
Factors associated with surgical refusal and non-surgical candidacy in stage 1 kidney cancer: a National Cancer Database (NCDB) analysis

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Introduction: We aim to identify factors associated with surgical refusal and non-surgical candidacy in clinical stage I kidney masses and to evaluate their impact on overall survival (OS).

Materials and methods: We conducted a retrospective cohort study using the National Cancer Database of patients with clinical stage I kidney cancer between 2004 and 2017. Logistic regression was used to determine baseline sociodemographic-, clinical-, and treatment facility-related factors associated with surgical refusal and non-surgical candidacy. Patients were 1:1 propensity score-matched and Cox regression analysis evaluated the impact of surgical refusal and non-surgical candidacy on OS.

Results: Compared to those who underwent surgery, those who refused surgery and those who were non-surgical candidates were more likely to be older, female, non-Hispanic (NH) Black, uninsured, have multiple comorbidities, and traveled a shorter distance to care. Similarly, compared to non-surgical candidates, those who refused surgery were more likely to be younger and have a tumor size ≥ 4.0 cm. Those who refused surgery had significantly lower median survival time and worse OS than those who underwent surgery (HR: 3.18, 95% CI: 2.85, 3.54). Non-surgical candidates had significantly lower median survival time and lower OS than those who had surgery (HR: 4.16, 95% CI: 3.84, 4.51).

Conclusion: Various socioeconomic, demographic, and clinical factors are associated with patients refusing to undergo surgery, which in turn leads to lower overall survival rates in stage I kidney cancer patients. Recognizing these factors will enable healthcare professionals to address and potentially alleviate these issues, ultimately ensuring that patients receive the most appropriate care.

Key Words: surgery refusal, surgical refusal, kidney cancer, renal cancer, stage I

Introduction

A localized stage I kidney cancer can be treated with surgery or managed with active surveillance (AS).

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Current management guidelines suggest that AS is a reasonable option for small ($< 2\text{-}4$ cm) kidney masses, especially in elderly or comorbid patients.¹⁻³ However, there is approximately a 2% risk of progression to metastasis while on AS.⁴ Therefore, surgery may be preferred to AS in patients, both of which are preferred to outright treatment refusal.⁵ Some patients may not be medically fit for surgery, have larger masses or other significant competing health risks, which preclude surgical intervention and thus obviate the need for AS. However, for most patients, the standard of care for

localized stage I kidney cancer is a surgical intervention due to excellent long-term cancer-specific survival of over 90%.^{1,6}

Despite this benefit, there is still a cohort of patients, not on active surveillance, that refuses surgical treatment for kidney stage I masses that could otherwise have been managed operatively. Understanding the clinical and socioeconomic factors that culminate in the refusal of surgery is crucial in optimizing care, expanding access and improving outcomes for this cohort of patients. Analyzing this subgroup can provide a more nuanced view of variables influencing surgery refusal and mortality. This study primarily aims to identify sociodemographic, clinical, and facility-related factors associated with patients’ refusal of surgery as well as factors that predict eligibility as a surgical candidate in clinical stage I kidney masses; secondarily, we report differences in overall survival (OS) for patients treated with surgery, those on active surveillance, non-surgical candidates, and those that refuse surgery.⁷⁻⁹

Materials and methods

Study design and setting

We conducted a retrospective cohort study using data obtained from the National Cancer Database (NCDB), a clinical oncology database responsible for collecting information from more than 1,500 Commission on Cancer (CoC)--accredited facilities.¹⁰ The data is provided via hospital registries and used to track patient disease, treatment, and outcomes. The NCDB is responsible for over 34 million historical records and the capture of more than 70% of cancer diagnoses in the US.¹⁰ This study was approved with a waiver of informed consent by the institutional review board of the Icahn School of Medicine at Mount Sinai owing to the retrospective nature of the study.

Study population

Patients with the primary site code 64.9, specifying kidney cancer based on the International Classification of Disease for Oncology (3rd edition), were included for

