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# Oncologic Outcomes and Predictors in Patients with Stage PT3aNxM0 Renal Cell Carcinoma Following Radical Nephrectomy

## ABSTRACT

**Objective:** The objective of this study is to evaluate oncologic outcomes in patients with PT3aNxM0 renal cell carcinoma following radical nephrectomy and also to investigate these outcomes in each specific subgroup of PT3a renal cell carcinoma and to determine predictive factors of recurrence, metastasis, and mortality.

**Materials and methods:** In this retrospective cohort study, we included 94 patients with stage PT3a renal cell carcinoma who had undergone radical nephrectomy from 2011 to 2016. All patients who had survived had at least 60 months of follow-up. Demographic and clinical data were collected; univariable and multivariable Cox proportional hazards regression analysis was performed to identify predictors of metastasis, recurrence, and cancer-related mortality.

**Results:** Patients' mean age was 58.07 ± 11.17 years and 62/94 (65.9%) were male. The mean follow-up time was 48.1 ± 25.5 months. Forty-three patients (45.7%) had experienced cancer-related mortality. The mean cancer-specific survival time was 60.94 months and the mean metastasis-free and local recurrence-free survival times were 57.06 and 88.72 months, respectively. Metastasis and local recurrence had occurred in 42 (44.6%) and 4 (4.25%) patients, respectively. After performing multivariate analysis, higher nuclear Fuhrman's grade ($P < .001$) and simultaneous involvement of the renal vein and perinephric fat ($P < .001$) were found to be predictive of cancer-related mortality. Advanced nuclear Fuhrman's grade was the only independent predictor of metastasis ($P = .001$).

**Conclusion:** Based on our results, advanced nuclear Fuhrman's grade and sarcomatoid change can independently predict mortality in patients with stage PT3aNxM0 renal cell carcinoma. Close monitoring during the follow-up period is recommended in patients with the mentioned risk factors.

**Keywords:** Kidney cancer, outcomes, recurrence, tumor staging, survival

## Introduction

Renal cell carcinoma (RCC) accounts for3% of all cancers and is the third most common urologic cancer.[1] An increasing number of incidental RCC cases are being detected; this is mostly attributed to the advancement in imaging methods, like magnetic resonance imaging, spiral computed tomography (CT), and ultrasound, which have enabled more precise detection of kidney masses.[2]

A lower stage of RCC is associated with a relatively favorable treatment outcome. In the case of organ-confined RCC, the neoplastic lesion can be treated by surgery, with 5-year survival rates nearing 85%.[3] In patients with tumors smaller than 4 cm at presentation, metastasis can be detected in up to 7.1% of cases and the 5-year survival rate is estimated to be at least 95%[4,5]; oncologic outcomes become worse in patients with tumor upstaging.[6] Several studies have been conducted to identify factors associated with recurrence, metastasis, cancer-specific survival (CSS), and overall survival in patients with RCC who undergo radical nephrectomy



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(RN).[7,8] Predictors of recurrence and metastasis are crucial to identify potential candidates for enrollment in clinical trials that use adjuvant systemic therapy; however, there is still no consensus on risk factors that are predictive of disease recurrence in patients with RCC.[9]

For the first time, in the 2002 AJCC TNM staging system, renal sinus invasion was added as an additional route to PT3a.[10] According to the 2010 AJCC TNM staging system, PT3a staging is diagnosed when the tumor grossly extends into the renal vein or invades the perirenal and/or renal sinus fat but does not extend beyond Gerota's fascia.[11] Each of the 3 mentioned subgroups of PT3a stage represents a different tumor behavior. Some studies have reported that patients with stage T3a RCC who have renal sinus fat involvement have a significantly worse prognosis compared with those with perinephric fat involvement.[12,13] On the other hand, some other studies have shown no significant difference in terms of survival rates in patients with different types of stage T3a RCC.[14,15]

In this study, we aim to evaluate oncologic outcomes in patients with stage PT3a RCC who undergo RN as the primary outcome. Our secondary objective is to investigate oncologic outcomes in each specific subgroup of PT3a and determine predictors of recurrence, metastasis, and mortality in this population.

