Published in final edited form as:

World J Urol. 2016 April ; 34(4): 539–544. doi:10.1007/s00345-015-1644-y.

Histologic subtype impacts cancer-specific survival in patients with sarcomatoid-variant renal cell carcinoma treated surgically

Daniel P. Nguyen¹, Antoni Vilaseca¹, Emily A. Vertosick², Renato B. Corradi¹, Karim A. Touijer^{1,3}, Nicole E. Benfante¹, Daniel D. Sjoberg², and Paul Russo^{1,3}

Paul Russo: russop@mskcc.org

¹Urology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, 353 East 68th Street, New York, NY 10065, USA

²Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, 307 East 63rd Street, New York, NY 10065, USA

³Weill Cornell Medical College, New York, NY, USA

Abstract

Purpose—To report survival outcomes of patients treated surgically for sarcomatoid-variant renal cell carcinomas (sRCC) and to assess whether the underlying histologic subtype is an independent predictor of outcome.

Methods—One hundred and fifty-one patients underwent surgery at a referral center between 1991 and 2014 and had sRCC in final pathology. Kaplan–Meier curves for metastasis-free survival and cancer-specific survival (CSS) were calculated, and the log-rank test assessed differences between clear cell sRCC and nonclear cell sRCC. Cox regression models were generated to test the prognostic value of histologic subtype.

Results—Of 151 patients, 120 (79 %) had clear cell sRCC and 31 (21 %) had nonclear cell sRCC. Ninety-eight (65 %) patients had M0/Mx disease at presentation. Among those M0/Mx patients, metastasis-free survival probabilities were 49 % at 2 years [95 % confidence interval (CI) 38–60] and 39 % at 5 years (95 % CI 28–50), while CSS probabilities were 50 % at 2 years (95 % CI 41–58) and 32 % at 5 years (95 % CI 24–41). There was no significant difference in metastasis-free survival between clear cell and nonclear cell sRCC ($p = 0.8$). However, patients with nonclear cell sRCC had significantly lower CSS than patients with clear cell sRCC ($p = 0.035$). In multivariable analyses, nonclear cell sRCC conferred a higher risk of cancer-specific death compared with clear cell sRCC (HR 2.30, 95 % CI 1.38–3.82, $p = 0.001$).

Correspondence to: Paul Russo, russop@mskcc.org.

Author contributions D. P. Nguyen: Protocol/project development, Data collection or management, Data analysis, Manuscript writing/editing. A. Vilaseca Cabo: Data collection or management, Manuscript writing/editing, Data analysis. E. A. Vertosick: Data analysis, Manuscript writing/editing. R. B. Corradi: Data collection or management. K. A. Touijer: Manuscript writing/editing. N. E. Benfante: Data collection or management. D. D. Sjoberg: Data analysis, Manuscript writing/editing. P. Russo: Protocol/project development, Manuscript writing/editing.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standard The creation and retrospective review of the MSKCC Kidney Cancer Database was approved by the Institutional Review Board and therefore conforms to the ethical standards laid down in the 1964 Helsinki Declaration and its later amendments. No information with the potential to disclose patient identities was included.

Conclusions—In a cohort of patients treated surgically, the underlying histologic subtype of sRCC had an impact on CSS. These results present valuable information for individual counseling and patient selection in clinical trials.

Keywords

Renal cell carcinoma; Sarcomatoid; Survival; Nephrectomy

Introduction

Sarcomatoid differentiation of renal cell carcinoma (RCC) may arise in any histologic subtype, and it is widely considered to portend a poor prognosis [1–5]. However, it is not clear whether the underlying histologic subtype of sarcomatoid-variant RCC (sRCC)—i.e., conventional clear cell, papillary, chromophobe, collecting duct, and unclassified— influences the natural history of the disease. A prior study at this institution suggested better progression-free survival among patients with metastatic sRCC in the presence of conventional clear cell histology [1]. Conversely, studies of the general RCC population that included mostly patients with clinically localized disease found better outcomes in patients with nonconventional clear cell histologic subtypes, notably papillary and chromophobe RCC [6].

