Cytoreductive Nephrectomy for T4NxM1 Renal Cell Carcinoma: The M.D. Anderson Cancer Center Experience

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OBJECTIVES Although cytoreductive nephrectomy may provide a survival benefit in metastatic renal cell carcinoma, patients with locally advanced lesions may be denied cytoreduction because of a perceived worse outcome and increased morbidity. We reviewed our experience with cytoreductive nephrectomy in patients with contiguous organ involvement (Stage T4NxM1) to evaluate the outcome and morbidity.

METHODS From 1993 to 2004, 498 patients underwent cytoreductive nephrectomy for renal cell carcinoma. Of those, 23 patients had Stage T4NxM1 disease. The analyzed variables included surgical complications, palliation of symptoms, and survival.

RESULTS The median patient age was 55 years (range 35 to 73), with a median tumor size of 15 cm (range 7 to 30). The median overall and disease-specific survival was 6.8 months (range 1.4 to 25.7). The distribution of the histologic type was conventional in 16, papillary in 2, and unclassified in 5. Sarcomatoid features were present in 9 patients. In 2 patients, surgery was aborted because of unresectable disease. Three patients developed postoperative complications (one wound dehiscence, one pancreatic collection, and one seizure). The median length of stay was 7 days (range 5 to 19). Of the 7 patients with local symptoms, 5 experienced postoperative palliation. Most patients (79%) received postoperative systemic therapy after a median of 39 days (range 24 to 114). Five patients did not receive systemic therapy because of disease progression. The median disease-specific survival for the patients who received systemic therapy was 7.1 months (range 1.4 to 25.7), but only 2.5 months (range 0 to 5.2) for those who had not ($P = 0.003$).

CONCLUSIONS Cytoreductive nephrectomy in Stage T4NxM1 renal cell carcinoma is feasible and provides significant palliation in symptomatic patients; however, the survival benefit is unclear. Our retrospective series has demonstrated that the prognosis in these patients is poor. UROLOGY 69: 835–838, 2007. Published by Elsevier Inc.

In 2006, it has been estimated that 38,890 new patients will have been diagnosed with renal cancer and 12,840 will have died of their disease.[1] Most deaths from renal cell carcinoma (RCC) are from metastatic disease, despite treatment with various systemic therapies. The role of cytoreductive radical nephrectomy as a part of multimodal therapy for patients with metastatic RCC has gained acceptance in the urologic community. It is evident that cytoreductive extirpation of the primary tumor can be performed safely, provide palliation of symptoms when present, and potentially improve survival.[2–4] The exact timing of cytoreductive surgery (before or after systemic therapy) remains controversial. The role of cytoreductive nephrectomy in patients with metastatic RCC in whom the primary tumor is also grossly invading adjacent organs (Stage T4NxM1) has not been clearly evaluated. Intuitively, surgical resection of such lesions could be accompanied by increased surgical morbidity, significant blood loss, and a prolonged hospital stay. These locally advanced tumors may also be associated with more aggressive tumor biology and a worse prognosis. Surgery in this subset of patients is highly selective, with an uncertain survival benefit. We reviewed our experience with cytoreductive nephrectomy in patients with Stage T4NxM1 RCC to evaluate the treatment outcome and morbidity.

MATERIAL AND METHODS

An institutional review board-approved search was performed of our renal cancer database. From 1993 to 2004, 498 patients

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Table 1. Baseline clinical characteristics of patients with T4M1 renal cell carcinoma

