Delayed nephrectomy has comparable long-term overall survival to immediate nephrectomy for cT1a renal cell carcinoma: A population-based analysis.

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Highlights

- We examined long-term overall survival (OS) of patients managed with delayed vs immediate nephrectomy for cT1a renal cancer.
- Delaying surgery for >6 months for cT1a renal cancer did not affect overall survival with a median follow-up of 82.5 months.
- These findings suggest that a period of observation for >6 months is safe and this may allow identification of renal masses, which will benefit from surgical resection.

Abstract

Objective

Early surgical resection remains the recommended treatment option for most small renal mass (≤4 cm). We examined long-term overall survival (OS) of patients managed with delayed and immediate nephrectomy of cT1a renal cancer.

Patient and methods

We utilized the National Cancer Database (2005-2010) to identify 14,677 patients (immediate nephrectomy: 14,050 patients vs late nephrectomy: 627 patients) aged <70 years with Charlson Comorbidity Index (CCI) 0 and cT1aN0M0 renal cell carcinoma (RCC). Immediate nephrectomy and late nephrectomy were defined as nephrectomy performed <30 days and >180 days from diagnosis respectively. Inverse probability of treatment weighting (IPTW)–adjusted Kaplan-Meier curves and Cox proportional hazards regression analyses were used to compare OS of patients in the two treatment arms. Influence of patient age and CCI on treatment effect was tested by interactions. Sensitivity analysis was performed to explore the outcome of delaying nephrectomy for >12 months.

Results

Median patient age was 55 years with a median follow-up of 82.5 months. IPTW-adjusted Kaplan-Meier curves suggest no significant difference between treatment arms (immediate nephrectomy [<30 days] vs delayed nephrectomy [>180 days]) (Hazard ratio, 0.96; 95% confidence interval, 0.73 to 1.26; p=0.77). This outcome was consistent between all patients regardless of age (p=0.48). Sensitivity analysis report no difference in OS even if nephrectomy was delayed by >12 months (p=0.60).

Conclusion

We report that delayed and immediate nephrectomy for cT1a RCC confers comparable long-term OS. These findings suggest that a period of observation of between 6-12 months is safe to allow identification of renal masses, which will benefit from surgical resection.

Keywords: delay; kidney cancer; nephrectomy; overall survival; renal cell carcinoma; small renal mass

1. Introduction

Kidney cancer is the 8th most common cancer with an increasing incidence over the last 20 years [1, 2]. The main driver of the increasing incidence of kidney cancer is the routine use of cross sectional and ultrasonography imaging which has led to incidental diagnosis of asymptomatic T1 renal lesions [3]. Fear of disease progression and metastatic potential has prompted recommendations for early surgical resection of T1a (≤4 cm) cancers although the 2009 National Comprehensive Cancer Network (NCCN) guidelines has recently advocated active surveillance as an option of small renal masses <2 cm [4].

The decision to delay surgery for small renal mass has several advantages. The fact that most patients with kidney cancer are >60 years old imply that most patients have co-morbidities and delaying surgery for several months would allow a period of “prehabilitation” which in turn has been shown to decrease postoperative complications [5, 6]. Further, 13-33% of small renal mass <4 cm have benign histology following surgical resection and while a substantial proportion of small renal mass remain radiologically static, those with metastatic potential are most likely to exhibit a significant growth rate [7-9]. A period of radiological assessment may therefore allow identification of patients harboring renal cell cancer (RCC).

Given recent shifts toward the promotion of active surveillance for many small renal masses, we sought to characterize outcomes for delayed nephrectomy of cT1a RCC. We examined the National Cancer Database (NCDB), a cohort with long-term follow up with the primary objective to compare the long-term overall survival of patients managed with immediate versus delayed nephrectomy of cT1a RCC.

2. Material and methods

2.1 Data source

Data used in this retrospective study was from the National Cancer Database (NCDB), a cancer registry from >1,500 Commission of Cancer (CoC)- accredited hospitals in the United States and Puerto Rico. Data captured in this registry include new cancer diagnosis, treatment and follow-up outcome. Specifically, this includes data on patient demographics and clinical characteristics, clinical and pathological stage, cancer histology, treatment modality and overall survival. The NCDB captures 86% of kidney cancer cases in the United States and has been validated against the Surveillance, Epidemiology and End Results (SEER) database suggesting good consistency [10, 11]. A waiver was obtained before commencement of the study by the Brigham and Women's Hospital Institutional review board in accordance with institutional regulation when using deidentified previously collected patient data.