In this era of increasingly individualized care and in light of a renewed interest in adjuvant therapies for RCC [7], we hypothesized that a better characterization of patients treated by surgery for sRCC may be helpful for individual counseling and for patient selection in clinical trials. Patient stratification based on underlying tumor histology has been performed in recent clinical trials targeting patients with metastatic sRCC [8]. However, the impact of underlying histology subtype on sRCC outcome has not been studied extensively, especially in the case of surgically treated patients.

Herein, we report survival outcomes of patients treated surgically for sRCC and assess whether the underlying histologic subtype has prognostic value.

Methods

Patients

After obtaining institutional review board approval, we identified 151 patients who underwent radical nephrectomy or partial nephrectomy at Memorial Sloan Kettering Cancer Center (MSKCC) from 1991 to 2014 and whose tumors had sarcomatoid features in the pathologic specimen. Baseline patient characteristics were abstracted from a prospectively maintained institutional database and included patient age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, and smoking history.

Pathology

Histologic subtype was assigned based on recommendations of the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (AJCC), and the Heidelberg classification system [9], which categorizes RCC into conventional clear cell,

papillary, chromophobe, collecting duct, and unclassified RCC subtypes [10]. Tumor and nodal classifications were attributed according to the 2002 AJCC TNM classification system [11]. sRCC was characterized by pleomorphic spindle cells and/or giant cells reminiscent of sarcoma, along with epithelial cells that typify RCC [2, 12]. Tumor size and the presence of positive surgical margins were documented. The percentage of sarcomatoid differentiation was not included in the analyses, notably because it was not available for all patients and because it does not uniformly add prognostic value [1–4, 13, 14].

Metastasis-free survival and cancer-specific survival (CSS)

The typical follow-up schedule at our institution includes office visits with review of general health, physical examination, abdominal computed tomography or ultrasound, chest radiography, and laboratory exams every 6 months for 3 years and then annually thereafter. Analysis of distant metastases was based on the first evidence of distant relapse in clinical and radiologic findings and was assessed for only those patients classified as M0/Mx at diagnosis. For patients who died during the duration of the study, the cause of death was determined by the investigators through review of medical records or death certificates.

Statistical analysis

Kaplan–Meier survival analysis was used to calculate the probability of metastasis-free survival and CSS. For the purpose of our analyses, nonconventional clear cell histologic subtypes were grouped together because each subtype represented only a few cases. A log-rank test was computed to test for differences in metastasis-free survival or CSS. Adjusting for pathologic classification (T1/T2 vs. T3/T4), tumor size, and surgical margin status, multivariable Cox regression models for the risk of distant metastasis and cancer-specific death were generated to assess whether the underlying histologic subtype of sRCC was an independent predictor of outcome. Additionally, the model for cancer-specific death was adjusted for metastatic status at presentation. Twenty-five patients who died of RCC were not listed as having had distant metastases; for metastasis-free survival analyses, we assumed that these 25 patients had metastases at the time of death. Patients who had metastases at diagnosis (M1) were excluded from the analyses of time-to-distant metastasis. All statistical analyses were completed using Stata 13 (StataCorp, College Station, TX, USA). A two-sided p value <0.05 was considered significant.

Results

Of 151 patients, 120 (79 %) had conventional clear cell sRCC and 31 (21 %) had nonconventional clear cell sRCC (Table 1). In all, 111 of 151 patients (74 %) had pathologic classification T3 or greater, and 36 of 151 (24 %) had lymph-node-positive disease. Ninety-eight of 151 patients (65 %) had no evidence of metastatic disease at presentation.

