# Renal Tumors in Young Adults

## A Single-Center Experience From a Developing Country

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Received May 2011
Accepted October 2011

**Purpose:** To determine the pattern and outcome of renal tumors in young adults in a large surgical series in Pakistan.

**Materials and Methods:** We retrospectively analyzed 133 young adults (age: ≥ 16 to ≤ 40 years) with 136 renal tumors, who underwent surgical treatment for suspected renal cancer from 1994 till 2010. The clinical and pathological parameters were determined and their impact on final outcome was analyzed.

**Results:** The mean age of the patients was 33.3 ± 6.2 years. Of 136, 121 (88.9%) renal tumors were malignant and 15 (11%) were benign. Among malignancies, 76 (62.7%) patients had stage I or II tumors, 22 (18.1%) stage III, and 23 (19%) stage IV at surgery. The overall cancer-specific survival for malignant tumors at 1, 5, and 10 years was 97%, 83%, and 83%, whereas the cancer-free survival (CFS) was 80%, 63%, and 37%, respectively. Patients with age ≤ 35 years had 1 and 5-year CFS of 83% and 71%, respectively, as compared with 76% and 49% for patients > 35 years ($P = .02$; odds ratio = 2.3; $P = .03$). Regarding tumor size, 1 and 5-year CFS for tumors ≤ 10 cm was 93% and 75%, while tumors > 10 cm showed CFS of 56% and 41%, respectively ($P = .0001$; odds ratio = 4.2; $P = .0001$). For stage I tumors, CFS at 1 and 5 years was 98% and 84%; for stage II, 82% and 63%; and for stage III, 62% and 50%, respectively. One-year survival for stage IV was 48% only ($P = .0001$).

**Conclusion:** A wide heterogeneity of renal tumors is seen in young adults with delayed presentation.

**Keywords:** epidemiology, nephrectomy, outcome, kidney neoplasms, renal cell carcinoma, young adults

## INTRODUCTION

Renal tumors comprise a diverse spectrum of neoplastic lesions with patterns that are relatively distinct for children and adults. Adult renal tumors have a predilection to occur in older patients and are infrequent in adults younger than 40 years. A wide variety of both benign and malignant tumors arise from different components of the renal tissue, especially tubular epithelium. Renal cell carcinoma (RCC) is the most common renal tumor in adults with the mean age of 62 years at occurrence.[1] Only approximately 5% of all the kidney tumors in adults occur below the age of 40 years.[2] The incidence of renal tumors is on the rise throughout the world and across all age groups, particularly during the last few decades.[3,4]

It is now believed that renal tumors in young adults differ from their counterparts in older adults in clinical behavior, biology, histology, and the long-term outcome.[5,6] However, the evidence for this, in the few published studies on the subject, is far from conclusive.[5] We have earlier reported, in the first detailed report from Pakistan, the pattern of renal tumors in a preliminary report that included all the adults.[7] To the best of our knowledge, there is no data on the pattern of renal tumors and their behavior in young adults in Pakistan. The aim of this retrospective study was to analyze different aspects of renal tumors in young adults based on a large surgical series of renal tumors from a single institution in Pakistan and to compare them with the previously published literature.

## MATERIALS AND METHODS

The study was conducted at the department of adult urology, Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan over a period of 16 years from November 1994 till July 2010. Medical records of 133 patients with 136 renal tumors who underwent surgical treatment for suspected renal cancer and were ≤ 40 years were retrospectively analyzed.

Data were collected in terms of age, gender, duration of symptoms, tumor size, laterality, and palpability of tumor. Laboratory findings, including hemoglobin and renal functions, were also recorded. World Health Organization (2004) classification of adult renal tumors was employed for the pathological classification of tumors.[8] Fuhrman nuclear grading system was used for RCC.[9] Robson staging system was applied for assessing the extent of spread of malignant tumors.[10] Disease status was also determined in terms of stability or progression of disease at the last follow-up.

