Comparison of the effects of open and endovascular aortic aneurysm repair on long-term renal function using chronic kidney disease staging based on glomerular filtration rate

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Objective: **It has been suggested that endovascular aneurysm repair (EVAR) in concert with serial contrast-enhanced computed tomography (CT) surveillance adversely impacts renal function. Our primary objectives were to assess serial renal function in patients undergoing EVAR and open repair (OR) and to evaluate the relative effects of method of repair on renal function.**

Methods: **A thorough retrospective chart review was performed on 223 consecutive patients (103 EVAR, 120 OR) who underwent abdominal aortic aneurysm (AAA) repair. Demographics, pertinent risk factors, CT scan number, morbidity, and mortality were recorded in a database. Baseline, 30- and 90-day, and most recent glomerular filtration rate (GFR) were calculated. Mean GFR changes and renal function decline (using Chronic Kidney Disease [CKD] staging and Kaplan-Meier plot) were determined. EVAR and OR patients were compared. CKD prevalence (≥stage 3, National Kidney Foundation) was determined before repair and in longitudinal follow-up. Observed-expected (OE) ratios for CKD were calculated for EVAR and OR patients by comparing observed CKD prevalence with the expected, age-adjusted prevalence.**

Results: **The only baseline difference between EVAR and OR cohorts was female gender (4% vs 12%, $P = .029$). Thirty-day GFR was significantly reduced in OR patients ($P = .047$), but it recovered and there were no differences in mean GFR at a mean follow-up of 23.2 months. However, 18% to 39% of patients in the EVAR and OR groups developed significant renal function decline over time depending on its definition. OE ratios for CKD prevalence were greater in AAA patients at baseline (OE 1.28-3.23, depending upon age group). During follow-up, the prevalence and severity of CKD increased regardless of method of repair (OE 1.8-9.0). Deterioration of renal function was independently associated with age >70 years in all patients (RR 2.92) and performance of EVAR compared with OR (RR 3.5) during long-term follow-up.**

Conclusions: **Compared with EVAR, OR was associated with a significant but transient fall in GFR at 30 days. Renal function decline after AAA repair was common, regardless of method, especially in patients >70 years of age. However, the renal function decline was significantly greater by Kaplan-Meier analysis in EVAR than OR patients during long-term follow-up. More aggressive strategies to monitor and preserve renal function after AAA repair are warranted. (J Vasc Surg 2008;47:1141-9.)**

Since its introduction in 1991, endovascular aneurysm repair (EVAR) has been well-accepted for patients with favorable anatomy due to reductions in early morbidity and mortality compared with open abdominal aortic aneurysm (AAA) repair.[1-3] However, EVAR is associated with unique and procedure-specific complications such as endoleak, stent graft migration and collapse, and endograft limb occlusions. For these reasons, EVAR patients require close follow-up with serial contrast-enhanced computed tomography (CT) surveillance, creating the potential for adverse effects on renal function due to the endoluminal manipulations and contrast administration required to place the endograft, as well as the risks of nephrotoxicity from repetitive contrast administration associated with serial CT scans.

The issue of renal function deterioration after EVAR is important. Numerous authors have analyzed the problem from a variety of perspectives. Initially, most published studies focused on the incidence of early postoperative renal insufficiency (30 to 90 days). Existing reporting standards generally focus on early postoperative renal function decline.[4-7] Recently, published investigations have examined the potential adverse effects of EVAR on long-term renal function. Progressive renal function decline is likely to be multifactorial and may be attributable to pre-existing renal dysfunction, a host of comorbidities, the AAA repair procedure itself, device-type, and the diagnostic and therapeutic procedures required to evaluate and treat endograft-related complications during follow-up. Pertinent questions, which various investigators have sought to answer, generally concern

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Competition of interest: Dr Mills has served as a paid consultant for Bard, Inc and has received author's royalties from Elsevier Ltd.

Presented at the Twenty-second Annual Meeting of the Western Vascular Society, Kona, Hawaii, Sept 9, 2007.

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0741-5214/$34.00

doi:10.1016/j.jvs.2008.01.039

seven issues: (1) what is the prevalence of baseline renal insufficiency in AAA patients?[8-10]; (2) does EVAR adversely impact renal function compared with open AAA repair (OR), and if so, how frequently?[11-20]; (3) among patients undergoing EVAR, is there a difference in the development of renal function deterioration following infrarenal (IR) vs suprarenal (SR) fixation?[14-16,21-30]; (4) do surveillance CT scans contribute to renal function deterioration after EVAR?[16]; (5) what are the risk factors for declining renal function after EVAR and OR?[16,18,19]; (6) can EVAR be done safely in patients with pre-existing renal impairment?[11,31-34]; and (7) does baseline renal insufficiency increase perioperative and long-term morbidity and mortality?[8]

Nearly all published studies of the effect of EVAR on renal function are limited by short follow-up, lack of open control groups, variable definitions of postoperative renal dysfunction, use of serum creatinine level (SCr) instead of creatinine clearance (CrCl) or glomerular filtration rates (GFR) as a measure of renal function, and a multitude of other confounding variables. Some authors have reported no long-term effect of EVAR on renal function [15,17,21,30] while others have found a significant decline in renal function over time.[3,14,16,22,24,25,29] A recent meta-analysis reported no difference in renal function after EVAR compared with open repair,[35] but most studies were short-term and the definitions of renal function decline were highly variable. No study has attempted to differentiate expected serial declines in renal function due to the effects of age and pre-existing renal function opposed to procedure-related deterioration.

We were concerned about the potential adverse effect of serial contrast administration as part of contemporary EVAR surveillance protocols on renal function. We, therefore, analyzed a consecutive series of patients who underwent EVAR and OR at two affiliated academic institutions to determine the impact of AAA repair on long-term renal function.

