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Safety of Presurgical Targeted Therapy in the Setting of Metastatic Renal Cell Carcinoma

Brian F Chapin[a], **Scott E Delacroix Jr.**[a], **Stephen H. Culp**[a], **Graciela M. Nogueras Gonzalez**[b], **Nizar M. Tannir**[c], **Eric Jonasch**[c], **Pheroz Tamboli**[d], and **Christopher G. Wood**[a,*]

[a]Department of Urology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

[b]Department of Biostatistics, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

[c]Department of Genitourinary Medical Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

[d]Department of Pathology, University of Texas M.D. Anderson Cancer Center, Houston, TX, USA

Abstract

Background—In patients with metastatic renal cell carcinoma (mRCC), the timing of systemic targeted therapy in relation to cytoreductive nephrectomy (CN) is under investigation.

Objective—To evaluate postoperative complications after the use of presurgical targeted therapy prior to CN.

Design, setting, and participants—A retrospective review of all patients who underwent a CN at The University of Texas M.D. Anderson Cancer Center from 2004 to 2010 was performed. Inclusion in this study required documented evidence of mRCC, with treatment incorporating CN.

*Corresponding author. The University of Texas M.D. Anderson Cancer Center, 1515 Holcombe Blvd, Unit 1373, Houston, TX 77030 USA. Tel: 713-563-7463; Fax: 713-792-3474. cgwood@mdanderson.org (C.G. Wood).

Author contributions: Christopher G. Wood had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Wood, Chapin.
Acquisition of data: Chapin, Delacroix, Culp, Tamboli.
Analysis and interpretation of data: Nogueras Gonzalez, Chapin, Delacroix.
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Interventions—Patients receiving presurgical systemic targeted therapy prior to CN were compared to those undergoing immediate CN.

Measurements—Complications were assessed using the modified Clavien system for a period of 12 mo postoperatively.

Results and limitations—Presurgical therapy was administered to 70 patients prior to CN (presurgical), while 103 patients had an immediate CN (immediate). A total of 232 complications occurred in 57% of patients (99 of 173). Use of presurgical systemic targeted therapy was predictive of having a complication >90 d postoperatively ($p = 0.002$) and having multiple complications ($p = 0.013$), and it was predictive of having a wound complication ($p < 0.001$). Despite these specific complications, presurgical systemic targeted therapy was not associated with an increased overall complication risk on univariable or multivariate analysis ($p = 0.064$ and $p = 0.237$) and was not predictive for severe (Clavien ≥3) complications ($p = 0.625$). This study is limited by its retrospective nature. As is inherent to any retrospective study reporting on complications, we are limited by reporting bias and the potential for misclassification of specific complications.

Conclusions—Despite an increased risk for specific wound-related complications, overall surgical complications and the risk of severe complications (Clavien ≥3) are not greater after presurgical targeted therapy in comparison to upfront cytoreductive surgery.

Keywords

Cytoreductive nephrectomy; Metastatic renal cell carcinoma; Targeted therapy; Complications

1. Introduction

Cytoreductive nephrectomy (CN) is currently a common practice in the multimodality treatment of patients with metastatic renal cell carcinoma (mRCC) as a result of two prospective randomized trials demonstrating a survival benefit in patients randomized to CN followed by interferon-α (IFN-α) compared to IFN-α alone [1,2]. Over the past 6 yr, contemporary systemic “targeted” therapies have essentially replaced immunotherapies as the standard treatment for patients with mRCC. Although level I evidence supporting CN prior to contemporary systemic therapy is lacking, the use of CN has remained an integral part of treatment for mRCC.

Several aspects of CN are under evaluation, including the optimal timing of surgery in the course of systemic treatment, the safety of administrating presurgical systemic therapy, and determining how better to select patients who may derive the greatest benefit from CN [3–7]. In a phase 2 study performed at The University of Texas M.D. Anderson Cancer Center (MDACC), we evaluated the feasibility and safety of presurgical treatment with bevacizumab in patients with mRCC [4]. This was the first trial in patients with mRCC to evaluate the safety of presurgical treatment with antiangiogenesis therapy. Without a control for comparison, definitive statements could not be made regarding the relative risks of surgical morbidity associated with presurgical therapy.