Patients with benign tumors and incomplete follow-up or who were lost to follow-up were excluded from the survival analysis. Follow-up duration was calculated from the date of surgery to the date of death or last follow-up.

**Statistical Analysis**

Statistical analysis was performed by SPSS software (the Statistical Package for the Social Sciences, Version 10.0, SPSS Inc, Chicago, Illinois, USA). Simple descriptive statistics, such as mean ± standard deviation, were used for continuous variables, such as age, while numbers (percentages) were used for categorical variables. The survival analysis was done using the Kaplan-Meier method, log-rank test, and multiple regression procedure of Cox. *P* values of less than .05 were considered statistically significant.

## RESULTS

A total of 1391 adult patients were treated surgically for suspected renal cancer during the study period. Among these, 133 (9.50%) patients were ≤ 40 years old and constituted the study population of the present study. Their mean age was 33.3 ± 6.2 years (range, 16 to 40 years). Majority (66.40%) were > 30 years, while 39 (29.30%) were between 21 and 30 years, and only 5 (3.70%) patients were ≤ 20 years. The male to female ratio was 1.1:1, with 71 (53.30%) men and 62 (46.70%) women.

Clinical features at the time of presentation are

**Table 1.** Clinical features at the time of presentation in 133 young adults with suspected renal cancer.

| Signs/Symptoms | Number (%) |
|---|---|
| Flank pain | 99 (72.40) |
| Hematuria | 70 (52.60) |
| Abdominal mass | 12 (9.00) |
| Symptoms triad | 30 (22.50) |
| Incidental finding | 11 (8.20) |
| Fever | 5 (3.70) |
| Weight loss | 2 (1.50) |

shown in Table 1. It is seen that flank pain was the most common symptom, observed in 99 (72.40%) patients, followed by hematuria in 70 (52.60%). Blood hemoglobin was > 10 g/dL in 95 (71.42%) patients, while the remaining 38 (28.60%) had hemoglobin ≤ 10 g/dL. Eight (6.0%) patients were in renal failure at the time of presentation, while the remaining 125 (94.0%) patients had normal renal function. On examination, 77 (56.60%) renal tumors were palpable.

The mean duration of symptoms, laterality, and size of the tumor along with type of the surgery, Robson stage, and follow-up periods are shown in Table 2. Among malignant tumors, 76 (62.70%) patients had their tumors confined within Gerota's fascia (Stage I or II), 22 (18.10%) had stage III, and 23 (19.0%) had stage IV at the time of surgery.

On pathological examination, 121 (88.90%) renal tumors were malignant, while the remaining 15 (11.0%) were benign. The histopathological diagnoses of these tumors specimens are presented in Table 3.

**Table 2.** Clinicopathological characteristics of 133 young adults with suspected renal cancer.

| | |
|---|---|
| Mean duration of symptoms, month | 7.0 ± 2.4 |
| Site of tumor, n (%) | |
| Right | 67 (49.20%) |
| Left | 65 (47.90%) |
| Bilateral | 4 (2.90%) |
| Size of tumor, cm, n (%) | |
| 1 to 3 | 4 (2.90%) |
| 4 to 7 | 22 (16.10%) |
| 8 to 10 | 54 (39.40%) |
| 11 to 15 | 40 (29.40%) |
| > 15 | 16 (11.70%) |
| Mean tumor size, cm | 10.4 ± 10.2 |
| Surgery, n (%) | |
| Radical or palliative nephrectomy | 129 (94.80%) |
| Partial nephrectomy | 6 (4.40%) |
| Robson staging (for malignant cancers only), n (%) | |
| I | 58 (47.90%) |
| II | 18 (14.80%) |
| III | 22 (18.10%) |
| IV | 23 (19.00%) |
| Patient status at the last follow-up, n (%) | |
| Stable | 66 (48.20%) |
| Disease progressed | 20 (14.90%) |
| Lost to follow-up | 39 (29.80%) |
| Expired | 8 (5.90%) |

