Survival after partial and radical nephrectomy for high-risk disease: A propensity-matched comparison

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Abstract

Introduction: Increasingly, partial nephrectomy has been applied to high-risk disease without evidence that its survival benefits can be extrapolated to this entity. We aimed to compare overall survival after partial vs. radical nephrectomy in patients with high-risk renal cell carcinoma.

Methods: Using the National Cancer Data Base, we identified patients who underwent partial or radical nephrectomy for high-risk disease between 2003 and 2006. High-risk disease was defined as the presence of adverse pathological features within the primary tumour, namely high-grade or unfavourable histology, T3 stage, or both. After matching the partial and radical nephrectomy groups based on propensity scores, 1680, 276, and 76 patients with high-grade or unfavourable histology, T3 stage, or both adverse pathologic features, respectively, were available for analysis. Five-year overall survival was compared after partial vs. radical nephrectomy for each high-risk cohort using the Kaplan-Meier and log rank tests.

Results: Partial nephrectomy was associated with a statistically significant improvement in five-year overall survival compared to radical nephrectomy for small tumours (median size 3.0 cm; interquartile range 2.1–4.5 cm) with high-grade or unfavourable histology (87% vs. 81%; p<0.01) or with pT3a stage (82% vs. 71%; p<0.01). For patients concomitantly harbouring both adverse pathologic features, no difference in survival was detected (p=0.21).

Conclusions: Partial nephrectomy is associated with survival benefits in patients with adverse pathologic features, suggesting that renal preservation is not only safe, but also potentially beneficial for high-risk disease. Due to inherent selection bias associated with partial nephrectomy use, prospective validation of these findings is needed.

Introduction

Partial nephrectomy (PN) is the optimal treatment for clinical T1 renal masses.[1] This recommendation is supported by numerous retrospective studies, which have demonstrated its superior functional and survival outcomes and at least equivalent cancer control relative to radical nephrectomy (RN).[2,3] Accordingly, PN use has increased over the last 10–15 years, with nearly half of all T1 renal tumours now being managed with PN.[4,5] Recently, this trend has been associated with increasing PN use for renal cell carcinoma (RCC) with adverse pathologic factors that independently predict cancer-specific death.[6-10] The role of PN for this high-risk RCC is ill-defined. Several retrospective studies have investigated the comparative effectiveness of PN vs. RN for high-risk disease, but have failed to detect a survival difference in this setting.[11-14] Despite its flaws, the only level 1 evidence comparing PN and RN demonstrated a survival advantage for RN, calling into question the long-held belief that PN is necessarily better than RN for the elective management of small renal masses.[15,16] We sought to compare survival outcomes between PN and RN for high-risk disease in a large, nationally representative cohort of American patients in the National Cancer Data Base (NCDB).

Methods

NCDB participant user file

The NCDB was established in 1989 as a joint project of the American Cancer Society and the Commission on Cancer (CoC) of the American College of Surgeons. It is a nationwide, hospital-based cancer registry that captures comprehensive clinical data on approximately 70% of all newly diagnosed malignancies in the U.S. annually. A data use agreement exists between the American College of Surgeons and each of its CoC-accredited hospitals. A detailed description of the NCDB has been published previously.[6] We used the NCDB's 2011 participant user file for kidney and renal pelvis cancers. Institutional review board approval was obtained prior to study initiation.

Study population

We identified 120 926 patients who had been diagnosed with RCC from 2003–2006, based on International Classification of Diseases for Oncology, third edition primary site codes. Diagnoses prior to 2003 were excluded because the Charlson comorbidity index (CCI) variable was not available, and diagnoses after 2006 were excluded to avoid patients with less than five years followup. We restricted the cohort to patients with clinical T1-T2, pathological T1-T3a, non-metastatic RCC who underwent PN or RN (n=30 287). Patients with other primary cancers were excluded to avoid potential confounding (n=5227). Cases diagnosed but not treated at the reporting facility were excluded due to incomplete followup (n=131).

Three cohorts were identified from the study population based on the presence of adverse pathologic features (APF): 1) RCC with high-grade or unfavourable histology (n=5150); 2) RCC with pT3a stage (n=1265); and 3) RCC with high-grade or unfavourable histology and pT3a stage (n=491).