METHODS

The study was approved by the Institutional Review Boards of both institutions. Retrospective data were collected on 223 consecutive patients undergoing EVAR and OR at University Medical Center (UMC) and the Southern Arizona Veterans Affairs Health Care System (SAVAHCS) in Tucson, Arizona from January 2001 to December 2006. Twenty-nine patients undergoing juxtarenal OR were included; however, all patients with ruptured aneurysms and those with preoperative dialysis-dependent renal failure were excluded. Patient demographics (age, gender, and weight), comorbidities (coronary disease, hypertension [HTN], hyperlipidemia, diabetes mellitus, and tobacco use), maximum aneurysm diameter, follow-up length, major morbidity, and mortality were recorded in Microsoft Excel (Microsoft, Redmond, Wash). In addition, the presence of renal artery stenosis, use of ACE (angiotensin converting enzyme) inhibitors and nonsteroidal anti-inflammatory drugs (NSAID), and number of contrast studies and total contrast volume were recorded; baseline, 30- and 90-day, and most recent SCr levels were collected.

Baseline, 30- and 90-day, and most recent glomerular filtration rate (GFR) were estimated using the Cockcroft-Gault equation: GFR = (140-age) × weight/72 × SCr × (0.85 if female). The modification of diet in renal disease (MDRD) study equation was not used since there were very few African American patients in this series, and the recording of self-identified race was inconsistent and inaccurate. Changes in mean GFR and chronic kidney disease (CKD) stage[36] as well as the incidence of >10% and >20% postoperative decline in GFR were calculated for both EVAR and OR cohorts.

Methodology for analyzing long-term renal function in study patients. Our primary objective was the evaluation of long-term rather than acute renal function decline after AAA repair. There is a published, validated classification for the evaluation and management of CKD that has clinical and prognostic significance: the CKD staging system (NKF/KDOQI -National Kidney Foundation/Kidney Disease Outcomes Quality Initiative).[36] This system was therefore applied in our study.

We stratified baseline renal function as normal (stage 1 and 2: GFR > 60 ml/min/1.73m^2) and abnormal (CKD ≥ 3, GFR < 60). During long-term follow-up, we chose to define renal function decline differently for each subgroup. For normal patients, a sustained drop in GFR to <60 (ie, development of CKD) was defined as renal function decline. Minor GFR fluctuations in patients who remain in stage 1 or 2 have not been shown to have clinical significance. In contrast, for patients whose GFR drops to "<60, the prevalence of complications of CKD increases, as does the risk of cardiovascular disease." [36] Therefore, progression to stage 3 is clinically relevant.

The second issue was how to define renal function decline in patients with pre-existing CKD at study entry. CKD stage 3 patients have a 30 < GFR < 60 ml/min/1.73m^2, stage 4 patients have a GFR < 30 ml/min/1.73m^2, and stage 5 patients (excluded from study) are receiving renal replacement therapy. The natural history of most forms of CKD tends to be progressive, but the slope of serial GFR decline is variable. In the MDRD study, mean GFR decline in CKD patients over 2 years was 4 ml/min/1.73m^2/y and was unrelated to baseline GFR. Rapid decline was defined as a fall in GFR > 4/y and slow decline as <4/yr (guidelines 2 and 13).[36] Since the majority of study patients with pre-existing CKD had a baseline GFR in the range of 40 < GFR < 59, a >20% reduction in GFR over 2 years would equate to rapid GFR decline (>4/y). We therefore defined renal function decline in CKD patients as a GFR reduction of >20% (more rapid than expected for CKD patients as a group) or the need for permanent renal replacement therapy.

All patients were classified into CKD stages 1 to 4 prior to intervention. CKD 5 patients undergoing hemodialysis at the time of AAA repair were excluded. CKD stage was recalculated for all patients based on GFR at most recent follow-up visit. Observed CKD stage distribution at base-

Table I. Patient demographics

	OR	*EVAR*	P *value*
Age (range)	72.4 (52-86)	73.2 (55-90)	.42
Gender (n[%])			.02
Male	105 (88%)	99 (96%)	
Female	15 (12%)	4 (4%)	
Body weight (kg)	78.7 (49-117)	81.3 (44-144)	.56
Risk factors (n[%])			
Diabetes mellitus	15 (12.7%)	15 (14.7%)	.67
Cardiac disease	51 (43.6%)	46 (15.3%)	.89
Hypertension	100 (84.7%)	83 (80.6%)	.41
Hyperlipidemia	68 (58.1%)	69 (70.0%)	.18
RAS	10 (10.9%)	4 (3.8%)	.09
Smokers (active)	47 (39.8%)	27 (28.1%)	.20
NSAID	7 (7.1%)	15 (14.6%)	.11
ACE inhibitor	29 (29.9%)	42 (41.2%)	.10
Aneurysm size (cm±standard deviation)	5.9 ± 1.0	5.8 ± 1.1	.09
Number of CT (n ± standard deviation)	1.4 ± 2.2	5.1 ± 4.1	<.001
Length of follow-up [months [range])	20.7 (0-86)	24.7 (0-67)	.16

OR, Open abdominal aortic aneurysm repair; *EVAR*, endovascular abdominal aortic aneurysm repair; *RAS*, renal artery stenosis; *NSAID*, non-steroidal anti-inflammatory drugs; *ACE*, angiotensin-converting enzyme; *CT*, contrast computed tomography scan.

line and at maximum longitudinal follow-up, stratified by patient age (40 to 59 years, 60 to 69 years, and > 70 years) was compared with the expected distribution of CKD stages in the general population (NHANES III, Table 26, guidelines Part IV).[36] OE (observed-expected) ratios were calculated to determine whether clinically significant progression of CKD occurred after aneurysm repair over time. OE ratios are an accepted method of evaluating the prevalence of given diseases or treatment outcomes in small populations compared with a large population-based data base.[37]

Statistical analysis. Freedom from renal dysfunction over time was calculated by means of the Kaplan-Meier method using the definitions of renal function decline outlined above. We planned to use the log-rank test to detect differences between the two treatment methods. Since the two curves cross, the follow-up time was divided into two periods—short- and long-term follow-up. The log-rank test was computed separately for the two periods. These results were confirmed with an extended Cox model with two heaviside functions. Statistical analyses were performed using SPSS software (SPSS, Inc, Chicago, Ill) with differences of $P < .05$ considered statistically significant. Poisson confidence intervals (CI) for OE ratios were calculated using a website calculator[38] and the CI used was 95% Poisson exact.