Median follow-up for survivors was 3.1 years (interquartile range 0.6–6.2 years). Of 98 M0/Mx patients, 51 developed metastases. Of the entire cohort of 151 patients, 93 died from their disease. Median metastasis-free survival among patients without metastases at presentation was 1.9 years [95 % confidence interval (CI) 1.1–5.8], and median CSS among all patients was 1.8 years (95 % CI 1.0–3.1). Overall, 2- and 5-year metastasis-free survival

probabilities among M0/Mx patients were 49 % (95 % CI 38–60 %) and 39 % (95 % CI 28–50 %), respectively. CSS probabilities among all patients were 50 % (95 % CI 41–58 %) at 2 years and 32 % (95 % CI 24–41 %) at 5 years. There was no significant difference in metastasis-free survival between conventional clear cell and nonconventional clear cell sRCC ($p = 0.8$) (Fig. 1). However, CSS differed significantly between conventional clear cell and nonconventional clear cell sRCC, as patients with nonconventional clear cell sRCC exhibited lower CSS than patients with conventional clear cell sRCC ($p = 0.035$) (Fig. 2).

Next, multivariable Cox regression models were used to assess whether the underlying histology of sRCC is predictive of distant metastasis or cancer-specific death when controlling for pathologic stage, tumor size, surgical margin status, and metastatic status at presentation. We found no evidence that the underlying histology subtype was an independent predictor of distant metastasis ($p = 0.8$) (Table 2). However, tumor histology was predictive of cancer-specific death: Nonconventional clear cell sRCC was associated with a significantly higher risk of cancer-specific death when compared to conventional clear cell sRCC (HR 2.30, 95 % CI 1.38–3.82, $p = 0.001$).

Discussion

According to UICC and AJCC recommendations, sRCC should not be considered a distinct histologic subtype [10]. Rather, sRCC is considered representative of a common pathway of high-grade RCC transformation [15]. The reported incidence of sRCC ranges from 5 to 8 % of all RCC cases [2–4] and may account for an even higher percentage in patients with locally advanced tumors. In this study, we investigated whether the underlying histologic subtype of sRCC impacts survival among patients who underwent surgical tumor removal. Overall, prognosis was poor in this population. However, a subset of patients benefited from surgery and showed prolonged CSS. In particular, conventional clear cell sRCC was associated with lower risk of cancer-specific death compared with nonconventional clear cell sRCC.

A few previous studies have investigated similar questions; however, patients with metastatic disease at presentation were either studied exclusively or comprised a large proportion of the patients studied. Molina et al. [1] showed that progression-free survival after systemic therapy was better for those patients with metastatic sRCC whose tumors had a conventional clear cell histologic background. However, no multivariable analyses were reported for their study. Similarly, Golshayan et al. [13] showed that patients with metastatic sRCC and underlying conventional clear cell histology were more likely to respond to vascular endothelial growth factor–targeted therapy. Conversely, in studying 120 patients with sRCC, 66 of whom had clinically localized disease, Cheville et al. [3] found that the underlying histologic subtype of sRCC was not predictive of death after surgery. However, their study included only 16 patients with nonconventional clear cell histology, precluding definitive conclusions. Their results were in agreement with those from Shuch et al. [4], who reported that histology did not impact prognosis in a cohort of 104 surgically treated sRCC patients, most of whom had metastatic disease. Our study contrasts with these previous reports by the fact that it represents a larger surgical series including a majority of patients with clinically localized sRCC.