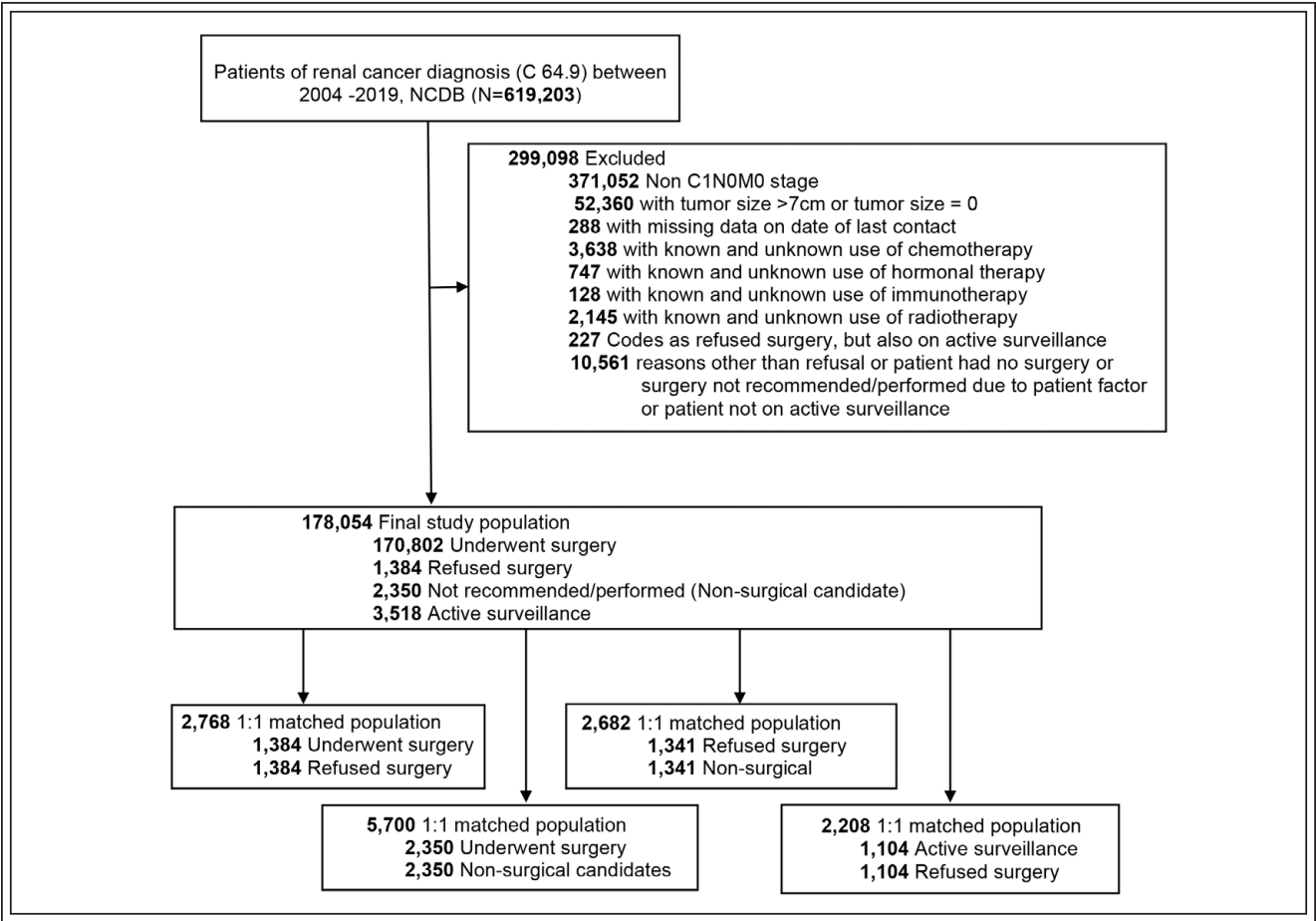


Figure 1. Schematic diagram of the selection criteria for study cohort.

initial screening. Overall, 619,203 patients, older than 18 years and diagnosed with kidney cancer between 2004 and 2019 were identified. To be considered for further analysis, patients must have CT1N0M0 kidney cancer and either received surgery, refused surgery, underwent active surveillance, or surgery was not recommended or performed as part of the first course of treatment or due to patient risk factors. The primary analysis excluded those with missing information on last contact and vital status, had tumor size greater than 7 cm, received any other form of treatment (systemic or radiotherapy), or had no information on the use of other treatments, Figure 1. Overall, 178,054 patients who were managed between 2004 and 2017 were included for analysis.

Main outcomes

The primary outcomes of this study are surgical refusal and surgical candidacy, which were defined using the variable “reason for no surgery of the primary site.” As defined by the NCDB, if surgery was recommended by the physician but refused by either the patient, the patient’s family, or guardian and directly noted in a patient’s record, the patient was considered to have refused surgery. Similarly, if surgery was not recommended or performed as part of the first course of treatment or due to patient risk factors, the patient was considered a non-surgical candidate. Both groups were compared to patients who had surgery.

Secondary outcomes

We also compared OS between the four cohorts of patients: patients treated with surgery, those on active surveillance, non-surgical candidates, and those who refuse surgery. OS was defined as the time from the date of diagnosis to (1) the date of death from any cause or (2) the date of the last follow up.

Covariates

Variables of interest included sociodemographic, clinical-, and treatment facility-related information. The sociodemographic covariates included age, sex, race/ethnicity, insurance status, median income, distance to care, and rurality. The NCDB determined the median income by matching the zip code of the patient at the time of diagnosis to the 2012 American Community Survey data. Distance to care was defined based on the variable, CROWFLY, and it represents the distance between the centroid of the patient’s zip code and the reporting facility’s zip code, estimated using the Haversine formula. The clinical covariates included the Charlson-Deyo score, tumor size, and

year of diagnosis. Facility-related factors included facility location and facility type. Facility type was categorized as Community Cancer Program (CCP), Comprehensive Community Cancer Program (CCCP), Academic/Research Program (AP), and Integrated Network Cancer Program (INCP) while the facility location was categorized based on the 9 US census divisions.

Statistical analysis

Categorical variables are presented as frequencies and percentages. The relationship between surgical refusal or surgical candidacy and other covariates was evaluated using the chi-square test or the Fisher exact test. An unknown category was included for variables with missing data. Unadjusted and adjusted logistic regression models were used to determine factors that were predictors of surgical refusal and non-surgical candidacy in the unmatched cohort. All variables were included in the adjusted models.

We used a propensity score matching to determine the probability of surgical refusal/ surgical candidacy based on observed characteristics. The propensity scores were estimated using a probit regression model, including all covariates. Using the propensity scores, patients were matched in a 1:1 fashion without replacement by using the nearest neighbor-matching algorithm within a caliper of the maximum distance set at 0.2 of the standard deviation of the logit of the propensity score. Covariate balance was evaluated using the standardized mean differences, and a difference less than 0.1 (10%) was considered a negligible imbalance.

OS from the time of diagnosis was evaluated in the matched cohorts using a Kaplan-Meier survival analysis. A log-rank test was used to compare survival curves. The association between surgical refusal/ surgical candidacy and OS was estimated with a Cox regression analysis controlling for the propensity score in the matched cohort.

To determine if patients who refused surgery were different from those that elected for active surveillance or those who were non-surgical candidates, we compared baseline characteristics and survival outcomes between the cohorts of patients, who refused surgery to those on active surveillance and those who were non-surgical candidates in multiple propensity-matched analyses. The absolute standardized mean differences between all comparison groups were < 0.1. All analyses were conducted using Stata/MP, version 14.1 (StataCorp, College Station, TX, USA). P values were 2-sided, and the significance level was set at 0.05.

TABLE 1. Baseline demographic, clinical, and tumor-related characteristics between patients who refused surgery and those who underwent surgery, NCDB 2004–2017