## Materials and Methods

### Study Design and Participants

In this retrospective cohort study, we included all consecutive patients with stage PT3a RCC who had undergone RN in our center from 2011 to 2016. All patients who had survived had at least 60 months of follow-up. Exclusion criteria were lymph node involvement, presence of metastasis at the time of diagnosis, and loss to follow-up. This study was conducted in accordance with the 1964 Declaration of Helsinki, and the study protocol was approved by our institutional review board (No: Ir.sbmu.unrc.rec.1398.1). Informed consent was obtained from all participants to access, analyze, and publish their data. The STROBE checklist was used to prepare this manuscript.

### Variables

Patients' demographic data including sex, age, body mass index (BMI), social history, family history, and past medical history (such as diabetic mellitus, hypertension, chronic kidney disease, etc.) were recorded. A complete pre-operative evaluation including blood sample test (for preoperative preparation), chest x-ray (CXR) or chest CT scan (to rule out distant metastasis), abdominopelvic CT, and other necessary examinations (to confirm the diagnosis) was performed.

**MAIN POINTS**

- *PT3a staging is diagnosed when the tumor grossly extends into the renal vein or invades the perirenal and/or renal sinus fat but does not extend beyond Gerota's fascia (new classification).*
- *Cancer-related mortality was positively correlated with lower body mass index, larger tumor size, higher nuclear Fuhrman's grade, and the presence of sarcomatoid change or undifferentiated carcinoma.*
- *Higher nuclear Fuhrman's grade and simultaneous involvement of renal vein and perinephric fat predicted mortality of cancer and higher nuclear Fuhrman's grade was the only independent predictor of metastasis in this patient population.*

After surgery, pathologic specimens were evaluated by 2 expert uropathologists to detect tumor size, stage, pathologic subtype, nuclear Fuhrman's grade, surgical margin and tumor invasion status, and sarcomatoid change. A baseline chest and abdominal CT scan was obtained within 3 to 6 months following surgery. Then, an abdominal CT and CXR were obtained every 6 months for the first 3 years and annually thereafter. Furthermore, in case of any unusual symptoms, specific imaging was performed depending on the site of involvement. The length of time after primary treatment for cancer that the patient survives without local recurrence and distant metastasis in follow-up evaluation is considered as local recurrence-free survival and metastasis-free survival, respectively. Cancer-specific survival was defined as the duration from the date of treatment until death due to RCC than other causes.

### Statistical Methods

We reported categorical data as frequency (%) and quantitative data are reported as mean ± SD. The Kaplan–Meier estimator of survival probability was represented by a curve along with log-rank test. The univariable Cox regression analysis was applied for continuous predictors of metastasis, local recurrence, and cancer-related mortality. Multivariable Cox proportional hazards regression analysis was used to identify predictors of metastasis and cancer-related mortality. Those variables which had $P < .2$ in the univariable analysis were candidates for the multivariable regression analysis. All statistical tests were performed utilizing Statistical Package for Social Sciences version 26.0 (IBM SPSS Corp.; Armonk, NY, USA). Two-tailed $P$-values $< .05$ were considered statistically significant.

## Results

Ninety-four patients (male/female: 62/32; mean age ± SD: 58.07 ± 11.17 years old) with stage PT3a RCC who fulfilled the inclusion criteria were included in the analysis. The mean follow-up time was 48.1 ± 25.5 months (range: 7-92). Thirty-three patients (35.1%) were smokers and 6/92 (6.4%) reported positive family history of kidney tumor. Just over half (52%) of the tumors were located on the right side. Regarding the type of surgery, 77 (81.9%) patients underwent open and 17 (18.9%) were considered for laparoscopic nephrectomy. Following pathologic evaluation of nephrectomy specimen, clear cell carcinoma, papillary cell carcinoma, chromophobe cell carcinoma, and collecting duct carcinoma were diagnosed in 73 (77.7%), 7 (7.4%), 6 (6.4%), and 3 (3.2%) patients, respectively, and undifferentiated carcinoma was reported in 5 (5.3%) patients. Sarcomatoid change was found in 21 (22.3%) and nuclear Fuhrman's grade I, II, III, and IV were found in 1 (1.1%), 22 (25.3%), 35 (40.2%), and 29 (33.3%) patients, respectively. Renal sinus, perinephric fat, and renal vein involvement were, respectively, observed in 45 (48.4%), 15 (16.1%), and 8 (8.6%) patients. Simultaneous involvement of renal sinus and perinephric fat, renal sinus and vein, and perinephric fat and renal vein occurred in 14 (15.1%), 7 (7.5%), and 3 (3.2%) patients. Simultaneous involvement of perinephric fat, renal sinus, and renal vein was found in only 1 patient. Tables 1, 2, and 3 show patients' demographic and clinical data based on death, metastasis, and local recurrence status.