Study variables

The NCDB contains data pertaining to patient demographics and comorbidity burden; cancer grade, stage, and histology; first course treatment(s); and overall survival. The study variables included: age, sex, CCI, race, income level, insurance type, county, hospital type, hospital surgical volume, tumour size, pT stage, tumour histology, and tumour grade. Age and tumour size were treated as continuous variables; all other variables were categorical. Missing data for the income, insurance, county, and grade variables were included as unknowns. CCI was calculated based on International Classification of Disease, ninth edition, clinical modification, secondary diagnosis codes and was categorized as 0 (no comorbidities), 1, or >1. Race was categorized as White, African-American, Hispanic, or other. Income levels were estimates based on 2000 U.S. census data that were stratified into annual income quartiles: lowest (<$30 000), lower middle ($30 000–$35 000), middle ($35 000–$46 000), and upper middle (>$46 000). Insurance type included no health insurance, social (Medicare/Medicaid), and private/managed care. County was categorized as urban, metropolitan, or rural according to data from the 2003 U.S. Department of Agriculture Research Service. Using classifications developed by the CoC, hospitals were designated as academic, comprehensive, community, or other hospitals. Surgical volume was calculated based on the hospital's overall surgical volume (2003–2006). Surgical volume was stratified into tertiles (<8, 8–21, >21 total cases), and hospitals were classified as low-, intermediate-, or high-volume. Pathological T stage included pT1-T3a. RCC histology was categorized as clear-cell, papillary, chromophobe, unfavourable subtype/variant (i.e., collecting duct, medullary, sarcomatoid, or rhabdoid), unclassified RCC, and other. Histologic grade, based on the American Joint Committee on Cancer grading system, was categorized as low-grade (G1/G2) and high-grade (G3/G4).

Study outcomes

The primary outcome was five-year overall survival (OS), which was calculated from the date of surgery to the date of death from all causes or censored at the date of last contact.

Propensity matching

We observed a greater proportion of large, higher-stage, histologically aggressive tumours within the controls (RN) vs. the cases (PN) (Table 1). Using 1:1 propensity score-matching based on the nearest neighbour algorithm, 90% or more of cases were matched to controls, and no additional matches could be made with the given data, confirming the completeness of the match. P values comparing cases to controls were not significant after matching for two out of three cohorts, confirming good matching.

Statistical analyses

Differences between the PN and RN groups were assessed by univariate analysis using the Mann-Whitney U-test for continuous variables and the chi-squared test for categorical variables. The PN and RN groups were compared in terms of OS using the Kaplan-Meier method and log-rank test. In order to adjust for covariates, which remained unbalanced after propensity-matching, the association between surgery type (PN or RN) and OS was analyzed using a multivariable Cox proportional hazards model. Statistical tests were performed using SAS® University Edition (SAS Institute Inc., Cary, NC, U.S.). P values <0.05 were considered statistically significant.

Results

In the final study cohorts, there were 1680, 276, and 76 patients with high-grade or unfavourable histology (HG/UH), pT3a stage (T3), or both APF, respectively (Table 2). The HG/UH and T3 cohorts were well matched. In the combined HG/UH and T3 cohort, elderly and male patients were over-represented among PN cases.

Median followup in months was 69 (interquartile range [IQR]) 48–83), 68 (IQR 47–82), and 61 (IQR 32–81) for the HG/UH, T3, and combined cohorts, respectively. Within the cohorts, followup did not differ significantly between the PN and RN groups (p>0.05).

