Effect of Transcatheter Aortic Valve Implantation on Renal Function in Patients With Previous Renal Dysfunction

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The study aims to investigate the incidence of immediate renal function improvement in renal dysfunction patients who had transcatheter aortic valve implantation (TAVI). TAVI patients with ≥ moderate reduced renal function [estimated GFR ≤ 60 ml/min/1.73 m^2] at baseline were identified from a prospectively maintained database. Patients were divided into 3 groups based on percent change [(discharge eGFR − baseline eGFR/baseline GFR) × 100] in eGFR post-TAVR. Improvement ≥ 10%, no change, Decline ≥ 10%. Multivariable logistic regression was performed to identify factors that predicted improvement/decline in GFR postprocedure. Out of 677 patients, 359 (53%) had eGFR ≤ 60 ml/min/1.73 m^2. Of these, 188 (52%) had an improvement in eGFR ≥ 10%, 125 (34%) had no change and 48 (14%) observed decline ≥ 10%. All groups had similar proportions of females and age was comparable in patient groups. Patients in whom a decline in eGFR was observed had significantly higher Society of thoracic Surgeons scores (10.7 vs 8.2 vs 8.2; p = 0.007) and incidence of liver disease (6% vs, 0% vs 2%; p = 0.014) than the no-change or improved groups respectively. On multivariable analysis, independent predictors of decline/improvement in eGFR were being female, low left ventricular ejection fraction and baseline liver dysfunction. In conclusion, over half of patients with compromised renal function who underwent TAVI experience an immediate improvement in kidney function post-TAVI. Being female, baseline liver dysfunction and a low left ventricular ejection fraction is associated with an immediate decline in eGFR. **Published by Elsevier Inc. (Am J Cardiol 2019;124:85−89)**

Transcatheter aortic valve implantation (TAVI) has successfully evolved as an intervention of choice in severe aortic stenosis (AS) patients with high and intermediate surgical risk for valve replacement.[1−4] In addition to the plethora of co-morbidities in TAVI patients, concomitant baseline renal dysfunction is described in a greater proportion of TAVI patients.[5] Reports from previous registries have documented an incidence of severe renal dysfunction in about 29% to 34% of TAVI patients.[5,6]

Studies have shown that, patients with baseline renal dysfunction do worse than their counterparts without renal disease after TAVI.[6] Furthermore, the presence of kidney disease is a risk factor for worsening kidney function post-TAVI. Pre-existing kidney impairment is therefore a concern in AS patients scheduled for valve replacement since this risk has been associated with a 2- to 6-fold increase in both short- and long-term mortality rates.[7]

Renal dysfunction in AS patients can be explained by the decrease in cardiac output thus leading to decreased renal perfusion and venous pressure. As such, it is possible that, post-TAVI, an improvement in cardiac output can lead to improved renal function. We hypothesized that in patients with severe symptomatic AS and reduced baseline renal function, TAVI may improve postprocedural renal function. This hypothesis was evaluated in patients who underwent TAVI at a single center.

Methods

A prospectively-maintained IRB approved TAVI database was queried to identify all patients who had TAVI at a single center between June 2012 and December 2016. Patients who fulfilled the criteria for AS per the American College of Cardiology/American Heart Association guidelines[8] were included in the study. Preoperative assessment was done by a heart team that included at least 2 cardiac surgeons and an interventional cardiologist. Transcatheter aortic valve implantation was proposed as a treatment option for patients who were deemed noneligible for surgical valve replacement based on their overall surgical risk. The Society of thoracic Surgeons risk score and frailty status of patients were 2 main elements used to risk stratify patients.

Frailty was assessed using a frailty index that represented the different domains of frailty previously described

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by Freid et al.[9] Our method of assessing frailty has been previously described in detail.[10] In brief, patients were assigned a score of 0 or 1 when deemed as nonfrail or frail per the 4 domains of frailty. A combined score ranging from 0 to 4 that consisted of scores from frailty components was developed. Patients were classified as frail if their total frailty score was equal to or greater than 3 out of 4 and nonfrail if less than 3 out of 4.

