function in Figure 1.

Patient 1:

The first patient is a 75-year-old male with a history of chronic obstructive pulmonary disease (COPD), Diabetes Mellitus type 2 (DM2), with severe tricuspid regurgitation (functional etiology). Angiography showed mild to moderate left anterior descending lesion and a chronically occluded right coronary artery. Echocardiography showed an ejection fraction of 60% to 65% and prolapse of the septal leaflet of the first tricuspid valve. He had a right heart catheterization which showed an RA pressure of 23 mmHg, PA pressure of 49 mmHg systolic

/17mmHg diastolic pressure, and pulmonary capillary wedge pressure of 18 mmHg with a cardiac output of 3.1 L/minute by Fick equation.

The tricuspid repair with the MitraClip was performed with a baseline serum creatinine of 0.9. No iodinated contrast was administered during the repair. The serum creatinine rose slightly to a peak of 1.1 mg/dL which did not meet the definition for AKI, and fell promptly back to baseline of 0.9mg/dL. From a technical standpoint, the regurgitant lesion was repaired with no additional morbidity or mortality.

Patient 2:

The second patient had two repair deployments of the MitraClip system. This 68-year-old Caucasian female with history of breast cancer status post anthracycline chemotherapy and radiation developed of radiation induced tricuspid valve insufficiency and radiation-induced pericardial constriction. Left heart angiography showed no coronary artery disease. Echocardiography revealed a decreased right ventricular ejection fraction of 45%, a preserved left ventricular ejection fraction of 55-60%, severe tricuspid regurgitation, mild diastolic dysfunction, mild aortic stenosis, and evidence of constrictive physiology. Right heart catheterization showed a Kussmaul sign consistent with constrictive physiology and confirmed severe tricuspid regurgitation. Right atrial pressure was 18 mmHg with prominent Y descents and V wave to 22 mmHg, right ventricular systolic pressure of 26 mmHg and diastolic pressure of 11 mmHg, pulmonary artery systolic pressure of 24 mmHg and diastolic pressure of 16 mmHg, a wedge pressure of 12 mmHg (equal to estimated left atrial pressure), and cardiac output of 3.5 L/min by Fick's equation with a cardiac index of 2.21 L/min.

The patient's tricuspid valve was repaired with the MitraClip, without iodinated contrast. The serum creatinine had risen prior to the procedure and it remained at baseline of 1.7 and 1.9 mg/dL. After procedure no significant rise in serum creatinine was noted but it did increase from 1.74 to 1.96 mg/dL the day post procedure, and remained stable at this level. Another episode of AKI remote to the procedure (a week later) caused the serum creatinine to rise up to a peak of 2.43 mg/dL eventually before it dropped down to pre hospitalization baseline levels of 1.1-1.2 by 1/31/2017. The tricuspid incompetence was thus repaired without any incident.

Patient 3:

The third patient is a 23-year-old male with a history of Acute Lymphoblastic Leukemia (ALL) s/p bone marrow transplant. He had a history of end stage renal disease on dialysis Tuesdays-Thursdays-and-Saturdays (TTS), and severe tricuspid regurgitation due to malcoaptation. He was considered to be an extremely poor surgical candidate given his comorbidities, which included cirrhosis from congestive hepatopathy and agreed to transcatheter tricuspid valve repair. Left heart angiography did not show any coronary lesions that required intervention. Echocardiography revealed mildly reduced biventricular systolic function with an estimated ejection fractions of 40-45%. Severe tricuspid valve regurgitation was noted due to restriction of the posterior tricuspid leaflet. Volume overload was confirmed on echocardiography. Right heart catheterization showed a right atrial pressure of 21 mmHg, pulmonary arterial pressures of 28 mmHg systolic and 20 mmHg diastolic, a wedge pressure of 20 mmHg, and cardiac output of 5.5 L/min and a cardiac index of 3.35 L/min by Fick equation.

Two MitraClips were placed on the anterior/septal and posterior/septal tricuspid valve leaflets and no iodinated contrast was administered during tricuspid valve repair. Renal function was marginal at the start of procedure with a serum creatinine of 7.52 mg/dL and an estimated glomerular filtration rate of 13 ml/min, with no discernable change in renal function due to ongoing intermittent hemodialysis. The patient completed the procedure with good improvement in valve function without other morbidity or mortality.