	Unmatched cohort		p value	SMD	Propensity-matched cohort		SMD
	Underwent surgery n (%)	Refused surgery n (%)			Underwent surgery n (%)	Refused surgery n (%)	
Age, yrs	170,802 (99.20)	1,384 (0.80)	< 0.001	0.843	1,384 (50)	1,384 (50)	0.000
18-49	31,052 (18.18)	85 (6.14)			83 (6.00)	85 (6.14)	
50-69	93,145 (54.53)	348 (25.14)			352 (25.43)	348 (25.14)	
≥ 70	46,605 (27.29)	951 (68.71)			949 (68.57)	951 (68.71)	
Sex			< 0.001	0.153			0.007
Female	67,154(39.32)	649 (46.89)			654 (47.25)	649 (46.89)	
Male	103,648 (60.68)	735 (53.11)			730 (52.75)	735 (53.11)	
Race/ethnicity			< 0.001	0.066			0.040
Non-Hispanic White	133,613 (78.23)	983 (71.03)			1,042(75.29)	983 (71.03)	
Non-Hispanic Black	20,417 (11.95)	268 (19.36)			211 (15.25)	268 (19.36)	
Hispanic	9,889 (5.79)	86 (6.21)			69 (4.99)	86 (6.21)	
Other	5,413 (3.17)	34 (2.46)			41 (2.96)	34 (2.46)	
Unknown	1,470 (0.86)	13 (0.94)			21 (1.52)	13 (0.94)	
Insurance status			< 0.001	0.529			0.053
Uninsured	4,397 (2.57)	54 (3.90)			29 (2.10)	54 (3.90)	
Private Insurance	78,847 (46.16)	167 (12.07)			195 (14.09)	167 (12.07)	
Medicaid	9,330 (5.46)	93 (6.72)			55 (3.97)	93 (6.72)	
Medicare	73,828 (43.22)	1,029(74.35)			1,060(76.59)	1,029(74.35)	
Other Government	2,281 (1.34)	16 (1.16)			14 (1.01)	16 (1.16)	
Unknown	2,119 (1.24)	25 (1.81)			31 (2.24)	25 (1.81)	
Median income ^b			< 0.001	0.000			0.019
< \$40,227	28,222 (16.52)	276 (19.94)			246 (17.77)	276 (19.94)	
\$40,227-\$50,353	33,714 (19.74)	289 (20.88)			296 (21.24)	289 (20.88)	
\$50,354-\$63,332	35,397 (20.72)	273 (19.73)			276 (19.94)	273 (19.73)	
≥ \$63,333	54,067 (31.65)	357 (25.79)			407(29.41)	357 (25.79)	
Unknown	19,402 (11.36)	189 (13.66)			161 (11.63)	189 (13.66)	
Charlson-Deyo score			< 0.001	0.173			0.045
CDS 0	115,238 (67.47)	864 (62.43)			876 (63.29)	864 (62.43)	
CDS 1	39,393 (23.06)	288 (20.81)			308 (22.25)	288 (20.81)	
CDS ≥ 2	16,171 (9.47)	232 (16.76)			200 (14.45)	232 (16.76)	
Tumor size, cm			< 0.001	0.200			0.020
≤ 4	118,575 (69.42)	829 (59.90)			828 (60.48)	829 (59.90)	
4.1-7.0	52,227 (30.58)	555 (40.10)			556 (40.17)	555 (40.10)	
Rurality			< 0.001	0.124			0.011
Metro	137,615 (80.57)	1,180(85.26)			1,180 (85.26)	1,180 (85.26)	
Urban	23,035 (13.49)	147 (10.77)			152 (10.98)	148(10.77)	
Rural	3,015 (1.77)	23 (1.66)			23 (1.66)	23 (1.66)	
Unknown	7,137 (4.18)	32 (2.31)			29 (2.10)	32 (2.31)	
Distance to care, miles			< 0.001	0.121			0.005
≤ 7.0	50,885 (29.79)	698 (50.43)			624 (45.09)	698 (50.43)	
7.1 -20.8	50,839 (29.76)	329 (23.77)			353 (25.51)	329 (23.77)	
> 20.9	51,460 (30.13)	199 (14.38)			267 (19.29)	199 (14.38)	
Unknown	17,618 (10.31)	158 (11.42)			140 (10.12)	158 (11.42)	

TABLE 1 (cont'd). Baseline demographic, clinical, and tumor-related characteristics between patients who refused surgery and those who underwent surgery, NCDB 2004–2017

	Unmatched cohort		p value	SMD	Propensity-matched cohort		SMD
	Underwent surgery n (%)	Refused surgery n (%)			Underwent surgery n (%)	Refused surgery n (%)	
Facility type			< 0.001	0.237			0.023
CCP	7,447 (4.36)	124 (8.96)			99 (7.15)	124 (8.96)	
CCCP	57,243 (33.51)	521 (37.64)			530 (38.29)	521 (37.64)	
AP	65,032 (38.07)	441 (31.86)			468 (33.82)	441 (31.86)	
INCP	31,905 (18.68)	274 (19.80)			260 (18.79)	274 (19.80)	
Unknown	9,175 (5.37)	24 (1.73)			25 (1.95)	24 (1.73)	
Facility location, US states			< 0.001	0.097			0.030
Pacific	15,540 (9.10)	117 (8.45)			132 (9.54)	117 (8.45)	
New England	9,519 (5.57)	90 (6.50)			78 (5.64)	90 (6.50)	
Middle Atlantic	26,144 (15.31)	235 (16.98)			239 (17.27)	235 (16.98)	
South Atlantic	34,318 (20.09)	274 (19.80)			284 (20.52)	274 (19.80)	
East North Central	29,813 (17.45)	282 (20.38)			295 (21.32)	282 (20.38)	
East South Central	12,646 (7.40)	72 (5.20)			70 (5.06)	72 (5.20)	
West North Central	13,750 (8.05)	129 (9.32)			111 (8.02)	129 (9.18)	
West South Central	13,908 (8.14)	127 (9.18)			105 (7.59)	127 (9.18)	
Mountain	5,989 (3.51)	34 (2.46)			43 (3.11)	34 (2.46)	
Unknown	9,175 (5.37)	24 (1.73)			27 (1.95)	24 (1.73)	
Year of diagnosis			< 0.001	0.116			0.007
2004–2011	88,651 (51.90)	798 (57.66)			793 (57.30)	798 (57.66)	
2012–2017	82,151 (48.10)	586 (42.34)			591 (42.70)	586 (42.34)	

CCP = Community Cancer Program; CCCP = Comprehensive Community Cancer Program; AP = Academic/Research Program; INCP = Integrated Network Cancer Program; SMD = standardized mean difference (< 0.1 is negligible imbalance)

^bmedian household income within a patient's area of residence by comparing zip codes, categorized as equally proportioned quartiles among all US zip codes based on the 2016 American Community Survey data