2.2 Patient selection

A total of 465,126 patients were identified with a diagnosis of kidney cancer or renal pelvis cancer (International Classification of Diseases of Oncology, 3rd Edition code C64) between January 2004 to December 2015 [12]. According to the American Joint Committee on Cancer (AJCC) 7th edition classification we restricted the patient cohort to cT1a N0 M0 renal cancer [13]. Only patients treated with radical or partial nephrectomy were included for analysis. Patients with urothelial carcinoma were excluded, as were those treated with thermal ablation. All patients comprised of aged <70 years with Charlson comorbidity index (CCI) 0. This was to exclude co-morbid and elderly patients to reduce case selection bias which we might not be able to adjust for. Patients were restricted to those diagnosed between 2005 to 2010 to ensure adequate patient follow-up. This excluded 450,449 patients leaving 14,677 patients for analysis (Figure 1).

2.3 Variables of interest

Surgical treatment was defined as treatment by either radical nephrectomy, partial nephrectomy, local tumor excision or any nephrectomy in continuity with the resection of other organs. Delayed nephrectomy was defined as nephrectomy performed >180 days from diagnosis while immediate nephrectomy was defined as nephrectomy performed <30 days from diagnosis.

Other variables of interest include: age at diagnosis (<48 years, 48-55.9 years, 56-61.9 years, ≥62 years [based on quartiles]), sex (male, female), race (black, white, other), year of diagnosis (2004-2005, 2006-2007, 2008-2009, 2010-2011), insurance status (Private, Medicaid, Medicare or other government [including TRICARE, Military, VA and Indian/ Public Health Service], uninsured), median household income within the ZIP code (≤$37,999, $38,000-$47,999, $48,000-$62,999, ≥ $63,000) and median proportion of individuals within the ZIP code without a high school diploma (≤6.9%, 7%-12.9%, 13%-20.9%, ≥ 21%), great circle distance (≤5.3, 5.4-12.1, 12.2-28.6, ≥28.7 miles) (distance in miles between a patient's residence based on the ZIP code centroid or city and the street address of the facility), urban/rural status (metropolitan, urban county, rural county), treating institution (academic, non-academic) and hospital surgical volume (continuous).

2.4 Statistical analysis

We performed inverse probability of treatment weighting (IPTW)- adjusted analyses to account for patient age, sex, race, CCI, year of diagnosis, education, insurance status, distance from treating hospital, nephrectomy caseload and urban/ rural status which may influence patient selection for treatment selection and available from the NCDB. A propensity score model based on a goodness-of-fit statistic which included linear and nonlinear covariates categorized according to clinically relevant cut-offs was used as previously described [14]. This represents an acceptable statistical method to reduce case selection bias between treatment arms [15]. To evaluate whether covariables were balanced, standardize difference approach plots were utilized. Standardized differences of ≥10 were considered significant. Kaplan-Meier curves were calculated to compare overall survival between patients receiving immediate nephrectomy vs delayed nephrectomy [16]. This was determined by the number of months from date of diagnosis till the date on which the patient was last contacted or died. Hazard ratios (HR) were assessed using an IPTW-adjusted Cox proportional hazards regression model. Interactions between patient age and year of diagnosis variables were tested within the IPTW-adjusted Cox model. A post hoc power analysis confirms that the current sample size is sufficient to detect a hazard ratio of 0.89 between treatment modality assuming an 80% power and 5% significance. Statistical analyses were performed using Stata version 15.0 (StataCorp, Texas, USA). Statistical significance was defined as two-sided $p<0.05$.

3. Results

The median age of the study cohort was 55 years (Interquartile range [IQR], 47, 62). A total of 14,050 patients (95.7%) had an immediate nephrectomy and the remaining 627 patients (4.3%) had a delayed nephrectomy. Median delay to time of nephrectomy from diagnosis was 8.1 months (IQR: 6.8, 11.2). Median follow-up was 82.5 months (IQR, 66.7, 102.3) during which 63 patients (10.1%) in the delayed nephrectomy arm and 1,350 patients (9.6%) in the immediate nephrectomy arm died.

The weighted and unweighted patient baseline, cancer and hospital characteristics stratified according to treatment arm is shown in Table 1. White patients (84.9% vs 79.9%), patients with private insurance (69.8% vs 63.8%) and patients treated in non-academic hospitals (50.0% vs 42.3%) were significantly more likely to be treated with immediate nephrectomy. Patients under Medicaid (9.7% vs 5.8%), greater distance to treating hospital (32.7% vs 25.0%), patients treated at academic hospitals (49.9% vs 39.5%) and higher mean surgical volume (7.8 vs 5.7) were significantly more likely to be treated with delayed nephrectomy. Multivariable logistic regression confirmed that patients with higher education [13-20.9% without a high school diploma (OR, 1.30; 95% CI, 1.01 to 1.68; p=0.043), 7-12.9% without a high school diploma (OR, 1.66; 95% CI, 1.26 to 2.19; p<0.001) and <7% without high school diploma (OR, 1.83; 95% CI, 1.32 to 2.53; p<0.001)] and non-academic treating hospital (OR, 1.23; 95% CI, 1.01 to 1.50; p=0.042) were more likely to have an immediate nephrectomy. Patients insured through Medicaid (OR, 1.81; 95% CI, 1.35 to 2.42; p<0.001), non-insured patients (OR, 1.86; 95% CI, 1.24 to 2.79; =0.003), living ≥28.7 miles from hospital (OR, 1.38; 95% CI, 1.07 to 1.79; p=0.013) and patient with higher income [$38,000-$47,999/ year (OR, 1.55; 95% CI, 1.16 to