Preoperative screening also included transesophageal echocardiography, cardiac catheterization, thoracic, and abdominal computer tomography. Patients with inadequate iliofemoral access based on imaging findings were recommended a nontransfemoral (TF) approach for TAVI. In these patients, TAVI was performed via the transapical, transaortic, subclavian, and transaxillary routes. The final study population did not include patients who attempted TAVI, but later had it converted to an open procedure.

All patients who had TAVI underwent both pre-and postprocedural hydration based on their respective individual cardiac performance. The Cockcroft gault formula was used to estimate Glomerular filtration rate (eGFR) at baseline and postprocedure for all patients. Reduced renal function was defined as eGFR $\leq$ 60 ml/min. Patients with eGFR < 15% including patients on dialysis were excluded since variations in eGFR are not accurate in these patients. Baseline and discharge creatinine values during hospital stay postprocedure were used to calculate baseline and post-TAVI eGFR. Patients were divided into 3 groups based on percent change [(discharge eGFR − baseline eGFR/baseline eGFR) × 100] in eGFR post-TAVR. Improved eGFR (discharge eGFR $\geq$ 10% baseline) worsened eGFR (discharge eGFR at < 10% baseline) and no change (not fitting either previous groups). The institutional review board at our institution approved the study, and all patients provided written informed consent. Pre-and postoperative clinical and echocardiographic data of patients were collected and compared among patient groups. Data collected included baseline clinical and demographics and periprocedural. Patient's co-morbidities were obtained using the definitions provided by the Society of Thoracic Surgeons data collection system. Perioperative morbidities were defined per criteria defined by the second version of the Valve and Academic Research Consortium (VARC-2).[11]

All continuous variables are reported as mean ± SD and compared using analysis of variance (ANOVA) or the Wilcoxon rank sum test when noted. Categorical variables are reported as percentages and numbers and compared using the chi-squared or Fisher's exact test. For logistic regression analysis, improvement/decline in GFR was chosen as the outcome variable. Covariates that were considered for selection were age, sex, body mass index, New York Heart Association (NYHA) class, frailty status, previous history of (hypertension, dyslipidemia, chronic lung disease, pulmonary hypertension, coronary artery disease, cerebrovascular accident, chronic renal failure, liver dysfunction, chronic atrial fibrillation, permanent pacemaker placement), procedure approach, and echocardiographic parameters (left ventricular ejection fraction, mean aortic valve gradient, moderate-severe mitral valve regurgitation, moderate to severe aortic valve regurgitation). Backward selection in a stepwise manner at a p entry of 0.25 and exit level of 0.10 was used to identify variables that were associated with an improvement/decline in eGFR. Selected variables were placed in a multivariable logistic regression model to determine independent factors associated with improvement/decline in eGFR. Hosmer-Lameshow chi-square statistics was used to assess goodness of fit of the model. The beta estimates, their 95% confidence intervals and standard error for each variable were reported. All statistical analysis was performed using the JMP Version 10.0 software (SAS. Institute, Inc. Cary, North Carolina).

Results

Of 677 patients who had TAVI during the study period, eGFR was estimated to be $\leq$ 60 ml/min in 359 (53%). Table 1 shows the baseline demographics and clinical characteristics of all patients included in the study. One hundred eighteen (52%) had an improvement in eGFR $\geq$ 10%, 123 (34%) had no change and 48 (14%) observed a decline $\geq$ 10%. All groups had similar proportions of females and age was comparable in patient groups. Decline patients had significantly higher Society of thoracic Surgeons scores (10.7 vs 8.2 vs 8.2; p = 0.007) and incidence of liver disease (6% vs, 0% vs 2%; p = 0.014) than the no-change or improved groups respectively. Previous history of cerebrovascular accident, pacemaker placement, and the presence of liver dysfunction was more frequent in decline patients than improved or no change groups.