Results

Surgical refusal compared to patients who underwent surgery

We identified a total of 172,186 patients diagnosed with CT1N0M0 kidney cancer. Among these, 170,802 (99.2%) underwent surgery, while 1,384 (0.8%) refused surgery. The baseline demographic, clinical, and tumor-related characteristics before and after propensity score matching are presented in Table 1. In the adjusted model, Table 2, the likelihood of refusing surgery varied significantly across different demographic and clinical factors. Patients aged 70 years and older and those aged 50–69 were 5.61 and 1.33 times more likely to refuse surgery compared to those aged 18–49, respectively. Male patients were less likely to refuse surgery compared to female patients (adjusted odds ratio (aOR) = 0.82, 95% confidence interval (CI) [0.74, 0.91]), while non-Hispanic Black patients exhibited a higher likelihood of refusal

compared to non-Hispanic White patients (aOR = 1.78, 95% CI [1.53, 2.07]). Hispanic patients and those of other races did not show significant differences in refusal rates. Uninsured patients were over five times more likely to refuse surgery compared to those with private insurance (aOR = 5.75, 95% CI [4.20, 7.88]). Medicaid recipients and those with Medicare also showed an increased likelihood of refusal (aOR = 4.03, 95% CI [3.10, 5.23] and aOR = 2.54, 95% CI [2.11, 3.06], respectively). Income levels were inversely related to surgical refusal, with patients from the highest income bracket ($\geq$ \$63,333) being less likely to refuse surgery (OR = 0.78, 95% CI [0.66, 0.94]).

Patients with higher comorbidity scores (CDS $\geq$ 2) (aOR = 1.35, 95% CI [1.16, 1.57]) and tumor size between 4.1–7.0 cm (OR = 1.39, 95% CI [1.25, 1.55]) were more likely to refuse surgery. Additionally, geographical factors, such as rurality and distance to care, impacted surgical refusal. Patients living more

TABLE 2. Logistic regression showing the relationship between covariates, surgical refusal and non-surgical candidacy in the unmatched cohorts, NCDB 2004–2017

	Surgical refusal		Non-surgical candidacy	
	Unadjusted model OR (95% CI)	Adjusted model OR (95% CI)	Unadjusted model OR (95% CI)	Adjusted model OR (95% CI)
Age, years				
18-49	1.00	1.00	1.00	1.00
50-69	1.36 (1.08, 1.73)	1.33 (1.01, 1.76)	2.99 (2.35, 3.80)	2.10 (1.62, 2.72)
≥ 70	7.45 (5.97, 9.31)	5.61 (4.21, 7.48)	14.52 (11.50, 18.34)	7.80 (5.98, 10.16)
Sex				
Female	1.00	1.00	1.00	1.00
Male	0.73 (0.66, 0.82)	0.82 (0.74, 0.91)	0.84 (0.77, 0.91)	0.92 (0.85, 1.00)
Race/ethnicity				
Non-Hispanic White	1.00	1.00	1.00	1.00
Non-Hispanic Black	1.78 (1.56, 2.04)	1.78 (1.53, 2.07)	1.32 (1.17, 1.47)	1.31 (1.15, 1.48)
Hispanic	1.18 (0.95, 1.47)	1.18 (0.93, 1.49)	0.82 (0.69, 1.00)	0.88 (0.72, 1.08)
Other	0.85 (0.61, 1.20)	0.96 (0.68, 1.36)	0.77 (0.59, 1.00)	0.85 (0.65, 1.12)
Unknown	1.20 (0.69, 2.08)	1.38 (0.79, 2.40)	0.86 (0.53, 1.38)	1.02 (0.63, 1.66)
Insurance status				
Private Insurance	1.00	1.00	1.00	1.00
Uninsured	5.79 (4.26, 7.89)	5.75 (4.20, 7.88)	2.81 (2.10, 3.76)	3.19 (2.37, 4.29)
Medicaid	4.71 (3.65, 6.07)	4.03 (3.10, 5.23)	2.87 (2.32, 3.56)	2.60 (2.09, 3.24)
Medicare	6.58 (5.59, 7.75)	2.54 (2.11, 3.06)	5.68 (5.05, 6.38)	2.06 (1.81, 2.36)
Other Government	3.31 (1.98, 5.54)	2.97 (1.77, 5.00)	1.64 (0.99, 2.70)	1.26 (0.76, 2.09)
Unknown	5.57 (3.65, 8.50)	3.57 (2.33, 5.49)	3.41 (2.36, 4.94)	2.32 (1.59, 3.38)
Median income ^b				
< \$40,227	1.00	1.00	1.00	1.00
\$40,227-\$50,353	0.88 (0.74, 1.03)	1.01 (0.85, 1.20)	0.86 (0.76, 0.98)	0.90 (0.79, 1.03)
\$50,354-\$63,332	0.79 (0.67, 0.93)	0.89 (0.74, 1.07)	0.86 (0.76, 0.98)	0.88 (0.77, 1.01)
≥ \$63,333	0.68 (0.58, 0.79)	0.78 (0.66, 0.94)	0.76 (0.67, 0.85)	0.79 (0.69, 0.91)
Unknown	0.99 (0.83, 1.19)	2.39 (1.63, 3.50)	0.94 (0.81, 1.09)	1.16 (0.79, 1.72)
Charlson-Deyo score				
CDS 0	1.00	1.00	1.00	1.00
CDS 1	0.98 (0.85, 1.11)	0.80 (0.70, 0.91)	1.42 (1.28, 1.57)	1.17 (1.06, 1.30)
CDS ≥ 2	1.91 (1.65, 2.21)	1.35 (1.16, 1.57)	3.56 (3.21, 3.93)	2.60 (2.35, 2.88)
Tumor Size, cm				
≤ 4	1.00	1.00	1.00	1.00
4.1-7.0	1.52 (1.36, 1.69)	1.39 (1.25, 1.55)	1.14 (1.04, 1.24)	1.02 (0.94, 1.11)
Rurality				
Metro	1.00	1.00	1.00	1.00
Urban	0.75 (0.63, 0.89)	1.04 (0.83, 1.27)	0.93 (0.83, 1.05)	1.14 (0.99, 1.32)
Rural	0.89 (0.59, 1.35)	1.32 (0.85, 2.04)	0.70 (0.49, 1.00)	0.88 (0.61, 1.29)
Unknown	0.52 (0.37, 0.74)	0.82 (0.54, 1.17)	0.53 (0.40, 0.69)	0.73 (0.55, 0.96)
Distance to care, miles				
≤ 7.0	1.00	1.00	1.00	1.00
7.1 -20.8	0.47 (0.41, 0.54)	0.59 (0.51, 0.67)	0.64 (0.57, 0.70)	0.75 (0.68, 0.84)
> 20.9	0.28 (0.24, 0.33)	0.34 (0.28, 0.40)	0.42 (0.37, 0.47)	0.47 (0.41, 0.54)
Unknown	0.65 (0.55, 0.77)	0.32 (0.21, 0.48)	0.75 (0.65, 0.86)	0.67 (0.45, 1.00)

