Outcome of elective total aortic arch replacement in patients with non–dialysis-dependent renal insufficiency stratified by estimated glomerular filtration rate

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Objective: Little is known about the impact of preoperative renal function stratified by estimated glomerular filtration rate (eGFR) on outcomes of total aortic arch replacement (TAR). The current study addressed this issue and identified a cutoff value of eGFR for the requirement of postoperative renal replacement therapy.

Methods: From January 2000 to May 2011, 229 consecutive patients who did not require preoperative hemodialysis were retrospectively studied after elective TAR. Patients were grouped into the following categories: those with normal renal function (eGFR >90 mL/min/1.73 m^2; n = 11) and those with mild (eGFR, 60-90 mL/min/1.73 m^2; n = 86), moderate (eGFR, 30-59 mL/min/1.73 m^2; n = 111), or severe (eGFR <30 mL/min/1.73 m^2; n = 21) renal dysfunction. Linear trend tests demonstrated that the lower categories of eGFR were associated with a higher age, hypertension, coronary artery disease, peripheral arterial disease, and a higher EuroSCORE II.

Results: The overall hospital mortality was 2.2%. A lower categories of eGFR were an independent risk factor for hospital mortality (odds ratio, 0.91; $P = .002$) and postoperative renal replacement therapy (odds ratio, 0.94; $P < .002$). A cutoff value for the requirement of postoperative renal replacement therapy was 26.0 mL/min/1.73 m^2. Patients in the lower categories of eGFR had significantly higher hospital mortality ($P = .03$) and more morbidities, such as renal replacement therapy ($P < .01$), postoperative permanent neurologic deficits ($P = .013$), and prolonged mechanical ventilatory support ($P < .01$). Midterm survival and freedom from major adverse cerebrocardiovascular events were worse across the levels of the lower categories of eGFR.

Conclusions: Preoperative eGFR is a strong predictor of short- and midterm outcomes in contemporary TAR. (J Thorac Cardiovasc Surg 2014;147:966-72)

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Short- and long-term outcomes of total aortic arch replacement (TAR) have been improving over the past decade.[1,2] However, the procedure is likely to be associated with more visceral organ dysfunction than are other cardiac procedures because the procedure is accompanied by ischemia-reperfusion injury caused by the lower body circulatory arrest. The overall incidence of acute kidney injury after aortic surgery has been reported to be high compared with other cardiac operations.[3,4] Patients with chronic kidney disease, a universal independent risk factor for short- and long-term outcomes according to risk adjustment models,[5] are at a higher risk for postoperative de novo renal replacement therapy (RRT), such as continuous hemodiafiltration (CHDF) and/or hemodialysis (HD). Previous studies also identified postoperative RRT as one of the risk factors for mortality in thoracic aortic surgery[6,7]; therefore, we believe that it is of considerable importance to determine the risk factors for predicting the need for RRT.

The glomerular filtration rate (GFR) is considered to be a more accurate measure of renal function than is the serum creatinine level,[8] and estimated GFR (eGFR) was shown to be a reliable predictor of outcomes in patients with acute myocardial infarction[9] and major adverse cerebrocardiovascular events (MACCE) in a large community-based population.[10] A worse outcome also has been reported in patients with renal dysfunction not requiring dialysis who underwent coronary artery bypass grafting (CABG).[11] However, little is known about the prognostic utility of eGFR in patients undergoing TAR. The aim of the present study was to address this issue and to determine a preoperative, clinically relevant cutoff value of eGFR that predicts postoperative de novo RRT.

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Abbreviations and Acronyms

CABG	= coronary artery bypass grafting
CHDF	= continuous hemodiafiltration
eGFR	= estimated glomerular filtration rate
GFR	= glomerular filtration rate
HD	= hemodialysis
MACCE	= major adverse cerebrocardiovascular events
OR	= odds ratio
RRT	= renal replacement therapy
TAR	= total aortic arch replacement

PATIENT PROFILES AND METHODS

This study was approved by our institutional review board, and the need for individual consent was waived. We retrospectively studied 229 consecutive patients with a mean age of 71.7 ± 11.5 years who had undergone elective TAR through a median sternotomy between January 2000 and May 2011 and did not require preoperative HD. Preoperative creatinine levels were measured, and the GFR was estimated from the Japanese equation (eGFR [mL/min/1.73 m^2] = 194 × [serum creatinine]$^{-1.094}$ × [patient age]$^{-0.287}$ × 0.739 [if patient is female]) because the estimation of eGFR is limited by differences in creatinine generation among ethnicities.[12] Patients were grouped into the following categories: those with normal renal function (eGFR >90 mL/min/1.73 m^2; n = 11) and those with mild (eGFR, 60-90 mL/min/1.73 m^2; n = 86), moderate (eGFR, 30-59 mL/min/1.73 m^2; n = 111), or severe (eGFR <30 mL/min/1.73 m^2; n = 21) renal dysfunction.