RESULTS

The OR and EVAR groups were comparable (Table I). The distribution of age, weight, and virtually all comorbidities did not differ between study groups. The only significant baseline difference was gender with 12% women in the OR group compared with 4% in the EVAR cohort ($P = .02$). The mean number of CT scans also differed significantly, 1.4 for OR patients vs 5.1 for EVAR patients ($P < .001$), as would be expected for patients undergoing EVAR surveillance. Mean follow-up was 23.2 months and did not differ significantly between study groups.

Early postoperative renal dysfunction reflected by a lower mean GFR at 30-days was more common after OR than EVAR ($P < .047$), but this effect was transient and there was no difference in mean GFR between EVAR and OR patients at 90 days or anytime thereafter (Table II). Juxtarenal OR patients had a slightly greater 30-day decline in GFR than infrarenal OR patients, but this difference was not statistically significant ($P = .11$). There was also no difference between these two OR sub-groups during long-term follow-up. However, in both OR and EVAR patients, there was a significant decline in renal function, no matter how it was defined, in a substantial proportion of patients during follow-up (Table III). Rates for ≥10% GFR decline in EVAR and OR patients, respectively, were 38% and 39%; ≥20% GFR decline 21% and 21%; and ≥1 CKD stage increase in 21% and 18.4%. The incidence of renal function deterioration did not differ between groups when evaluated by any of these three methods.

CKD staging. The baseline CKD stage distributions of AAA patients in both EVAR and OR groups by deciles of age were compared with the expected ratios in a large population-based study.[36] For every age-group except 60 to 69 years, study patients had worse baseline renal function than the age-adjusted general population, with OE ratios ranging from 1.17 to 3.8 depending on the subgroup (Tables IV and V).

We then compared CKD stage distribution at last available follow-up visit for AAA study patients with the age-adjusted CKD distribution expected in the general population (Tables IV and V). During follow-up, after both OR and EVAR, OE ratios increased in nearly every age group and ranged from 1.8 to 9.0, with the most striking increase in patients >70 years of age.

Freedom from renal dysfunction. Freedom from renal dysfunction for OR and EVAR patients was computed according to Kaplan-Meier for all patients (Fig, *A*), for those with normal baseline renal function (Fig, *B*), and for those with preexisting CKD (Fig, *C*). Since in each instance the curves cross (30 months for overall analysis, 36 months for patients with normal baseline renal function, and 24 months for patients with pre-existing CKD), short- and long-term results were compared.

In all three cases, no short-term differences could be detected ($P \geq .38$). In contrast, the freedom from renal dysfunction during long-term follow-up was significantly higher in OR compared with EVAR patients ($P = .03$). Interestingly, the deterioration of renal function could be shown to occur 12 months earlier in patients with pre-existing CKD compared with those with normal baseline renal function.

Table II. Mean glomerular filtration rates in open vs endovascular repair patients at baseline, 30-day, 90-day, and long-term follow-up

	Baseline	*30-day*	*90-day*	*Last available*
OR	70.9 ± 25.4	62.5 ± 28.1	63.6 ± 29.4	66.5 ± 30.7
EVAR	71.3 ± 30.7	70.6 ± 31.6	68.2 ± 32.1	65.5 ± 29.0
P value	0.91	0.047	0.44	0.82

EVAR, Endovascular abdominal aortic aneurysm repair; *OR,* open abdominal aortic aneurysm repair.
GFR unit= mL/min/1.73m^2.
Data are reported as mean ± standard deviation.

Table III. Long-term decline in glomerular filtration rates and change in chronic kidney disease (CKD) stage observed in open and endovascular abdominal aortic aneurysm repair groups

	OR	*EVAR*
10% GFR decline[a]	46 (38%)	40 (39%)
20% GFR decline[a]	25 (21%)	22 (21%)
CKD stage decline[b]	25 (21%)	19 (18.4%)

CKD, Chronic kidney disease; *EVAR,* endovascular abdominal aortic aneurysm repair; *GFR,* glomerular filtration rate; *OR,* open abdominal aortic aneurysm repair.
[a]Reported as number of patients (percentage) with 10% or 20% GFR decline compared with baseline GFR.
[b]CKD change ≥ 1 stage.

Table IV, A. Comparison of chronic kidney disease (CKD) stage at baseline and long-term follow-up for all abdominal aortic aneurysm study patients compared to chronic kidney disease (CKD) stage distribution expected for age

	Baseline	*Last follow-up*	*Expected for age*
Age group 40-59 (n=12)			
CKD 1	5 (41.7%)	5 (41.7%)	55.7%
2	7 (58.3%)	6 (50.0%)	42.7%
3	0 (0.0%)	1 (8.3%)	1.8%
4	0 (0.0%)	0 (0.0%)	—
Age group 60-69 (n=56)			
CKD 1	22 (38.6%)	20 (37.0%)	38.5%
2	30 (52.6%)	23 (42.6%)	53.8%
3	5 (8.8%)	9 (16.7%)	7.1%
4	0 (0.0%)	2 (3.7%)	—
Age group ≥70 (n=154)			
CKD 1	15 (9.8%)	14 (9.6%)	25.5%
2	52 (34.0%)	47 (32.2%)	48.5%
3	79 (51.6%)	68 (46.6%)	24.6%
4	7 (4.6%)	16 (11.0%)	1.3%
5	0 (0.0%)	1 (0.7%)	

CKD, Chronic kidney disease.
Reported as number (%) of patients.
Expected distribution of chronic kidney disease stages based on data from the National Health and Nutrition Examination Survey (NHANES III [1988-1994]). N = 15,000, based on one-time assessment of glomerular filtration rate.[36]

These results were confirmed with a Cox regression (Table VI), which showed a short-term relative risk of 0.920 for EVAR compared with OR (P = .859) and, therefore, no significant difference in renal dysfunction between the two methods. In contrast, the hazard ratio for renal dysfunction for long-term follow-up increased to 3.553 (P = .03) for EVAR and showed a significantly increased risk of renal dysfunction. In addition, patients over 70 year of age, independently of the treatment method, had an increased risk of renal dysfunction (RR = 2.92, P = .01)(Table VI).