TABLE 2 (cont'd). Logistic regression showing the relationship between covariates, surgical refusal and non-surgical candidacy in the unmatched cohorts, NCDB 2004–2017

	Surgical refusal		Non-surgical candidacy	
	Unadjusted model OR (95% CI)	Adjusted model OR (95% CI)	Unadjusted model OR (95% CI)	Adjusted model OR (95% CI)
Facility type				
CCP	1.00	1.00	1.00	1.00
CCCP	0.55 (0.45, 0.67)	0.65 (0.53, 0.79)	0.66 (0.56, 0.78)	0.73 (0.62, 0.87)
AP	0.41 (0.33, 0.50)	0.57 (0.46, 0.71)	0.53 (0.45, 0.63)	0.73 (0.61, 0.87)
INCP	0.52 (0.42, 0.64)	0.63 (0.50, 0.78)	0.60 (0.50, 0.71)	0.68 (0.56, 0.81)
Unknown	0.16 (0.10, 0.24)	0.61 (0.35, 1.04)	0.04 (0.02, 0.08)	0.23 (0.11, 0.47)
Facility location, US states				
Pacific	1.00	1.00	1.00	1.00
New England	1.26 (0.95, 1.65)	1.27 (0.96, 1.68)	0.98 (0.79, 1.21)	0.96 (0.77, 1.19)
Middle Atlantic	1.19 (0.96, 1.49)	1.24 (0.99, 1.57)	0.96 (0.81, 1.13)	0.94 (0.79, 1.11)
South Atlantic	1.06 (0.85, 1.32)	0.99 (0.79, 1.24)	0.95 (0.81, 1.11)	0.89 (0.76, 1.05)
East North Central	1.26 (1.01, 1.56)	1.13 (0.90, 1.42)	1.06 (0.91, 1.24)	0.93 (0.79, 1.09)
East South Central	0.76 (0.56, 1.02)	0.77 (0.57, 1.09)	0.68 (0.55, 0.84)	0.67 (0.53, 0.83)
West North Central	1.25 (0.97, 1.60)	1.30 (1.00, 1.63)	1.07 (0.89, 1.28)	1.05 (0.86, 1.27)
West South Central	1.21 (0.94, 1.56)	1.21 (0.93, 1.57)	0.91 (0.75, 1.11)	0.93 (0.76, 1.13)
Mountain	0.75 (0.51, 1.10)	0.78 (0.53, 1.14)	0.93 (0.72, 1.20)	0.97 (0.75, 1.25)
Unknown	0.35 (0.22, 0.54)	-	0.06 (0.03, 0.12)	-
Year of diagnosis				
2004-2011	1.00	1.00	1.00	1.00
2012-2017	0.79 (0.71, 0.88)	0.80 (0.72, 0.89)	0.99 (0.91, 1.08)	0.99 (0.91, 1.08)

CCP = Community Cancer Program; CCCP = Comprehensive Community Cancer Program

AP = Academic/Research Program; INCP = Integrated Network Cancer Program

SMD = standardized mean difference (< 0.1 is negligible imbalance)

^bmedian household income within a patient's area of residence by comparing zip codes, categorized as equally proportioned quartiles among all US zip codes based on the 2016 American Community Survey data.

than 20.9 miles from care facilities were significantly less likely to refuse surgery (aOR = 0.34, 95% CI [0.28, 0.40]). Facility type influenced refusal rates, with those treated at Comprehensive Community Cancer Programs (CCCP) being less likely to refuse surgery (aOR = 0.65, 95% CI [0.53, 0.79]). Other results are presented in Table 2. In the matched cohort [n = 1384 (50%) per group], the median follow up time is 59.07 months (interquartile range [IQR]: 23.92–93.60). Those who refused surgery had significantly lower median survival time than those who underwent surgery (46.13 vs. 133.52 months, log-rank $p < 0.001$), Figure 2. The median 5-year overall survival (OS) was 77% for those that had surgery and 41% for those that refused surgery. In the Cox regression analysis, those who refused surgery had a worse survival rate compared to those who underwent surgery (hazard ratio [HR]: 3.18, 95% CI [2.58, 3.54]), Table 3.

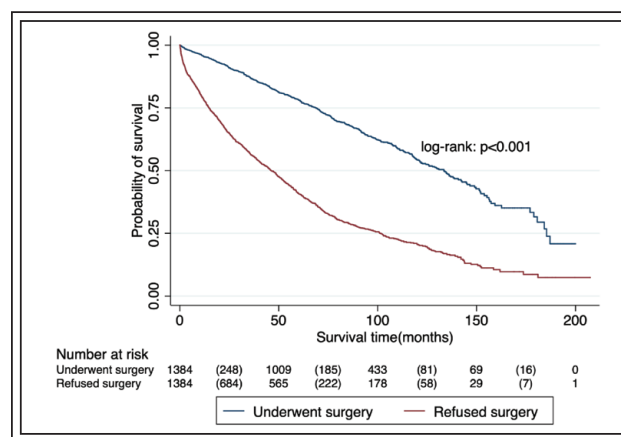


Figure 2. Overall survival among patients who refused surgery compared to those who underwent surgery in a propensity matched cohort.

TABLE 3. Cox regression analysis predicting overall survival among the propensity-matched cohorts

	Overall survival HR (95% CI)
Refusal	
Underwent surgery	Ref
Refused surgery	3.18 (2.85, 3.54)
Surgical candidacy	
Underwent surgery	Ref
Non-surgical candidate	4.16 (3.84, 4.51)

Non-surgical candidates compared to patients who underwent surgery

We identified 2,359 non-surgical candidates. The baseline demographic, clinical, and tumor-related characteristics before and after propensity score matching are presented in Table 4. In the adjusted model, patients aged ≥ 70 were 7.8 times more likely to be deemed non-surgical candidates compared to those aged 18-49 (aOR = 7.80, 95% CI [5.98, 10.16]), while those aged 50-69 also had higher odds (aOR = 2.10, 95% CI [1.62, 2.72]). Non-Hispanic Black patients had increased odds of non-surgical candidacy compared to non-Hispanic White patients (aOR = 1.31, 95% CI [1.15, 1.48]). Uninsured patients had more than three times the odds of being non-surgical candidates compared to those with private insurance (aOR = 3.19, 95% CI [2.37, 4.29]), and patients with Medicare were also more likely (aOR = 2.06, 95% CI [1.81, 2.36]). Conversely, higher-income patients ($\geq \$63,333$) had a lower

likelihood of being deemed non-surgical candidates (aOR = 0.79, 95% CI [0.69, 0.91]).