Values for baseline mean aortic valve area, transaortic gradient, and left ventricular ejection fraction did not differ in the 3 groups. Compared with improved or no-change patients, a fewer proportion of patients who had a decline in eGFR underwent TAVI as an elective procedure. Furthermore, patients who had a decline in eGFR were more likely to undergo the procedure via a nontransfemoral approach compared to their no-change or improved counterparts. Postoperatively, mean serum creatinine levels were documented to be 1.3 in improved patients, 1.4 in no change patients, and 1.3 in decline patients. Estimated GFR at baseline was similar in all 3 groups. Illustrated in Figure 1 is the mean serum creatinine of all 3 groups at baseline, post-TAVR and discharge. Comparing postoperative outcome in the 3 patient groups, decline patients had a significantly higher rate of new onset atrial fibrillation (10% vs 3% vs 2%, p = 0.048), and a prolonged length of stay (7 vs 5 vs 5, p = 0.038) days. Also, decline patients were more likely to be discharged to a location other than home and reported a higher incidence of dialysis during follow-up. The incidence of vascular complications and arrythmias requiring pacemaker implantation were similar in all patient groups. Twenty-one percent (n = 10) of decline patients required dialysis in long term follow-up (Table 2). On logistic regression analysis, female gender, baseline liver dysfunction, and left ventricular ejection fraction were independently associated an immediate decline or improvement in GFR (Table 3).

Discussion

In a contemporary analysis of TAVI patients with baseline renal dysfunction, we found that (1) the incidence of

Table 1
Baseline clinical and echocardiographic characteristics

	Estimated glomerular filtration rate (eGFR)			
Variable	Improved (n = 188)	No change (n = 123)	Declined (n = 48)	p value
Age (years)	85 ± 6	84 ± 7	84 ± 8	0.755
Women	115 (61%)	64 (52%)	34 (70%)	0.058
Body mass index (kg/m^2)	25.9 ± 5.2	26.1 ± 5.3	27.3 ± 5.6	0.248
NYHA class (III or IV)	138 (74%)	100 (82%)	39 (79%)	0.063
STS score (%)	8.2 ± 6.5	8.2 ± 5.2	10.7 ± 6.5	**0.007**
Frail	52 (28%)	38 (32%)	20 (42%)	0.201
Nonelective	63 (33%)	45 (36%)	27 (56%)	**0.016**
Hypertension	160 (86%)	108 (88%)	45 (94%)	0.264
Dyslipidemia	142 (76%)	87 (70%)	34 (70%)	0.542
Chronic lung disease	46 (26%)	23 (19%)	17 (35%)	0.063
Pulmonary hypertension	52 (28%)	35 (28%)	14 (29%)	0.980
Coronary artery disease	119 (64%)	79 (64%)	38 (79%)	0.097
Cerebrovascular accident	19 (11%)	22 (18%)	11 (23%)	0.043
Liver dysfunction	0 (0%)	2 (2%)	3 (6%)	0.008
Chronic atrial fibrillation	52 (28%)	44 (36%)	13 (27%)	0.287
Pacemaker placement	28 (15%)	30 (25%)	5 (10%)	0.041
Previous				
CABG	35 (19%)	21 (16%)	12 (25%)	0.449
BAV	7 (4%)	5 (4%)	6 (13%)	0.087
PCI	44 (23%)	31 (25%)	11 (23%)	0.912
Trans femoral approach	143 (76%)	88 (72%)	28 (59%)	**0.049**
Echocardiography				
Ejection fraction (%)	49 ± 15	53 ± 16	51 ± 15	0.160
Aortic valve area (cm^2)	0.6 ± 0.3	0.6 ± 0.2	0.7 ± 0.2	0.843
Mean gradient (mm Hg)	48 ± 16	45 ± 16	45 ± 18	0.265
Mod-Severe MR	125 (66%)	77 (63%)	30 (63%)	0.741
Mod-Severe AR	61 (32%)	42 (34%)	14 (29%)	0.819
Estimated GFR (/min)	46 ± 13	46 ± 12	47 ± 12	0.764

NYHA = New York Heart Association; STS = Society of thoracic Surgeons; CABG = coronary artery bypass graft; BAV = balloon aortic valvuloplasty; PCI = percutaneous coronary intervention; MR = mitral valve regurgitation; AR = aortic valve regurgitation; GFR = glomerular filtration rate.