Table 1. Patient, hospital, and clinical characteristics of three high-risk RCC cohorts by surgery type before propensity matching

	HG/UH (N=5150)					T3 (N=1265)					HG/UH and T3 (N=491)				
	RN (n=4216)		PN (n=934)			RN (n=1125)		PN (n=140)			RN (n=452)		PN (n=39)		
Variable	**n**	**%**	**n**	**%**	**p value**	**n**	**%**	**n**	**%**	**p value**	**n**	**%**	**n**	**%**	**p value**
Diagnosis year					0.02					0.26					0.36
2003	775	18.4	144	15.4		260	23.1	22	15.7		95	21.0	6	15.4	
2004	1009	23.9	205	21.9		249	22.1	34	24.3		99	21.9	10	25.6	
2005	1130	26.8	255	27.3		281	25.0	40	28.6		114	25.2	14	35.9	
2006	1302	44.7	330	54.6		335	42.	44	45.8		144	46.8	9	30.0	
Age (years)					0.01					0.10					0.04
Median (IQR)	61	(52–71)	61	(51–69)		63	(54–74)	63	(54–70)		64	(55–75)	59	(52–66)	
Sex					0.02					0.28					0.32
Female	1539	36.5	303	32.4		397	35.3	43	30.7		151	33.4	10	25.6	
Male	2677	63.5	631	67.6		728	64.7	97	69.3		301	66.6	29	74.4	
Charlson comorbidity index					0.68					0.12					0.97
0	3017	71.6	665	71.2		771	68.5	84	60.0		307	67.9	26	66.7	
1	861	20.4	200	21.4		264	23.5	41	29.3		104	23.0	9	23.1	
>1	338	8.0	69	7.4		90	8.0	15	10.7		41	9.1	4	10.3	
Race					0.66					0.61					0.83
White	3356	79.6	757	81.0		930	82.7	118	84.3		376	83.2	34	87.2	
African-American	455	10.8	89	9.5		84	7.5	11	7.9		34	7.5	3	7.7	
Hispanic	237	5.6	49	5.2		71	6.3	5	3.6		27	6.0	1	2.6	
Other	168	4.2	39	4.4		40	3.7	6	4.5		15	3.4	1	2.6	
Income level					0.62					0.55					0.11
Lowest	542	12.9	122	13.1		135	12.0	19	13.6		54	11.9	9	23.1	
Lower-middle	738	17.5	162	17.3		206	18.3	21	15.0		91	20.1	3	7.7	
Middle	1089	25.8	220	23.6		311	27.6	33	23.6		133	29.4	9	23.1	
Upper-middle	1608	38.1	371	39.7		413	36.7	60	42.9		151	33.4	15	38.5	
Unknown	239	5.7	59	6.3		60	5.3	7	5.0		23	5.1	3	7.7	
County					0.70					0.16					0.90
Urban	614	14.6	131	14.0		192	17.1	19	13.6		73	16.2	8	20.5	
Metropolitan	3256	77.2	720	77.1		834	74.1	115	82.1		341	75.4	28	71.8	
Rural	78	1.9	15	1.6		26	2.3	2	1.4		10	2.2	1	2.6	
Unknown	268	6.4	68	7.3		73	6.5	4	2.9		28	6.2	2	5.1	

HG/UH: high-grade or unfavourable hstology; IQR: interquartile range; PN: partial nephrectomy; RCC: renal cell carcinoma; RN: radical nephrectomy; T3: pathological T3a stage.

RCC with HG/UH

At the time of last contact, 350 (21%) patients had died, including 8.0% (135/1680) treated with PN and 13% (215/1680) treated with RN. The five-year OS for the total cohort was 84% (Fig.1). The five-year OS was 87% for PN and 81% for RN (p<0.01; Fig. 2A). PN was associated with a 34% decreased hazard of death (hazard ratio [HR] 0.66, 95% confidence interval [CI] 0.53–0.82; p<0.01; Table 3).

RCC with T3

At the time of last contact, 75 (27%) patients had died, including 9.8% (27/275) treated with PN and 17% (48/275) treated with RN. The five-year OS for the total cohort was 77% (Fig. 1). The five-year OS was 82% for PN and 71% for RN (p<0.01; Fig. 2B). PN was associated with a 46% decreased hazard of death (HR 0.54, 95% CI 0.34–0.87; p=0.01; Table 3).

RCC with HG/UH and T3

At the time of last contact, 29 (38%) patients had died, including 16% (12/76) treated with PN and 22% (17/76) treated with RN. The five-year OS for the total cohort was 65% (Fig. 1). OS was not significantly different between approaches (p=0.21; Fig. 2C). After adjusting for unbalanced covariates, namely age and sex, on Cox multivariable analysis, the results were unchanged (p=0.28; Table 3).