At the time of this study, 43/94 (45.7%) patients had died due to cancer-related reasons. The mean time from surgery to death was 21.2 ± 13.45 months (range: 13-60). The mean CSS time was 60.94 (95% CI: 53.65-68.23) months. Metastasis and local recurrence occurred in 42

**Table 1.** Univariable and Multivariable Cox Model Results to Explore the Effect of Demographic and Clinical Characteristic Variables on Cancer-Specific Survival Among Patients with PT3aNxM0 Renal Cell Carcinoma Who Underwent Radical Nephrectomy in Labbafinejad Hospital from 2011 to 2016.

| | Status | | Univariable Cox Model | | Multivariable Cox Model | |
|---|---|---|---|---|---|---|
| | Censored | Dead | HR (CI) | *P* | HR (CI) | *P* |
| Median age (IQR) | 57 (51, 65) | 58 (52, 70) | 1.01 (0.98-1.04) | .232 | | |
| Median BMI (IQR) | 29 (28, 30.5) | 28 (24, 30) | 0.86 (0.78-0.94) | .001 | 0.96 (0.88-1.04) | .369 |
| Median tumor size (IQR) | 80 (64, 116) | 101 (70, 130) | 1.01 (1.00-1.02) | .011 | 1.01 (0.99-1.02) | .072 |
| Sex (n = 93) | | | | | | |
| Male (%) | 34 (66.6) | 28 (66.6) | Ref | | | |
| Female (%) | 17 (33.4) | 14 (33.4) | 1.00 (0.52-1.90) | .996 | | |
| Smoker (n = 94) | | | | | | |
| Yes (%) | 19 (37.2) | 14 (32.5) | Ref | | | |
| No (%) | 32 (62.8) | 29 (67.5) | 0.88 (0.46-1.66) | .694 | | |
| DM (n = 94) | | | | | | |
| Yes (%) | 8 (15.6) | 9 (20.9) | Ref | | | |
| No (%) | 43 (84.4) | 34 (79.1) | 0.80 (0.38-1.67) | .563 | | |
| HTN (n = 94) | | | | | | |
| Yes | 8 (15.6) | 9 (20.9) | Ref | | | |
| No | 43 (84.4) | 34 (79.1) | 0.95 (0.52-1.74) | .889 | | |
| CKD (n = 94) | | | | | | |
| Yes | 3 (5.8) | 1 (2.3) | Ref | | | |
| No | 48 (94.2) | 42 (97.7) | 2.14 (0.29-15.56) | .452 | | |
| Anemia (n = 94) | | | | | | |
| Yes | 4 (7.8) | 7 (16.2) | Ref | | | |
| No | 47 (92.2) | 36 (83.8) | 1.58 (0.70-3.57) | .263 | | |
| Family history (n = 94) | | | | | | |
| Yes | 2 (3.9) | 4 (9.3) | Ref | | | |
| No | 49 (96.1) | 39 (90.7) | 1.89 (0.67-5.31) | .223 | | |
| Tumor side (n = 94) | | | | | | |
| Right | 28 (54.9) | 21 (48.8) | Ref | | | |
| Left | 23 (45.1) | 22 (51.2) | 0.80 (0.44-1.45) | .467 | | |
| Surgery type (n = 94) | | | | | | |
| Open | 41 (80.3) | 36 (83.7) | Ref | | | |
| Laparoscopy | 10 (19.7) | 7 (16.3) | 0.80 (0.35-1.79) | .589 | | |
| T3a type (n = 94) | | | | | | |
| Sinus | 26 (50.9) | 19 (44.2) | Ref | | Ref | |
| Perinephric fat | 8 (15.6) | 7 (16.3) | 1.25 (0.52-2.98) | .610 | 1.37 (0.48-3.85) | .551 |
| Vein | 7 (13.7) | 1 (2.3) | 0.25 (0.03-1.88) | .180 | NA | .977 |
| mix | 10 (19.6) | 16 (37.2) | 1.89 (0.97-3.69) | .061 | 1.34 (0.65-2.73) | .418 |
| Fuhrman grade(n = 87) | | | | | | |
| Low grade (1 & 2) | 21 (45.7) | 2 (4.9) | Ref | | Ref | .014 |
| High grade (3 & 4) | 25 (54.3) | 39 (95.1) | 10.06 (2.42-41.75) | .001 | 6.57 (1.46-29.60) | |
| Sarcomatoid change (n = 94) | | | | | | |
| Yes | 1 (1.9) | 20 (46.5) | 6.669 (3.469-12.819) | <.001 | Ref | .012 |
| no | 50 (98.1) | 23 (53.5) | Ref | | 2.68 (1.24-5.78) | |
| Pathology (n = 94) | | | | | | |
| Clear cell | 41 (80.4) | 32 (74.4) | Ref | | Ref | |
| Papillary | 4 (7.8) | 3 (7) | 0.79 (0.24-2.61) | .710 | 0.76 (0.09-6.05) | .799 |
| Chromophobe | 6 (11.8) | 0 (0) | NA | .974 | NA | .987 |
| Collecting duct | 0 (0) | 3 (7) | 2.46 (0.75-8.09) | .136 | 2.46 (0.68-8.91) | .170 |
| Undifferentiated | 0 (0) | 5 (11.6) | 3.14 (1.21-8.16) | .018 | 1.34 (0.47-3.83) | .574 |