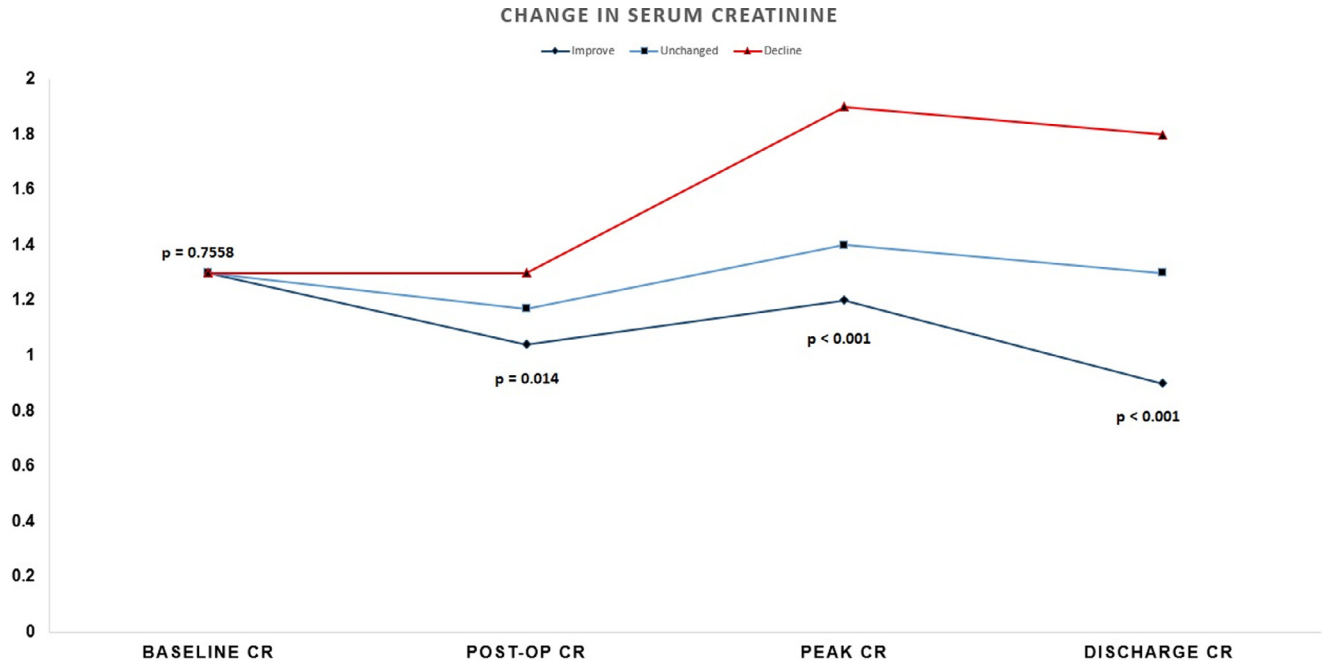

Figure 1. Changes in serum creatinine levels in all 3 patient groups at baseline, postoperatively, peak and discharge.

Table 2
Postoperative and follow-up clinical outcomes

Variable	Estimated glomerular filtration rate			p value
	Improved (n = 188)	No change (n = 123)	Declined (n = 48)	
Contrast volume used (ml)	164 ± 76	163 ± 91	162 ± 88	0.975
New onset atrial fibrillation	5 (3%)	2 (2%)	4 (10%)	0.043
Arrythmia requiring PPM	15 (8%)	5 (4%)	6 (13%)	0.138
Stroke	2 (1%)	2 (2%)	0 (0%)	0.513
Major Bleeding	9 (5%)	2 (2%)	3 (6%)	0.209
Length of stay (days)	5 ± 5	5 ± 6	7 ± 7	0.037
Discharge disposition				
Home	122 (65%)	74 (60%)	19 (40%)	0.021
Dialysis	7 (4%)	2 (2%)	6 (13%)	0.006
Mortality				
In-hospital	5 (3%)	5 (4%)	4 (8%)	0.025
30-day	8 (4%)	3 (4%)	7 (15%)	0.039
1-year	21 (11%)	13 (11%)	12 (25%)	0.044

PPM = permanent pacemaker.