As our experience with presurgical targeted therapy has grown at MDACC, we are obligated to remain critical of the outcomes associated with this treatment paradigm and to report on the safety with respect to surgical morbidity. In addition to published outcomes from other surgical series, our own experience has raised concerns regarding the potential effects of this sequence of therapy on postoperative outcomes. To validate our concerns, we assessed postoperative complications occurring with the use of presurgical systemic targeted therapy and compared these results to complications occurring after immediate CN in a contemporary series of patients.

2. Materials and methods

2.1. Patient population

After approval from the institutional review board at MDACC, we performed a retrospective review on all surgical patients with mRCC from 2004 to 2010. Inclusion criteria encompassed all patients with pathologically confirmed RCC (any histology) and preoperative findings of M1 disease. A total of 173 patients were identified and available for analysis. Presurgical systemic targeted therapy was administered to 70 patients (presurgical), while the remaining 103 patients received immediate CN (immediate). The majority of patients underwent a percutaneous biopsy to establish histology prior to receiving presurgical therapy. Several patients presenting with poor performance status (PS) or on therapy prior to evaluation at our institution may not have had a biopsy prior to initiation of therapy. Presurgical therapy was not knowingly administered to patients with non–clear-cell histology. Multiple systemic treatments were used, including a monoclonal antibody against vascular endothelial growth factor (VEGF), VEGF receptor inhibitors, mammalian target of rapamycin inhibitors, epidermal growth factor receptor inhibitors, or a combination of agents with or without cytotoxic chemotherapy. Patients receiving systemic therapy did so as a result of three scenarios: (1) inclusion in our previously reported presurgical clinical trial, (2) patients on systemic therapy prior to evaluation at MDACC, or (3) patients who did not meet clinical trial criteria to enroll in one of our protocols but were treated off protocol per patient or physician preference.

2.2. Clinical evaluation

Preoperative, operative, and postoperative characteristics were recorded for each patient. Duration of systemic therapy and time from last treatment dose to surgery were calculated. The primary end point was any postoperative complication occurring within 12 mo. Complications were captured by review of the electronic medical record, including urology clinic visits, medical oncology visits, urgent care visits, consults, review of radiographic imaging, and review of acquired medical documents from hospital and physician visits outside of our center when these were available. Complications were assessed by time and event (for those with multiple complications) and were classified using the modified Clavien system [8]. There were 45 categorized postoperative events (Table 1). Superficial wound dehiscence (at minimum, a separation of skin edges requiring dressing changes), wound infection (required intravenous or oral antibiotics), and fascial dehiscence (evisceration) were assessed independently and also subsequently grouped as *wound complications*.

2.3. Statistical analysis

Summary statistics were used to describe the clinical and demographic characteristics of the study population. Student *t* tests (or Wilcoxon rank-sum test) were used to assess differences between patients with complications and patients without complications for continuous variables. We used the Fisher exact test to assess differences between patients with complications and patients without complication for categoric variables. We analyzed preoperative, operative, and postoperative characteristics to determine predictors of having any postoperative complications, and then more specifically for wound complications. Univariable and multivariate logistic regression models were used to determine statistically significant predictors as well as known clinical predictors of surgical complications for overall complication risk, and then more specifically for predictors of wound complications. Statistical analysis was performed using Stata/SE v.11.0 statistical software (StataCorp, College Station, TX, USA).

3. Results

3.1. Patient characteristics and outcomes

Baseline demographics were similar between the two groups (Table 2). The only statistically significant baseline difference was clinical N-stage (45.7% with clinically positive nodes in the presurgical group vs 29.1% in the immediate group; $p = 0.035$). Median follow-up for the entire cohort was 19.2 mo (range: 1.1–77.7), and median length of stay was 6 d (range: 1–107).

3.2. Presurgical and adjuvant systemic therapies

Presurgical systemic targeted therapies administered to patients prior to nephrectomy are listed in Figure 1. Duration of therapy prior to CN was a median of 1.4 mo (range: 0.2–19.6) and varied based on the reason for receiving presurgical therapy. The interval from last dose of systemic therapy to surgery was based on the specific therapy administered. The median time from last dose to surgery for bevacizumab- and sunitinib-containing regimens was 32 and 11 d, respectively. Postoperative systemic therapy was administered equally to both groups (presurgical group: 85.7%; immediate group: 74.8%; $p = 0.089$), although median time from surgery to start of postoperative therapy was less in the presurgical group (presurgical group: 1.2 mo; immediate group: 1.7 mo; $p < 0.001$).