Patient 4:

The fourth patient is a 77-year-old male with established aortic and mitral valvular disease and atrial fibrillation due to a childhood rheumatic fever with prior mechanical aortic and mitral valve replacements. He had been rate controlled and placed on warfarin anticoagulation for his atrial fibrillation. He was free of anginal symptoms without obstructive coronary artery disease on left heart catheterization. Echocardiography showed normal left ventricular function with an ejection fraction of 55-60%, enlarged right ventricle and mildly reduced systolic function of the right ventricle, right sided volume overload, aortic and mitral valve mechanical prostheses, severe tricuspid regurgitation, and moderate aortic atherosclerosis. Right heart catheterization showed a right atrial pressure of 25mmHg, pulmonary artery pressure of 44mmHg systolic, and 15mmHg pulmonary artery diastolic pressure. A wedge pressure of 22 mmHg was noted and cardiac output was 5.95L/min by Fick's equation with a cardiac index of 3 L/minute. Tricuspid valve disease was thought to be due to rheumatic fever.

This patient's MitraClip repair of his tricuspid valve was performed with an increase in serum creatinine from baseline of 1.2-1.4 to 1.7-1.9 before the repair was attempted. The etiology was thought to be due to pre-renal azotemia due to cardio renal syndrome caused by underlying renal hypoperfusion from tricuspid valve dysfunction. The serum creatinine increased post valvular repair to 2.6 mg/dL, despite no iodinated contrast. The patient developed oliguria in face of volume overload with urine output decreased to 700 ml the day after the repair. The next day the patient became symptomatic due to volume overload despite a continuous infusion of loop diuretics and adjunctive therapy with metolazone thiazide diuretics. Continuous renal replacement therapy was initiated, with intermittent dialysis two days later. He recovered his renal function two weeks later. Urine output increased 1.9 L with

improvement of serum creatinine to 2.41 mg/dL and eventual recovery to baseline serum creatinine of 1.1-1.2 mg/dL. The valvular function improved post transcatheter procedure but the patient suffered a significant episode of AKI peri procedurally.

Patient 5:

The fifth patient is a 71-year-old female with Diabetes Mellitus type 2, hypertension, early cirrhosis/congestive hepatopathy, sick sinus syndrome with atrial fibrillation on warfarin anticoagulation, and chronic kidney disease stage III with serum creatinine of 1.2-1.3 on baseline. She had no angina symptoms and no evidence of myocardial perfusion defects on myo-view. Echocardiography showed normal left ventricular ejection fraction of 50-55%, enlarged right ventricle with mildly reduced systolic function, bi atrial enlargement, mild aortic stenosis is noted, mildly elevated pulmonary artery pressures and severe tricuspid valve dysfunction with evidence for malcoaptation due to chamber enlargement or resulted in chamber enlargement. Right heart catherization showed right atrial pressure of 15mmHg, pulmonary artery systolic pressure of 36 mmHg systolic/25mmHg with a diastolic pulmonary capillary wedge pressure of 25 mmHg, and cardiac output of 4.7 L/min by Fick equation.

The patient's MitraClip repair was performed with 2 clips applied to the tricuspid valve, using no iodinated contrast. The patient tolerated the procedure well but her serum creatinine rose from baseline of 1.24 mg/dL (during this hospitalization to 1.82mg/dL - a rise of 0.58 mg/dL). The renal function then stabilized without oliguria, need for dialysis, or electrolyte abnormalities. Renal function decreased to a new baseline with a creatinine of 1.4-1.7 mg/dL and remained at this level after the procedure for almost one year. The valve function improved and aside from the limited AKI no other morbidity occurred post procedure.

Patient 6:

The sixth patient is a 76-year-old male with hypertension, atrial fibrillation, congestive heart failure (right sided), aortic valve insufficiency (status post mechanical aortic valve), congestive hepatopathy, chronic kidney disease (stage IIIb) with baseline serum creatinine of 2.5-2.7 mg/dL, and liver cirrhosis. The patient presented to UCLA with decompensated heart failure and symptomatic tricuspid regurgitation. His tricuspid valve regurgitation was listed as functional and remained symptomatic despite optimal medical therapy. No anginal symptoms were noted prior to beginning of cardiovascular intervention.