In our series, median metastasis-free survival among M0/Mx patients was 23.4 months and median CSS among all patients was 21.6 months. These numbers are slightly higher than those derived from older surgical series that reported median CSS ranging from 8 to 19 months [2, 3]. This difference may reflect the downward stage shift associated with modern imaging [16], leading to a higher number of sRCC cases diagnosed earlier, as localized disease. Although our findings may seem intuitive, they do confirm what has become accepted in clinical practice: sRCC is locally aggressive and is characterized by great metastatic potential. It has been postulated that the poor prognosis of sRCC is related to evidence of epithelial–mesenchymal transition (EMT), a process during which tumor cells lose their epithelial features and acquire mesenchymal characteristics as well as invasive properties [17]. Sarcomatoid elements in RCC are characterized by molecular alterations associated with EMT, including increased expression of vimentin and Snail and low expression of E-cadherin [18]. It has also been proposed that aggressive features of sRCC are related to robust hypoxia signatures [19]. Having said that, we show for the first time in a surgical series including mostly patients with clinically localized sRCC that conventional clear cell histology is associated with a survival benefit. In fact, 50 and 32 % of patients with conventional clear cell sRCC were alive at 2 and 5 years after surgery, respectively. Further molecular studies are warranted to dissect the mechanisms underlying the potential survival advantage conferred by conventional clear cell histology in the setting of sRCC. Future research should also confirm the previously suggested hypothesis that patients with metastatic conventional clear cell sRCC respond better to systemic therapies [1, 13]. Unfortunately, detailed data on salvage therapies were not available for the current cohort. Of note, a potential explanation as to why no difference was found in the model for metastasis-free survival is that patients who were metastatic at diagnosis were excluded from that model, since they already had metastasis. This may have reduced the power of the analysis to detect a difference in metastasis-free survival by histology, as evidenced by the wide confidence interval.

Recent years have seen the advent of targeted therapies in metastatic RCC, which have had a profound effect on patient survival [20–25]. Their proven efficacy in the advanced setting has led to current evaluation in the adjuvant setting for intermediate- to high-risk RCC [7]. These advances in therapy, however, have not translated into significant survival benefits for patients whose tumors exhibit sarcomatoid features [1, 13, 14]. Similarly, clinical trials investigating cytotoxic chemotherapy containing doxorubicin and/or gemcitabine regimens have yielded disappointing results in sRCC [8, 26, 27]. Therefore, all of these agents are unlikely to be effective in the adjuvant setting in cases of sRCC. Novel effective therapies are urgently needed. Interestingly, the presence of intratumoral immune cells expressing programmed cell death-1 (PD-1) is associated with sarcomatoid differentiation in RCC [28]. PD-1 inhibitors therefore represent a highly anticipated class of agents in the treatment of RCC [29]. Our results, derived from patients with mostly localized sRCC, provide helpful information for patient counseling as well as evidence-based rationale for patient stratification utilizing underlying histologic subtype in clinical trials, thereby achieving relatively homogeneous treatment groups with respect to risk.

Our study is retrospective in nature and therefore subject to potential selection bias, such as including only patients fit for surgery. We did not perform a central pathologic review.

However, pathologic specimens were assessed by dedicated urologic pathologists accustomed to evaluating malignancies using international guidelines [10]. The percentage of sarcomatoid differentiation was not available for all tumors and thus was not used as a factor for this analysis. However, based on previous studies, this variable does not uniformly add prognostic value [1–4, 13, 14]. In addition, considering the large size of most sRCC tumors, calculating the percentage of sarcomatoid differentiation may be random and misrepresentative of the true proportion. In fact, reporting the percentage of sarcomatoid differentiation is not required according to the Institutional Society of Urological Pathology 2012 Consensus Conference guidelines [30].

Conclusions

In a cohort of patients treated surgically for sRCC, the underlying histologic subtype had an impact on CSS. Nonconventional clear cell histology was associated with lower CSS than conventional clear cell histology and was an independent predictor of cancer-specific death. These results present valuable information for individual counseling and provide a rationale for patient stratification in clinical trials.

Acknowledgments

Daniel P. Nguyen is a research fellow and is supported by research grants from the Nuovo-Soldati, the Arnold U. und Susanne Huggenberger-Bischoff, the Bangerter Foundations and the Swiss Urological Association (Switzerland). This work was also supported by a National Cancer Institute Cancer Center Support Grant (P30 CA008748) to principal investigator Craig B. Thompson, MD, and by the Sidney Kimmel Center for Prostate and Urologic Cancers. The authors thank Editor Victoria Sahadevan Fossland, MD, for her review of the manuscript.