BMI, body mass index; CKD, chronic kidney disease; DM, diabetes mellitus; HR, hazard ratio; HTN, hypertension; NA, could not estimate due to small sample size.

**Table 2.** Univariable and Multivariable Cox Model Results to Explore the Effect of Demographic and Clinical Characteristic Variables on Cancer Metastasis-Free Survival Among Patients with PT3aNxM0 Renal Cell Carcinoma Who Underwent Radical Nephrectomy in Labbafinejad

| | Status | | Univariable Cox Model | | Multivariable Cox Model | |
|---|---|---|---|---|---|---|
| | Censored | Metastasis | HR (CI) | *P* | HR (CI) | *P* |
| Median age (IQR) | 58 (51, 65) | 58 (54, 68) | 1.01 (0.98-1.03) | .528 | | |
| Median BMI (IQR) | 29 (27.6, 30.7) | 28 (24, 29.9) | 0.87 (0.80-0.96) | .005 | 0.96 (0.88-1.05) | .421 |
| Median tumor size (IQR) | 82.5 (64.5, 118) | 100.5 (73, 130) | 1.01 (1.00-1.02) | .040 | 1.00 (0.99-1.01) | .240 |
| Sex (n = 93) | | | | | | |
| Male (%) | 32 (62.7) | 30 (71.4) | Ref | .529 | | |
| Female (%) | 30 (71.4) | 12 (28.6) | 0.80 (0.41-1.57) | | | |
| Smoker (n = 94) | | | | | | |
| Yes (%) | 17 (32.7) | 16 (38.1) | ref | .807 | | |
| No (%) | 35 (67.3) | 26 (61.9) | 1.08 (0.57-2.01) | | | |
| DM (n = 94) | | | | | | |
| Yes (%) | 10 (19.2) | 7 (16.6) | ref | .914 | | |
| No (%) | 42 (80.8) | 35 (83.4) | 1.04 (0.46-2.35) | | | |
| HTN (n = 94) | | | | | | |
| Yes | 24 (46.1) | 20 (47.6) | ref | .946 | | |
| No | 28 (53.9) | 22 (52.4) | 1.02 (0.55-1.87) | | | |
| CKD (n = 94) | | | | | | |
| Yes | 2 (3.8) | 2 (4.8) | Ref | .955 | | |
| No | 50 (96.2) | 40 (95.2) | 0.96 (0.23-3.97) | | | |
| Anemia (n = 94) | | | | | | |
| Yes | 5 (9.6) | 6 (14.3) | ref | .325 | | |
| No | 47 (10.4) | 36 (85.7) | 1.54 (0.65-3.67) | | | |
| Family history (n = 94) | | | | | | |
| Yes | 2 (3.8) | 4 (9.5) | ref | .263 | | |
| No | 50 (96.2) | 38 (90.5) | 1.80 (0.64-5.05) | | | |
| Tumor side (n = 94) | | | | | | |