Surgical Protocol

The details of TAR at our institute have been reported previously.[1] The cannulation site and type of arterial cannulation for cardiopulmonary bypass are particularly important. Both transesophageal echocardiography and epiaortic ultrasound were routinely applied to investigate the ascending aorta and to determine proper cannulation site.[13] The ascending aorta or aortic arch perfusion was selected in the majority of cases (n = 216, 94.3%). A 24F dispersion arterial cannula (Duraflo II; Edwards Lifesciences LLC, Irvine, Calif) was inserted near the aortic root with perfusion toward the aortic valve in 123 (53.5%) patients with atherothrombotic aorta. After the tympanic temperature had fallen to 20°C to 23°C and rectal temperature below 30°C, the aortic arch aneurysm was opened, and antegrade selective cerebral perfusion was initiated. A 14F or 16F balloon-tipped cannula was inserted from inside the aorta into the brachiocephalic artery, and 12F cannulas were positioned in the left common carotid and left subclavian arteries. The distal aortic arch or the descending aorta was divided from inside the aorta to avoid injury to the recurrent nerve during circulatory arrest to the lower body. A gelatin-impregnated quadrifurcated Dacron graft (Gelweave; Vascutek Ltd, Terumo Corporation, Inchinnan Renfrewshire, Scotland, United Kingdom, or J Graft Shield Neo, Japan Lifeline, Tokyo, Japan) or Triplex (Terumo Corporation, Tokyo, Japan) was used. After completion of the distal anastomosis of the prosthetic graft, lower body circulation was reinstituted through a branch graft, and the tympanic/rectal temperature was rewarmed early. The proximal anastomosis of the graft was completed, followed by coronary reperfusion. Finally, the aortic arch vessels were reconstructed.

Indications for Postoperative RRT

The indications for RRT (CHDF/HD) were oliguria less than 0.5 mL/kg/h, volume overload, refractory pulmonary edema despite high doses of diuretics for 6 to 12 hours, difficult-to-control hyperkalemia, and/or metabolic acidosis. CHDF was applied for patients with hemodynamic instability.

Definitions of Permanent and Transient Neurologic Deficit, Atherothrombotic Aorta, and MACCE

Using the definition of the Mount Sinai group,[14] we defined a permanent neurologic deficit as the presence of deficits that persisted on hospital discharge. We defined a transient neurologic deficit as delayed awakening, transient loss of orientation, slurred language, agitation, poor response to commands, or transient hemiparesis that recovered by the time of hospital discharge. When a fragile and spiculated atheroma that exceeded 5 mm in thickness was confirmed by computed tomography in the ascending aorta or aortic arch but did not include the aneurysm itself, an "atherothrombotic aorta" was diagnosed.[15] MACCE were defined as death from any cause, the presence of myocardial ischemic events, congestive heart failures, arrhythmias requiring hospitalization (atrial fibrillation, pacemaker, or implantable cardioverter-defibrillator), and neurologic deficits (stroke or brain hemorrhage).

Statistical Analysis

Data were processed using SPSS 11.0 software (SPSS Inc, Chicago, Ill). Continuous values are expressed as the mean ± standard deviation. Data were analyzed by the χ^2 test or Fisher's exact test for categorical variables. We assessed linear trends by the Cochran-Armitage test for dichotomous outcomes and the Jonckheere-Terpstra test for continuous outcomes (Tables 1 and 2). Stepwise logistic regression analysis was performed to identify the risk factors for hospital mortality and RRT (Tables 3 and 4). Clinically relevant variables with $P < .05$ on univariate analysis were incorporated into the multivariate models to identify significant independent factors predictive of postoperative RRT. Calculation of the area under the curve of the receiver operating characteristics with a 95% confidence interval was used to assess the most clinically useful level of eGFR for predicting the need for postoperative RRT. A cutoff value for the highest sensitivity and specificity was identified. Survival was assessed by the Kaplan-Meier method. A Cox proportional hazard analysis, into which all preoperative variables in the patient profiles were incorporated, was used to determine the risk factors for late mortality.

RESULTS

Patient profiles are shown in Table 1. There were 47 (20.5%) octogenarians in the cohort. All of the dissections were chronic aortic dissection. One hundred eleven (48.5%) patients had concurrent procedures: CABG in 75, aortic root operation in 25 (reimplantation = 6, Bentall procedure = 5, sinotubular junction plication = 13, partial remodeling = 1), aortic valve replacement in 4, mitral valve repair in 2, maze procedure in 8, and abdominal aortic replacement in 5. When we compared baseline patient profiles across the degree of preoperative eGFR, the patients with lower categories of eGFR were significantly older, had lower incidence of aortic dissection, and were more likely to have hypertension, coronary artery disease, and peripheral artery disease. There were significant trends across the quartile in the EuroSCORE II[16] and Japan score,[5] indicating that patients with lower categories of eGFR were at higher risk (Table 1).

The operation time and cardiopulmonary bypass time were significantly longer in patients with lower categories of eGFR. The results on mortality and morbidities are shown in Table 2. Overall 30-day mortality was 0%, and hospital mortality was 2.2% (5/229). The causes of death