## Outcome Analysis

We analyzed 94 patients who were on regular follow-up for their cancer-free status after surgery by

**Table 3.** Histopathological diagnoses of 136 renal tumors specimens from 133 young adults with suspected renal cancer

| Tumor types | Number (%) |
|---|---|
| Malignant tumors | 121 (88.90) |
| RCC clear cell variant | 84 (69.40) |
| RCC papillary variant | 11 (9.00%) |
| RCC chromophobe variant | 3 (2.40%) |
| RCC sarcomatoid | 2 (1.60%) |
| Transitional cell carcinoma | 9 (7.40%) |
| Primitive neuroectodermal tumor | 5 (4.10%) |
| Synovial sarcoma | 2 (1.60%) |
| Non-hodgkin lymphoma | 2 (1.60%) |
| Squamous cell carcinoma | 1 (0.80%) |
| Leiomyosarcoma | 1 (0.80%) |
| Malignant fibrous histiocytoma | 1 (0.80%) |
| Benign tumors | 15 (11.00%) |
| Angiomyolipoma | 11 (73.30%) |
| Oncocytoma | 3 (20.00%) |
| Schwannoma | 1 (6.60%) |

RCC indicates renal cell carcinoma.

**Table 4.** Outcome analysis of 94 young adults with malignant renal tumors and regular follow-up

| Variables | 1 year | 5 years | 10 years | *P* |
|---|---|---|---|---|
| Overall cancer-specific survival | 97 | 83 | 83 | - |
| Overall cancer-free survival | 80 | 63 | 37 | - |
| Patient age, y | | | | .02 |
| ≤ 35 | 83 | 71 | - | |
| > 35 | 76 | 49 | - | |
| Tumor palpability | | | | .008 |
| Non-palpable tumors | 93 | 75 | - | |
| Palpable tumors | 66 | 52 | - | |
| Tumor size, cm | | | | .0001 |
| ≤ 10 | 93 | 75 | - | |
| > 10 | 56 | 41 | - | |
| Tumor stage (Robson) | | | | .0001 |
| Stage I | 98 | 84 | - | |
| Stage II | 82 | 63 | - | |
| Stage III | 62 | 50 | - | |
| Stage IV | 48 | - | - | |
| Histological type | | | | .03 |
| Renal cell carcinoma | 86 | 71 | - | |
| Non-Renal cell carcinoma | 65 | 42 | - | |

*All figures are in percentages.

using Kaplan-Meier method. The minimum follow-up period for inclusion in the outcome analysis was one year. The overall cancer-specific survival rates at 1, 5, and 10 years were 97%, 83%, and 83% whereas the cancer-free survival (CFS) rates were 80%, 63%, and 37%, respectively (Figure 1). Various clinicopathologic characteristics of these tumors were analyzed to determine their effect on the progression of disease (Table 4). Patients ≤ 35 years had better outcome with 1 and 5-year CFS rates of 83% and 71%, respectively. The corresponding figures were 76% and 49%, respectively, for patients older than 35 years [*P* = .02; odds ratio (OR) = 2.3; 95% confidence interval (CI) = 1.1 to 4.9; *P* = .03].

Cancer-free survival rates on the basis of tumor palpability were also analyzed, which confirmed the better survival for the group who had non-palpable tumors. Palpable tumors had 1 and 5-year survival rates of 66% and 52%, while non-palpable tumors had CFS rates of 93% and 75% at 1 and 5 years, respectively (*P* = .008; OR = 2.8; 95% CI = 1.2 to 6.4; *P* = .01; Figure 2).

Regarding tumor size, of 94 patients, 60 (64%) with tumors measuring ≤ 10 cm had good prognosis compared to 34 (36%) who had tumors > 10 cm in size. One- and 5-year CFS rates for tumors of ≤ 10 cm were 93% and 75%, while the tumors > 10 cm showed CFS rates of 56% and 41%, respectively (*P* = .0001; OR = 4.2; 95% CI = 1.97 to 9.1; *P* = .0001).