| Right | 30 (57.7) | 19 (45.2) | ref | | | |
| Left | 22 (42.3) | 23 (51.8) | 0.65 (0.35-1.21) | .217 | | |
| Surgery type (n = 94) | | | | | | |
| Open | 41 (78.8) | 36 (85.7) | Ref | .427 | | |
| Laparoscopy | 11 (21.2) | 6 (14.3) | 0.70 (0.29-1.67) | | | |
| T3a type (n = 94) | | | | | | |
| Sinus | 27 (51.9) | 18 (42.8) | Ref | | Ref | |
| Perinephric fat | 8 (15.3) | 7 (16.7) | 1.23 (0.51-2.95) | .638 | 0.88(0.28-2.71) | .832 |
| Vein | 6 (11.5) | 2 (4.8) | 0.52 (0.12-2.24) | .381 | 0.35 (0.04-2.80) | .327 |
| Mix | 11 (21.1) | 15 (35.7) | 1.81 (0.91-3.61) | .090 | 1.15 (0.55-2.39) | .698 |
| Fuhrman grade(n = 87) | | | | | | |
| Low grade (1 & 2) | 21 (44.7) | 2 (5) | Ref | .001 | Ref | .020 |
| High grade (3 & 4) | 26 (55.3) | 38 (95) | 10.396 (2.500-43.224) | | 6.0 (1.32-27.12) | |
| Sarcomatoid change (n = 94) | | | | | | |
| Yes | 2 (3.8) | 19 (45.2) | 6.251 (3.195-12.231) | <.001 | 3.22 (1.42-7.31) | .005 |
| No | 50 (96.2) | 23 (54.8) | Ref | | | |
| Pathology (n = 94) | | | | | | |
| Clear cell | 43 (82.7) | 30 (71.4) | Ref | | Ref | |
| Papillary | 4 (7.7) | 3 (7.1) | 0.84 (0.25-2.76) | .780 | 0.81 (0.10-6.53) | .851 |
| Chromophobe | 5 (9.6) | 1 (2.4) | 0.30 (0.04-2.26) | .248 | 0.43 (0.05-3.39) | .426 |
| Collecting duct | 0 (0) | 3 (7.1) | 6.06 (1.77-20.70) | .004 | 6.65 (1.73-25.46) | .006 |
| Undifferentiated | 0 (0) | 5 (11.9) | 5.68 (2.11-15.30) | .001 | 2.31 (0.73-7.28) | .150 |

BMI, body mass index; CKD, chronic kidney disease; DM, diabetes mellitus; HR, hazard ratio; HTN, hypertension.

(44.6%) and 4 (4.25%) patients after a mean duration of 15.9 ± 11.38 (range 4-42) and 35.2 ± 30.35 (range 8-63) months, respectively. The mean metastasis-free survival and local recurrence-free survival time were 57.06 (95% CI: 49.14-64.98) and 88.72 (95% CI: 85.55-91.59) months, respectively. Figure 1A and B contains Kaplan–Meier CSS and metastasis-free survival estimation in PT3a different subtypes.