TABLE 1. Patient profiles

Variables	Total	Normal eGFR >90 (mL/min/1.73 m^2)	Mild eGFR dysfunction 60-90	Moderate eGFR dysfunction 30-59	Severe eGFR dysfunction <30	P value
No. of patients, (%)	229	11 (4.7)	86 (36.9)	111 (47.6)	21 (9.0)	
Age, y, mean ± SD	71.7 ± 11.5	45.0 ± 20.8	70.7 ± 10.9	74.3 ± 7.4	76.7 ± 4.2	.0001
Octogenarian	47 (20.5)	1 (9.1)	15 (17.4)	27 (24.3)	4 (19.0)	.25
Male gender	175 (76.4)	6 (54.5)	66 (76.7)	86 (77.5)	17 (81.0)	.32
Dissection	24 (10.5)	5 (45.5)	10 (11.6)	9 (8.1)	0 (0)	.0038
Atherothrombotic aorta	35 (15.3)	0 (0)	12 (14.0)	19 (17.1)	4 (19.0)	.21
Serum Cr level (mg/dL)	1.10 ± 0.7	0.62 ± 0.09	0.78 ± 0.11	1.13 ± 0.23	2.75 ± 1.06	<.0001
eGFR (mL/min/1.73 m^2)	56.9 ± 19.9	101.1 ± 10.3	71.4 ± 7.5	48.0 ± 7.9	20.0 ± 6.6	<.0001
Diabetes mellitus	34 (14.8)	1 (9.1)	11 (12.8)	19 (17.1)	3 (14.3)	.39
Hypertension	195 (85.2)	6 (54.5)	71 (82.6)	101 (91.0)	17 (81.0)	.043
Dyslipidemia	91 (39.7)	1 (9.1)	35 (40.7)	46 (41.4)	9 (42.9)	.301
History of smoking	160 (69.9)	7 (63.6)	62 (72.1)	79 (71.2)	12 (57.1)	.58
Old cerebral infarction	17 (7.4)	0 (0)	3 (3.5)	14 (12.6)	0 (0)	.19
Extracranial carotid artery stenosis	27 (11.8)	0 (0)	9 (10.5)	15 (13.5)	3 (14.3)	.23
Coronary artery disease	75 (32.8)	1 (9.1)	21 (24.4)	42 (37.8)	11 (52.4)	.0015
Left ventricular EF (≤40%)	11 (4.8)	0 (0)	4 (4.7)	6 (5.4)	1 (4.8%)	.64
Chronic atrial fibrillation	13 (5.7)	0 (0)	7 (8.1)	5 (4.5)	1 (4.8)	.54
Chronic obstructive pulmonary disease	22 (9.6)	0 (0)	8 (9.3)	10 (9.0)	4 (19.0)	.25
Peripheral arterial disease	11 (4.8)	0 (0)	2 (2.3)	6 (5.4)	3 (14.3)	.031
Concurrent procedure	111 (48.5)	4 (36.4)	39 (45.3)	55 (49.5)	13 (61.9)	.16
EuroSCORE	7.3 ± 2.7	3.6 ± 2.7	6.9 ± 2.4	7.6 ± 2.6	9.1 ± 2.1	.0004
EuroSCORE II	4.5 ± 2.9	1.9 ± 1.2	3.8 ± 2.5	4.8 ± 3.0	7.2 ± 2.6	.0004
Japan score (30-d mortality)	4.9 ± 2.8	2.8 ± 2.1	4.2 ± 1.8	4.9 ± 2.7	8.8 ± 3.7	<.0001
Japan score (30-d mortality + complications)	22.2 ± 10.0	17.1 ± 10.4	20.3 ± 8.5	21.5 ± 8.0	36.6 ± 13.5	<.0001

eGFR, Estimated glomerular filtration rate; *SD*, standard deviation; *Cr*, creatinine; *EF*, ejection fraction.

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were bowel necrosis in 3 patients (severe eGFR, n = 2; moderate eGFR dysfunction, n = 1), pulmonary dysfunction in 1 patient (severe eGFR dysfunction), and sepsis in 1 patient (mild eGFR dysfunction). Comparing the hospital mortality across the quartile of eGFR, the most striking increase was observed in patients with severe eGFR dysfunction ($P = .03$). Serious complications of permanent neurologic deficit and prolonged ventilation were observed in a significantly greater number of patients with lower categories of eGFR ($P = .013$ and $P < .01$, respectively). Postoperative renal failure requiring RRT occurred in 11 (4.8%) patients; of these patients, 10 (4.4%) were supported by CHDF and 4 (1.7%) by HD. As expected, the incidence of postoperative RRT (CHDF/HD) was greater in patients with lower categories of eGFR, particularly with severe eGFR ($P < .01$).

Table 3 shows the univariate and multivariate analyses for hospital mortality. Age, atherothrombotic aorta, serum creatinine level, eGFR, chronic obstructive pulmonary disease, and operation time were identified as risk factors by univariate analysis. By multivariate analysis, age (odds ratio [OR], 1.33; $P = .04$) and a lower level of eGFR (OR, 0.91; $P = .002$) were determined to be risk factors for postoperative hospital mortality, whereas serum creatinine level was not.

Table 4 shows the univariate and multivariate analyses for postoperative RRT. Age, serum creatinine level, eGFR, coronary artery disease, operation time, and minimum tympanic temperature were identified as risk factors by univariate analysis. However, neither lower body circulatory arrest time nor minimum rectal temperature was a risk factor. By multivariate analysis, however, serum creatinine level (OR, 4.2; $P < .0001$) and a lower level of eGFR (OR, 0.94; $P = .002$) were risk factors for postoperative RRT. Details for the 11 patients requiring postoperative RRT are shown in Table E1. Their mean age and preoperative eGFR were 77.9 ± 3.0 years old and 29.4 ± 23.4 mL/min/1.73 m^2, respectively. Accordingly, the average EuroSCORE II and Japan scores were as high as 6.5 ± 3.4 and 9.5 ± 4.8, respectively. Eight of the 11 patients underwent concomitant CABGs, which was reflected by a longer operation time (549.2 ± 181.7 minutes) and cardiopulmonary bypass time (200.8 ± 65.5 minutes), although the lower body circulatory arrest time was shorter and body temperatures were lower when compared with the overall patient group. Hospital mortality among patients with postoperative RRT was as high as 36.4% (4/11) versus 0.4% (1/218) among patients without RRT ($P < .0001$).