3.3. Surgical parameters

Surgical and perioperative parameters are listed in Table 3. Significant differences were not apparent between the two groups with regards to most surgical parameters. Patients receiving presurgical therapy were more likely to have undergone a regional lymphadenectomy (78.6% vs 61.2%; $p = 0.02$) and thus were more likely to be diagnosed with pathologic node-positive disease (48% vs 28.2%; $p = 0.047$). Although the percentage of patients undergoing laparoscopic CN was not different between groups ($p = 0.225$), use of laparoscopy was associated with a decreased risk of overall postoperative complications (odds ratio [OR]: 0.1; 95% confidence interval [CI], 0.0–0.3; $p < 0.001$).

3.4. Postoperative outcomes

3.4.1. Complications—Postoperative complications, as classified by the modified Clavien system, included 232 events occurring in 57% of patients (99 of 173) within 12 mo of CN. The majority of complications (65.1%) occurred within 30 d of CN; however, an additional 57 events (24.6%) occurred between 31 and 90 d, while another 24 events (10.3%) occurred after 90 d and were more likely in those who had received presurgical therapy (15.9% vs 3.8%; $p = 0.002$). Significant (Clavien ≥3) complications comprised 29.7% (69 of 232) of all events and occurred equally in both groups (presurgical group: 29.4% vs immediate group: 30.2%; $p = 0.999$). Although presurgical therapy was not significantly associated with an increased overall complication rate (65.7% vs 51.4%; $p = 0.085$), patients receiving presurgical therapy who developed a subsequent postoperative complication were more likely to have multiple events (76% vs 51%; $p = 0.013$). When analyzing the risk of experiencing a specific complication, presurgical therapy was associated with an increased rate of superficial wound dehiscences (24.3% vs 5.8%; $p < 0.001$) and wound infections (12.9% vs 2.9%; $p = 0.015$). Although not statistically significant, there were two facial dehiscences, both occurring in the presurgical group. Equivalent risks were noted in the remaining categorized complications, including deep vein thrombosis (DVT) or pulmonary embolism (PE) and hemorrhage.

3.4.2. Wound complications—We performed a univariable analysis to determine predictors of having a wound complication for all patients undergoing CN (Table 4). When accounting for all statistically significant covariates (body mass index [BMI] ≥30, use of presurgical therapy), baseline significant differences (clinical node status), and known risk factors for wound complications (diabetes, smoking history, and duration of surgery), a multivariate analysis confirmed that presurgical targeted therapy remained a significant predictor of having a wound complication (Table 4; OR: 4.14; 95% CI, 1.6–10.6; $p = 0.003$).

3.4.3. Perioperative morbidity (all patients)—Univariable analysis was again used to determine preoperative predictors of having any complication within 12 mo of CN for all patients (Table 5). When accounting for all statistically significant variables in addition to the use of presurgical therapy, only Eastern Cooperative Oncology Group (ECOG) PS (OR: 2.40; 95% CI, 1.2–4.8; $p = 0.013$) and an elevated clinical T-stage (OR: 8.95; 95% CI, 1.1–79.6; $p = 0.042$) remained significant predictors of having a postoperative complication after CN.

3.4.4. Perioperative morbidity—Eighteen deaths (10.4%) were attributed to postoperative complications. These occurred in nine patients from each of the two groups. The majority (16 of 18) occurred within 90 d of surgery, while two occurred after 90 d—both in the presurgical group—and were associated with complications occurring as a result of the development and subsequent treatment or management of chylous ascites. Deaths resulting from disease progressions were not categorized as postoperative complications.

3.4.5. Presurgical patients only—We further evaluated the presurgical group alone to determine preoperative predictors of the overall complication rate in this subpopulation (Table 6). Using all statistically significant variables in addition to ECOG PS as a measure

of clinical fitness, the multivariate analysis revealed that only a decline in serum albumin while on systemic therapy was a significant predictor of having a complication (OR: 4.20; 95% CI, 1.3–14.1; $p = 0.021$).

4. Discussion

Although the paradigm of presurgical therapy in this population appears to hold promise in initial clinical trials, currently, the proper integration of surgery and systemic therapy in the treatment of patients with mRCC is unknown. Until the results of ongoing clinical trials are known, upfront CN followed by systemic therapy will remain an integral part of the treatment of mRCC in properly selected patients [9,10]. As in any advance in medicine, proven patient safety is of paramount importance and must be assessed before any analysis of efficacy can be made.