Table 1 (cont'd). Patient, hospital, and clinical characteristics of three high-risk RCC cohorts by surgery type before propensity matching

	HG/UH (N=5150)					T3 (N=1265)					HG/UH and T3 (N=491)				
	RN (n=4216)		PN (n=934)			RN (n=1125)		PN (n=140)			RN (n=452)		PN (n=39)		
Variable	**n**	**%**	**n**	**%**	**p value**	**n**	**%**	**n**	**%**	**p value**	**n**	**%**	**n**	**%**	**p value**
Hospital type					<0.01					<0.01					0.74
Academic	1566	37.1	513	54.9		441	39.2	75	53.6		188	41.6	19	48.7	
Comprehensive	2296	54.5	373	39.9		576	51.2	60	42.9		229	50.7	18	46.2	
Community	300	7.1	42	4.5		94	8.4	4	2.9		28	6.2	2	5.1	
Other	54	1.3	6	0.6		14	1.2	1	0.7		7	1.5	0	0.0	
Hospital surgical volume					<0.01					<0.01					0.67
Low	1394	33.1	210	22.5		420	37.3	36	25.7		172	38.1	12	30.8	
Intermediate	1476	35.0	281	30.1		382	34.0	46	32.9		156	34.5	15	38.5	
High	1346	31.9	443	47.4		323	28.7	58	41.4		124	27.4	12	30.8	
Tumour size (cm)					<0.01					<0.01					<0.01
Median (IQR)	5.5	(3.8–7.8)	3.0	(2.2–4.0)		6.5	(4.6–8.5)	3.0	(2.0–4.0)		7.0	(5.0–9.5)	3.0	(2.3–4.5)	
Histology					<0.01					<0.01					<0.01
Clear cell	1392	33.0	300	32.1		457	40.6	35	25.0		174	38.5	3	7.7	
Papillary	389	9.2	179	19.2		91	8.1	32	22.9		35	7.7	10	25.6	
Chromophobe	241	5.7	73	7.8		54	4.8	9	6.4		21	4.6	4	10.3	
Aggressive type	88	2.1	6	0.6		33	2.9	0	0.0		22	4.9	0	0.0	
Unclassified RCC	1808	42.9	335	35.9		435	38.7	59	42.1		168	37.2	19	48.7	
Other	298	7.1	41	4.4		55	4.9	5	3.6		32	7.1	3	7.7	
Clinical T stage					<0.01					<0.01					<0.01
T1	2877	68.2	894	95.7		599	53.2	130	92.9		219	48.5	34	87.2	
T2	1339	31.8	40	4.3		526	46.8	10	7.1		233	51.6	5	12.8	
Pathological T stage					<0.01					-					-
T1	2661	63.1	859	92.0		-		-			-		-		
T2	1103	26.2	36	3.9		-		-			-		-		
T3a	452	10.7	39	4.2		1125	100.0	140	100.0		452	100.0	39	100.0	
Grade					-					0.01					-
Low-grade	-		-			517	46.0	83	59.3		-		-		
High-grade	4216	100.0	934	100.0		452	40.2	39	27.9		452	100.0	39	100.0	
Unknown/Not applicable	-		-			156	13.9	18	12.9		-		-		
Followup (months)					0.15					0.01					0.18
Median (IQR)	67	(43–82)	69	(49–81)		65	(35–81)	70	(55–82)		60	(26–76)	64	(43–80)	

HG/UH: high-grade or unfavourable hstology; IQR: interquartile range; PN: partial nephrectomy; RCC: renal cell carcinoma; RN: radical nephrectomy; T3: pathological T3a stage.

Discussion

High-risk RCC harbouring one or more APF has been treated increasingly with PN over the last decade, despite a lack of evidence of the safety of PN in this setting.[6] Our results demonstrate superior or at least equivalent survival for patients with high-risk RCC treated with PN. For RCC with HG/UH or T3, PN was an independent significant predictor of improved OS, after adjusting for age, comorbidity burden, tumour size, and other risk factors for all-cause mortality. For RCC with both APF, the OS curve for PN was better than that for RN, but this difference was not statistically significant, likely due to insufficient power (n=76).