The area under the curve of receiver operating characteristics for preoperative eGFR for predicting postoperative de novo RRT was 0.82 ($P < .0001$), and the best cutoff value of preoperative eGFR for predicting postoperative RRT after

TABLE 2. Operation characteristics, hospital mortality and postoperative complications

Variables	Total	Normal eGFR >90 (mL/min/1.73 m^2)	Mild eGFR dysfunction 60-90	Moderate eGFR dysfunction 30-59	Severe eGFR dysfunction <30	*P* value
No. of patients	229	11 (4.7)	86 (36.9)	111 (47.6)	21 (9.0)	
Operation time (min)	415.1 ± 136.1	413.5 ± 160.6	403.1 ± 140.3	412.0 ± 119.3	481.2 ± 177.3	.026
CPB time (min)	173.2 ± 52.0	160.3 ± 45.2	168.6 ± 53.0	177.3 ± 50.3	177.2 ± 60.3	.052
Myocardial ischemic time (min)	77.2 ± 39.6	77.7 ± 31.9	75.8 ± 46.8	78.8 ± 36.3	74.3 ± 32.4	.18
SCP time (min)	89.3 ± 22.1	90.7 ± 26.1	90.4 ± 21.8	89.3 ± 23.1	84.3 ± 16.0	.82
Lower body circulatory arrest time (min)	38.8 ± 12.1	41.0 ± 13.7	38.3 ± 11.4	40.2 ± 12.2	31.0 ± 14.7	.88
Minimum tympanic temperature (°C)	21.5 ± 1.7	22.0 ± 2.0	21.8 ± 1.5	21.3 ± 1.5	20.4 ± 2.3	1.00
Minimum rectal temperature (°C)	25.9 ± 2.3	26.8 ± 1.8	26.3 ± 2.1	25.7 ± 2.1	24.5 ± 3.3	1.00
Thirty-day mortality	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	NA
Hospital mortality	5 (2.2)	0 (0)	1 (1.2)	1 (0.9)	3 (14.3)	.03
PND	6 (2.6)	0 (0)	0 (0)	4 (3.6)	2 (9.5)	.013
TND	20 (8.7)	0 (0)	6 (7.0)	11 (9.9)	3 (14.3)	.15
Mediastinitis	5 (2.2)	1 (9.1)	0 (0)	3 (2.7)	1 (4.8)	.41
Prolonged ventilation (≥48 h)	30 (13.1)	0 (0)	8 (9.3)	10 (9.0)	12 (57.1)	<.01
RRT	11 (4.8)	0 (0)	2 (2.3)	1 (0.9)	8 (38.1)	<.01
Continuous hemodiafiltration	10 (4.4)	0 (0)	2 (2.3)	1 (0.9)	7 (33.3)	<.01
Hemodialysis	4 (1.7)	0 (0)	2 (2.3)	0 (0)	2 (9.5)	.47
Gastrointestinal tract (necrosis)	2 (0.9)	0 (0)	0 (0)	1 (0.9)	1 (4.8)	.094

eGFR, Estimated glomerular filtration rate; *CPB*, cardiopulmonary bypass, *SCP*, selective cerebral perfusion, *PND*, permanent neurologic deficit, *TND*, transient neurologic deficit; *RRT*, renal replacement therapy.

TAR was determined to be 26.0 mL/min/1.73 m^2 (sensitivity, 72.7%; specificity, 95.8%).

A midterm follow-up was completed for 93% of the patients, and the mean follow-up period was 29.6 ± 28.2 months (range, 0.3-114.8 months; median, 19.7 months). Figure 1 shows the Kaplan-Meier survival curves for the patients stratified by the preoperative eGFR. The survival was clearly stratified and worse across the lower categories of eGFR. The Cox proportional hazard analysis (Table E2) showed that atherothrombotic aorta, chronic obstructive pulmonary disease, and lower eGFR were risk factors for midterm mortality. In Figure E1, data are shown for freedom from MACCE, which was also stratified across the levels of preoperative eGFR. However, no stratification existed for freedom from aorta-related death (figure not shown).

DISCUSSION

This retrospective study determined that preoperative patient profiles and the short-term, and midterm outcomes after elective TAR were clearly stratified by universally used eGFR, whereas creatinine level has significant limitations in this role because the definition of renal insufficiency using serum creatinine level varies.

Preoperative renal dysfunction is one of the strongest risk factors that predict poor short- and long-term outcomes; these poor outcomes occurred more frequently in patients with renal dysfunction not requiring dialysis that underwent CABG.[11] Recent literature demonstrated the risk factors for postoperative acute kidney injury defined by RIFLE criteria (RIFLE = risk, injury, failure, loss, end stage) after thoracic aortic surgery,[17] and a higher RIFLE classification was associated with worse short-term outcomes. However, little is known about the impact of preoperative renal function on outcomes after TAR, which involves an ischemic insult against the kidneys.