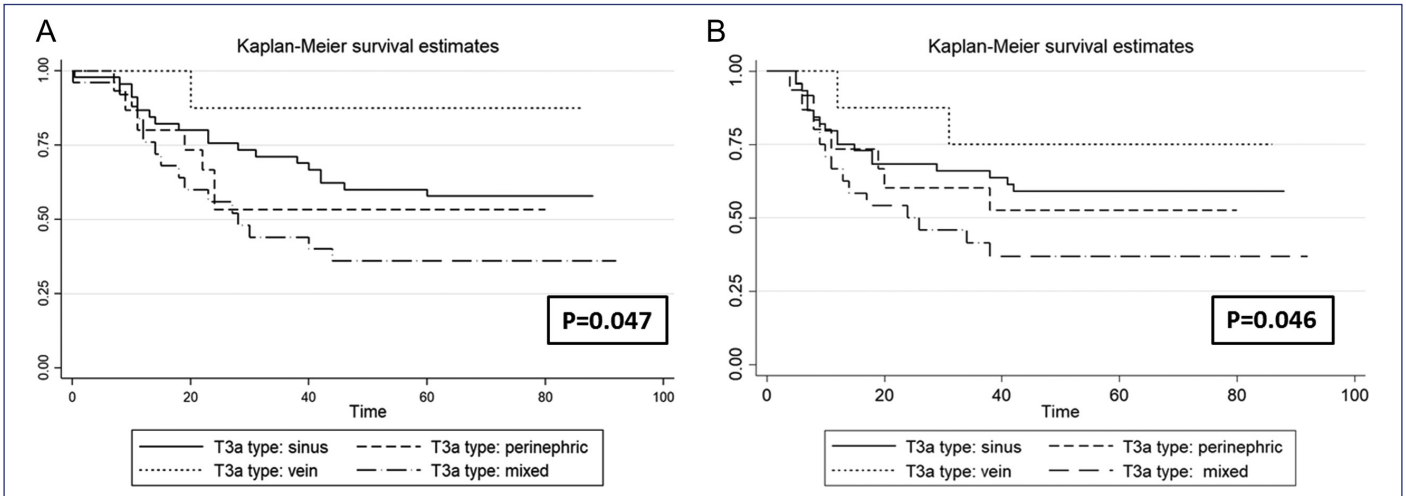


**Figure 1. a,b. Kaplan–Meier cancer-specific survival (a) and metastasis-free survival (b) estimation in PT3a different subtypes in patients who underwent radical nephrectomy (stage PT3a) in Labbafinejad hospital from 2011 to 2016.**

As shown in Table 1, cancer-related mortality had a positive relationship with lower BMI, larger tumor size, higher nuclear Fuhrman's grade, and the presence of sarcomatoid change or undifferentiated carcinoma. Also, there was a relationship between metastasis and lower BMI, larger tumor size, higher nuclear Fuhrman's grade, sarcomatoid change, and pathological subtypes of undifferentiated carcinoma or collecting duct carcinoma (Table 2). Local recurrence had a relationship with lower BMI and sarcomatoid change (Table 3). After performing multivariate analysis, higher nuclear Fuhrman's grade and sarcomatoid change predicted mortality of cancer (Table 1). Higher nuclear Fuhrman's grade, sarcomatoid change, and collecting duct pathologic subtype were the independent predictors of metastasis (Table 2). The multivariate analysis of local recurrence was not feasible due to a small number of patients with local recurrence.

## Discussion

In the current study, we aimed to investigate the oncologic outcomes of patients with stage T3aNxM0 RCC who had undergone RN and determine its predictive factors. Based on our results, 45.7% of patients had died from cancer-related reasons after 60 months of surgery. In a study by Mager et al.[16] cancer-specific death occurred in 42% of patients, which was very similar to our finding. Also, the mean CSS time in our patients was 60.94 months. Tang et al[17] reported a median overall survival time of 63 months. In the evaluation of 413 patients, Mager et al[16] reported 50 months of the CSS in the whole study cohort (range: 0-328 months). These findings were in accordance with our results.

In the present study, the mean metastasis-free and local recurrence-free survival times were 57.06 and 88.72 months, respectively. Metastasis and local recurrence had developed in 44.6% and 4.25% of patients (respectively) at 5-years follow-up. Jeong et al[18] reported that the 2-year recurrence-free survival was less favorable in the pT3a upstaging group (87.3%, $P < 0.001$). In a study by Tang et al.[17] distant metastasis was found in approximately 25% of patients before surgery. The 5-year overall survival and CSS rate were estimated to be 53.6% and 54.4%, respectively, in all patients; for N0M0 patients, the five-year overall survival and CSS rate were 71.8% and 73.2%, respectively. Mager et al[16] reported the 5-year CSS rate to be 47.6% in their cohort of patients.