We used propensity-matching to address the inherent differences between patients undergoing PN and RN and to adjust for patient factors which may affect OS, including age and comorbidity. Optimal matching necessitated the exclusion of larger tumours, which had been treated mostly with RN; therefore, the median tumour size of the analyzed cohorts was only 3.0–3.7 cm (IQR 2.1–4.5). For this reason, although both PN and RN are being used to treat larger tumours, our study only addresses the comparative

Table 2. Patient, hospital, and clinical characteristics of three high-risk RCC cohorts by surgery type after propensity matching

	HG/UH (n=1680)					T3 (n=276)					HG/UH and T3 (n=76)				
	RN		PN			RN		PN			RN		PN		
Variable	**n**	**%**	**n**	**%**	**p value**	**n**	**%**	**n**	**%**	**p value**	**n**	**%**	**n**	**%**	**p value**
Diagnosis year					0.76					0.09					0.38
2003	143	17.0	134	16.0		39	28.3	22	15.9		11	28.9	6	15.8	
2004	199	23.7	194	23.1		27	19.6	33	23.9		8	21.1	10	26.3	
2005	228	27.1	222	26.4		37	26.8	39	28.3		8	21.1	13	34.2	
2006	270	47.4	290	52.7		35	34.0	44	46.8		11	40.7	9	31.0	
Age (years)					0.19					0.09					0.04
Median (IQR)	61	(52–70)	61	(52–70)		63	(54–72)	65	(54–74)		64	(54–73)	70	(59–76)	
Sex					0.47					0.52					0.02
Female	292	34.8	278	33.1		48	34.8	43	31.2		19	50.0	9	23.7	
Male	548	65.2	562	66.9		90	65.2	95	68.8		19	50.0	29	76.3	
Charlson comorbidity index					0.49					0.54					0.87
0	599	71.3	600	71.4		90	65.2	84	60.9		23	60.5	25	65.8	
1	167	19.9	178	21.2		38	27.5	39	28.3		11	28.9	9	23.7	
>1	74	8.8	62	7.4		10	7.2	15	10.9		4	10.5	4	10.5	
Race					0.98					0.94					0.53
White	673	80.1	671	79.9		113	81.9	116	84.1		29	76.3	33	86.8	
African-American	82	9.8	85	10.1		14	10.1	11	8.0		4	10.5	3	7.9	
Hispanic	50	6.0	47	5.6		5	3.6	5	3.6		4	10.5	1	2.6	
Other	35	4.3	37	4.6		6	4.5	6	4.5		1	2.7	1	2.7	
Income level					0.13					0.98					0.71
Lowest	83	9.9	116	13.8		18	13.0	19	13.8		7	18.4	9	23.7	
Lower-middle	158	18.8	153	18.2		25	18.1	21	15.2		7	18.4	3	7.9	
Middle	216	25.7	204	24.3		31	22.5	32	23.2		7	18.4	8	21.1	
Upper-middle	336	40.0	313	37.3		57	41.3	59	42.8		15	39.5	15	39.5	
Unknown	47	5.6	54	6.4		7	5.1	7	5.1		2	5.3	3	7.9	
County					0.80					0.33					0.64
Urban	116	13.8	126	15.0		20	14.5	19	13.8		4	10.5	8	21.1	
Metropolitan	648	77.1	641	76.3		110	79.7	113	81.9		30	78.9	27	71.1	
Rural	17	2.0	13	1.5		0	0.0	2	1.4		1	2.6	1	2.6	
Unknown	59	7.0	60	7.1		8	5.8	4	2.9		3	7.9	2	5.3	

HG/UH: high-grade or unfavorable histology; IQR: interquartile range; PN: partial nephrectomy; RCC: renal cell carcinoma; RN: radical nephrectomy; T3: pathological T3a stage.