Previous studies and risk stratification systems like the EuroSCORE and Japan score have used serum creatinine as the preoperative determinant for the degree of renal failure. Serum creatinine is generally accepted to be an insensitive indicator of renal function. Compared with creatinine levels, eGFR has been noted as the most reliable index of renal function according to the National Kidney Foundation guidelines.[8] The recently revised EuroSCORE II also uses the creatinine clearance calculated by the Cockcroft-Gault formula for the risk model in contemporary cardiac surgery.[16] In the current study, the Japanese formula for eGFR developed by collaborators was applied to take into consideration the differences in creatinine generation among ethnicities.[12] Patients with lower categories of eGFR tended to be older, have more comorbidities, and consequently higher scores for the EuroSCORE II and Japan scoring systems. These associations have been shown to be similar even with different modes of cardiovascular operations.[11,18]

Go and associates[10] reported the close relationship between eGFR and MACCE in a large community-based population. Anavekar and associates[9] demonstrated that even mild renal disease, as assessed by eGFR, should be considered a major risk factor for cardiovascular complications after a myocardial infarction. In the literature, other researchers have demonstrated that mild renal dysfunction

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TABLE 3. Risk factors for hospital mortality identified by univariate and multivariate analysis

	Hospital mortality			
	Univariate		Multivariate	
Variables	OR (95% CI)	P	OR (95% CI)	P
Age, y, mean ± SD	1.25 (1.03-1.54)	.028	1.33 (1.01-1.74)	.04
Octogenarian	6.14 (0.99-37.9)	.051		
Atherothrombotic aorta	9.00 (1.44-56.0)	.02	15.5 (0.82-291.7)	.07
Serum Cr level (mg/dL)	4.13 (2.09-8.14)	<.0001	17.0 (0.79-366.5)	.07
eGFR (mL/min/1.73 m^2)	0.92 (0.87-0.98)	.005	0.91 (0.83-1.00)	.02
Diabetes mellitus	0.57 (0.07-4.62)	.60		
Hypertension	0.69 (0.08-6.38)	.74		
Dyslipidemia	0.37 (0.04-3.39)	.38		
Smoking	0.28 (0.05-1.71)	.17		
Extracranial carotid artery stenosis	1.90 (0.21-17.7)	.57		
Coronary artery disease	8.62 (0.95-78.5)	.056		
Left ventricular EF (≤40%)	5.35 (0.55-52.4)	.15		
COPD	6.80 (1.07-43.1)	.04	2.50 (0.13-47.8)	.54
Concurrent procedure	4.37 (0.48-39.8)	.19		
Operation time (min)	1.01 (1.00-1.01)	.017	1.01 (1.00-1.01)	.10
CPB time (min)	1.01 (1.00-1.02)	.48		
Myocardial ischemic time (min)	0.99 (0.96-1.02)	.56		
SCP time (min)	1.00 (0.97-1.04)	.83		
Lower body circulatory arrest time (min)	0.93 (0.85-1.02)	.10		
Minimum tympanic temperature (°C)	0.87 (0.50-1.55)	.65		
Minimum rectal temperature (°C)	1.00 (0.68-1.47)	.98		

Variables of sex (female), dissection, old cerebral infarction, peripheral arterial disease, and concurrent procedure were not tested because hospital mortality was not observed in patients with the factors. *OR*, Odds ratio; *CI*, confidence interval; *SD*, standard deviation; *Cr*, creatinine; *eGFR*, estimated glomerular filtration rate; *EF*, ejection fraction; *COPD*, chronic obstructive pulmonary disease; CPB, cardiopulmonary bypass; *SCP*, selective cerebral perfusion.

TABLE 4. Risk factors for postoperative renal replacement therapy (CHDF, HD) identified by univariate and multivariate analysis

	Postoperative renal replacement therapy			
	Univariate		Multivariate	
Variables	OR (95% CI)	P	OR (95% CI)	P
Age, y, mean ± SD	1.11 (1.00-1.23)	.048	1.12 (0.98-1.28)	.11
Octogenarian	1.52 (0.39-5.96)	.55		
Male gender	3.29 (0.41-26.3)	.26		
Serum Cr level (mg/dL)	5.11 (2.55-10.2)	<.0001	4.20 (2.12-8.30)	<.0001
eGFR (mL/min/1.73 m^2)	0.93 (0.90-0.97)	<.0001	0.94 (0.90-0.98)	.002
Diabetes mellitus	0.57 (0.07-4.62)	.60		
Hypertension	1.75 (0.22-14.1)	.60		
Dyslipidemia	1.89 (0.56-6.41)	.30		
Smoking	0.50 (0.15-1.69)	.26		
Extracranial carotid artery stenosis	3.09 (0.77-12.5)	.11		
Coronary artery disease	5.91 (1.52-23.0)	.01	1.95 (0.38-9.88)	.42
Chronic atrial fibrillation	1.75 (0.21-14.8)	.61		
COPD	2.24 (0.45-11.1)	.32		
Concurrent procedure	3.03 (0.78-11.7)	.11		
Operation time (min)	1.01 (1.00-1.01)	.002	1.00 (1.00-1.01)	.08
CPB time (min)	1.01 (1.00-1.02)	.07		
Myocardial ischemic time (min)	1.00 (0.98-1.02)	.91		
SCP time (min)	0.98 (0.95-1.02)	.34		
Lower body circulatory arrest time (min)	0.96 (0.91-1.02)	.20		
Minimum tympanic temperature (°C)	0.53 (0.34-0.82)	.005	0.73 (0.44-1.19)	.20
Minimum rectal temperature (°C)	0.87 (0.68-1.12)	.28		

Variables of dissection, old cerebral infarction, and peripheral arterial disease were not tested because renal replacement therapy was not observed in patients with the factors. *OR*, Odds ratio; *CI*, confidence interval; *SD*, standard deviation; *Cr*, creatinine; *eGFR*, estimated glomerular filtration rate; *COPD*, chronic obstructive pulmonary disease; *CPB*, cardiopulmonary bypass, *SCP*, selective cerebral perfusion.