Patients with higher Charlson-Deyo Scores ≥ 2 were more likely to be non-surgical candidates (aOR = 2.60, 95% CI [2.35, 2.88]). Distance to care was inversely related to non-surgical candidacy, with those living more than 20.9 miles from care facilities being less likely to be non-surgical candidates (aOR = 0.47, 95% CI [0.41, 0.54]). Patients treated at CCCP (OR = 0.73, 95% CI [0.62, 0.87]) and other specialized facilities had lower odds of being non-surgical candidates. Other results are presented in Table 2.

A total of 5,700 patients were included in the matched analysis: underwent surgery (n = 2,350 [50.00%]) and non-surgical candidates (n = 2,350 [50.00%]). The overall median follow up time in this cohort is 50.79 months (IQR: 17.41-83.84). The median 5-year overall survival (OS) was 76% for those who had surgery and 29% for those that are non-surgical candidates. Non-surgical candidates had significantly lower median survival time (26.25 vs. 117.59 months, log-rank p < 0.001) and worse survival rate (HR: 4.16, 95% CI [3.84, 4.51]) than those who underwent surgery, Figure 3 and Table 3.

Comparison between patients on active surveillance and those who refuse surgery

We compared patients who refused surgery to those on active surveillance to assess cohort differences. A total of 4,902 patients were analyzed, with 3,518 (71.77%) on active surveillance and 1,384 (28.23%) who refused surgery. In the adjusted model, patients aged 50-69 and ≥ 70 were less likely to refuse surgery compared to those aged 18-49 (aOR = 0.64, 95% CI [0.43, 0.96] and aOR = 0.71, 95% CI [0.47, 1.06], respectively). Similarly, male patients showed a decreased likelihood of refusing surgery. Non-Hispanic Black patients and those uninsured or on Medicaid exhibited higher odds of surgical refusal (aOR = 1.39, 95% CI [1.13, 1.73]; aOR = 1.96, 95% CI [1.24, 3.11]; aOR = 1.96, 95% CI [1.34, 2.85], respectively). Larger tumor size (4.1-7.0 cm) strongly correlated with surgical refusal (OR = 4.20, 95% CI [3.55, 4.50]), while greater distance to care was associated with decreased likelihood (OR = 0.46, 95% CI [0.36, 0.58]). Among those who refused surgery, median survival time was significantly lower (51.06 vs. 80.03 months, log-rank p < 0.001), indicating worse survival (HR: 1.49, 95% CI [1.33, 1.66]) compared to patients on active surveillance. Median 5-year overall survival (OS) rates were 57% for patients on active surveillance and 44% for those who refused surgery.

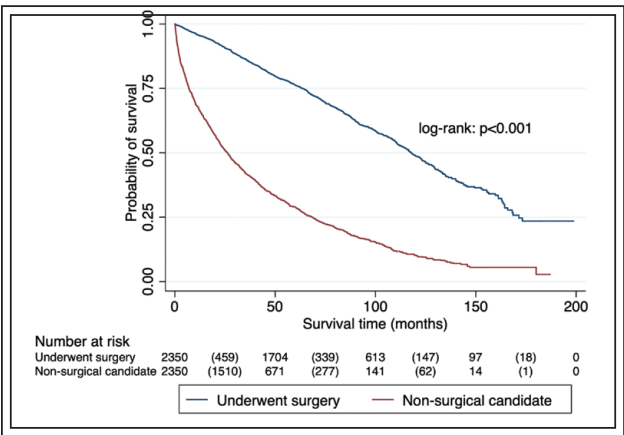


Figure 3. Overall survival among patients who underwent surgery compared to non-surgical candidates in a propensity matched cohort.

TABLE 4. Baseline demographic, clinical, and tumor-related characteristics between non-surgical candidates and those who underwent surgery, NCDB 2004–2017

	Unmatched cohort		p value	Propensity-matched cohort			
	Underwent surgery n (%)	Non-surgical candidate n (%)		SMD	Underwent surgery n (%)	Non-surgical n (%)	SMD
Age, years	170,802 (93.64)	2,359 (1.36)	< 0.001	0.930	2,350 (50.00)	2,350 (50.00)	0.006
18-49	31,052 (18.18)	74 (3.15)			61 (2.60)	74 (3.15)	
50-69	93,145 (54.53)	663 (28.21)			680 (28.94)	663 (28.21)	
≥ 70	46,605 (27.29)	1,613 (68.64)			1,609 (68.47)	1,613 (68.64)	
Sex			< 0.001	0.086			0.026
Female	67,154 (39.32)	1,204 (43.57)			1,017 (43.28)	1,204 (43.57)	
Male	103,648 (60.68)	1,326 (56.43)			1,333 (56.72)	1,326 (56.43)	
Race/ethnicity			< 0.001	0.022			0.026
Non-Hispanic White	133,613 (78.23)	1,804 (76.77)			1,875 (76.79)	1,804 (76.77)	
Non-Hispanic Black	20,417 (11.95)	363 (15.45)			293 (12.47)	363 (15.45)	
Hispanic	9,889 (5.79)	110 (4.68)			112 (4.77)	110 (4.68)	
Other	5,413 (3.17)	56 (2.38)			50 (2.13)	56 (2.38)	
Unknown	1,470 (0.86)	17 (0.72)			20 (0.85)	17 (0.72)	
Insurance status			< 0.001	0.542			0.041
Uninsured	4,397 (2.57)	53 (2.26)			26 (1.11)	53 (2.26)	
Private Insurance	78,847 (46.16)	338 (14.38)			372 (15.83)	338 (14.38)	
Medicaid	9,330 (5.46)	115 (4.89)			68 (2.89)	115 (4.89)	
Medicare	73,828 (43.22)	1,797 (76.47)			1,828 (77.79)	1,797 (76.47)	
Other Government	2,281 (1.34)	16 (0.68)			16 (0.68)	16 (0.68)	
Unknown	2,119 (1.24)	31 (1.32)			40 (1.70)	31 (1.32)	
Median income ^b			< 0.001	0.013			0.008
< \$40,227	28,222 (16.52)	451 (19.19)			432 (18.38)	451 (19.19)	
\$40,227-\$50,353	33,714 (19.74)	465 (19.79)			478 (20.34)	465 (19.79)	
\$50,354-\$63,332	35,397 (20.72)	489 (20.81)			470 (20.00)	489 (20.81)	
≥ \$63,333	54,067 (31.65)	654 (27.83)			680 (28.94)	654 (27.83)	
Unknown	19,402 (11.36)	291 (12.38)			290 (12.34)	291 (12.38)	
Charlson-Deyo score			< 0.001	0.437			0.020
CDS 0	115,238 (67.47)	1,184 (50.39)			1,198 (50.98)	1,184 (50.39)	
CDS 1	39,393 (23.06)	575 (24.47)			583 (24.81)	575 (24.47)	
CDS ≥ 2	16,171 (9.47)	591 (25.15)			569 (24.21)	591 (25.15)	
Tumor size, cm			0.004	0.060			0.004
≤ 4	118,575 (69.42)	1,566 (66.64)			1,570 (66.81)	1,566 (66.64)	
4.1-7.0	52,227 (30.58)	784 (33.36)			780 (33.19)	784 (33.36)	
Rurality			< 0.001	0.114			0.014
Metro	137,615 (80.57)	1,960 (83.40)			1,984 (84.43)	1,960 (83.40)	
Urban	23,035 (13.49)	306 (13.02)			295 (12.55)	306 (13.02)	
Rural	3,015 (1.77)	30 (1.28)			19 (0.81)	30 (1.28)	
Unknown	7,137 (4.18)	54 (2.30)			52 (2.21)	54 (2.30)	
Distance to care, miles			< 0.001	0.081			0.026
≤ 7.0	50,885 (29.79)	1,012 (43.06)			952 (40.51)	1,012 (43.06)	
7.1 -20.8	50,839 (29.76)	642 (27.32)			647 (27.53)	642 (27.32)	
> 20.9	51,460 (30.13)	433 (18.43)			483 (20.55)	433 (18.43)	
Unknown	17,618 (10.31)	263 (11.19)			268 (11.40)	263 (11.19)	