Existing studies that have examined the impact of targeted therapy on the primary tumor would suggest that a dramatic reduction in primary tumor size or stage is not realized with the current generation of targeted therapies [5,10,11]. That said, there is some evidence that this approach can be used as a selection criterion to identify patients suitable for CN. In our phase 2 trial of presurgical bevacizumab, 6 of the 50 patients were considered unsuitable for CN after receiving presurgical therapy [4]. Whether this is viewed as successful use of presurgical therapy as a litmus test or a missed opportunity is unknown. Similarly, there is a published prospective clinical trial showing the safety of administering 3 mo of sunitinib followed by nephrectomy in 20 patients [12]. This report did not use a valid classification system or compare perioperative morbidity with a contemporary group of patients undergoing immediate CN.

The safety of the presurgical therapy paradigm was evaluated previously in a retrospective study at our institution. In this report, we reviewed a mixed cohort of 48 patients (metastatic and locally advanced) who received presurgical therapy and compared the surgical outcomes to a cohort of 58 patients who underwent immediate surgery. There were no statistically significant differences in the incidence of perioperative (30-d) morbidity and mortality [13]. Similar to Hellenthal et al, this study lacked a standardized classification system of postoperative complications. Recent urologic oncologic literature has demonstrated that a fair percentage of complications may not be captured within the 30-d postoperative interval and suggested that a period of 90 d may be necessary when reporting surgical outcomes [14]. After observing several late postoperative complications (>90 d) in presurgically treated RCC patients, we felt that evaluating postoperative outcomes for 12 mo would more accurately define surgical risk. In addition, significant discrepancies exist in the reporting of complications in the literature, and a standard needs to be developed to consistently assess outcomes among techniques and across institutions [15]. While an attempt to modify the Clavien system has been made by Shabsigh et al at Memorial Sloan-Kettering Cancer Center (MSKCC), this system is only minimally modified from that described by Clavien and does not address specific urologic and oncologic issues resulting from surgical intervention [9]. In the absence of a validated and standardized urologic classification system, we have used the modified Clavien system and attempted to address the 10 established basic reporting criteria as discussed in the MSKCC publication.

In line with our previously reported series, presurgical therapy was not an independent predictor for overall postoperative complication risk ($p = 0.085$). Importantly, its use was also not associated with significant (Clavien ≥3) complications ($p = 0.625$). These findings demonstrate the safety of the use of presurgical systemic therapy prior to CN. By evaluating postoperative complications from within 30 d to within 12 mo, we demonstrate that patients treated with presurgical therapy were more likely to have late complications and/or multiple events. With this added time interval, we captured an additional 81 events, which accounted for 35% of the captured postoperative complications. It should be pointed out that patients receiving presurgical therapy were more likely to undergo a lymph node dissection (LND; $p = 0.02$), likely because of a higher incidence of clinically positive lymph node disease. Despite this association, those patients undergoing LND were not shown to have a statistically significant increased overall complication risk ($p = 0.072$; data not shown in results). Wound-related complications were the most frequent complications observed in this group. When evaluating predictors of this outcome, presurgical systemic therapy was an independent risk factor for having a wound complication. This is consistent with other reports in breast and colorectal cancer describing delayed wound healing with the use of presurgical therapies [16–18]. In addition, we identified that a decline in serum albumin while on therapy was associated with having a postoperative complication ($p = 0.015$). Albumin is a marker of chronic nutritional status and has been shown to be a prognostic factor for morbidity and mortality in other published oncologic series [19–21]. These findings support the need for further evaluation of markers of preoperative nutritional status in surgical series.

Our study is limited, as it is a retrospective review and is subject to all the inherent biases related to reporting of postoperative complications, including inconsistent follow-up and the potential for misclassifications in the medical records. Discrepancies may be seen particularly in patients enrolled in clinical trials having shorter-interval evaluations, potential closer follow-up with more frequent wound evaluations, and more attention paid to small deviations from standard postoperative findings. In addition, although the majority of patients received presurgical therapy through enrollment in a clinical trial, there was likely selection bias when deciding which patients would receive presurgical therapy off protocol. Although this study does demonstrate equivalent postoperative surgical risks between the two groups, with an association between the use of presurgical therapy and wound complications, this study is not designed to prove causality. Consequently, because of the small numbers of patients receiving the specific agents in this study, the risks attributed to any individual therapy may be underappreciated. Several different presurgical therapies were administered, with a majority of the patients receiving bevacizumab. Bevacizumab is known to have a longer half-life (20 d) than most of the tyrosine kinase inhibitors, and this may complicate timing of surgical interventions. Nevertheless, bevacizumab was not an independent predictor of overall complication risk in our series (Table 6).