2.08; p=0.003), $48,000-62,999/ year (OR, 1.73; 95% CI, 1.27 to 2.35; p=0.001), <63,000/ year (OR, 1.90; 95% CI, 1.33 to 2.69; p<0.001) were independently more likely to have a delayed nephrectomy.

Unweighted Kaplan Meier analysis for overall survival comparing immediate and delayed nephrectomy (immediate nephrectomy [<30 days] vs delayed nephrectomy [>180 days]) confirmed no significant difference (HR, 0.95; 95% CI, 0.75 to 1.22, p=0.71). There was no difference in RCC subtype (p=0.74) and upstaging at pathology (p=0.72) between treatment arms. Following IPTW adjustment weighted Kaplan Meier analysis, there was no significant difference between treatment arms (HR, 0.96; 95% CI, 0.73 to 1.26; p=0.77) (Figure 3). Patient characteristics were similar between the two patient cohorts after IPTW adjustment. Interaction terms suggest that overall survival between treatment arms were not influenced by patient age (HR, 0.99; 95% CI, 0.96 to 1.02; p=0.48) or year of diagnosis (all p>0.05) in the delayed surgery arm. Categorizing patients into three treatment arms, immediate nephrectomy, delayed nephrectomy and nephrectomy performed 31-180 days from cancer diagnosis suggest no difference in overall survival (Supplementary Figure 1). Sensitivity analysis of patients delaying radical nephrectomy beyond 365 days (325 patients) confirmed that there was no difference in overall survival compared to immediate nephrectomy (HR, 0.90; 95% CI, 0.61 to 1.34; p=0.60).

4. Discussion

Based on the analysis of this large retrospective multicenter registry, we report comparable long-term overall survival for delayed vs immediate radical nephrectomy with a long median follow-up of 82.5 months. Sensitivity analysis confirmed that even when nephrectomy was delayed beyond 12 months, there was still no difference in overall survival when compared to immediate nephrectomy.

Where cancer is concerned, physicians have long believed that immediate surgical resection should be performed and assumed that early definitive treatment is superior to delayed treatment. Patients culturally prioritize treatment to eradicate cancer [17]. In the case of prostate cancer, early treatment with radical prostatectomy or radiation was wide-spread before the last decade. These treatments did not clearly improve life expectancy or disease-specific mortality but subjected many patients to the long-term side effects of treatment [18]. This problem is not confined to oncology. Recent randomized evidence has shown that patients with stable angina treated with either medical therapy or percutaneous coronary intervention had similar outcomes contrary to conventional practice [19]. Often, it is often easier to prescribe treatment, but physicians should acknowledge that “Less is More”.

Current recommendations by the American Urological Association (AUA) state that partial nephrectomy should be performed for T1a renal cancers and thermal ablation is an option for renal mass ≤3 cm [20]. The role of active surveillance is reserved for comorbid or elderly patients. The question of interest is do small renal tumors need immediate definitive treatment? Our results suggest that delayed surgical intervention is not inferior to immediate nephrectomy. We report comparable overall survival rates for both treatment arms relative to a large nephrectomy series reporting 5-year overall survival of between 87-100% in patients ≤64 years [21].

Results of our investigation add to the growing body of research that supports delayed intervention for small renal masses. Many recent studies are drawn from single center small case series. Our study provides compelling evidence from a large, national dataset that delayed nephrectomy is a safe approach. A delay in surgery of between 14-15.8 months was not associated with disease upstaging at final histology [22, 23]. Further, patients under surveillance for ≥3 months (median: 15.8 months) before nephrectomy did not have a significant difference in overall survival at a median of 60 months compared to matched patients with immediate nephrectomy [23]. Indeed, previous analysis of Surveillance, Epidemiology, and End Results Medicare-linked database suggest that a delay in nephrectomy for 3 months in patients with RCC was not associated with a lower cancer specific survival [24].