was the most prevalent in the patients undergoing CABG or valve surgery, whereas in the current study, moderate dysfunction was the most prevalent type. Therefore, we should pay more attention to patients undergoing TAR. As for hospital mortality, we found no increase in patients with mild and moderate renal dysfunction. However, hospital mortality was increased to as high as 14.3% in patients with severe dysfunction. Hillis and associates[11] confirmed that an eGFR level of 60 mL/min/1.73 m^2 (mild dysfunction) was the most useful in predicting 30-day mortality in patients undergoing CABG. There was no 30-day mortality in the current study, and therefore we cannot compare the level of preoperative eGFR in predicting early mortality to previous studies. However, a lower preoperative level of eGFR was proven to be a risk factor for hospital mortality (OR, 0.91; 95% confidence interval, 0.83-1.00; $P = .02$) by multivariate analysis, whereas serum creatinine level was not. Renal dysfunction requiring postoperative RRT leads to increased postoperative mortality. Bove and associates[19] reported that hospital mortality was 40.9% in patients with acute renal failure and increased to 63.8% when RRT was indicated. With regard to thoracic aortic surgery involving deep hypothermic circulatory arrest, both Estrera and associates[7] and

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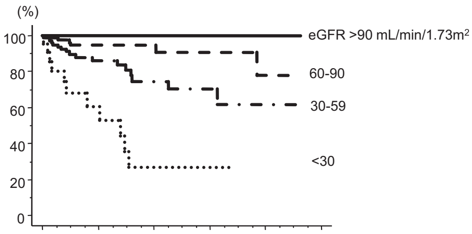


Number at risk	0	24	48	72	96	(months)
>90 mL/min/1.73m²	11	7	4	2	1	
60-90	86	45	26	14	6	
30-59	111	41	21	10	1	
<30	21	8	3	2	0	

FIGURE 1. Survival curve across the quartile stratified by preoperative estimated glomerular filtration rate *(eGFR)* showing survival at 36 months after surgery of 100.0% ± 0% (normal eGFR), 94.5% ± 2.7% (mild), 80.8% ± 5.3% (moderate), and 35.4% ± 13.3% (severe eGFR dysfunction).

Augoustides and associates[6] identified postoperative RRT as one of the risk factors for mortality. In the current study, hospital mortality among patients with postoperative RRT was as high as 36.4% (4/11) versus 0.4% (1/218) among patients without the therapy ($P < .0001$). Estimated GFR (OR, 0.94; $P = .002$) and serum creatinine level (OR, 4.2; $P < .0001$) were risk factors for postoperative RRT according to multivariate analysis. However, neither lower body circulatory arrest time nor minimum rectal temperature, which was supposed to have an impact on the degree of renal ischemic insult, was a risk factor. The analysis suggests that it might be difficult to prevent the postoperative deterioration of renal function in patients with severe renal dysfunction by lowering the degree of the rectal temperature alone. In comparison with eGFR, our data suggested that creatinine level was also a strong predictor with regard to postoperative renal dysfunction but was less sensitive for predicting hospital mortality. We believe that eGFR could be a more accurate predictor for comorbidities except renal dysfunction than serum creatinine level inasmuch as eGFR was calculated using 3 independent variables of gender, age, and serum creatinine. Hence, we identified the importance of risk factors for predicting postoperative de novo RRT and a cutoff value of preoperative eGFR predictive of RRT. Eventually, we confirmed that eGFR was a risk factor for the requirement of de novo RRT, and an eGFR level of 26 mL/min/1.73 m^2 (severe dysfunction) was the critical threshold below which RRT was likely to be needed postoperatively. Although Englberger and associates[20] reported that deep hypothermic circulatory arrest and preoperative serum creatinine were not risk factors for acute kidney injury in thoracic aortic surgery, we confirmed that severe renal dysfunction assessed by eGFR might deserve special attention. The cutoff value is critical to the field of aortic surgery because the procedure induces renal ischemia during the distal anastomosis. The finding will help surgeons to better identify patients at risk of de novo RRT after TAR and perform additional perioperative renal protection, such as lower body perfusion during distal anastomosis[21] or pharmacologic intervention. Hybrid thoracic endovascular aortic repair is expected to be an alternative to open surgery in this era. However, Benedetto and associates[22] failed to supports the superiority of hybrid procedure relative to open surgery using a meta-analysis. The selection remains controversial.

With regard to morbidities, lower categories of eGFR were significantly associated with more permanent neurologic deficit and prolonged ventilation. Zierer and associates[23] demonstrate that unilateral antegrade cerebral perfusion offers at least equal brain protection as bilateral antegrade cerebral perfusion by reducing the incidence of embolism arising from surgical manipulation on the arch vessels. Inasmuch as patients with lower categories of eGFR have greatly accelerated vascular disease and a very high cardiac risk,[24] it might be one of the alternatives to bilateral perfusion for brain protection so long as the circle of Wills in the brain is preserved.

Both midterm survival and freedom from MACCE were compromised at the lower categories of eGFR. The Cox proportional hazard analysis determined that atherothrombotic aorta, preoperative lower categories of eGFR, and chronic obstructive pulmonary disease had an adverse impact on midterm mortality. Our previous study also determined that patients with atherothrombotic aorta (shaggy aorta) had decreased midterm survival compared with patients without atherothrombotic aorta.[15] Taken together, our data have elucidated that preoperative eGFR could play a pivotal role in predicting outcomes after contemporary TAR.