5. Conclusions

The use of presurgical therapy in patients with mRCC does not result in an increased overall complication rate or an increased risk of severe complications requiring an intervention (Clavien ≥3) when compared to immediate CN. However, there is an increased risk of

wound complications and having multiple complications in patients treated with presurgical targeted therapy. Further insight into the role of nutritional status while on systemic therapy and prior to surgery may aid in identifying higher-risk surgical patients. Although it appears that the use of presurgical therapy in patients with mRCC is safe, we advocate that it be limited to patients deemed initially unresectable or to individuals enrolled in clinical trials.

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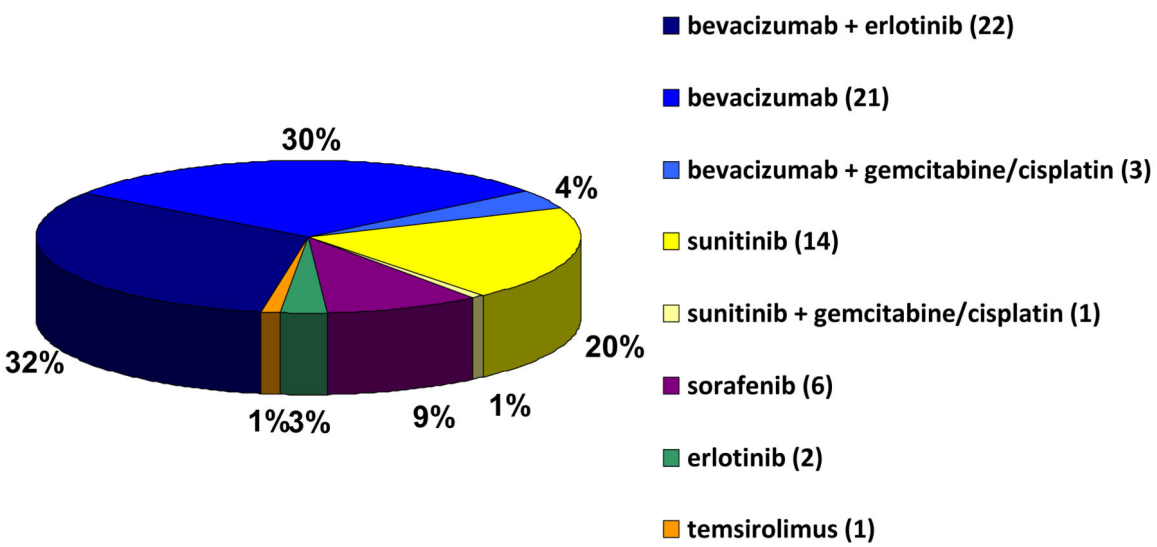

Fig. 1. Presurgical systemic therapies administered prior to cytoreductive nephrectomy

Table 1

Two hundred thirty-two postoperative complications captured within 12 mo from surgery

Event	*n*	Event	*n*
Hematologic (*n* = 25):		Lymphatic (*n* = 14):	
Bleeding	3	Chylous ascites	12
Retroperitoneal hematoma	2	Lymphocele	2
DVT	7		
PE	13		
Incisional complications (*n* = 40):		Pulmonary (*n* = 23):	
Superficial wound dehiscence	23	Pneumonia	6
Wound infection	12	Respiratory failure (requiring intubation)	12
Fascial dehiscence	2		
Incisional hernia	3	Pleural effusion	5
Genitourinary/renal (*n* = 28):		Cardiovascular (*n* = 12):	
Urinary retention	2	MI	2
Ureteral obstruction (requiring stent placement)	1	Arrhythmia	5
		Hypertension	5
Acute renal failure (not requiring dialysis)	10	Neurologic (*n* = 4):	
		CVA	1
Dialysis	3	Subdural hematoma	1
Dehydration/failure to thrive	10	Seizure	1
Epididymitis	2	Cerebral edema	1
Gastrointestinal (*n* = 27):			
Pancreatitis	2	Miscellaneous (*n* = 48):	
Ileus	15	Postoperative transfusion (<30 d)	
Splenic laceration	1	Unplanned ICU stay	
TPN	8	Retained foreign object	
Small bowel obstruction	1	Prolonged drain	
Infectious (*n* = 11):		Reoperation	
UTI	2	Uncontrolled pain (requiring narcotics)	
Line sepsis	3		
Intraperitoneal/retroperitoneal fluid collection	6	Death	
		Addisonian crisis	
		Other	