Further, approximately 13-33.3% of small renal masses ≤4 cm are benign at histopathological analysis [8, 9]. A recent report of renal masses on surveillance demonstrated absent growth in size for 23% of masses with a median follow-up of 29 months [8]. A period of surveillance will indeed allow better selection of patients who will benefit from treatment reducing the overtreatment of small renal masses. A systematic review of 259 patients on active surveillance suggest that patients who developed disease progression were older (75 years vs 67 years), had larger tumor size (4.3 cm vs 2.3 cm), higher tumor volume (66 cm^3 vs 15 cm^3), progressive linear growth rate over time (0.8 cm/year vs 0.4 cm/year) and volumetric growth rate (27 cm^3/year vs 6 cm^3/year) suggesting that these features may trigger the need for definitive therapy [8].

Renal biopsy of small renal lesions may play a role in improving case selection in who would benefit from delayed surgery. Traditional concerns of tumor seeding is rare and in lesions ≤4 cm, renal biopsy was diagnostic in 90% of cases [25]. Benign lesions can be safely discharged with no follow-up and renal cancer patients with low risk histological features can be followed with active surveillance [26]. The future role of predictive genomic biomarkers to indolent lesions are promising but require further validation [27]. Indeed, multi-region gene expression profiling of small renal mass suggest that such tumors are less heterogenous and a single needle biopsy is sufficient to characterize the cancer and may have a role in selecting patients who will benefit from active surveillance [28].

Delayed surgery would provide an opportunity for prehabilitation, where a supervised exercise program, optimization of nutrition and a smoking succession program can be administered prior to surgery [29]. Prehabilitation has been shown to promote earlier return to normal activity particularly following major surgery [6]. Even a period of simple walking regime and breathing exercises before surgery has been shown to be efficacious [30].

Our study has limitations. The retrospective nature of NCDB data suggest that there will be case selection bias associated with delayed definitive treatment. Although, we attempted to account for this by propensity score adjustment, we may not have accounted for all confounding factors. Comorbidity might also be underestimated in NCBD which may affect weighting of each treatment arm [31]. This was evident when patients not treated with any modality were added to the delayed nephrectomy cohort to attempt to define active surveillance. This resulted in a benefit favoring immediate nephrectomy, which we would attribute to unaccounted case selection, as we are unable to determine the reason why these patients did not receive treatment.

We also cannot determine if patients with delayed nephrectomy were actually actively surveyed or their nephrectomy was delayed for administrative or for patient optimization. NCDB also does not capture cancer specific survival hence only overall survival is captured. Further, we are unable to determine if patients had a renal biopsy prior to delayed nephrectomy. Finally, while we performed a sensitivity analysis for an interval nephrectomy after a period of 12 months, we used 6 months for the primary analysis as only 325 patients had a nephrectomy delayed for >12 months.

5. Conclusion

We report that delayed and immediate definitive surgical treatment for cT1a RCC confers comparable long-term overall survival. The findings of this study support the fact that immediate surgery has no survival advantage even when surgery is delayed for >12 months. Hence, we hypothesize that a period of observation is safe to allow identification of renal masses which will benefit from surgical resection. Renal biopsy may aid in the selection of such patients.

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Supplementary Figure:

Supplementary Figure 1: Weighted Kaplan Meier analysis for overall survival for patients with delayed nephrectomy vs immediate nephrectomy (HR: 1.00, 95% CI: 0.77-1.30, p=0.991) and nephrectomy performed between day 31-180 from diagnosis (HR: 1.10, 95% CI: 0.84-1.44, p=0.478).

Supplementary Table 1: Summary of key results.

Figure 1: Inclusion and exclusion criteria used to determine study cohort.

