CLINICAL STUDY

Mortality and Renal Replacement Therapy after Renal Artery Stent Placement for Atherosclerotic Renovascular Disease

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ABSTRACT

Purpose: To identify risk factors for progression to renal replacement therapy (RRT) and all-cause mortality in patients who underwent renal artery (RA) stent placement for atherosclerotic renal artery stenosis (RAS).

Materials and Methods: A retrospective study from June 1996 to June 2009 identified 1,052 patients who underwent RA stent placement. Glomerular filtration rate at time of RA stent placement was estimated from serum creatinine level and divided into chronic kidney disease (CKD) stages 1–5. Univariate and multivariable Cox proportional hazards models were used to determine which factors were associated with each endpoint.

Results: Times to progression to all-cause mortality and RRT were similar for CKD stages 1/2/3A and served as the reference group. In multivariable analysis, high-grade proteinuria ($P < .001$) and higher CKD stage (5 vs 1/2/3A [$P < .001$], 4 vs 1/2/3A [$P < .001$], 3B vs 1/2/3A [$P = .02$]) remained independently associated with increased risk of progression to RRT. Angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB) use was associated with decreased risk of progression to RRT ($P = .03$). Higher CKD stage (5 vs 1/2/3A [$P < .001$], 4 vs 1/2/3A [$P = .004$]), carotid artery disease ($P < .001$), diabetes mellitus ($P = .002$), and high-grade proteinuria ($P < .001$) remained independently associated with all-cause mortality. Statin use was associated with decreased risk of all-cause mortality ($P < .001$).

Conclusions: Patients with atherosclerotic RAS who undergo RA stent placement and have high-grade proteinuria and CKD stage 3B/4/5 have increased risk of progression to RRT. Patients with high-grade proteinuria, CKD stage 3B/4/5, carotid artery disease, or diabetes have increased risk for all-cause mortality after renal artery stent placement. Patients receiving ACEI/ARBs have a decreased risk of progression to RRT, and patients receiving statins have a decreased risk of all-cause mortality.

ABBREVIATIONS

ACEI = angiotensin-converting enzyme inhibitor, ARB = angiotensin receptor blocker, ASTRAL = Angioplasty and STent for Renal Artery Lesions, CI = confidence interval, CKD = chronic kidney disease, CORAL = Cardiovascular Outcomes in Renal Atherosclerotic Lesions, GFR = glomerular filtration rate, HR = hazard ratio, RA = renal artery, RAS = renal artery stenosis, RRT = renal replacement therapy, STAR = Stenting in Renal Dysfunction Caused by Atherosclerotic Renal Artery Stenosis, USRDS = United States Renal Data System

Atherosclerotic renal artery stenosis (RAS) is a recognized contributor to uncontrolled hypertension and/or worsening of renal function (1,2). Restoring blood flow with either surgical or endovascular revascularization can improve management of refractory renovascular hypertension and can sometimes salvage renal function (3–6). However, identifying patients likely to benefit from endovascular intervention is a major challenge. In recent years, prospective, randomized controlled trials have failed to demonstrate a major additional benefit for patients who have been treated with angioplasty and/or stent placement versus medical therapy for RAS (7–11).

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Several weaknesses have been identified with these trials, including the small number of patients, crossover, selection bias, and potential of underpowering of the trials (8,12,13). Observational studies and results of registries suggest that technically successful revascularization confers a substantial survival benefit to some "high-risk" patient subsets (5,6,14–20). Because this patient population often includes older patients with the presence of extensive comorbid cardiovascular disease, identifying predictors for all-cause mortality and/or progression to renal replacement therapy (RRT) with hemodialysis, peritoneal dialysis, or kidney transplantation is an important goal in planning therapy.

The purpose of the present study was to evaluate the factors that contribute to progression to RRT and all-cause mortality in patients with chronic kidney disease (CKD) with atherosclerotic RAS who have undergone renal artery (RA) stent placement using the resources of the United States Renal Data System (USRDS) and the Social Security Death Index. It is hypothesized that patients with advanced CKD (stage 3B or greater) would have worse outcomes compared with patients with CKD stage 1/2/3A. This information is important for interpreting completed and ongoing clinical trials, for designing future clinical trials, and for clinical management of patients with comorbid risks to better determine which patients may benefit from RA stent placement.