Limitations

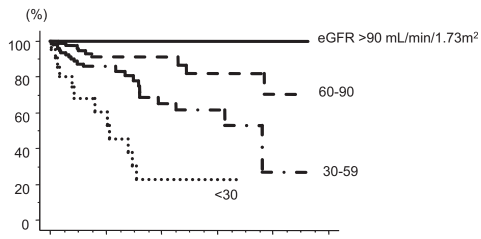
This is a retrospective study from a single center. The logistic regression analysis for hospital mortality was limited by the small number of events, because our surgical approach generally provided satisfactory outcomes. Patients requiring preoperative HD were excluded because of the small number of these cases (n = 4, no hospital mortality). The completion of midterm follow-up was relatively low (93%) and the mean follow-up period was short (29.6 ± 28.2 months; range, 0.3-114.8 months; median, 19.7 months).

CONCLUSIONS

Hospital mortality in patients requiring postoperative RRT was quite high. Preoperative eGFR was a strong predictor for short-term and midterm outcomes in TAR. Patients with severe renal dysfunction (eGFR <30) and associated preoperative comorbidities may be predisposed to adverse outcomes after TAR.

References

1. Okada K, Omura A, Kano H, Sakamoto T, Tanaka A, Inoue T, et al. Recent advancements of total aortic arch replacement. *J Thorac Cardiovasc Surg*. 2012;144:139-45.
2. Sakata R, Fujii Y, Kuwano H. Thoracic and cardiovascular surgery in Japan during 2009: annual report by the Japanese Association for Thoracic Surgery. *Gen Thorac Cardiovasc Surg*. 2011;59:636-67.
3. Hobson CE, Yavas S, Segal MS, Schold JD, Tribble CG, Layon AJ, et al. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. *Circulation*. 2009;119:2444-53.
4. Roh GU, Lee JW, Nam SB, Lee J, Choi JR, Shim YH. Incidence and risk factors of acute kidney injury after thoracic aortic surgery for acute dissection. *Ann Thorac Surg*. 2012;94:766-71.
5. Motomura N, Miyata H, Tsukihara H, Takamoto S. Risk model of thoracic aortic surgery in 4707 cases from a nationwide single-race population through a web-based data entry system: the first report of 30-day and 30-day operative outcome risk models for thoracic aortic surgery. *Circulation*. 2008;118:S153-9.
6. Augoustides JG, Pochettino A, Ochroch EA, Cowie D, Weiner J, Gambone AJ, et al. Renal dysfunction after thoracic aortic surgery requiring deep hypothermic circulatory arrest: definition, incidence, and clinical predictors. *J Cardiothorac Vasc Anesth*. 2006;20:673-7.
7. Estrera AL, Miller CC III, Huynh TT, Porat EE, Safi HJ. Replacement of the ascending and transverse aortic arch: determinants of long-term survival. *Ann Thorac Surg*. 2002;74:1058-64.
8. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002;39:S1-266.
9. Anavekar NS, McMurray JJ, Velazquez EJ, Solomon SD, Kober L, Rouleau JL, et al. Relation between renal dysfunction and cardiovascular outcomes after myocardial infarction. *N Engl J Med*. 2004;351:1285-95.
10. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu CY. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. *N Engl J Med*. 2004;351:1296-305.
11. Hillis GS, Croal BL, Buchan KG, El-Shafei H, Gibson G, Jeffrey RR, et al. Renal function and outcome from coronary artery bypass grafting: impact on mortality after a 2.3-year follow-up. *Circulation*. 2006;113:1056-62.
12. Matsuo S, Imai E, Horio M, Yasuda Y, Tomita K, Nitta K, et al. Revised equations for estimated GFR from serum creatinine in Japan. *Am J Kidney Dis*. 2009;53:982-92.
13. Glas KE, Swaminathan M, Reeves ST, Shanewise JS, Rubenson D, Smith PK, et al. Guidelines for the performance of a comprehensive intraoperative epiaortic ultrasonographic examination: recommendations of the American Society of Echocardiography and the Society of Cardiovascular Anesthesiologists; endorsed by the Society of Thoracic Surgeons. *Anesth Analg*. 2008;106:1376-84.
14. Ergin MA, Galla JD, Lansman L, Quintana C, Bodian C, Griepp RB. Hypothermic circulatory arrest in operations on the thoracic aorta: determinants of operative mortality and neurologic outcome. *J Thorac Cardiovasc Surg*. 1994;107:788-97.
15. Okada K, Omura A, Kano H, Inoue T, Oka T, Minami H, et al. Effect of atherothrombotic aorta on outcomes of total aortic arch replacement. *J Thorac Cardiovasc Surg*. In press.
16. Nashef SA, Roques F, Sharples LD, Nilsson J, Smith C, Goldstone AR, et al. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41:734-44.
17. Arnaoutakis GJ, Bihorac A, Martin TD, Hess PJ Jr, Klodell CT, Ejaz AA, et al. RIFLE criteria for acute kidney injury in aortic arch surgery. *J Thorac Cardiovasc Surg*. 2007;134:1554-60.
18. Dhanani J, Mullany DV, Fraser JF. Effect of preoperative renal function on long-term survival after cardiac surgery. *J Thorac Cardiovasc Surg*. In press.
19. Bove T, Calabro MG, Landoni G, Aletti G, Marino G, Crescenzi G, et al. The incidence and risk of acute renal failure after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2004;18:442-5.
20. Englberger L, Suri RM, Greason KL, Burkhart HM, Sundt TM III, Daly RC, et al. Deep hypothermic circulatory arrest is not a risk factor for acute kidney injury in thoracic aortic surgery. *J Thorac Cardiovasc Surg*. 2011;141:552-8.
21. Matsuyama S, Tabata M, Shimokawa T, Matsushita A, Fukui T, Takanashi S. Outcomes of total arch replacement with stepwise distal anastomosis technique and modified perfusion strategy. *J Thorac Cardiovasc Surg*. 2012;143:1377-81.
22. Benedetto U, Melina G, Angeloni E, Codispoti M, Sinatra R. Current results of open total arch replacement versus hybrid thoracic endovascular aortic repair for aortic arch aneurysm: a meta-analysis of comparative studies. *J Thorac Cardiovasc Surg*. 2013;145:305-6.
23. Zierer A, El-Sayed AA, Papadopoulos N, Moritz A, Diegeler A, Urbanski PP. Selective antegrade cerebral perfusion and mild (28°C-30°C) systemic hypothermic circulatory arrest for aortic arch replacement: results from 1002 patients. *J Thorac Cardiovasc Surg*. 2012;144:1042-50.
24. Jardine AG, McLaughlin K. Cardiovascular complications of renal disease. *Heart*. 2001;86:459-66.