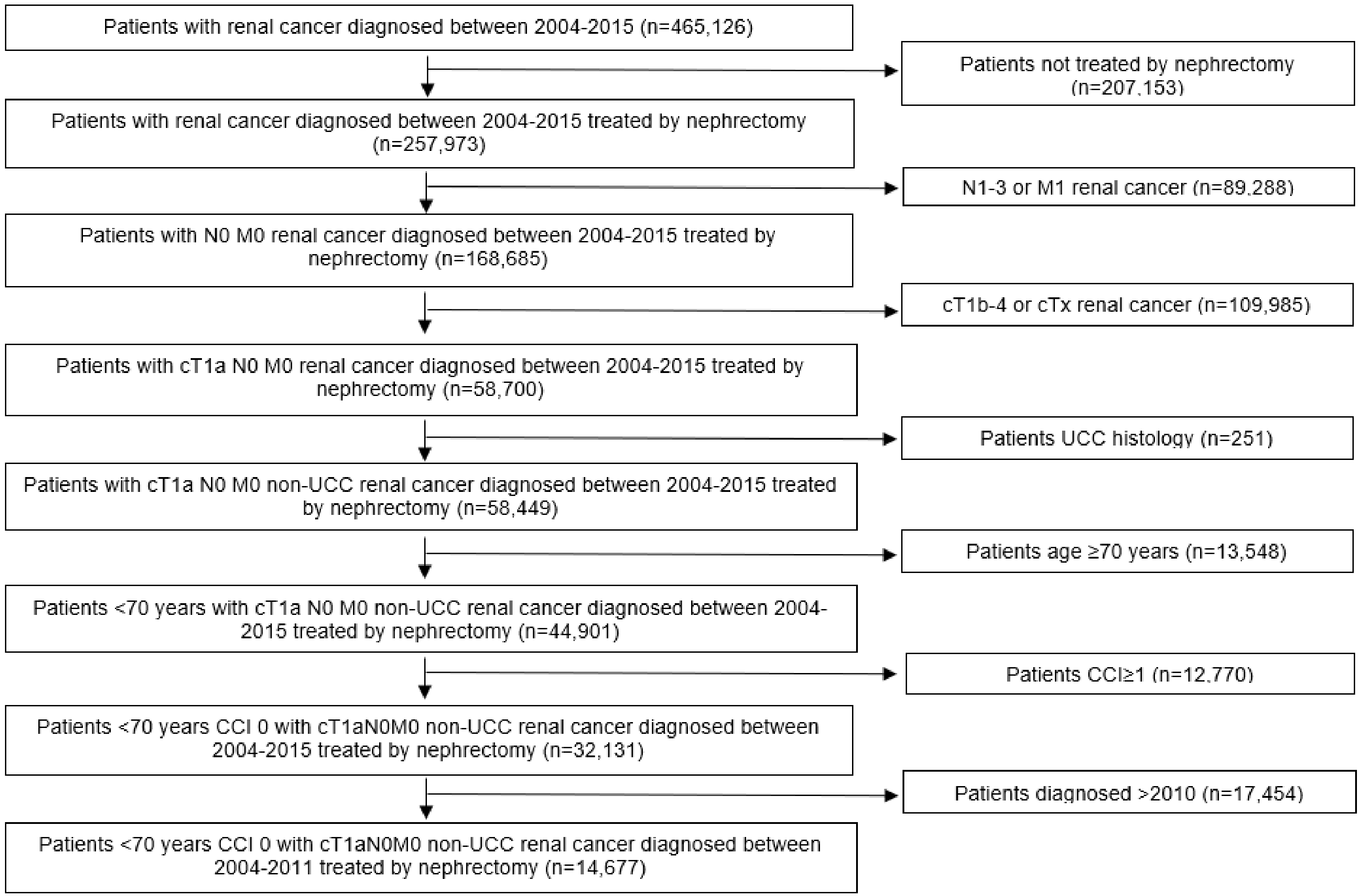


Figure 2: Weighted Kaplan Meier analysis for overall survival for patients with delayed nephrectomy vs immediate nephrectomy (HR: 0.96, 95% CI: 0.73-1.26, p=0.766).