References

1. Molina AM, Tickoo SK, Ishill N, Trinos MJ, Schwartz LH, Patil S, et al. Sarcomatoid-variant renal cell carcinoma: treatment outcome and survival in advanced disease. *Am J Clin Oncol*. 2011; 34:454–459. [PubMed: 21127411]
2. de Peralta-Venturina M, Moch H, Amin M, Tamboli P, Hailemariam S, Mihatsch M, et al. Sarcomatoid differentiation in renal cell carcinoma: a study of 101 cases. *Am J Surg Pathol*. 2001; 25:275–284. [PubMed: 11224597]
3. Cheville JC, Lohse CM, Zincke H, Weaver AL, Leibovich BC, Frank I, et al. Sarcomatoid renal cell carcinoma: an examination of underlying histologic subtype and an analysis of associations with patient outcome. *Am J Surg Pathol*. 2004; 28:435–441. [PubMed: 15087662]
4. Shuch B, Bratslavsky G, Shih J, Vourganti S, Finley D, Castor B, et al. Impact of pathological tumour characteristics in patients with sarcomatoid renal cell carcinoma. *BJU Int*. 2012; 109:1600–1606. [PubMed: 22221668]
5. Pal SK, Jones JO, Carmichael C, Saikia J, Hsu J, Liu X, et al. Clinical outcome in patients receiving systemic therapy for metastatic sarcomatoid renal cell carcinoma: a retrospective analysis. *Urol Oncol*. 2013; 31:1826–1831. [PubMed: 22608544]
6. Teloken PE, Thompson RH, Tickoo SK, Cronin A, Savage C, Reuter VE, et al. Prognostic impact of histological subtype on surgically treated localized renal cell carcinoma. *J Urol*. 2009; 182:2132–2136. [PubMed: 19758615]
7. Tobert CM, Uzzo RG, Wood CG, Lane BR. Adjuvant and neoadjuvant therapy for renal cell carcinoma: a survey of the Society of Urologic Oncology. *Urol Oncol*. 2013; 31:1316–1320. [PubMed: 22264501]
8. Haas NB, Lin X, Manola J, Pins M, Liu G, McDermott D, et al. A phase II trial of doxorubicin and gemcitabine in renal cell carcinoma with sarcomatoid features: ECOG 8802. *Med Oncol*. 2012; 29:761–767. [PubMed: 21298497]