We found simultaneous involvement of the renal vein and perinephric fat to be associated with the risk of mortality in RCC patients. Moreover, higher nuclear Fuhrman's grade was an independent predictor for both mortality and metastasis. This was the main finding of our study, which has not been reported in previous studies. Although high-grade tumor is associated with poor prognosis, to date, the Fuhrman grade has not been significantly involved in determining treatment plans and making treatment decisions.[19,20]

Thus far, only a few studies have aimed to evaluate mortality, metastasis, and local recurrence rates in patients with T3aNxM0 RCC and have determined its risk factors. In another study, Tang et al[17] aimed to identify factors associated with prognosis in patients with RCC and venous tumor thrombus. They found that patients with RCC and venous tumor thrombus, especially cases with early tumor thrombus, could have relatively promising long-term survival rates. In their study, Fuhrman's grade was not significantly related to prognosis. However, this could be partly attributed to the small number of patients with advanced Fuhrman grades in their study.

Although surgery (radical and partial nephrectomy) is considered the gold standard treatment for RCC, recurrence rates still remain as high as 7%, 26%, and 39% for T1, T2, and T3 stages, respectively.[21] In a study of 91 patients, Shimizu et al[22] identified a recurrence rate of 28.6% in patients with pT3aN0M0 RCC. They found that a tumor size > 7 cm significantly affects recurrence-free survival (HR 2.98, $P = .013$). Other studies had also reported that a tumor size > 7 cm increases cancer-specific mortality (HR 1.71, $P < .001$) in patients with pT3a RCC compared with tumors smaller than 7 cm. In fact, it was shown that a 1-cm increase in tumor size was associated with a 7% increase in cancer-specific mortality.[23] We also found that tumor size was significantly higher in patients who had experienced death or metastasis. In a previous retrospective study on 37 patients with RCC and vascular invasion who underwent surgery, tumor size, lymph

**Table 3.** Univariable Cox Model Results to Explore the Effect of Demographic and Clinical Characteristic Variables on Local Recurrence-Free Survival Among Patients with PT3aNxM0 Renal Cell Carcinoma Who Underwent Radical Nephrectomy in Labbafinejad

| | Status | | Univariable Cox Model | |
|---|---|---|---|---|
| | Censored | Recurrence | HR (CI) | *P* |
| Median age (IQR) | 58 (52, 66) | 62 (50.5, 65.66) | 1.005 (0.916-1.103) | .916 |
| Median BMI (IQR) | 29 (26.2, 30.2) | 25 (21.2, 29) | 0.675 (0.481-0.947) | .023 |
| Median tumor size (IQR) | 90 (70, 120) | 102.5 (64, 154.5) | 1.015 (0.987-1.044) | .293 |
| Sex (n = 93) | | | | |
| Male (%) | 59 (66.3) | 3 (75) | 0.614 (0.063-5.931) | .673 |
| Female (%) | 30 (33.7) | 1 (25) | | |
| Smoker (n = 94) | | | | |
| Yes (%) | 30 (33.3) | 3 (75) | 6.065 (0.625-58.804) | .120 |
| No (%) | 60 (66.7) | 1 (25) | | |
| DM (n = 94) | | | | |
| Yes (%) | 16 (17.8) | 3 (75) | 0.560 (0.058-5.429) | .617 |
| No (%) | 74 (82.2) | 1 (25) | | |
| HTN (n = 94) | | | | |
| Yes | 43 (47.8) | 3 (75) | 2.631 (0.273-25.313) | .402 |
| No | 47 (52.2) | 1 (25) | | |
| CKD (n = 94) | | | | |
| Yes | 4 (4.4) | 0 (0) | NA | .776 |
| No | 86 (95.6) | 100 (100) | | |
| Anemia (n = 94) | | | | |
| Yes | 10 (11.1) | 1 (25) | 3.100 (0.320-30.008) | .329 |
| No | 80 (88.9) | 3 (75) | | |
| Family history (n = 94) | | | | |
| Yes | 84 (93.3) | 4 (100) | NA | .760 |
| No | 6 (6.7) | (0) | | |
| Tumor side (n = 94) | | | | |
| Right | 47 (52.2) | 2 (50) | 0.893 (0.126-6.341) | .910 |
| Left | 43 (47.8) | 2 (50) | | |
| Surgery type (n = 94) | | | | |
| Open | 73 (81.1) | 4 (100) | NA | .532 |
| Laparoscopy | 17 (18.9) | 0 (0) | | |
| T3a type (n = 94) | | | | |
| Sinus | 45 (50) | 0 (0) | NA | .919 |
| Perinephric fat | 14 (15.5) | 1 (25) | | .956 |
| Vein | 8 (8.9) | 0 (0) | | 1.000 |
| Mix | 23 (25.6) | 3 (75) | | .953 |
| Fuhrman grade(n=87) | | | | |
| Low grade (1 & 2) | 23 (27.7) | 0 (0) | NA | .375 |
| High grade (3 & 4) | 60 (72.3) | 4 (100) | | |
| Sarcomatoid change (n = 94) | | | | |
| Yes | 19 (21.2) | 2 (50) | 12.226 (1.193-125.302) | .035 |
| No | 71 (78.9) | 2 (50) | | |
| Pathology (n = 94) | | | | |
| Clear cell | 69 (76.7) | 4 (100) | NA | .982 |
| Papillary | 7 (7.8) | 0 (0) | | .719 |
| Chromophobe | 6 (6.7) | 0 (0) | | .672 |
| Collecting duct | 3 (3.3) | 0 (0) | | .855 |
| Undifferentiated | 5 (5.5) | 0 (0) | | .799 |