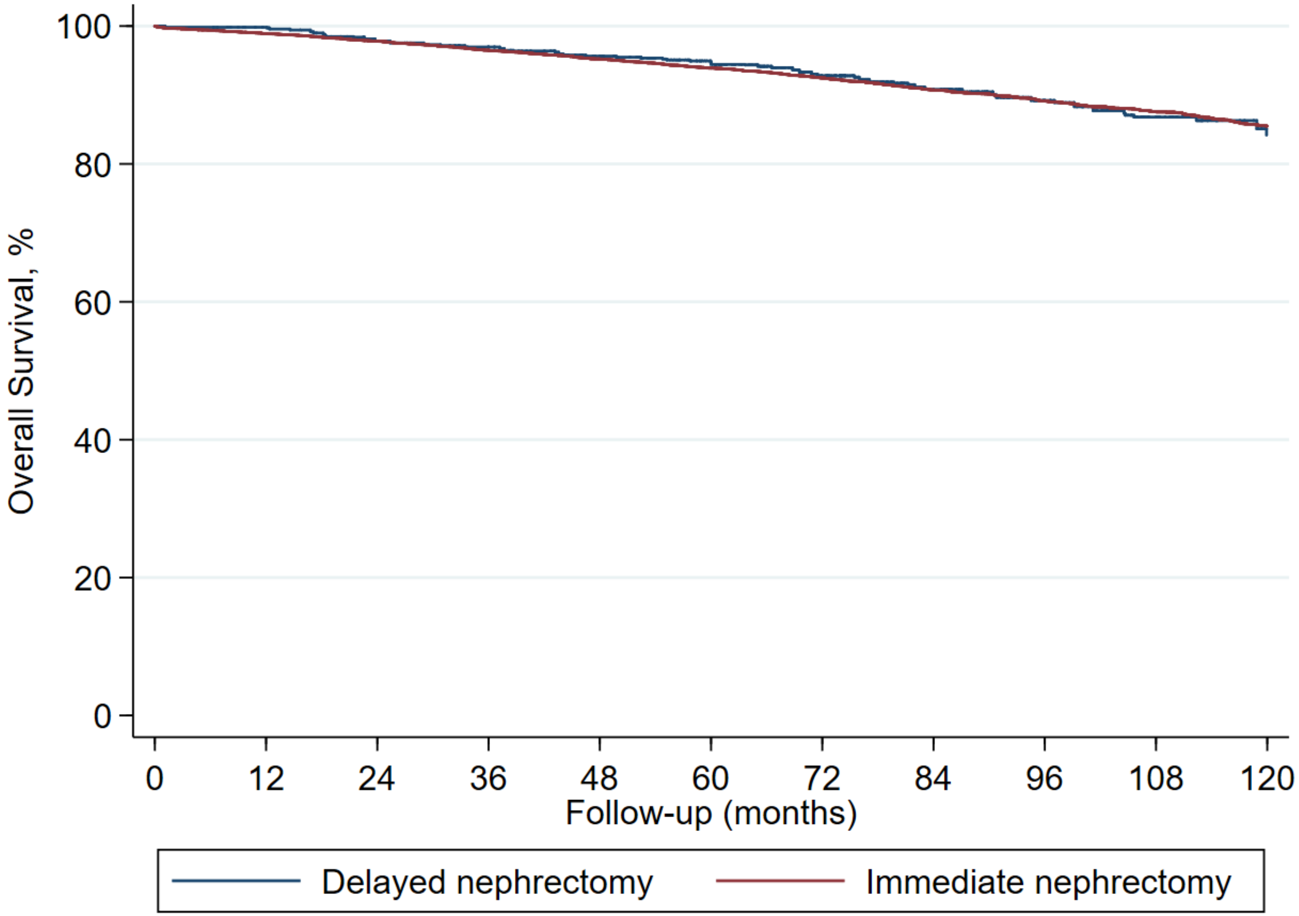
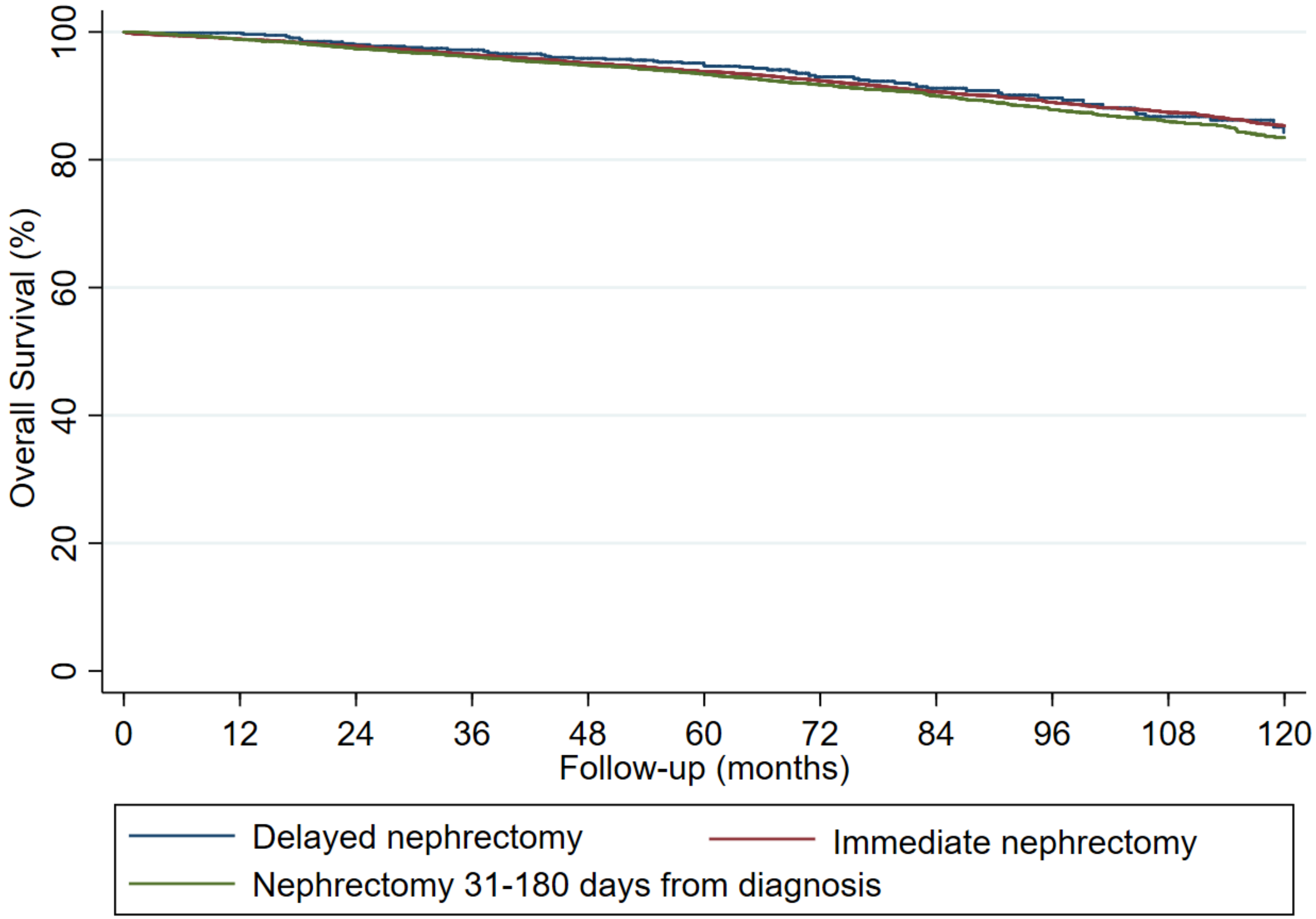