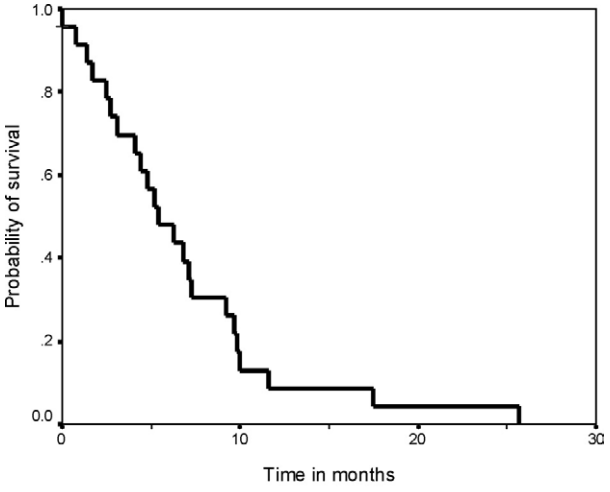
Age (yr)	
Median	55
Range	35–73
Primary tumor size (cm)	
Median	15
Range	7–30
Site of metastasis* (n)	
Pulmonary	20 (87)
Bone	4 (17)
Liver	3 (13)
Other	6 (26)
ECOG status (n)	
0–1	22 (96)
2	1 (4)
Preoperative local symptoms (n)	
Gross hematuria	2 (9)
Pain	5 (22)
None	16 (69)
Operative characteristics	
Time to systemic therapy (days)	
Median	39
Range	24–113
Length of stay (days)	
Median	7
Range	5–19
Surgical complications (n)	3 (13)
Estimated blood loss (mL)	
Mean	2,445
Range	225–15,000

ECOG = Eastern Cooperative Oncology Group.
Data in parentheses are percentages.
* Eight patients had two sites and one had three sites of metastasis.

had undergone cytoreductive nephrectomy for metastatic RCC. Of those, 23 patients had undergone cytoreductive nephrectomy for Stage T4NxM1 disease and formed the basis of this report. Each patient had undergone a preoperative metastatic workup that included blood tests, a chest x-ray, and computed tomography of the abdomen and pelvis. After surgery, the patients were followed up with routine blood tests, chest x-rays, computed tomography of the abdomen and pelvis, and bone scans (if indicated) to assess for the extent of the tumor burden. Brain imaging was obtained in patients with neurologic symptoms. The collected variables included Eastern Cooperative Oncology Group performance status at surgery, TNM stage, tumor size, site of metastasis, surgical complications, length of hospital stay, estimated blood loss, resection of adjacent organs, histologic type, palliation of symptoms, time to systemic therapy, disease progression, and time of death. Overall and disease-specific survival were estimated using the Kaplan-Meier method. Statistical analysis was performed using commercially available software (SPSS, Chicago, Ill).

RESULTS

The baseline clinical characteristics of the patients with Stage T4NxM1 RCC are described in Table 1. The median patient age was 55 years (range 35 to 73), with a median tumor size of 15 cm (range 7 to 30). Clinical Stage T4 disease was suspected on preoperative imaging in most patients (14 of 23, 61%). The sites of clinical



	3 months	5 months	10 months	15 months	25 months
Cumulative # events	7	11	20	21	23
Patients at risk	24	16	11	3	1

Figure 1. Kaplan-Meier estimate of overall survival for patients with T4NxM1 RCC who underwent cytoreductive nephrectomy.

metastasis at surgery were the lungs in 18, bone in 2, liver in 3, pancreas in 1, submandibular gland in 1, and distant lymph nodes in 2. Nine patients had more than one site of distant metastatic disease. The distribution of the histologic type was conventional in 16, papillary in 2, and unclassified in 5. Sarcomatoid features were present in 9 patients. Most patients (22 of 23) presented with an Eastern Cooperative Oncology Group performance status of 0 to 1; 1 patient had an Eastern Cooperative Oncology Group performance status of 2. The median overall and disease-specific survival was 6.8 months (range 1.4 to 25.7; Fig. 1). Virtually all patients (22 of 23, 96%) were dead of disease at the last follow-up. In 2 patients, the surgery was aborted because of unresectable disease. One of these patients was alive at 21 months after the aborted surgery. Of the 21 patients in whom cytoreductive nephrectomy was successful, 15 required major adjacent organ resection because of extensive disease involvement (6 colectomy, 5 partial hepatectomy, 2 splenectomy, and 2 combined splenectomy with partial pancreatectomy). Six other patients had gross disease that extended outside Gerota's fascia but did not require adjacent organ resection. Three patients (14%) had positive surgical margins on the final analysis. Three patients developed postoperative complications (one wound dehiscence, one pancreatic collection, and one seizures of unknown etiology). All complications were managed conservatively. All patients were discharged from the hospital after a median hospital stay of 7 days (range 5 to 19). None of the patients died in the perioperative period. Of 7 patients with local symptoms (5 with significant abdominal pain and 2 with recurrent gross hematuria), 5 experienced postoperative palliation. Most patients (79%) received postoperative systemic therapy a median of 39 days