DVT = deep vein thrombosis; PE = pulmonary embolism; MI = myocardial infarction, CVA = cerebrovascular accident; TPN = total parenteral nutrition; ICU = intensive care unit; UTI = urinary tract infection.

Table 2

Summary statistics of baseline demographic and clinical characteristics by presurgical therapy

Characteristic	No. (%)			*p* value
	All patients (*n* = 173)	Immediate surgery (*n* = 103)	Presurgical therapy (*n* = 70)	
Age, yr, median (range)	60.1 (20.9–80.0)	59.7 (26.1–80.0)	61.4 (20.9–76.8)	0.891
Gender:				0.317
Male	121 (69.9)	69 (67)	52 (74.3)	–
Female	52 (30.1)	34 (33)	18 (25.7)	–
Clinical T category:				0.090
T1 and T2	91 (52.6)	60 (58.3)	31 (44.3)	–
T3 and T4	81 (46.8)	43 (41.7)	38 (54.3)	–
Missing	1 (0.6)	0 (0)	1 (1.4)	–
Clinical N category:				0.035
N0	111 (64.2)	73 (70.9)	38 (54.3)	–
N1 and N2	62 (35.8)	30 (29.1)	32 (45.7)	–
Histology:				0.608
Clear	149 (86.1)	87 (84.5)	62 (88.6)	–
Papillary	11 (6.4)	8 (7.8)	3 (4.3)	–
Chromophobe	2 (1.2)	1 (1.0)	1 (1.4)	–
Translocation	1 (0.6)	0 (0)	1 (1.4)	–
Unclassified	10 (5.8)	7 (6.8)	3 (4.3)	–
Fuhrman grade:				0.216
II	7 (4.0)	3 (2.9)	4 (5.7)	–
III	54 (31.2)	37 (35.9)	17 (24.3)	–
IV	112 (64.7)	63 (61.2)	49 (70.0)	–
Laterality:				0.420
Right	84 (48.6)	54 (52.4)	30 (42.9)	–
Left	87 (50.3)	48 (46.6)	39 (55.7)	–
Bilateral	2 (1.2)	1 (1)	1 (1.4)	–
Follow-up, mo, median (range)	19.2 (1.1–77.7)	20.4 (1.1–77.7)	19.0 (3.3–60.4)	0.347
BMI>30	53 (30.6)	29 (28.2)	24 (34.3)	0.406
Current smoker (yes)	32 (18.5)	15 (14.6)	17 (24.3)	0.107
Diabetic (yes)	26 (15)	15 (14.6)	11 (15.7)	0.832
Charlson:				0.161
Charlson <8	76 (43.9)	50 (48.5)	26 (37.1)	–

Characteristic	No. (%)			*p* value
	All patients (*n* = 173)	Immediate surgery (*n* = 103)	Presurgical therapy (*n* = 70)	
Charlson ≥8	97 (56.1)	53 (51.5)	44 (62.9)	–
ECOG:				0.229
ECOG <2	161 (93.1)	98 (95.1)	63 (90)	–
ECOG ≥2	12 (6.9)	5 (4.9)	7 (10)	–
Metastases:				0.490
1	125 (72.30)	72 (69.9)	53 (75.7)	–
>1	48 (27.7)	31 (30.1)	17 (24.3)	–
MSKCC risk stratification*:				0.352
Favorable 0	3 (1.7)	3 (2.9)	0 (0)	–
Intermediate 1–2	110 (63.6)	63 (61.2)	47 (67.1)	–
Poor >2	60 (34.7)	37 (35.9)	23 (32.9)	–

BMI = body mass index; ECOG = Eastern Cooperative Oncology Group.

*One point assigned to all presurgical patients when assessing time from diagnosis to treatment [23].