Table 1: Baseline patient characteristics for unmatched and matched patient cohort

Variable	Unweighted patient cohort				Weighted patient cohort			
	All patients (n=14,677)	Immediate nephrectomy (n=14,050)	Delayed nephrectomy (n=627)	Standard differences	All patients	Immediate nephrectomy	Delayed nephrectomy	Standard differences
Age at diagnosis, n (%)								
<48 years	3,897 (26.5)	3,755 (26.7)	142 (22.7)	9.5	25.6	26.6	24.6	4.6
48-55.9 years	3,595 (24.5)	3,431 (24.4)	164 (26.1)	-4.0	24.9	24.4	25.5	-2.4
56-61.9 years	3,223 (22.0)	3,007 (21.9)	146 (23.3)	-3.3	22.2	21.9	22.5	-1.4
≥62 years	3,962 (27.0)	3,787 (27.0)	175 (27.9)	-2.1	27.2	27.0	27.4	-0.9
Sex, n (%)								
Male	9,092 (62.0)	8,689 (61.8)	403 (64.3)	-5.0	61.6	62.0	61.3	1.4
Female	5,585 (38.0)	5,361 (38.2)	224 (35.7)	5.0	38.4	38.0	38.7	-1.4
Race, n (%)								
White	12,430 (84.7)	11,929 (84.9)	501 (79.9)	13.2	84.6	84.7	84.5	0.5
Black	1,636 (11.1)	1,551 (11.0)	85 (13.6)	-7.7	11.2	11.1	11.2	-0.,1
Other	426 (2.9)	392 (2.8)	34 (5.4)	-13.3	3.0	2.9	3.1	-0.8
Unknown	185 (1.3)	178 (1.3)	7 (1.1)	1.4	1.2	1.3	1.2	0.1
Year of diagnosis:								
2004	1,170 (8.0)	1,127 (8.0)	43 (6.8)	4.4	7.7	8.0	7.5	1.9
2005	1,335 (9.1)	1,285 (9.2)	50 (8.0)	4.2	9.0	9.1	8.9	0.8
2006	1,480 (10.1)	1,418 (10.1)	62 (9.9)	0.7	9.7	10.1	9.4	2.3
2007	1,707 (11.6)	1,633 (11.6)	74 (11.8)	-0.6	11.7	11.6	11.8	-0.5
2008	2,633 (17.9)	2,510 (17.9)	123 (19.6)	-4.5	18.1	17.9	18.2	-0.7
2009	3,210 (21.9)	3,069 (21.8)	141 (22.5)	-1.6	22.1	21.9	22.3	-1.0
2010	3,142 (21.4)	3,008 (21.4)	134 (21.4)	0.1	21.7	21.4	22.0	-1.4
Insurance status, n (%)								
Private	10,211 (69.6)	9,811 (69.8)	400 (63.8)	12.8	69.5	69.6	69.4	0.3
Medicare	2,976 (20.3)	2,847 (20.3)	129 (20.6)	-0.8	20.4	20.3	20.4	-0.4
Medicaid/ other government	883 (6.0)	822 (5.8)	61 (9.7)	-14.5	5.9	6.0	5.8	0.8
Uninsured	420 (2.8)	392 (2.8)	28 (4.5)	-9.0	2.8	2.9	2.8	0.6
Unknown	187 (1.3)	178 (1.3)	9 (1.4)	-1.5	1.4	1.3	1.6	-2.4
Median income quartiles within ZIP code, n (%)								
≤$37,999	2,246 (15.3)	2,158 (15.4)	88 (14.0)	3.7	13.5	15.5	11.6	11.4
$38,000-47,999	3,028 (20.6)	2,886 (20.5)	142 (22.7)	-5.1	21.0	20.6	21.4	-1.9
48,000-62,999	3,968 (27.0)	3,794 (27.0)	174 (27.8)	-1.7	27.5	27.0	28.1	-2.7
≥$63,000	5,282 (36.0)	5,063 (36.0)	219 (34.9)	2.3	37.0	35.9	38.0	-4.4
Unknown	153 (1.0)	149 (1.1)	4 (0.6)	4.6	1.0	1.0	0.9	1.7
Quartiles of no high school degree, n (%)								
≥21%	2,238 (15.3)	2,116 (15.1)	122 (19.5)	-11.7	14.9	15.2	14.5	2.0

