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Original article

End-stage renal disease secondary to renal malignancy: Epidemiologic trends and survival outcomes

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Abstract

Objectives: Loss of renal parenchyma after surgery may contribute to chronic kidney disease; however, the long-term consequences of chronic kidney disease may differ by cause. We analyzed the outcomes of patients with end-stage renal disease (ESRD) based on various medical and surgical causes.

Materials and methods: In the United States Renal Data System from the period 1983 to 2007, patients with renal tumors, traumatic surgical loss, diabetes, or other known causes were identified. The annual incidence, prevalence, and influence of age, race, sex, and primary cause on survival were evaluated.

Results: Of 1.3 million patients, 6,812 (0.49%) had renal malignancy–related ESRD (RM-ESRD). An increased over time was noted in the standardized incidence rates of patients with RM-ESRD ($R^2 = 0.973$, $P < 0.0001$). Patients with RM-ESRD had a worse median survival (1.9 vs. 3.4 y, $P < 0.0001$), whereas those with ESRD related to nonmalignant surgical loss had improved survival (3.8 y) compared to diabetic ESRD ($P < 0.0001$). The 5-year cancer-specific mortality was higher for RM-ESRD (30.9% vs. 5.5%, $P < 0.0001$) compared to ESRD from other known causes; however, the non–cancer-specific mortality was improved compared to patients with ESRD with diabetic causes ($P < 0.0001$). Limitations include retrospective analysis and lack of specific clinical data, such as cancer grade.

Conclusions: The incidence of RM-ESRD is increasing, possibly owing to the increased rate of renal cell carcinoma treatment. Although overall survival for RM-ESRD was worse than either that of nonmalignant surgical loss or other known causes, non–cancer-specific mortality was decreased compared to diabetic causes, likely due to systemic effects by cause of ESRD.

Keywords: End-stage renal disease; Renal cell carcinoma; Dialysis; Survival

1. Introduction

Historically, partial nephrectomy has been reserved for individuals with hereditary syndromes, chronic kidney disease (CKD), bilateral tumors, or a solitary kidney. The past 2 decades have seen a shift toward renal preservation with nephron-sparing surgery, especially as retrospective data suggest that patients treated with radical nephrectomy have a greater risk of renal and cardiovascular complications [1,2]. Despite partial nephrectomy being considered the gold standard for the management of the small renal mass (cT1a, ≤4 cm), most patients with normal renal function have been managed with radical nephrectomy [3–5]. Although partial nephrectomy may be less harmful to renal function when compared to radical nephrectomy, all forms of surgical therapy are associated with adverse renal

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and cardiovascular outcomes [6,7]. In recent years, the field has embraced active surveillance and thermal ablation to further limit renal dysfunction while maintaining improved oncologic outcomes [8,9].

Nephron loss after kidney cancer treatment can contribute to progression to end-stage renal disease (ESRD). The long-term effects on cardiovascular events and mortality may differ by cause of ESRD, whether it may be medically or surgically induced. When managing patients with renal malignancy who may progress to ESRD with treatment, clinicians are faced with a significant dilemma: risk metastatic progression without treatment or risk progression to ESRD with surgical intervention. Patients with metastatic renal cell carcinoma (RCC) and urothelial carcinoma are rarely curable; however, dialysis also has poor outcomes with a median survival of 3 years [10]. However, these data include all patients of ESRD, and it has been established that specific medical causes of ESRD, such as diabetes, have worse prognosis [11]. The outcomes of patients with surgical causes of ESRD may be different based on recent observations suggesting that those with surgical CKD have less long-term risks than medical causes [12,13].

To make an informed decision, patients must be presented with accurate data; however, there is limited information available on the outcome of patients with ESRD with renal malignancy or surgical loss to accurately counsel patients. In this study, we evaluated the epidemiologic trends of patients with renal malignancy–related ESRD (RM-ESRD) compared to those with medical causes of ESRD using a national comprehensive database.

2. Materials and methods

2.1. Data source and study population

The United States Renal Data System (USRDS) was used to identify individuals diagnosed with ESRD from 1983 to 2007 [14]. Demographic information, including sex, age, race, year of ESRD diagnosis, primary cause of ESRD, and date of last follow-up, was recorded. Specific ESRD causes investigated were renal malignancy (RM-ESRD), diabetic ESRD, benign kidney tumors-ESRD, traumatic surgical kidney loss-ESRD, and other known causes. The standardized incidence rates (SIR) of RCC per year were obtained from the surveillance, epidemiology, and end results (SEER) program and United States census information [15]. The RM-ESRD SIR was obtained by dividing the number of RM-ESRD cases per year by the US population adjusted to 100,000 patients per year. The percentage of RCC individuals with RM-ESRD was obtained by dividing the prevalence of RM-ESRD by the prevalence of RCC. For deceased patients, the primary cause of death was available from the Centers for Medicare and Medicaid Services ESRD Death Notification form. Death from cancer was listed as a cause; however, the specific type of cancer was not readily available. For overall survival, patients were censored if alive at the date of last follow-up. Cause-specific mortality was assessed using a Fine-Gray competing risk model for cumulative mortality.

2.2. Statistical analysis

Data analysis was performed using JMP Pro v.11.1 statistical software (SAS Institute Inc., Cary, NC). The chi-square test, analysis of variance, and generalized linear regression were used to evaluate differences between study groups and to examine trends over time. Kaplan-Meier estimates were performed to assess overall survival, whereas a Fine-Gray competing risk model was used to examine cumulative mortality over time. Differences in survival were compared by primary causes of ESRD using the log-rank test, whereas differences in cumulative mortality were evaluated with the Gray test. For survival analyses, owing to a low number of cases, benign kidney tumors and traumatic surgical loss were grouped into the same category called nonmalignant surgical loss ESRD (NMSL-ESRD). Cox proportional hazard models examined the influence of demographic variables (age, race, and sex) as independent predictors of overall survival. For the analysis of race, patients were compared as White vs. non-White. Hazards ratios evaluated the degree to which demographic variables and primary cause of ESRD contributed to survival. R version 3.3.0 with the cmprsk package was used to assess the cumulative mortality of both non–cancer-specific and cancer-specific causes. Significance was considered if $P \leq 0.05$.

3. Results

3.1. Patient characteristics

We identified 1,374,577 patients with ESRD in the USRDS database (Table 1). A total of 807,244 (58.7%), 6,812 (0.49%), 191 (0.01%), 1,589 (0.12%), and 558,741 (40.6%) patients had diabetic ESRD, RM-ESRD, benign kidney tumor-ESRD, traumatic surgical loss, and other known causes of ESRD, respectively. Differences in the primary cause of ESRD by race, age, and sex were evaluated. For patients with RM-ESRD, White, Black, Native American, Asian, and other race constituted 5,641 (83%), 1,024 (15%), 69 (1%), 52 (0.7%), and 26 (0.3%) patients, respectively. Similar to the expected frequency and age distribution, 78% of the patients with RM-ESRD were men, and the median (interquartile range) age was 68 (58–75).

The number of patients experiencing RM-ESRD, benign kidney tumors, and traumatic surgical loss per year (from 1983–2007) was evaluated (Fig. 1A). During this period, RM-ESRD steadily increased ($R^2 = 0.970$, $P < 0.0001$), while the number of ESRD cases attributed to benign kidney tumors and traumatic surgical loss only moderately