9. Kovacs G, Akhtar M, Beckwith BJ, Bugert P, Cooper CS, Delahunt B, et al. The Heidelberg classification of renal cell tumours. *J Pathol.* 1997; 183:131–133. [PubMed: 9390023]
10. Storkel S, Eble JN, Adlakha K, Amin M, Blute ML, Bostwick DG, et al. Classification of renal cell carcinoma: Work-group No. 1. Union Internationale Contre le Cancer (UICC) and the American Joint Committee on Cancer (AJCC). *Cancer.* 1997; 80:987–989. [PubMed: 9307203]
11. Greene, FL.; Page, DL.; Fleming, ID.; Fritz, AG.; Balch, CM.; Haller, DG., et al., editors. *AJCC cancer staging manual.* Springer; New York: 2002.
12. Farrow GM, Harrison EG Jr, Utz DC, ReMine WH. Sarcomas and sarcomatoid and mixed malignant tumors of the kidney in adults. I. *Cancer.* 1968; 22:545–550. [PubMed: 5673234]
13. Golshayan AR, George S, Heng DY, Elson P, Wood LS, Mekhail TM, et al. Metastatic sarcomatoid renal cell carcinoma treated with vascular endothelial growth factor-targeted therapy. *J Clin Oncol.* 2009; 27:235–241. [PubMed: 19064974]
14. Kunene V, Miscoria M, Pirrie S, Islam MR, Afshar M, Porfiri E. Sarcomatoid renal cell carcinoma: clinical outcome and survival after treatment with sunitinib. *Clin Genitourin Cancer.* 2014; 12:251–255. [PubMed: 24560086]
15. Delahunt B. Sarcomatoid renal carcinoma: the final common dedifferentiation pathway of renal epithelial malignancies. *Pathology.* 1999; 31:185–190. [PubMed: 10503259]
16. Kane CJ, Mallin K, Ritchey J, Cooperberg MR, Carroll PR. Renal cell cancer stage migration: analysis of the National Cancer Data Base. *Cancer.* 2008; 113:78–83. [PubMed: 18491376]
17. Kalluri R, Weinberg RA. The basics of epithelial–mesenchymal transition. *J Clin Invest.* 2009; 119:1420–1428. [PubMed: 19487818]
18. Bostrom AK, Moller C, Nilsson E, Elfving P, Axelson H, Johansson ME. Sarcomatoid conversion of clear cell renal cell carcinoma in relation to epithelial-to-mesenchymal transition. *Hum Pathol.* 2012; 43:708–719. [PubMed: 21992819]
19. Hammers HJ, Verheul HM, Salumbides B, Sharma R, Rudek M, Jaspers J, et al. Reversible epithelial to mesenchymal transition and acquired resistance to sunitinib in patients with renal cell carcinoma: evidence from a xenograft study. *Mol Cancer Ther.* 2010; 9:1525–1535. [PubMed: 20501804]
20. Escudier B, Eisen T, Stadler WM, Szczylik C, Oudard S, Siebels M, et al. Sorafenib in advanced clear-cell renal-cell carcinoma. *N Engl J Med.* 2007; 356:125–134. [PubMed: 17215530]
21. Escudier B, Pluzanska A, Koralewski P, Ravaud A, Bracarda S, Szczylik C, et al. Bevacizumab plus interferon alfa-2a for treatment of metastatic renal cell carcinoma: a randomised, double-blind phase III trial. *Lancet.* 2007; 370:2103–2111. [PubMed: 18156031]
22. Hudes G, Carducci M, Tomczak P, Dutcher J, Figlin R, Kapoor A, et al. Temsirolimus, interferon alfa, or both for advanced renal-cell carcinoma. *N Engl J Med.* 2007; 356:2271–2281. [PubMed: 17538086]
23. Motzer RJ, Escudier B, Oudard S, Hutson TE, Porta C, Bracarda S, et al. Efficacy of everolimus in advanced renal cell carcinoma: a double-blind, randomised, placebo-controlled phase III trial. *Lancet.* 2008; 372:449–456. [PubMed: 18653228]
24. Motzer RJ, Hutson TE, Tomczak P, Michaelson MD, Bukowski RM, Rixe O, et al. Sunitinib versus interferon alfa in metastatic renal-cell carcinoma. *N Engl J Med.* 2007; 356:115–124. [PubMed: 17215529]
25. Rini BI, Halabi S, Rosenberg JE, Stadler WM, Vaena DA, Ou SS, et al. Bevacizumab plus interferon alfa compared with interferon alfa monotherapy in patients with metastatic renal cell carcinoma: CALGB 90206. *J Clin Oncol.* 2008; 26:5422–5428. [PubMed: 18936475]
26. Escudier B, Droz JP, Rolland F, Terrier-Lacombe MJ, Gravis G, Beuzeboc P, et al. Doxorubicin and ifosfamide in patients with metastatic sarcomatoid renal cell carcinoma: a phase II study of the Genitourinary Group of the French Federation of Cancer Centers. *J Urol.* 2002; 168:959–961. [PubMed: 12187199]
27. Staehler M, Haseke N, Roosen A, Stadler T, Bader M, Siebels M, et al. Sorafenib after combination therapy with gemcitabine plus doxorubicine in patients with sarcomatoid renal cell carcinoma: a prospective evaluation. *Eur J Med Res.* 2010; 15:287–291. [PubMed: 20696639]