Number at risk	0	24	48	72	96 (months)
>90 mL/min/1.73m^2	11	7	4	2	1
60-90	86	44	25	14	6
30-59	111	40	20	9	1
<30	21	8	3	2	0

FIGURE E1. Freedom from major adverse cerebrocardiovascular events across the quartile stratified by preoperative estimated glomerular filtration rate *(eGFR)* showing the freedom at 36 months after surgery of 100% ± 0% (normal eGFR), 91.2% ± 3.5% (mild), 78.0% ± 5.6% (moderate), and 30.3% ± 12.3% (severe eGFR dysfunction).

TABLE E1. Details for patients who required postoperative RRT

No.	Age	Sex	EuroSCORE II	Japan score	Preop Cr	Preop eGFR	Concomitant procedure	Op time	CPB time	CA time	Min tympanic temp (°C)	Min rectal temp (°C)	Postop de novo RRT	Outcome at discharge	Causes of death
1	77	M	5.3	10.2	4.2	11.6	No	580	154	27	20.0	28.5	CHDF	Alive	
2	84	M	11.8	16.7	4.5	10.5	CABG	605	178	30	20.0	26.0	CHDF	Death	Bowel necrosis
3	79	M	6.4	4.0	0.78	72.6	CABG	840	185	45	20.3	27.3	CHDF/HD	Death	Sepsis
4	76	M	9.6	8.3	2.1	25.4	CABG	425	160	35	19.8	20.8	CHDF	Alive	
5	79	M	10.1	15.5	3.0	16.4	CABG	905	227	41	19.2	25.4	HD	Alive	
6	73	F	1.9	2.2	0.64	68.2	CABG	505	263	30	18.4	28.0	CHDF/HD	Alive	
7	75	M	3.4	8.0	2.6	19.9	No	300	143	28	19.0	24.2	CHDF	Alive	
8	78	M	8.6	12.6	2.0	26.0	CABG	556	368	63	19.7	21.6	CHDF	Alive	
9	80	M	8.3	12.8	4.1	11.8	CABG	464	157	2	21.7	24.6	CHDF/HD	Death	Pulmonary
10	80	M	2.3	4.0	1.1	51.2	CABG	422	178	40	20.7	26.3	CHDF	Alive	
11	76	M	3.5	10.0	4.7	10.3	No	439	196	0	22.1	23.9	CHDF	Death	Bowel necrosis

RRT, Renal replacement therapy; *M*, male; *F*, female; *Cr*, creatinine; *eGFR*, estimated glomerular filtration rate; *Op*, operation; *CPB*, cardiopulmonary bypass; *CA*, circulatory arrest; *Min*, minimum; *CABG*, coronary artery bypass grafting; *CHDF*, continuous hemodiafiltration; *HD*, hemodialysis.

ACD

TABLE E2. Cox proportional hazard analysis

Variables	OR (95% CI)	*P*
Age	1.07 (1.00-1.15)	.06
Female	1.37 (0.55-3.39)	.50
Dissection	1.81 (0.20-16.1)	.60
Atherothrombotic aorta	3.08 (1.27-7.46)	.01
eGFR (mL/min/1.73 m^2)	0.95 (0.93-0.97)	<.0001
Diabetes mellitus	1.21 (0.46-3.21)	.70
Hypertension	1.06 (0.38-2.96)	.92
Dyslipidemia	0.83 (0.38-1.82)	.64
History of smoking	0.91 (0.39-2.13)	.83
Old cerebral infarction	0.79 (0.17-3.77)	.77
Extracranial carotid artery stenosis	0.47 (0.13-1.66)	.24
Coronary artery disease (CABG)	1.63 (0.47-5.59)	.44
Low left ventricular EF (≤40%)	2.11 (0.64-6.99)	.22
COPD	3.25 (1.24-8.47)	.02
Peripheral arterial disease	0.76 (0.21-2.81)	.68
Concurrent procedure	1.04 (0.28-3.80)	.96

eGFR, Estimated glomerular filtration rate; *CABG*, coronary artery bypass grafting, *EF*, ejection fraction; *COPD*, chronic obstructive pulmonary disease; *OR*, odds ratio; *CI*, confidence interval.