Tumor stage was also analyzed for CFS and it was observed that for stage I tumors, CFS rates at 1 and 5 years were 98% and 84%, for stage II, 82% and 63%, and for stage III, 62% and 50%, respectively. On the other hand, 1-year survival for stage IV was 48% only (*P* = .0001; Figure 3).

Among patients with malignant tumors, prognosis

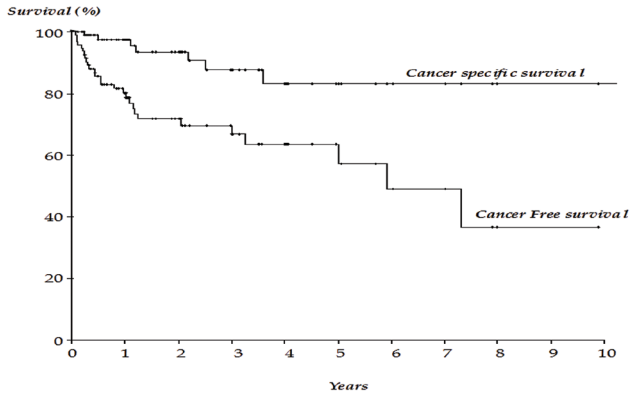


**Figure 1.** Cancer-specific and cancer-free survival following surgery for malignant renal tumors in 94 young adults.

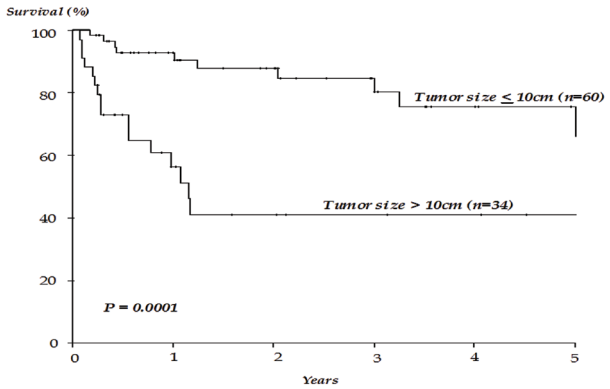


**Figure 2.** Cancer-free survival according to tumor size following surgery for malignant renal tumors in 94 young adults.

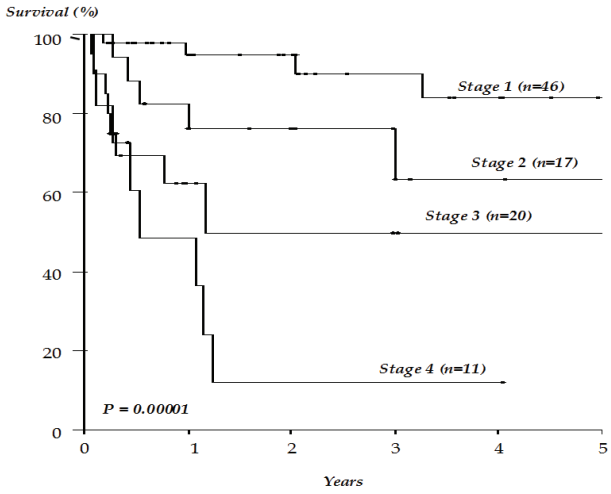


**Figure 3.** Cancer-free survival according to Robson stage of malignant renal tumors in 94 young adults following surgery.

of patients with RCC was better than non-RCC group. Among RCC cohort, 86% were disease-free at 1 year and 71% at 5 years compared to non-RCC group, who had 65% and 42% CFS rates at 1 and 5 years, respectively (OR for non RCC and RCC = 2.2; 95% CI = 1.0 to 4.8; $P = .03$).