28. Thompson RH, Dong H, Lohse CM, Leibovich BC, Blute ML, Cheville JC, et al. PD-1 is expressed by tumor-infiltrating immune cells and is associated with poor outcome for patients with renal cell carcinoma. *Clin Cancer Res.* 2007; 13:1757–1761. [PubMed: 17363529]
29. Pal SK, Singh P, Vogelzang NJ. PD-1/PD-L1 in renal cell carcinoma: projecting the way forward. *Clin Genitourin Cancer.* 2014; 13:257–260. [PubMed: 25160519]
30. Delahunt B, Cheville JC, Martignoni G, Humphrey PA, Magi-Galluzzi C, McKenney J, et al. The International Society of Urological Pathology (ISUP) grading system for renal cell carcinoma and other prognostic parameters. *Am J Surg Pathol.* 2013; 37:1490–1504. [PubMed: 24025520]

Number at risk						
Clear cell	78	23	17	11	7	2
Non-clear cell	20	5	4	2	2	1

Red line, nonconventional clear cell sRCC; blue line, conventional clear cell sRCC

Fig. 1. Kaplan–Meier curves showing estimates of metastasis-free survival in M0/Mx patients treated by surgery for sarcomatoid-variant renal cell carcinoma (sRCC). *Red line* nonconventional clear cell sRCC; *blue line* conventional clear cell sRCC

Fig. 2. Kaplan–Meier curves showing estimates of cancer-specific survival in patients treated by surgery for sarcomatoid-variant renal cell carcinoma (sRCC). *Red line* nonconventional clear cell sRCC; *blue line* conventional clear cell sRCC

Table 1

Clinical and pathologic characteristics of patients treated by surgery for sRCC, $n = 151$

Characteristic	Frequency (%) or median (IQR)
Age	62 (52, 71)
Female gender	29 (19)
BMI ($n = 142$)	28.1 (24.6, 31.9)
ASA score ($n = 144$)	
1	2 (1)
2	64 (45)
3	71 (49)
4	7 (5)
Smoking history ($n = 148$)	94 (64)
Partial nephrectomy	23 (15)
Pathologic tumor classification	
T1	19 (13)
T2	21 (14)
T3	96 (64)
T4	15 (10)
Pathologic nodal classification	
N0	65 (43)
N1	20 (13)
N2	16 (11)
Nx	50 (33)
Metastatic classification at presentation	
M0	94 (62)
M1	53 (35)
Mx	4 (3)
Tumor size (cm)	9.2 (6.5, 12.0)
Positive surgical margins	25 (17)
sRCC histologic subtype	
Conventional clear cell	120 (79)
Nonconventional clear cell	31 (21)

sRCC sarcomatoid-variant renal cell carcinoma; BMI body mass index; ASA American Society of Anesthesiologists; IQR interquartile range

Table 2

Multivariable Cox regression models for distant metastasis (including only M0/Mx patients at diagnosis) and cancer-specific death (including all patients) in patients treated by surgery for sRCC

	HR	95 % CI	p value
<i>Distant metastasis</i>			
sRCC			0.8
Conventional clear cell	Ref.		
Nonconventional clear cell	1.10	0.53–2.30	
<i>Cancer-specific death^a</i>			
sRCC			0.001
Conventional clear cell	Ref.		
Nonconventional clear cell	2.30	1.38–3.82	

Models adjusted for histology (conventional clear cell or nonconventional clear cell), pathologic stage (T1/T2 or T3/T4), tumor size (cm), lymph node dissection (yes/no), and surgical margin status

sRCC, sarcomatoid-variant renal cell carcinoma; HR hazard ratio; CI confidence interval

^aThe model for cancer-specific death was also adjusted for metastatic classification