effectiveness of PN and RN for high-risk, clinical T1 tumours. Irrespective of RCC risk, numerous observational studies have demonstrated improved OS with PN.[17-20] In a contemporary meta-analysis comparing PN and RN outcomes, PN was associated with a 19% reduction in all-cause mortality.[2] A recent instrumental variable analysis, which adjusts for selection bias and confounders — both known and unknown — in observational studies, arrived at similar results, with a 16% reduction in all-cause mortality attributed to PN.[21] This survival benefit is attributed to improved renal and cardiovascular functional outcomes with PN.[3,17,18]

Four observational studies, using data from 1976–2008, have examined the outcomes of PN for high-risk disease.[11-14] These studies all showed comparable oncologic outcomes for PN and RN. Only two studies examined OS, finding no difference between PN and RN; however, these studies were underpowered.[12,13] Within the largest published study, a population-based study using the Surveillance, Epidemiology, and End Results (SEER) database, Hansen et al failed to detect statistically significant cancer-specific mortality differences between PN and RN for large, high-grade, or T3 tumours. This study is consistent with our findings, suggesting that PN offers at least equivalent survival relative to RN for high-risk disease.[14] However, due to its lack of information on baseline comorbidity burden, this study was unable to assess the effect and potential benefit of PN on OS.

Recently, the survival benefits of PN have been called into question. The only prospective, randomized, controlled trial to

Table 2 (cont'd). Patient, hospital, and clinical characteristics of three high-risk RCC cohorts by surgery type after propensity matching

	HG/UH (n=1680)					T3 (n=276)					HG/UH and T3 (n=76)				
	RN		PN			RN		PN			RN		PN		
Variable	**n**	**%**	**n**	**%**	**p value**	**n**	**%**	**n**	**%**	**p value**	**n**	**%**	**n**	**%**	**p value**
Hospital type					0.82					0.56					0.68
Academic	447	53.2	432	51.4		71	51.4	75	54.3		15	39.5	18	47.4	
Comprehensive	350	41.7	360	42.9		57	41.3	58	42.0		19	50.0	18	47.4	
Community	39	4.6	42	5.0		9	6.5	4	2.9		3	7.9	2	5.3	
Other	4	0.5	6	0.7		1	0.7	1	0.7		1	2.6	0	0.0	
Hospital surgical volume					0.36					0.51					0.71
Low	180	21.4	203	24.2		27	19.6	35	25.4		12	31.6	12	31.6	
Intermediate	268	31.9	267	31.8		49	35.5	45	32.6		12	31.6	15	39.5	
High	392	46.7	370	44.0		62	44.9	58	42.0		14	36.8	11	28.9	
Tumour size (cm)					0.64					0.51					0.48
Median (IQR)	3.0	(2.4–4.3)	3.0	(2.4–4.5)		3.0	(2.1–4.5)	3.0	(2.1–4.5)		3.4	(2.5–4.5)	3.7	(2.9–4.5)	
Histology					0.71					0.53					0.98
Clear cell	268	31.9	279	33.2		42	30.4	35	25.4		3	7.9	3	7.9	
Papillary	145	17.3	133	15.8		35	25.4	31	22.5		10	26.3	10	26.3	
Chromophobe	59	7.0	65	7.7		10	7.3	9	6.5		4	10.5	3	7.9	
Aggressive type	3	0.4	6	0.7		0		0			0	0.0%	0	0.0	
Unclassified RCC	298	35.5	317	37.7		42	30.4	58	42.0		16	42.1	19	50.0	
Other	67	8.0	40	4.8		9	6.5	5	3.6		5	13.2	3	7.9	
Clinical T stage					0.03					0.02					0.53
T1	778	92.6	800	95.2		115	83.3	128	92.8		31	81.6	33	86.8	
T2	62	7.4	40	4.8		23	16.7	10	7.3		7	18.4	5	13.2	
Pathological T stage					0.24					-					-
T1	757	90.1	765	91.1		0	0.0	0	0.0		0	0.0	0	0.0	
T2	50	6.0	36	4.3		0	0.0	0	0.0		0	0.0	0	0.0	
T3a	33	3.9	39	4.6		138	100.0	138	100.0		38	100.0	38	100.0	
Grade					-					0.51					-
Low-grade	0	0.0	0	0.0		84	60.9	81	58.7		0	0.0	0	0.0	
High-grade	840	100.0	840	100.0		42	30.4	39	28.3		38	100.0	38	100.0	
Unknown/Not applicable	0	0.0	0	0.0		12	8.7	18	13.0		0	0.0	0	0.0	
Followup (months)					0.57					0.09					0.34
Median (IQR)	69	(48–83)	70	(48–83)		68	(47–82)	63	(41–83)		61	(32–81)	50	(22–82)	