BMI, body mass index; CKD, chronic kidney disease; DM, diabetes mellitus; HR, hazard ratio; HTN, hypertension; NA: Could not estimate due to small sample size.

node involvement, presence of metastasis, thrombus level, and histological tumor type were associated with overall survival.[24] In another study by Li et al.[25] T3a tumor size distinguished by the cutoff of 4 cm and 7 cm could more accurately predict CSS rather than a cutoff just by 7 cm or 4 cm. They recommended that for better clinical outcomes and improved survival stratification, sub-staging the

current T3aN0M0 stage by tumor size should be considered rather than relying solely on anatomical features.

According to our results, simultaneous involvement of renal vein and perinephric fat were risk factors for cancer-related mortality. In line with the results of our study, Shah et al[26] found that patients with different patterns of extra-renal extension (perinephric fat, renal sinus fat, or renal vein involvement; in isolation or in combination) were at significantly increased risk of disease progression (HR: 1.31; $P = .020$), cancer-specific mortality (HR 1.64, $P < .001$), and all-cause mortality (HR 1.32; $P = 0.008$). Similarly, Baccos et al[27] reported the combined involvement of renal vein and perinephric fat to be linked to a higher risk of cancer-specific mortality as perinephric fat infiltration alone.

We observed that sarcomatoid change was markedly associated with death, metastasis, and local recurrence in our patients. Despite this finding, previous studies have not noted any relationship between the presence of sarcomatoid change and oncologic outcomes. Nevertheless, in a study by Dutcher et al.[28] the long-term survival of 4 patients with advanced stage sarcomatoid RCC handled by chemotherapy was evaluated; 2 died from progression of the disease, 1 with recurrence of clear cell, and 1 with recurrence of sarcomatoid, after 3 and 6 years, respectively.

Retrospective design is the main limitation of this study. We recommend a prospective study with a larger sample size about this subject. Another limitation was that we excluded the patients with node involvement to eliminate the predictable bias. Lymphadenectomy during RN is not routine in our center so it did not perform for all the patients (only may when visible lymph node).

To our findings, the mean cancer-specific, metastasis-free, and local recurrence-free survival times in patients with stage PT3a RCC who underwent radical nephrectomy were 60.94, 57.06, and 88.72 months, respectively. Higher nuclear Fuhrman's grade and sarcomatoid change predicted mortality of cancer. Higher nuclear Fuhrman's grade, sarcomatoid change, and collecting duct pathologic subtype were the independent predictors of metastasis in this patient population. Close monitoring during the follow-up period is recommended in patients with the mentioned risk factors.

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***Informed Consent:*** *Written informed consent was obtained from all participants who participated in this study.*

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