DISCUSSION

The main objective of the present study was to determine if EVAR leads to a greater decline in renal function over time than would be expected for comparable patients undergoing OR. We generally obtain routine serial abdominal duplex ultrasound and CT scans at 1 to 3 months, 6 months, and then every 12 months after EVAR; more frequent scans are obtained if abnormalities of concern were detected, following re-intervention, and in patients with clinical signs or symptoms of graft-related problems. At both UMC and SAVAHCS, CT scans cannot routinely be obtained in patients with SCr > 1.5. In selected cases, CT scans are obtained in such patients after discussion between the radiology and vascular surgery attendings and after arrangements are made to administer N-acetylcysteine and hydrate the patients before and after contrast administration. We anecdotally noted that numerous EVAR patients during follow-up developed elevated SCr above the radiology department cut-off value (generating numerous conversations about whether the study should be cancelled, performed without contrast, or after the above-mentioned renal protective measures), and wondered whether the serial decline in renal function in these patients could be due to repetitive contrast administration. Surowiec et al recently reported that "a decrease in kidney function is seen after EVAR . . . . . likely related to the repetitive administration of contrast agent."[16]

Our review of over 30 reports addressing renal dysfunction after EVAR[1-35] revealed three major problems with the existing literature: (1) a classification system for baseline renal dysfunction is lacking; (2) a standard definition of postoperative renal dysfunction does not exist; and (3) with rare exceptions, follow-up is short, and data on serial renal function decline are not presented in Kaplan-Meier format. Similar to the evaluation of cancer survival or graft patency, mean percentage survival or patency at a given

Table IV, B. Comparison of observed chronic kidney disease (CKD) stage at baseline and at long-term follow up between open and endovascular aneurysm repair study patients with CKD stage distribution expected for age

	Baseline		*Last follow-up*		
	OR	*EVAR*	*OR*	*EVAR*	*Expected for age*
Age group 40-59 (n=12)					
CKD 1	2 (40.0%)	3 (42.9%)	1 (20.0%)	4 (57.1%)	55.7%
2	3 (60.0%)	4 (57.1%)	3 (60.0%)	3 (42.9%)	42.7%
3	0 (0.0%)	0 (0.0%)	1 (20.0%)	0 (0.0%)	1.8%
4	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	—
Age group 60-69 (n=56)					
CKD 1	11 (33.3%)	11 (45.8%)	8 (25.8%)	12 (52.2%)	38.5%
2	19 (57.6%)	11 (45.8%)	15 (48.4%)	8 (34.8%)	53.8%
3	3 (9.1%)	2 (8.3%)	6 (19.4%)	3 (13.0%)	7.1%
4	0 (0.0%)	0 (0.0%)	2 (6.4%)	0 (0.0%)	—
Age group ≥70 (n=154)					
CKD 1	9 (11.0%)	6 (8.5%)	9 (11.7%)	5 (7.2%)	25.5%
2	29 (35.4%)	23 (32.4%)	30 (38.9%)	17 (24.6%)	48.5%
3	40 (48.8%)	39 (54.9%)	29 (37.6%)	39 (56.5%)	24.6%
4	4 (4.9%)	3 (4.2%)	9 (11.7%)	7 (10.1%)	1.3%
5				1 (1.4%)	

CKD, Chronic kidney disease; *EVAR*, endovascular abdominal aortic aneurysm repair; *OR*, open abdominal aortic aneurysm repair.
Reported as number (%) of patients.
Expected distribution of chronic kidney disease stages based on data from the National Health and Nutrition Examination Survey (NHANES III [1988-1994]). N = 15,000, based on one-time assessment of glomerular filtration rate.[36]

Table V. Prevalence of chronic kidney disease in abdominal aortic aneurysm study patients at baseline and in long-term follow-up: observed-expected (OE) ratios compared with age-matched general population

	Observed-expected (OE) ratios	
OR		
CKD stages 3 + 4	Baseline	Long-term
60-69 y	1.28 (ns)	3.63[d]
>70 y	2.07[a]	1.9[e]
> 70 y (CKD 4)	3.75[b]	9.0[f]
EVAR		
CKD stages 3 + 4		
60-69 y	1.17 (ns)	1.84 (ns)
> 70 y	2.28[c]	2.57[g]
> 70 y (CKD 4 + 5)	3.25 (ns)	8.9[h]

CKD, Chronic kidney disease; *EVAR*, endovascular abdominal aortic aneurysm repair; *OR*, open abdominal aortic aneurysm repair; *ns*, not significant.
1. Glomerular filtration rate estimated by Cockcroft-Gault equation.
2. CKD defined as glomerular filtration rate <60 ml/min/1.73m^2 for >3 months.
3. Expected distribution of chronic kidney disease stages based on data from the National Health and Nutrition Examination Survey ([NHANES III [1988-1994]). N = 15,000, based on one-time assessment of glomerular filtration rate.
[a-h] 95% LCL-UCL (lower confidence level-upper confidence level), Poisson exact; $P < .05$
[a]CL 1.51-2.78
[b]CL 1.02-9.61
[c]CL 1.6 -3.02
[d]CL 1.57-7.16
[e]CL 1.34-2.62
[f]CL 4.11-17.07
[g]CL 1.88-3.43
[h]CL 3.85-17.57

mean follow-up interval is not meaningful. Life-table analysis of freedom from renal dysfunction during longitudinal follow-up is required to account for variable follow-up lengths.