METHODS AND MATERIALS

Institutional review board approval was obtained for this retrospective study. All patients undergoing stent placement for treatment of atherosclerotic RAS because of either hypertension or worsening renal function from June 1996 to June 2009 were included in the data set. Demographic data, comorbidity data, laboratory data from before and after the procedure, and catheter-related angiographic data through October 2011 were obtained from medical records. Embolic protection devices were not used on any of the patients in this study. There were 1,222 patients treated for renovascular disease. Patients were excluded if they had concomitant fibromuscular dysplasia and/or were treated for non-atherosclerotic RA disease. The study group comprised 1,052 patients after applying the exclusion criteria. Of these patients, 526 were female (50%), with a total mean age of 72.4 years ± 9.2 (range, 42–93 y). The median follow-up period was 3.8 years (range, 0–10.79 y; mean, 2.2 y ± 2.0). The patient demographics are presented in Table 1.

The primary endpoint was the progression to RRT. The secondary endpoint was all-cause mortality. Information on the need for RRT was obtained by querying the USRDS in October 2011. All-cause mortality data were obtained in August 2011 by querying the death data in the US Social Security Death Index and the health system medical records. RRT was defined as the need for hemodialysis, peritoneal dialysis, or renal transplantation at any time after stent placement or undergoing renal transplantation.

Definitions

Glomerular filtration rate (GFR) was estimated using the serum creatinine level obtained before the stent procedure using the Modification of Diet in Renal Disease formula: estimated GFR $= 186 \times (\text{serum creatinine})^{-1.54} \times \text{age}^{-0.203} \times 0.742$ (females) $\times$ 1.210 (African Americans) (21). Baseline creatinine data were collected and analyzed based on the latest creatinine level obtained within 30 days before the procedure. Each patient's CKD stage was based on his or her GFR at the time of the first RAS procedure. Patients were stratified into stages of renal disease based on the Kidney Dialysis Outcomes Quality Initiative classification, as follows: stage 1, GFR $>$ 90 mL/min/m^2; stage 2, GFR 60–89 mL/min/m^2; stage 3A, GFR 45–59 mL/min/m^2; stage 3B, GFR 30–44 mL/min/m^2; stage 4, GFR 15–29 mL/min/m^2; and stage 5, GFR $<$ 15 mL/min/m^2. Prediction of the 24-hour urinary protein excretion rate was obtained from a randomly collected urine specimen before the RA intervention and use of the following formula: 24-hour predicted proteinuria (g/L) per 1.73 m^2 body surface area = (urine [protein] $\times$ 0.088) $\div$ urine (creatinine) (22). The last available urine sample in the patient chart before intervention, obtained within 30 days of the procedure date, was used. High-grade proteinuria was defined as $>$ 300 mg/24 h. Low-grade proteinuria was defined as $\leq$ 300 mg/24 h.

Preliminary Kaplan-Meier plots of cumulative survival revealed that patients with CKD stage 1/2/3A had very similar risk of all-cause mortality and progression to RRT. For this reason, these stages were combined in the analyses. As this study was retrospective, all available data were used for each analysis. The sample size for each model was different for this reason and is included in the summary tables (Tables 2 and 3).

Refractory hypertension was defined as uncontrolled blood pressure despite the patient receiving 3 antihypertensive medications including diuretic therapy, a systolic pressure $>$ 140 mm Hg or diastolic pressure $>$ 90 mm Hg (23). For the purposes of this study, antianginal medications other than beta-blockers were not defined as blood pressure medications. Patients without refractory hypertension were not excluded from this study as an indication for RA stent placement because RA stent placement was performed for preserving kidney function in this population.

Medication usage at the time of stent placement was included in the analysis as well. Along with baseline hypertensive medications, use of statins, angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), calcium channel blockers,