HG/UH: high-grade or unfavorable histology; IQR: interquartile range; PN: partial nephrectomy; RCC: renal cell carcinoma; RN: radical nephrectomy; T3: pathological T3a stage.

address the comparative effectiveness of PN and RN in the elective setting did not find a significant improvement in OS with PN.[15] In fact, based on the initial intention-to-treat analysis in which 8–10% of the patients had high-risk disease, i.e., tumours >5 cm or ≥pT3 stage, PN resulted in inferior OS outcomes compared to RN. Despites its flaws, including poor accrual and 15% crossover between groups, this study represents the only level 1 evidence to date. The discrepancy between these results and those of prior observational studies may be explained by the effect of potential bias and confounders on OS comparisons between PN and RN in the elective setting.[16,22]

Our study has limitations. Due to its retrospective nature, our study is susceptible to bias. Although we adjusted for inherent biases in treatment selection using propensity-based matching, we were unable to adjust for unmeasured confounders not included in the NCDB, particularly preoperative renal function and unknown confounders, which may have biased our results. Furthermore, since cause-specific survival is not available in the NCDB, we relied on OS, which is a limitation. However, we adjusted for age and CCI in order to address the risk of non-cancer. Although this is the largest study to compare OS between PN and RN for

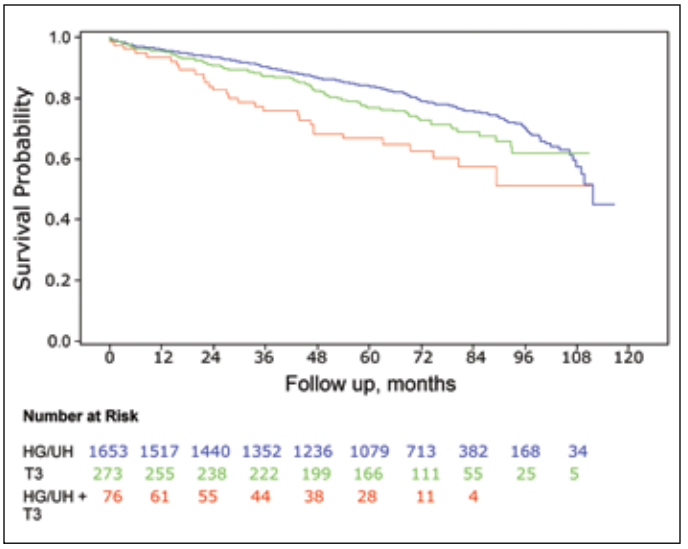

Fig. 1. Kaplan-Meier survival curves for RCC with HG/UH (blue), T3 (green), or HG/UH and T3 (red) after radical or partial nephrectomy. HG/UH: high-grade or unfavourable histology; RCC: renal cell carcinoma; T3: pathological T3a stage.

high-risk disease, a larger dataset would have helped. Lastly, despite the use of advanced statistical methods and a large representative national cohort, our study does not substitute for a prospective, randomized trial. In the absence of a trial, our study represents best available evidence on the topic.

Conclusion

PN offers at least equivalent and possibly improved survival relative to RN in RCC patients with small (<5 cm), high-risk tumours. Due to the retrospective nature of the study, the OS benefits of PN for high-risk disease may be influenced by bias.