To illustrate the conundrum, our review identified the following definitions of postoperative renal function decline: SCr levels > 1.1, 1.2, 1.3, 1.5, 1.7, 1.8, 2.0, 2.5, and 3.0; SCr rise > 1mg/dL above baseline; SCr rise >20%, >30% and 50% above baseline; GFR < 45; GFR decline > 10%, 20%; and need for hemodialysis. The number of definitions of renal insufficiency nearly equaled the number of reports.

The issue of the influence of SR vs IR fixation on renal function is also unresolved. Surowiec et al compared postoperative renal function using SCr in 146 EVAR patients, subgrouping them by IR vs SR fixation, with 65 consecutive OR patients.[16] Mean follow-up was 23.2 months. "At life-table analysis, renal impairment at 36 months was seen in 36% of patients in the IR group, 25% of patients in the SR group, and 19% of the OR group ($P < 0.04$ for IR fixation vs OR)." Macierewicz et al reported the evaluation of 30 EVAR patients with IR (11) and SR (19) fixation studied by postoperative technetium-labeled diethylene triamine penta-acetic acid (Tc-DTPA) scans and reported that coverage of renal ostia by bare struts did not effect on renal function.[30] Greenberg et al compared 80 open AAA repair patients with 190 patients undergoing EVAR with SR fixation using different definitions of renal dysfunction.[15] EVAR patients had less renal dysfunction prior to hospital discharge than OR patients; subsets of both groups had renal dysfunction prior to discharge and up to 12 months, but they reported that this "stabilized or improved at 12 to

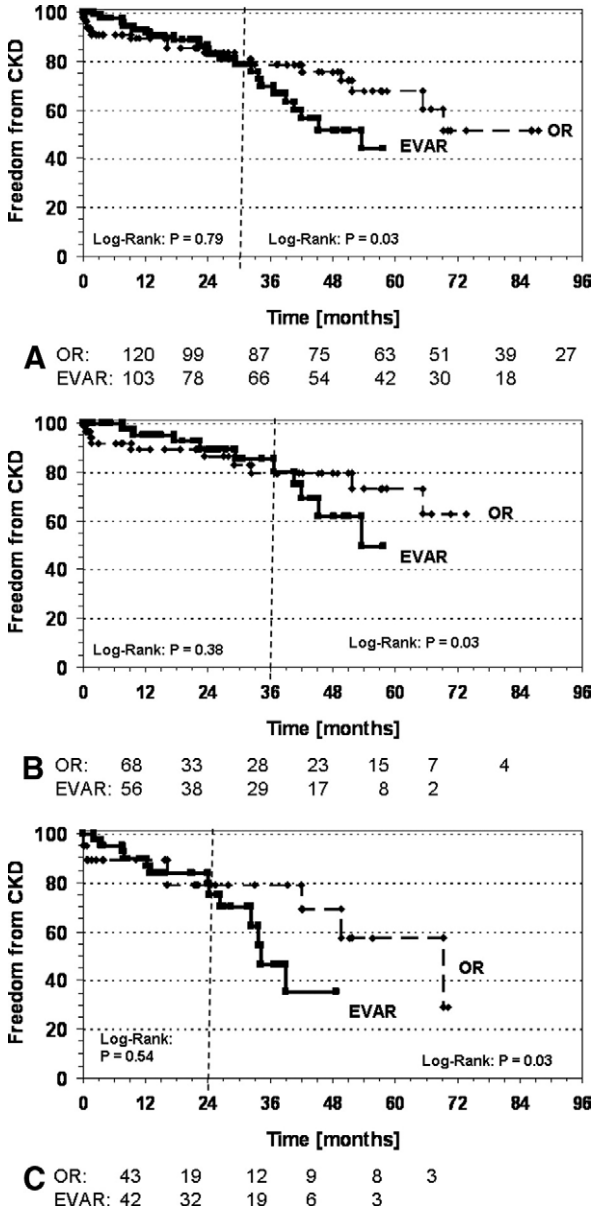

Fig. Kaplan Meier life-tables: renal function decline, OR vs EVAR. **A,** Plot for entire series: renal function decline defined as progression to chronic kidney disease (CKD) stage 3 or higher for patients without baseline CKD or >20% glomerular filtration rate (GFR) decline for patients with pre-existing CKD. **B,** Renal function decline after abdominal aortic aneurysm AAA repair for patients without pre-existing CKD. **C,** Renal function decline after AAA repair for patients with pre-existing CKD.

24 months". In contrast, several investigators have reported that SR is associated with a significantly increased risk of renal function decline compared with IR or OR patients.[25,26,29]

The primary reason for the disparate results reported in the literature regarding EVAR and long-term renal function stems from the lack of standardized definitions. The wide variability of definitions of renal dysfunction made it imperative to apply an appropriate renal function classification system to allow evaluation of long-term renal function decline after AAA repair. We believe that long-term assessment of the impact of EVAR, or for that matter, any series of endovascular diagnostic tests and procedures should be based on GFR and use CKD staging. The CKD staging system (NKF/KDOQI -National Kidney Foundation/ Kidney Disease Outcomes Quality Initiative) is the validated standard for the evaluation and management of chronic renal disease.[36] This staging system was therefore applied in our study.