Echocardiography showed mildly increased left ventricular size with borderline to normal systolic function (estimated ejection fraction-visual was 50-55%). The right ventricle showed normal size and systolic function. Bi-atrial enlargement was noted on echo and moderate to severe tricuspid regurgitation was noted on echocardiography. Mitral valve leaflets were thickened and calcified, while the aortic valve was replaced by a mechanical aortic prosthetic valve.

Right heart catherization showed right atrial pressure of 11mmHg, pulmonary artery systolic pressure of 23 mmHg systolic/10mm Hg diastolic, pulmonary capillary wedge pressure of 10 mmHg, and cardiac output of 5.7 L/min by Fick equation. The patient's mitra clip was performed without change in serum creatinine. The patient underwent a successful repair without incident. The serum creatinine even improved to 2.2 mg/dL 14 days later.

Patient 7:

The seventh and final patient is a 73-year-old male with hypertension, chronic atrial fibrillation, bioprosthetic aortic valve replacement, and mitral valve replacement. He had normal renal function pre procedure without CKD. He developed right sided congestive heart failure with cardiogenic ascites and congestive hepatopathy as well as edema and presented with symptomatic tricuspid regurgitation. He was graded as having severe tricuspid regurgitation clinically, with functional etiology.

Echocardiography showed an enlarged right atrium and ventricle with moderately reduced right ventricular ejection fraction. The left ventricular size and function was noted as normal (LVEF 55-60%). Functioning bioprosthetic valves were noted in the aortic and mitral positions.

Right heart catheterization showed a right atrial pressure of 26 mmHg, with a right ventricular pressure of 38 mmHg/15 mmHg. Pulmonary artery pressure, wedge, and cardiac output were not obtained. He had improvement of hemodynamics and serum creatinine was not elevated post operatively. He was discharged 48 hours post procedure with improved valve function without renal dysfunction or other complication.

Discussion and Conclusion

We have reported seven patients with MitraClip repairs of the tricuspid valve (Tri-clip repair) all of which were successful from a technical and cardiac outcomes standpoint. Two patients developed mild increases in serum creatinine, not meeting definition of AKI (>0.5mg/dL rise in serum creatinine). One patient developed severe symptomatic AKI post-procedure who needed transient continuous renal replacement therapy (CRRT) afterwards. One patient had a self-limited episode of AKI that resolved. Finally, one patient with ESRD did not have a discernible change in his marginal renal function as expected. Therefore 33% of all non ESRD patients in this series (2/6) and 50% of patients (2/4) with CKD but not ESRD developed AKI post percutaneous tricuspid valve repair.

In all cases the kidney injury was reversible, and only one patient required temporary hemodialysis and eventually re-covered renal function. Our small series survey suggests as the Tri-Clip procedure becomes increasingly utilized, it would be

prudent until a larger study is done to follow patients with CKD closely for the developed of post-procedure AKI. Radio-contrast did not identify persistent CKD after tricuspid valve repair, although there may be changes in intrarenal hemo-dynamics due to changes in sympathetic outflow or hormonal changes. As Tri-Clip procedure becomes more popular, larger studies will be needed to monitor patient with CKD to determine the indicence of post –procedure AKI, look for incidence of AKI post Tri-Clip repair, and to examine in these cases what changes contribute to renal injury.

