eMethods 1: Measurement of Post-operative Complications

For patients treated with partial or radical nephrectomy, we assessed the occurrence of post-operative complications during the index hospitalization or within 30 days of surgery. Guided by the published literature,[1-3] we identified specific ICD-9 codes for gastrointestinal (GI) complications, cardiac complications, acute renal failure excluding chronic dialysis,[3] genitourinary complications, post-operative hemorrhage, post-operative infection (e.g., pneumonia, Clostridium Difficile), wound complications, pulmonary failure, sepsis, neurologic complications, and miscellaneous technical complications related to surgery (Table). Each of these measures has been described previously by the Complications Screening Program and validated through chart review.[1,2]

Our catalogue of complications also included the following Patient Safety Indicators (PSIs, version 4.2) developed by the Agency for Healthcare Research and Quality: 1) foreign body left during procedure; 2) iatrogenic pneumothorax; 3) post-operative pulmonary embolism or deep vein thrombosis; and 4) accidental puncture or laceration (most often an injury to the GI tract, bladder, or blood vessel).[4,5] We selected these PSIs based on previous validation studies and compatibility with our dataset.[4-6]

Table: Claims-based definitions for post-operative complications

Complication	ICD-9 Codes / PSI	Reference
Accidental puncture or laceration	PSI 12	AHRQ PSI
Acute renal failure	584, 997.5	Waikar et al.[3]
Cardiac	410, 427.5, 785.51, 997.1	CSP
Foreign body left during procedure	PSI 5	AHRQ PSI
Gastrointestinal	530.82, 531-535, 560, 578.9, 997.4	CSP
Genitourinary	442.1, 445.81, 447.0, 567.89, 591, 593.3-5, 593.8, 593.82, 599.1, 599.6, 619.0, 788.8, 866, 867, 868.14, 868.04, 902.4, 997.72, 998.6, V44.6, V55.6, 39.53, 39.79, 55.02, 55.03, 55.12, 55.21, 55.22, 55.29, 55.8, 55.92, 55.93, 55.94, 56.0, 56.31, 56.39 56.6, 56.74, 56.75, 56.79, 56.8, 57.0, 57.93, 59.0, 59.2x, 59.8, 59.92, 59.93, 87.74, 88.45, 97.61, 97.62	
Post-operative hemorrhage	998.1, 998.11, 998.12, 34.43, 39.41, 39.49, 39.98, 54.12	CSP
Post-operative infection	008.45, 320, 481 - 486, 507, 510, 513, 519.2, 567.0-3, 567.8-9, 590.1-3, 590.8-9, 683, 997.31, 997.39	CSP
Miscellaneous technical	518.7, 997.2, 997.9, 998.81, 998.89, 998.9, 999.1, 999.2, 999.4-9, E874.0, E876, E878, E879, E911, E912	CSP
Neurologic	433-434, 997.0	CSP
Iatrogenic pneumothorax	PSI 6	AHRQ PSI
Pulmonary failure	518.4, 518.5, 518.7, 518.81, 518.82, 518.84, 799.1, 997.3, 997.31	CSP
Sepsis	038, 785.5, 790.7, 995.91, 995.92, 996.62, 998.0, 999.3, 999.31	CSP
Pulmonary embolism / deep vein thrombosis	PSI 12	AHRQ PSI
Wound	958.3, 998.13, 998.3, 998.5, 998.83	CSP

Abbreviations: ICD-9 – International Classification of Diseases, Ninth Revision, Clinical Modification; CSP – Complication Screening Program;[1,2] AHRQ PSI – Agency for Healthcare Research and Quality Patient Safety Indicator.[4-6]

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eMethods 2: Instrumental Variable and Modeling Specifications

Standard observational studies are vulnerable to residual confounding and selection bias, thereby limiting potential inferences, especially concerning causality. Randomized controlled trials provide one way to address these limitations. However, findings based on these highly-selected and homogenous study cohorts may not generalize to real-world practice. In settings where randomized controlled trials are not feasible or available, advanced econometric methods can attenuate the influence of unmeasured confounding variables in observational data. Instrumental variable analysis is one such technique. By capitalizing on naturally-occurring randomization that is not related directly to the outcome of interest, the instrumental variable approach can balance both measured and unmeasured confounding variables, thereby enhancing causal inference in the assessment of treatment effects for medical or surgical therapies.[1]

Creating the instrumental variable

We selected differential distance to a partial nephrectomy provider as our instrumental variable.[1] We defined this variable as the distance from the patient's residence to the nearest provider performing at least one partial nephrectomy minus the distance from the patient's residence to the nearest surgeon performing any kidney cancer surgery in the year of treatment.[1] We used the linear distance function in SAS version 9.2 (SAS Institute, Cary, NC), which calculates the number of miles between the centers of two zip codes, to determine the distance to the nearest partial nephrectomy provider and kidney cancer surgeon, respectively, for each patient. Because some providers may have adopted this technique during the latter portion of the study interval, surgeons were considered a partial nephrectomy provider only in the year(s) they performed this procedure.