Table 3
Summary statistics of surgical and pathologic parameters by presurgical therapy

Characteristic	No. (%)			*p* value
	All patients (*n* = 173)	Immediate surgery (*n* = 103)	Presurgical therapy (*n* = 70)	
Pathologic tumor size, cm, median (range)	10 (1.7–27)	10 (2–27)	10 (1.7–24)	0.397
Duration of surgery, min, median (range)	185 (61–665)	182 (61–649)	196 (62–665)	0.638
EBL, ml, median (range)	600 (25–14 000)	600 (25–14 000)	700 (50–8900)	0.464
Pathologic T category:				0.674
T1 and T2	27 (15.6)	15 (14.6)	12 (17.1)	–
T3 and T4	146 (84.4)	88 (85.4)	58 (82.9)	–
Pathologic N category:				0.047
Nx	55 (31.8)	40 (38.8)	15 (21.4)	–
N0	61 (35.3)	34 (33)	27 (38.6)	–
N1 and N2	57 (32.9)	29 (28.2)	28 (40)	–
LND:				0.020
None	55 (31.8)	40 (38.8)	15 (21.4)	–
Partial plus total	118 (68.2)	63 (61.2)	55 (78.6)	–
Matted nodes present	15 (12.7)	6 (9.5)	9 (16.4)	0.284
Presence of sarcomatoid features	29 (16.8)	14 (13.6)	15 (21.4)	0.214
Laparoscopic	31 (17.9)	15 (14.6)	16 (22.9)	0.225
PN	6 (3.5)	2 (1.9)	4 (5.7)	0.224

EBL = estimated blood loss; LND = lymph node dissection; PN = partial nephrectomy.

Table 4

Analysis of preoperative and postoperative characteristics by risk for wound complications for all patients undergoing cytoreductive nephrectomy

Characteristic	Univariable		Multivariate	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Presurgical targeted therapy*	4.42 (1.8–10.8)	<0.001	4.14 (1.6–10.6)	0.003
BMI ≥30*	2.46 (1.1–5.7)	0.035	2.44 (0.96–6.2)	0.060
Diabetic*	1.35 (0.5–4.0)	0.564	1.00 (0.3–3.3)	0.999
Smoker*	1.03 (0.4–3.0)	0.999	0.73 (0.2–2.3)	0.597
Duration of surgery* (per-minute increase)	1.00 (1.0–1.0)	0.361	1.00 (1.00–1.00)	0.929
Clinical N1 or N2*	1.84 (0.8–4.2)	0.190	1.31 (0.5–3.3)	0.563

OR = odds ratio; CI = confidence interval; BMI = body mass index.

*Included in multivariate analysis.

Table 5

Analysis of preoperative and postoperative characteristics by risk of overall complications for all patients undergoing cytoreductive nephrectomy

Characteristic	Univariable		Multivariate	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
ECOG ≥2*	9.1 (1.2–72.3)	0.036	9.0 (1.1–74.6)	0.003
Clinical N1 or N2*	2.5 (1.3–4.8)	0.007	1.83 (0.96–3.5)	0.068
Clinical T3 or T4*	2.0 (1.1–3.8)	0.023	8.95 (1.1–79.6)	0.042
Presurgical targeted therapy*	1.8 (0.97–3.4)	0.064	1.50 (0.77–2.9)	0.237
BMI ≥30	1.5 (0.8–2.9)	0.222	–	–

OR = odds ratio; CI = confidence interval; ECOG = Eastern Cooperative Oncology Group; BMI = body mass index.

*Included in multivariate analysis.

Table 6

Analysis of preoperative characteristics for risk of overall complications for patients receiving presurgical targeted therapy prior to cytoreductive nephrectomy

Characteristic	Univariable		Multivariate	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
Decline in serum albumin*	4.3 (1.3–14.1)	0.015	4.20 (1.3–14.1)	0.021
BMI ≥30*	3.8 (1.1–13.0)	0.031	2.35 (0.6–8.9)	0.208
Clinical T3 or T4*	2.7 (0.9–7.4)	0.063	1.74 (0.5–5.5)	0.352
ECOG ≥2*	3.5 (0.4–30.5)	0.265	2.59 (0.3–26.2)	0.420
Charlson ≥8	1.3 (0.4–4.0)	0.633	–	–
Received bevacizumab	1.4 (0.5–4.1)	0.515	–	–

OR = odds ratio; CI = confidence interval; BMI = body mass index; ECOG = Eastern Cooperative Oncology Group.

*Included in multivariate analysis.