Conflicts of Interest: The authors have no conflicts of interest to declare

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Figure 1

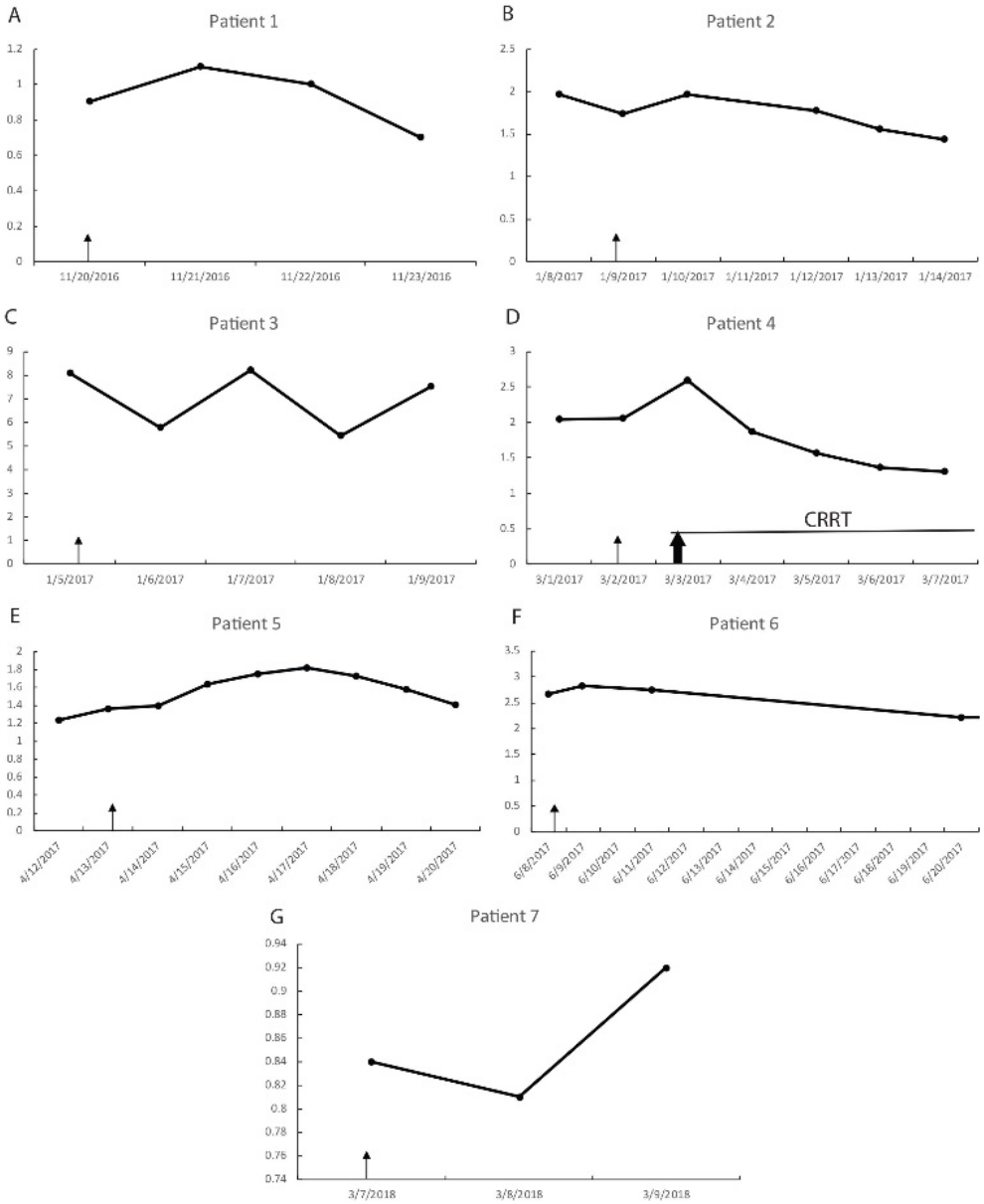

Figure 1: Time course of changes in serum creatinine in patients receiving the mitra-clip tricuspid valve repair. AKI=acute kidney injury, CRRT=continuous renal replacement therapy, Thin arrow: date of Triclip procedure, Thick arrow=start of CRRT.

Table 1 Clinical Cases Involving percutaneous tricuspid valve repair (TriClip) procedure

Patient #	Age	Gender	Race	Other valvular disease	CAD	DM2	Contrast used	Etiology of TR	CKD	ESRD	AKI	RRT
1	75	M	Hispanic	N	LAD	Y	0 ml	functional	N	N	N	N
2	68	F	Caucasian	N	N	N	0 ml	constrictive physiology	Y	N	N	N
3	23	M	Hispanic	N	N	N	0 ml	malcoaptation	N*	Y	N	chronic
4	77	M	Middle Eastern	AV, MV	N	N	0 ml	rheumatic fever	Y	N	Y	acute
5	71	F	Hispanic	N	N	Y	0 ml	malcoaptation	Y	N	Y	N
6	76	M	Middle Eastern	AV, calcified MV	N	N	0 ml	functional	Y	N	N	N
7	73	M	Hispanic	AV, MV	N	N	0 ml	functional	N	N	N	N

AKI=Acute kidney injury, AV= aortic valve, CAD=coronary artery disease, CKD=chronic kidney disease, ESRD=end stage renal disease, F=Female, LAD= coronary disease in left anterior descending coronary artery, M=Male, ml=milliiter, MV=mitral valve, N=No, RRT=renal replacement therapy , TR=tricuspid regurgitation, Y= yes. * This patient is labeled as "not CKD but yes ESRD"

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