Table VI. Relative risk (RR) of factors associated with renal function decline

Variable	*Parameter estimate*	$Pr > \chi^2$	*Relative risk ratio*
Age >70	1.07156	0.0104	2.920
Short follow-up*	−0.06857	0.8591	0.934
Long follow-up*	1.26217	0.0301	3.533

*EVAR versus OR

This approach leads to the important realizations that SCr is not reliable in making such determinations and that CKD prevalence in many subpopulations of patients with vascular disease, including AAA patients, is higher than most practitioners realize. For example, the incidence of CKD in our AAA patients >70 years was 56.2%, more than double that expected in the general population. Even in our younger AAA patients 40 to 59 years of age (there were only 12), although there were no CKD patients at baseline, the proportion of CKD 2:CKD1 patients was reversed compared with that expected (Table IV, A). Since we practice at tertiary referral centers, our patients may be more complex and have a higher incidence of renal insufficiency than AAA patients seen in community hospitals. However, the association of AAA and CKD has been reported by others, and our data appear to confirm it. Nakamura et al compared baseline renal function in AAA patients[10] to a patient cohort with HTN but without other risk factors for cardiovascular disease and showed by multiple methods, including renal scintigraphy, that moderate or severe renal dysfunction was present in 81% of AAA patients compared with 58% of HTN patients ($P < .0001$). Walsh and associates[8] identified preoperative renal insufficiency based on GFR in 33% of preoperative AAA patients. They also reported that GFR was a much more sensitive indicator of preoperative CKD than SCr. Using a preoperative SCr of 1.5 identified only 18/52 patients with CKD (GFR < 60 ml/min).

Critics may dispute our use of CKD stages and claim that it is overly sensitive. Many previous reports have used SCr, but SCr is influenced by a host of factors other than GFR including tubular secretion and generation and extrarenal creatinine excretion. These processes, especially SCr generation, vary greatly among individuals over time and the range of SCr levels in normal subjects is wide. SCr is an

insensitive indicator of renal dysfunction because levels do not begin to rise above the upper limits of normal until at least half of glomerular filtration has been lost.[8,36] GFR is accepted as the best overall index of kidney function in health and disease; normal GFR varies by age, gender, and body size. Unlike a rise in SCr, a decrease in GFR precedes the onset of kidney failure; therefore, a persistently reduced GFR < 60 is a specific indicator of CKD and applies regardless of age.[36]

GFR < 60 also appears to be associated with increased perioperative and long-term mortality in aneurysm patients following EVAR,[9] OR,[8,39] and thoracoabdominal aneurysm repair.[40] No such relationship existed for SCr levels and survival after aneurysm repair.[8,38] GFR measurements, thus, appear to have clinical and prognostic significance in AAA patients. Future studies should also examine the influence of reduced GFR on short- and long-term morbidity and mortality; if these impressions are confirmed, determination of diameter cut-off measurements for intervention may require adjustment and the decisions for aneurysm repair in individuals with reduced GFR carefully balanced against the anticipated risk of rupture. Examination of SCr alone, as is the usual habit among surgeons, is insensitive in identifying at-risk patients with CKD.

Early postoperative renal dysfunction was more common after OR than EVAR but this dysfunction was transient. This finding has been previously reported and is likely related to the hemodynamic effects of aortic cross-clamping, reperfusion injury, blood loss, transient hypotension, and perioperative fluid shifts.

We identified a significant decline in serial renal function during follow-up in a substantial proportion of patients, in line with most previous reports that have analyzed renal function decline by some arbitrary percentage reduction in GFR or SCr, with declining function in over 20% to 29% of patients at 2 to 3 years.[2,3,14,16,22,24,25] Nonetheless, unless CKD classification is utilized and CKD deterioration is compared with age-matched controls, it is difficult to differentiate any possible detrimental effects of aneurysm repair on long-term renal function from the natural history of CKD, which is one of progression. The issue is whether method of repair accelerates progression and what other comorbid factors influence renal function decline.

In OR and EVAR patients, we found that increasing age was strongly associated with renal function decline (RR 2.92 for age > 70 years). This finding has not, to our knowledge, been previously reported. The impact of age should be examined in larger multicenter studies or registry databases to determine whether this observation based on our series is valid and whether age should be considered in the decision for OR vs EVAR. The situation may prove analogous to carotid stenting, for which multiple studies have demonstrated higher stroke risks in octogenarians; age > 80 years is now thought to be a relative contraindication to carotid stenting.[41,42] Our analysis also strongly suggests that long-term renal function decline is associated with EVAR compared with OR, even for patients with normal renal function before intervention.

Limitations. The first limitation is the retrospective and nonrandomized nature of our study. Despite this weakness, OR and EVAR groups were quite similar at baseline except for gender, likely related to smaller access vessel diameter or possibly adverse anatomic characteristics of the aortic neck.

Second, we had 223 patients in our series, which limits the ability to perform meaningful subgroup analysis and to identify statistically significant risk factors for progressive renal function decline (type II error). Nonetheless, except for meta-analyses, most reports in the literature regarding post EVAR renal function have had similar numbers of patients (range 47 to 399), so nearly all published data suffer from this same limitation.

Third, our method of analysis has not been previously employed for long-term analysis of renal function in OR or EVAR patients. We believe our approach is logical, well-conceived, and evidence-based. SCr is certainly useful in recognizing major acute changes in renal function in surgical patients. An accurate estimation of GFR from SCr requires a steady state of balance (ie, relatively stable SCr from day to day, which may not be the case in many early postoperative OR and other surgical patients). SCr can provide important information about kidney function even when it is not in a steady state. For example, a daily doubling of SCr means there is complete shutdown of GFR. Estimated GFR, in contrast, overestimates true GFR when SCr is rising and underestimates GFR when SCr is falling (eg, during recovery phase of acute tubular necrosis).

However, if one wishes to analyze the chronic effects of endovascular procedures, which involve intraluminal manipulations in or near the renal arteries, device placement adjacent to or across the renal ostia and repetitive contrast administration on renal function, SCr levels are inappropriate and insensitive. Estimated GFR is much more accurate for assessing longitudinal changes in renal function.