Table 3
Factors associated with improved/decline eGFR after multivariable logistic regression

Variable	Estimate (95% CI)	Standard error	p value
Intercept			<0.0001
Improve	−2.4	2.16	
Decline	0.34	2.16	
Female	0.29 (0.02,0.57)	0.14	**0.036**
Liver dysfunction	−1.48 (−3.1, −0.3)	0.57	**0.012**
Preleft ventricular ejection fraction (%)	−0.02 (−0.03, 0.004)	0.009	**0.052**

renal impairment is common in high and intermediate surgical risk patients; (2) immediate improvement of ≥ 10% of in baseline GFR was seen in about half of patients with preoperative renal dysfunction while only 14% of these patients had a decline in GFR ≥ 10% postprocedure (3) female gender, baseline liver dysfunction and left ventricular ejection fraction are associated with improvement or decline in eGFR post-TAVI.

Findings from the present study confirm the high incidence of renal dysfunction in both high and intermediate surgical risk AS patients who underwent TAVI. The observed incidence of 53% from this single center series is comparable with what has been previously described in the literature. Data from the PARTNER trial documented an incidence of 72% out of 821 patients enrolled in the trial.[12] The pathophysiological consequence of cardiorenal syndrome is one of the several reasons for the observed high prevalence in this subgroup of patients. In addition, the high incidence of normally encountered risk factors for cardiovascular diseases such as dyslipidemia, diabetes, peripheral vascular disease, and hypertension further increases their risk of renal dysfunction.[5]

An immediate improvement of at least 10% of baseline eGFR was observed in one out of every 2 patients who had renal impairment, no change in one-third of them and only 14% observed a decline in their renal function. These results underscore the salutary immediate hemodynamic effect of TVAR on renal function. While the procedure itself may pose a risk to renal injury secondary to both diagnostic and intraoperative contrast requirement, it should be stated that, the above findings outweighs the risks of post-TAVI acute kidney injury. Comparing baseline characteristics among patients analyzed in the present study, those with improved eGFR after TAVI were more likely to have a lower frequency of liver dysfunction, pacemaker placement, cerebrovascular disease, and to have the procedure via a transfemoral approach. This suggests that, mechanical unloading the left ventricle with TAVI plays a bigger role on type 2 cardiorenal syndrome in this subset of patients. Compared with what has been reported in the literature, our observed rates of improvement are high. Another single center study reported improvement in renal function in 15% of patients at 30 days (defined as an absolute decrease in serum creatinine ≥ 0.3 mg/dl) and included all patients irrespective of baseline renal function.[13] Findings from the PARTNER trial described an improvement frequency of 42%. About two-thirds of the patients enrolled in the PARTNER trial either had an improvement or no change. This contrasts with our reported 85% which can be explained by the inclusion of more intermediate surgical risk patients who are deemed less sicker than those enrolled in the PARTNER trial.

Female gender, baseline liver dysfunction, and preoperative left ventricular ejection fraction was associated with an immediate decline or improvement in GFR. Our findings are like that reported by Boehar et al who found that, female gender and baseline left ventricular mass are predictors of decline or improvement.[12]

There are several limitations to the present study that if properly addressed can lead to a more comprehensive apprehension of the findings reported above. First, this study is a retrospective subanalysis of a single center and is subject to the limitations inherently present in such analyses. Patients with baseline eGFR < 15/minutes and those on dialysis were excluded from the present analysis since fluctuations in GFR are not accurate on patients with eGFR < 15. The clinical course in terms of mortality and outcome in this subset of patients cannot be deduced from the present analysis. The present study only considered an immediate improvement change which was defined as change in eGFR predischarge.

Long-term follow-up was not considered for the present analysis, but it would be interesting to note how these immediate changes persist in both short and long term. The study is likely not adequately powered to detect differences in some clinical end points in the groups with improved or worsened eGFR compared with the group who experienced no change, despite event rates that follow a consistent pattern of being lowest in the group with improved eGFR, intermediate in the group who experienced no change, and highest among the group with worsened eGFR. We used a clinically meaningful definition of improvement or worsening of eGFR, but other definitions such an absolute increase or decrease of serum creatinine of 0.3 mg/dl could be used as an extrapolation from the Valve Academic Research Consortium definitions.

In conclusion, decreased baseline eGFR was frequent in high and intermediate surgical risk patients with severe symptomatic AS. Over half of patients with compromised renal function who underwent TAVI experience an immediate improvement in kidney function post-TAVI.

Disclosures

The authors have no conflicts of interest to declare.

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