13-20.9%	3,551 (24.2)	3,388 (24.1)	163 (26.0)	-4.3	23.9	24.2	23.7	1.1
7-12.9%	4,829 (32.9)	4,638 (33.0)	191 (30.5)	5.5	33.3	32.9	33.7	-1.6
≤6.9%	3,910 (26.6)	3,763 (26.8)	147 (23.4)	7.7	26.9	26.7	27.2	-1.3
Unknown	149 (1.0)	145 (1.0)	4 (0.6)	4.3	1.0	1.0	0.9	1.4
Great circle distance (miles), n (%)								
≤5.3	3,488 (23.8)	3,352 (23.9)	136 (21.7)	5.2	23.8	23.8	23.8	-0.2
5.4-12.1	3,630 (24.7)	3,488 (24.8)	142 (22.7)	5.1	24.4	24.7	24.1	1.6
12.2-28.6	3,676 (25.0)	3,536 (25.2)	140 (22.3)	6.7	24.6	25.0	24.1	2.2
≥28.7	3,724 (25.4)	3,519 (25.0)	205 (32.7)	-16.9	26.1	25.4	26.9	3.4
Unknown	159 (1.1)	155 (1.1)	4 (0.6)	0.5	1.1	1.1	1.1	-0.3
Urban/ rural status of county, n (%)								
Metropolitan	12,127 (82.6)	11,606 (82.6)	521 (83.1)	-1.3	82.5	82.6	82.3	0.9
Urban	1,886 (12.9)	1,806 (12.9)	80 (12.7)	0.3	13.3	12.9	13.8	-2.9
Rural	228 (1.5)	215 (1.5)	13 (2.1)	-4.1	1.3	1.5	1.2	3.6
Unknown	436 (3.0)	423 (3.0)	13 (2.1)	0.6	2.9	3.0	2.7	1.4
Treating hospital, n (%)								
Academic	5,864 (39.9)	5,551 (39.5)	313 (49.9)	-21.1	39.9	40.0	29.8	0.2
Non-academic	7,289 (49.7)	7,024 (50.0)	265 (42.3)	15.5	50.2	49.7	50.8	-2.3
Unknown	1,524 (10.4)	1,475 (10.5)	49 (7.8)	9.3	9.9	10.3	9.4	3.5
Hospital surgical volume, mean (SE)	78.1 (5.7)	77.5 (5.7)	90.0 (7.8)	-17.9	79.2 (5.8)	78.1 (5.8)	80.3 (7.0)	-3.2

Supplementary Figure 1: Weighted Kaplan Meier analysis for overall survival for patients with delayed nephrectomy vs immediate nephrectomy (HR: 1.00, 95% CI: 0.77-1.30, p=0.991) and nephrectomy performed between day 31-180 from diagnosis (HR: 1.10, 95% CI: 0.84-1.44, p=0.478).



Supplementary Table 1: Summary of key results.

Key results	
Median delay to time of nephrectomy from diagnosis	8.1 months (IQR: 6.8, 11.2).
Median follow-up	82.5 months (IQR, 66.7, 102.3)
Unadjusted log-rank test between immediate (defined as <30 days) vs delayed nephrectomy (defined as >180 days)	HR, 0.95; 95% CI, 0.75 to 1.22, p=0.71
Adjusted log-rank test between immediate (defined as <30 days) vs delayed nephrectomy (defined as >180 days)	HR, 0.96; 95% CI, 0.73 to 1.26; p=0.77
Adjusted log-rank test between immediate (defined as <30 days) vs delayed nephrectomy (defined as >365 days)	HR, 0.90; 95% CI, 0.61 to 1.34; p=0.60

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