CONCLUSIONS

This study confirms previous observations that the baseline incidence of CKD is higher in AAA patients than age-matched controls. We recommend routine measurement of GFR prior to AAA repair because SCr alone, especially in the elderly, significantly underestimates the true incidence of CKD. OR transiently worsens renal function at 30 days, compared with EVAR, but OR patients recover by 90 days. We were also able to identify a significant difference in the incidence of long-term renal function decline for EVAR compared with OR patients; these differences were detected after 3 years in patients with normal baseline renal function and after 2 years in patients with pre-existing CKD, suggesting that serial contrast administration as part of EVAR surveillance was likely a contributing factor. Compared with expected rates of CKD incidence and severity in the age-matched general population, renal function significantly worsens after AAA repair by both OR and EVAR. Age >70 years strongly correlated with serial renal function decline in all patients. Although GFR is known to decline with age, "decreased GFR in the

elderly is an independent predictor of adverse outcomes" including not only CKD-related complications, but also cardiovascular events and mortality.[36] We therefore believe that our use of GFR to assess long-term renal function is appropriate. In addition, CKD staging has the potential to be a better method of evaluating chronic changes in renal function. Therefore, our described method of analysis using GFR and CKD stage should to be applied in the analysis of chronic renal function in larger populations of patients undergoing AAA repair. Unless such a standardized reporting methodology is utilized, it will be impossible to accurately determine the effects of different devices, SR vs IR fixation, repetitive contrast administration and a multitude of other clinically important issues on long-term renal function after endovascular therapy. Further study is necessary to determine the frequency with which EVAR patients require contrast CT scans and which patients are at greatest risk for CKD decline. Further investigation of noncontrast CT surveillance combined with duplex imaging and the development of less or nontoxic contrast agents are also important. Routine hydration and the use of oral N-acetylcysteine do not appear to provide sufficient protection from the deleterious effects of repetitive contrast administration.

The authors wish to thank Leann Chavez, MD, Hannah Zimmerman, MD, Zach Taylor, MD, and Steven Lee Pike for participating in the study by assisting with data collection and entry.

AUTHOR CONTRIBUTIONS

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Obtained funding: JM
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REFERENCES

1. Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R, et al; Dutch Randomized Endovascular Aneurysm Management (DREAM)Trial Group. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. N Engl J Med 2004;351:1607-18.
2. May J, White GH, Yu W, Ly CN, Waugh R, Stephen MS, et al. Concurrent comparison of endoluminal versus open repair in the treatment of abdominal aortic aneurysms: analysis of 303 patients by life table method. J Vasc Surg 1998;27:213-20.
3. Greenhalgh RM, Brown LC, Kwong GP, Powell JT, Thompson SG; EVAR trial participants. Comparison of endovascular aneurysm repair with open repair in patients with abdominal aortic aneurysm (EVAR trial 1), 30-day operative mortality results: randomized controlled trial. Lancet 2004;364:843-8.
4. Chaikof EJ, Blankensteijn JD, Harris PL, White Geoffrey H, Zarins CK, Bernhard VM, et al. Reporting standards for endovascular aortic aneurysm repair. J Vasc Surg 2002;35:1048-60.
5. Chaikof EL, Fillinger MF, Matsumura JS, Rutherford RB, White GH, Blankensteijn JD, et al. Identifying and grading factors that modify the outcome of endovascular aortic aneurysm repair. J Vasc Surg 2002;35:1061-6.
6. Sacks D, Marinelli DL, Martin LG, Spies JB. Reporting standards for clinical evaluation of new peripheral arterial revascularization devices. J Vasc Inter Radiol 1997;8:137-49.
7. Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. J Vasc Surg 1997;26:517-38.
8. Walsh SR, Tang T, Sadat U, Varty K, Boyle JR, Gaunt ME. Preoperative glomerular filtration rate and outcome following open abdominal aortic aneurysm repair. Vasc Endovasc Surg 2007;41:225-9.
9. Azizzadeh A, Sanchez LA, Miller CC 3rd, Marine L, Rubin BG, Safi HJ, et al. Glomerular filtration rate is a predictor of mortality after endovascular abdominal aortic aneurysm repair. J Vasc Surg 2006;43:14-8.
10. Nakamura S, Yoshihara F, Kamide K, Horio T, Nakahama H, Inenaga T, et al. Renal function in patients with abdominal aortic aneurysm. Comparison with hypertensive patients. Kidney Blood Press Res 2006; 29:67-73.
11. Parmer SS, Fairman RM, Karmacharya J, Carpenter JP, Velazquez OC, Woo EY. A comparison of renal function between open and endovascular aneurysm repair in patients with baseline chronic renal insufficiency. J Vasc Surg 2006;44:706-11.
12. Taylor PR, Reidy J, Scoble JE. Endovascular abdominal aortic aneurysm repair and renal function. Nephrol Dial Transplant 2006;21: 2362-5.
13. AbuRahma AF, Welch CA, Mullins BB, Dyer B. Computed tomography versus color duplex ultrasound for surveillance of abdominal aortic stent-grafts. J Endovasc Ther 2005;12:568-73.
14. Alsac JM, Zarins CK, Heikkinen MA, Karwowski J, Arko FR, Desgranges P, et al. The impact of aortic endografts on renal function. J Vasc Surg 2005;41:926-30.
15. Greenberg RK, Chuter TA, Lawrence-Brown M, Haulon S, Nolte L; Zenith Investigators. Analysis of renal function after aneurysm repair with a device using suprarenal fixation (Zenith AAA Endovascular Graft) in contrast to open surgical repair. J Vasc Surg 2004;39: 1219-28.
16. Surowiec SM, Davies MG, Fegley AJ, Tanski WJ, Pamoukian VN, Sternbach Y, et al. Relationship of proximal fixation to postoperative renal dysfunction in patients with normal serum creatinine concentration. J Vasc Surg 2004;39:804-10.
17. Jenkins MP, Onwudike M, Singh R, Bomanji J, Adiseshiah M. Endoluminal repair of abdominal aortic aneurysms causes more perioperative renal dysfunction than open repair. Br J Surg 2002;87:492.
18. Becquemin J, Bourriez A, D'Audiffret A, Zubilewicz T, Kobeiter H, Allaire E, et al. Midterm results of endovascular versus open repair for abdominal aortic aneurysm in patients anatomically suitable for endovascular repair. Eur J Vasc Endovasc Surg 2000;19:656-61.
19. Jordan WD, Alcocer F, Wirthlin DJ, Westfall AO, Whitley D. Abdominal aortic aneurysms in "high-risk" surgical patients: comparison of open and endovascular repair. Ann Surg 2003;237:623-9.
20. Arko FR, Hill BB, Olcott C, Harris EJ Jr, Fogarty TJ, Zarins CK. Endovascular repair reduces early and late morbidity compared to open surgery for abdominal aortic aneurysm. J Endovasc Ther 2002;9:711-8.
21. England A, Butterfield JS, Ashleigh RJ. Incidence and effect of bare suprarenal stent struts crossing renal ostia following EVAR. Eur J Vasc Endovasc Surg 2006;32:523-8.
22. Parmer SS, Carpenter JP; Endologix Investigators. Endovascular aneurysm repair with suprarenal versus infrarenal fixation: a study of renal effects. J Vasc Surg 2006;43:19-25.
23. Waasdorp E, van't Hullenaar C, van Herwaarden J, Kelder H, van de Pavoordt E, Overtoom T, et al. Renal function after endovascular aortic aneurysm repair: a single-center experience with transrenal versus infrarenal fixation. J Endovasc Ther 2007;14:130-7.
24. Sun Z, Mwipatayi BP, Semmens JB, Lawrence-Brown MM. Short to midterm outcomes of fenestrated endovascular grafts in the treatment of abdominal aortic aneurysms: a systematic review. J Endovasc Ther 2006;13:747-53
25. Raithel D, Qu L, Hetzel G. Infrarenal fixation is the safest option. Endovasc Today 2005;4(8):62-65.