Table 3. Cox proportional hazards for mortality after surgery for high-risk RCC

Variable	HR	95% CI	p value
A.		**HG/UH**	
Surgery (reference = radical nephrectomy)			<0.01
Partial nephrectomy	0.66	0.53–0.82	
B.		**T3**	
Surgery (reference = radical nephrectomy)			0.01
Partial nephrectomy	0.54	0.34–0.87	
C.		**HG/UH and T3**	
Surgery (reference = radical nephrectomy)			0.28
Partial nephrectomy	0.66	0.30–1.42	
Age	1.03	1.00–1.07	0.07
Sex (reference = female)			0.67
Male	0.84	0.38–1.86	

CI: confidence interval; HR: hazard ratio; RCC: renal cell carcinoma.

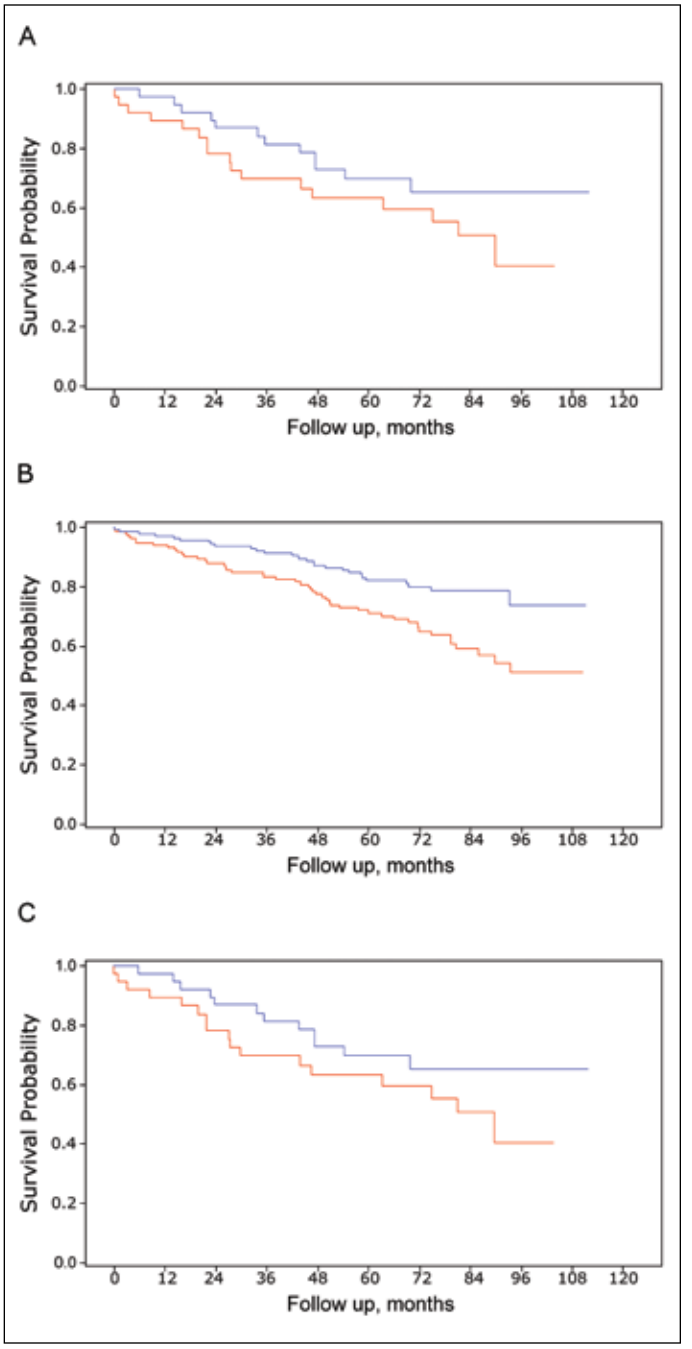

Fig. 2. Kaplan-Meier survival curves for PN (blue) and RN (red) for RCC with adverse pathologic features, HG/UH ***(A)***, T3 ***(B)***, or HG/UH and T3 ***(C)***. HG/UH: high-grade or unfavourable histology; PN: partial nephrectomy; RCC: renal cell carcinoma; RN: radical nephrectomy; T3: pathological T3a stage.

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Disclaimer: The American College of Surgeons and the Commission on Cancer have not verified and are not responsible for the analytic or statistical methodology employed, or the conclusions drawn from these data by the investigator.

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