TABLE 4 (cont'd). **Baseline demographic, clinical, and tumor-related characteristics between non-surgical candidates and those who underwent surgery, NCDB 2004–2017**

	Unmatched cohort			Propensity-matched cohort			
	Underwent surgery n (%)	Non-surgical candidate n (%)	p value	Underwent surgery SMD	candidate n (%)	Non-surgical n (%)	SMD
Facility type			< 0.001	0.304			0.019
CCP	7,447 (4.36)	176 (7.49)			139 (5.91)	176 (7.49)	
CCCP	57,243 (33.51)	898 (38.21)			944 (40.17)	898 (38.21)	
AP	65,032 (38.07)	816 (34.72)			792 (33.70)	816 (34.72)	
INCP	31,905 (18.68)	451 (19.19)			463 (19.70)	451 (19.19)	
Unknown	9,175 (5.37)	9 (0.38)			12 (0.51)	9 (0.38)	
Facility location, US states			< 0.001	0.134			0.018
Pacific	15,540 (9.10)	234 (9.96)			226 (9.62)	234 (9.96)	
New England	9,519 (5.57)	140 (5.96)			149 (6.34)	140 (5.96)	
Middle Atlantic	26,144 (15.31)	377 (16.04)			370 (15.74)	377 (16.04)	
South Atlantic	34,318 (20.09)	489 (20.81)			492 (20.94)	489 (20.81)	
East North Central	29,813 (17.45)	476 (20.26)			503 (21.40)	476 (20.26)	
East South Central	12,646 (7.40)	129 (5.49)			156 (6.64)	129 (5.49)	
West North Central	13,750 (8.05)	221 (9.40)			201 (8.55)	221 (9.40)	
West South Central	13,908 (8.14)	191 (8.13)			169 (7.19)	191 (8.13)	
Mountain	5,989 (3.51)	84 (3.57)			72 (3.06)	84 (3.57)	
Unknown	9,175 (5.37)	9 (0.38)			12 (0.51)	9 (0.38)	
Year of diagnosis			0.828	0.005			0.004
2004-2011	88,651 (51.90)	1,225 (52.13)			1,220 (51.91)	1,225 (52.13)	
2012-2017	82,151 (48.10)	1,125 (47.87)			1,130 (48.09)	1,125 (47.87)	

CCP = Community Cancer Program; CCCP = Comprehensive Community Cancer Program; AP = Academic/Research Program; INCP = Integrated Network Cancer Program; SMD = standardized mean difference (< 0.1 is negligible imbalance)

^bmedian household income within a patient's area of residence by comparing zip codes, categorized as equally proportioned quartiles among all US zip codes based on the 2016 American Community

Comparison between non-surgical candidates and those who refuse surgery

When comparing patients who refused surgery to non-surgical candidates, older patients had lower odds of surgical refusal, as did those with higher Charlson-Deyo scores (CDS 1, aOR = 0.67, 95% CI [0.56, 0.79]; CDS ≥2, aOR = 0.51, 95% CI [0.42, 0.61]). Conversely, non-Hispanic Black patients and uninsured individuals were more likely to refuse surgery (aOR = 1.34, 95% CI [1.10, 1.64]; aOR = 1.78, 95% CI [1.13, 2.80]). Larger tumor size increased the odds of surgical refusal (OR = 1.40, 95% CI [1.20, 1.60]), while longer distance to care was associated with decreased odds (OR = 0.70, 95% CI [0.56, 0.88]). The median survival time among those who refused surgery was significantly higher (45.17 vs. 26.41 months, log-rank $p < 0.0001$) and had a higher survival rate (HR: 0.73, 95% CI [0.66, 0.79]) compared to non-surgical candidates. The 5-year overall survival (OS) rates were 30% for non-surgical candidates and 41% for those who refused surgery.