26. Grego F, Frigatti P, Antonello M, Lepidi S, Ragazzi R, Iurilli V, et al. Suprarenal fixation of endograft in abdominal aortic aneurysm treatment: focus on renal function. Ann Surg 2004;240:169-78.
27. Mehta M, Cayne N, Veith FJ, Darling RC 3rd, Roddy SP, Paty PS, et al. Relationship of proximal fixation to renal dysfunction in patients undergoing endovascular aneurysm repair. J Cardiovasc Surg (Torino) 2004;45:367-74.
28. Alric P, Hinchliffe RJ, Picot MC, Braithwaite BD, MacSweeney ST, Wenham PW, et al. Long-term renal function following endovascular aneurysm repair with infrarenal and suprarenal aortic stent-grafts. J Endovasc Ther 2003;10:397-405.
29. Böckler D, Krauss M, Mansmann U, Halawa M, Lange R, Probst T, et al. Incidence of renal infarctions after endovascular AAA repair: relationship to infrarenal versus suprarenal fixation. J Endovasc Ther 2003;10:1054-60.
30. Macierewicz J, Walker SR, Vincent R, Wastie M, Elmarasy N, Hopkinson BR. Vascular surgical society of Great Britain and Ireland: perioperative renal function following endovascular repair of abdominal aortic aneurysm with suprarenal and infrarenal stents. Br J Surg 1999;86:696.
31. Park B, Mavanur A, Drezner AD, Gallagher J, Menzoian JO. Clinical impact of chronic renal insufficiency on endovascular aneurysm repair. Vasc Endovasc Surg 2006-2007;40:437-45.
32. Mehta M, Veith FJ, Lipsitz EC, Ohki T, Russwurm G, Cayne NS, et al. Is elevated creatinine level a contraindication to endovascular aneurysm repair? J Vasc Surg 2004;39:118-23.
33. Mehta M, Veith F. Endovascular repair of aortic aneurysms in patients with renal insufficiency. Perspect Vasc Surg Endovasc Ther 2004;16:15-23.
34. Vasquez J, Rahmani O, Lorenzo AC, Wolpert L, Podolski J, Gruenbaum S, et al. Morbidity and mortality associated with renal insufficiency and endovascular repair of abdominal aortic aneurysms: a 5-year experience. Vasc Endovascular Surg 2004;381438.
35. Ho P, Yiu WK, Cheung GC, Cheng SW, Ting AC, Poon JT. Systematic review of clinical trials comparing open and endovascular repair of abdominal aortic aneurysm. Surg Pract 2006;10:24-37.
36. www.kidney.org/professionals/kdoqi/guidelines
37. Glance LG, Dick AW, Osler TM, Mukamel DB. Accuracy of hospital report cards based on administrative data. HSR 2006;41(4 Part I): 1413-37.
38. http://www.quantitativeskills.com/sisa.statistics/smr.htm.
39. Powell RJ, Roddy SP, Meier GH, Villa MA, Estrera AL, Azizzadeh A, et al. Effect of renal insufficiency on outcome following infrarenal aortic surgery. Am J Surg 1997;174:126-30.
40. Huynh TT, van Eps RG, Miller CC, Gusberg RJ, Conte MS, Sumpio BE. Glomerular filtration rate is superior to serum creatinine for prediction of mortality after thoracoabdominal aortic surgery. J Vasc Surg 2005;42:206-12.
41. Hobson RW 2nd, Howard VJ, Roubin GS, Brott TG, Ferguson RD, Popma JJ, et al; CREST Investigators. Carotid artery stenting is associated with increased complications in octogenarians: 30-day stroke and death rates in the CREST lead-in phase. J Vasc Surg 2004;40:1106-11.
42. Stanziale SF, Marone LK, Boules TN, Brimmeier JA, Hill K, Makaroun MS, et al. Carotid artery stenting in octogenarians is associated with increased adverse outcomes. J Vasc Surg 2006;43:297-304.

Submitted Sep 20, 2007; accepted Jan 20, 2008.