Because the SEER registries are nationally-representative, but not geographically contiguous, we excluded from analysis patients meeting one or more of the following conditions: 1) patients treated in a SEER registry where no partial nephrectomy was performed that year (n=75); 2) patients whose primary zip code fell outside of a SEER registry or contiguous State (n=126); and 3) patients living in a Hospital Referral Region (Dartmouth Atlas of Healthcare[2]) with fewer than 8 kidney cancer surgeries over the entire study interval for the original SEER registries (n=28), or fewer than 5 for the 4 registries established in 2000 (n=20). After excluding these potential outliers, we identified the differential distance for 7,138 patients, or 97% of our initial sample.

Testing the instrumental variable

To be considered a suitable instrument, candidate variables must satisfy two conditions: 1) the variable must be highly associated with the treatment; and 2) the variable cannot be associated with the outcome except through its effect on the treatment.[1] We noted a significant correlation between differential distance and partial

nephrectomy use with an F-statistic of 97.3, thereby satisfying the first assumption.[3] While the second assumption cannot be directly tested, we observed no significant association between our instrument and overall survival when using a standard multivariable proportional hazards model (HR 1.03, 95% CI 0.99 – 1.07). To further assess the validity of our instrument, we examined the covariate balance across the differential distance categories. As noted in the table below, we observed improved balance in patient-level covariates across the categories of our instrument compared with the pooled sample.

Assessment of the two-stage residual inclusion model

We performed a variety of specification tests to assess the robustness of our findings. To determine whether these findings were sensitive to the choice of the parametric hazard function, we fit the second stage model using Gompertz, log-logistic, log-normal, and gamma distributions in addition to a Weibull distribution. Next, to ensure that our findings were not unduly influenced by the small number of patients with extremely long follow-up (ie, patients treated with partial and radical nephrectomy prior to 1999 and survived until 2009), we artificially censored all observations at 10 years to focus on short- and intermediate-term findings. Finally, we limited our sample to those patients with a differential distance less than 100 miles as greater distances may represent potential outliers. In each of the above scenarios, we noted no substantive change in our principal findings.

Table: Covariate balance for pooled sample and across differential distance categories using chi-squared testing