Discussion

Using information from the NCDB between 2004 and 2017, we identified sociodemographic-, clinical-, and facility-related factors associated with surgical refusal and non-surgical candidacy for stage I kidney cancer and evaluated the association of refusal of surgery and OS. Patients who refused surgery and those who were non-surgical candidates were more likely to be older, NH Black, uninsured, have a lower income, and have multiple co-morbidities, compared to those patients who underwent surgery. The baseline characteristics of patients who refused surgery were observed to be different from those patients on active surveillance and those who were non-surgical candidates for stage 1 kidney cancer. Compared to non-surgical candidates and patients on active surveillance, those who refused surgery were more likely to be younger, uninsured, and had higher tumor size. In the propensity-matched cohort, those who refused surgery had significantly worse OS,

with a 3.18-fold higher risk of death, compared to those who underwent surgery and a 1.49-fold risk compared to those on active surveillance. Conversely, they had better OS than those who were non-surgical candidates.

The differentiation of patients who have refused surgery, non-surgical candidates, and patients on active surveillance is of paramount importance in medical decision-making. Non-surgical candidates are individuals ineligible for surgery due to medical conditions or other factors, while patients on active surveillance are those who are closely monitored but are not yet undergoing treatment. The findings of the present study strongly indicate that the grouping together of these two patient categories with those who have refused surgery may be erroneous. Both groups, while not undergoing surgery, may not be receiving comparable levels of follow-up care as post-surgery patients. Consequently, it is imperative to accurately distinguish between these patient groups to ensure that they receive the tailored care they require.

Like our study, previous studies have reported factors for surgical refusal to include older age, minority race, single marital status, being uninsured, and a higher burden of comorbidities.⁷⁻¹² Older patients with advanced chronic diseases tend to refuse surgery due to fear of side effects and lack of prognostic details.¹³ In particular, older cancer patients have also been found to be more fearful of surgical interventions due to expected negative impacts on quality of life.¹⁰ These frail and elderly patients may be best suited for active surveillance if they have an appropriately sized tumor; in our primary analysis, the patients who underwent active surveillance and non-surgical candidates were excluded. Thus, the mere presence of comorbidities and old age do not entirely account for treatment refusal in the study population.

Unlike older patients, whose reasons for surgery refusal are often clinical, NH Black patients are more likely to refuse surgery because of a distrust of healthcare systems.¹⁴ Due to historical precedents, Black patients have been identified as more likely to be skeptical about diagnoses, more likely to support nonmedical cancer treatments, and more likely to be dissatisfied with patient-doctor communications.¹⁴ Hence, surgeons may find more success by opening lines of communication, easing patient concerns about prognosis and surgery-related adverse events, and directly addressing the maltreatment of minority groups in medicine.^{13,15} Like our findings, Navaneethan et al reported NH Black patients as less likely to undergo renal surgery compared to other groups.¹⁶ Their systematic review identified low socioeconomic status, low education attainment, and poor physician perception of post-

transplantation survival as factors leading to the refusal of renal transplantation in NH Black patients.

Insurance status is also strongly associated with surgery refusal. Uninsured cancer patients are less likely to follow treatment regimens and more likely to miss scheduled appointments.^{8,17} With the annual cost of initial care over \$38,000, renal cancer patients who are uninsured may be unable to afford required surgical interventions.¹⁸ This forces clinicians into scenarios where they feel compelled to bypass reimbursement rules, lower quality of care, or even refuse to see patients who cannot afford the cost of care.¹⁹ Decreased access to healthcare services for uninsured patients has been previously identified as a reason for poorer outcomes.²⁰ According to the National Kidney Foundation's Kidney Early Evaluation Program (KEEP) data, uninsured kidney patients were 82% more likely to die and 72% more likely to develop end-stage renal disease (ESRD) when compared to those with private insurance.²⁰ Other factors such as lower median income and lower education status are contributors to the refusal of surgery by way of financial toxicity and lack of understanding or misunderstanding of the consequences of surgery refusal. Our results suggest that the same racial and socioeconomic barriers that influence the refusal of other oncological surgeries are also responsible for patients refusing kidney cancer surgeries.

When these socioeconomic and demographic factors culminate in a patient's decision to forgo surgical management, we find there is an associated decrease in OS in the setting of stage I kidney cancer. This decrease in OS is likely due to the poor overall health of these patients, though the cause of death and cancer-specific mortality are not captured in the NCDB. Although we adjust for certain variables, large pooled databases are not always comprehensive with several uncaptured variables and possible confounders. Additionally, the NCDB variable that informs surgical refusal is cursory, and it does not capture borderline surgical candidates who refused surgery based on the risks during surgeon counseling, even though they could have undergone surgery. Nevertheless, OS and cancer-specific mortality benefits have been shown in surgically managed patients compared to those that refuse surgery across various oncological diseases.²¹⁻²³ Though a function of the underlying cancer stage and grade, overall and cancer-specific survival is strikingly lower in patients who refused surgery in these studies. Wang et al found that refusing surgery in localized hepatocellular carcinoma resulted in a 2.5-fold risk of cancer-specific mortality compared to those that had cancer-directed surgery.²¹ In breast cancer, after accounting for other prognostic factors including tumor characteristics and stage, women who

refused surgery had a 2.1-fold (95% confidence interval, 1.5-3.1) increased risk of dying of breast cancer compared with operated women.²² In non-metastatic pancreatic adenocarcinoma, median survival is 5.1 months versus 20.5 months in those who refused and accepted surgery, respectively.²³ In our cohort, the median survival was significantly lower in those who refused surgery than those who underwent surgery, which aligns with the reported data. The survival difference between groups underscores the importance of uncovering and understanding modifiable socioeconomic factors and patient motivations, which can result in mortality benefits by way of appropriate surgical management. The importance of patient-doctor communication in the surgical management of oncological disease is laid bare; understanding patient perspective and motivation are critical in providing high-level care.

Limitations

Our study has several limitations. Not all hospitals participate with the NCDB, leading to an inherent selection bias, which limits the generalizability of our results. The propensity score-matching used in our patient selection only accounts for observable differences but does not account for unobservable characteristics between the two groups, which may lead to unknown confounder effects. Also, the dataset used was from 2004-2017, and thus may not be representative of the current state of kidney cancer surgery. Lastly, our study only identified socioeconomic and clinical factors associated with surgical refusal; we did not identify patient-specific reasons leading to refusal. Future studies could apply the same or similar analyses with more robust data sources that account for and address possible biases.

Conclusion

Several socioeconomic, clinical, and demographical factors are associated with the refusal of kidney cancer surgery and non-surgical candidacy. The decision to refuse surgical intervention is associated with lower OS in patients with stage I kidney cancer. By better understanding, the factors associated with surgical refusal, future studies, and clinical practices can work to mitigate these issues and provide patients with appropriate management. □

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