		Pooled			0 miles			0.1-4 miles			4-13.6 miles			>13.6 miles		
Variable	**Categories**	**PN**	**RN**	**P**	**PN**	**RN**	**P**	**PN**	**RN**	**P**	**PN**	**RN**	**P**	**PN**	**RN**	**P**
Age	65-69	32.8	25.6	<0.01	30.6	23.2	<0.01	32.9	25.4	<0.01	33.3	26.7	<0.01	40.8	27.2	<0.01
	70-74	29.7	28.1		30.6	27.6		28.6	26.4		30.7	29.1		26.6	29.2	
	75-79	24.7	26.3		25.2	28.0		25.4	26.7		25.4	24.8		20.2	25.6	
	80-84	10.7	14.6		11.2	15.2		11.5	16.3		8.5	13.7		9.6	13.5	
	85 or older	2.1	5.4		2.2	6.0		1.6	5.2		2.1	5.7		2.8	4.6	
Race	Caucasian	82.3	83.7	<0.01	82.0	82.3	0.05	78.4	78.6	0.14	85.3	84.6	0.81	87.6	88.3	0.20
	African-American	7.8	7.8		8.1	10.5		10.3	11.6		6.5	6.1		2.8	3.4	
	Hispanic	5.1	5.5		5.3	4.1		5.2	6.1		4.4	5.7		5.5	6.3	
	Other	4.8	3.0		4.6	3.1		6.1	3.7		3.8	3.6		4.1	2.0	
Gender	Female	41.7	46.4	<0.01	42.3	45.1	0.19	41.1	47.1	0.03	42.8	46.9	0.17	39.0	46.5	0.04
Married	Yes	64.9	61.5	<0.01	64.1	61.3	0.18	62.5	56.8	0.03	70.5	60.9	<0.01	65.1	66.1	0.77
Income[a]	Low	30.3	33.3	<0.01	32.2	34.4	0.55	26.2	27.9	0.26	22.4	21.6	0.23	44.5	47.4	0.62
	Intermediate	31.1	32.9		30.7	31.4		32.7	34.8		28.9	33.0		32.6	32.9	
	High	36.3	31.1		34.3	31.9		39.5	34.8		46.6	42.1		20.6	17.1	
Education[a]	Low	29.5	33.6	<0.01	30.6	34.0	0.23	29.4	33.4	0.07	26.6	27.2	0.06	30.3	39.5	0.07
	Intermediate	30.9	33.0		29.1	29.8		29.8	31.4		28.9	34.0		43.1	36.6	
	High	37.3	30.6		37.5	33.8		39.1	32.7		42.5	35.4		24.3	21.3	
Residence	Rural	15.6	17.5	0.07	15.3	14.2	0.47	7.1	5.5	0.22	11.8	9.5	0.21	42.7	37.8	0.17
Charlson	0	57.6	57.9	0.96	56.3	57.4	0.13	56.7	56.5	0.68	61.7	57.6	0.39	58.3	59.7	0.40
	1	24.3	24.2		26.3	22.9		23.4	25.0		21.8	24.7		22.5	24.5	
	≥ 2	18.1	17.9		17.4	19.7		19.9	18.5		16.5	17.7		19.2	15.8	
Histology	Clear Cell	73.8	84.2	<0.01	73.5	81.0	<0.01	73.4	83.2	<0.01	76.1	84.5	<0.01	72.5	88.0	<0.01
	Papillary	14.7	7.7		14.6	10.3		15.3	8.6		12.7	6.6		16.5	5.7	
	Chromophobe	6.5	3.7		6.8	4.2		6.1	3.9		5.9	4.1		7.8	2.7	
	Oncocytoma	0.6	0.4		0.6	0.4		0.6	0.3		0.6	0.2		0.4	0.5	
	Other Histology	4.4	4.0		4.5	4.1		4.6	4.0		4.7	4.6		2.8	3.1	
Grade	Well-differentiated	18.9	17.7	<0.01	19.6	17.7	0.13	17.3	15.9	0.12	19.5	17.9	0.45	18.8	18.9	<0.01
	Mod-differentiated	41.7	38.9		41.4	40.4		41.7	40.1		39.2	35.0		46.8	40.0	
	Poor-differentiated	11.8	11.1		11.2	12.9		13.8	10.9		10.3	11.3		12.4	9.4	
	Undifferentiated	0.9	1.3		0.7	1.8		0.6	1.1		1.2	1.5		1.8	0.7	
	Unknown	26.7	31.0		27.1	27.2		26.6	32.0		29.8	34.3		20.2	31.0	

[a] A small number of patients (N=185) had missing income or education.
Abbreviations: RN – radical nephrectomy; PN – partial nephrectomy; P – p-value.

References

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[b] Income and education terciles are based on the median census-tract income and percentage of non-high school graduates, respectively. Income and education data were not available for 185 patients.

eTable 1: Cause of Death[a]

	Partial Nephrectomy (N=391)	Radical Nephrectomy (N=1,853)
Malignant		
Kidney	37 (9.5%)	222 (12.0%)
Breast	7 (1.8%)	18 (1.0%)
Gastrointestinal	24 (6.1%)	100 (5.4%)
Genitourinary except kidney	14 (3.6%)	67 (3.6%)
Hematologic	18 (4.6%)	45 (2.4%)
Other malignant disease[b]	22 (5.6%)	84 (4.5%)
Respiratory	19 (4.9%)	102 (5.5%)
Skin	5 (1.3%)	4 (0.2%)
Benign		
Cardiovascular including hypertension	100 (25.6%)	497 (26.8%)
Diabetes Mellitus	17 (4.3%)	63 (3.4%)
Infectious	9 (2.3%)	42 (2.3%)
Neurologic	25 (6.4%)	133 (7.2%)
Pulmonary	28 (7.2%)	117 (6.3%)
Other non-malignant disease[c]	51 (13.0%)	301 (16.3%)
Renal	15 (3.8%)	58 (3.1%)

[a] Cause of death is based on data available through SEER for patients who died on or before December 31, 2008.
[b] Other malignant disease includes cancers of the oral cavity, pharynx, bone, eye, brain, among others.
[c] Other non-malignant disease includes liver failure, ulcer disease, congenital anomalies, among others.