Subtypes of RCC were also analyzed for CFS. Clear cell variant of RCC (CCRCC) had 89% 1-year survival and 75% 5-year survival. Because of small number of patients in other types of RCC, only 1-year survival could be estimated, which was 53% for papillary RCC (PRCC) and 100% for the rest of the two types of RCC ($P = .01$)

The majority of patients with RCC had grade 2 nuclear features; therefore, only grade 2 survivals were estimated and found to be 91% at 1 year and 76% at 5 years.

## DISCUSSION

This study is one of the largest studies on the spectrum of renal tumors in young adults throughout the world and the first from this region. We, however, acknowledge the fact that this is a single center-based study and not truly representative of the population in Pakistan. The study has also inherent selection bias in that only those subjects, in whom surgery was carried out as part of treatment, were included, but it comes from a center of excellence for the kidney and urological diseases in the country and its catchment area extends more or less to the entire country. Therefore, we believe that the findings from this study are fairly representative of the prevailing renal tumor types in young adults from this country.

Approximately, 9% of adults with renal tumors in our study were either 40 years or less at the time of presentation. Published literature reports the incidence of 5% to 9% for renal tumors in younger patients [1,4]. The mean age of the patients in our study was 33.3 ± 6.2 years with male to female ratio of 1.1:1. Denzinger and colleagues reported the male to female ratio of 3.1:1,[5] while Eggener and asso-

ciates reported the ratio of 1.2:1,[11] the later being concordant with our study.

Symptomatology of renal tumors in these young patients is generally similar to that reported previously. In this study, approximately 8% of the patients were asymptomatic and were incidentally diagnosed during the workup of some other diseases. This incidence is less as compared with western studies, where incidental detection rates vary between 35% and 75%.[5,11-13] The main reason of this appears to be the lack of awareness among the masses and the inaccessibility of medical facilities. The mean duration of symptoms in our study was 7 months, while it was reported to be 84 weeks in another study,[14] which is markedly longer than our finding. Anemia is one of the major complications of renal tumors and its incidence has been reported to be up to 30%.[15] It was not infrequent in our study and approximately 29% of the patients had anemia at the time of presentation representing the outcome of hematuria, malignancy, and chronic disease.

In our study, only 6% of the patients had renal dysfunction, which is almost the same as that reported in other study.[11] Renal function is usually preserved in these patients, especially in young adults who have a healthy contra-lateral kidney and do not have co-morbidities, like diabetes and hypertension, which are prevalent in the elderly population.

Laterality of the renal tumors is of no clinical importance. Eggener and associates reported the occurrence of 54.6% and 45.4% for renal tumors on the right and left sides, respectively,[11] which was not statistically significant and is concordant with our study. Overall incidence of bilateral renal tumors is between 2% to 4%, but in young adults and in von Hippel-Lindau disease, it is more common.[16] However, there is a wide variation, as Eggener and coworkers[11] and Boykin and colleagues[14] did not report any bilateral renal tumors. On the other hand, Abou El Fettouh and associates reported that approximately 13% of the patients who were between 20 to 40 years had bilateral renal tumors.[17] We found bilateral renal tumors in 3% of our patients, which is comparable to most of the previous studies.[16]

Palpability of the tumors depends on the size of the tumors and the contour of the body. It was the size, and not the palpability of the tumor which affected the clinical outcome in these patients. In our study, only 19% of the patients had renal tumors ≤ 7.0 cm. While approximately 70% of the patients in the study by Eggener and colleagues had renal tumors < 7.5 cm,[11] indicating early diagnosis and prompt utilization of investigating tools.

Despite the larger size of the tumors reported in our study, we found that approximately 63% of the patients had organ confined disease. Cao and associates reported almost similar percentage of young patients with organ confined disease.[18] However, other studies have reported up to 90% of the patients with early stage disease at the time of presentation.[11,12] The disparity in the rates of early stage disease may partly be due to the lack of proper health services in our country.

Renal cell carcinoma is undoubtedly the most common renal malignancy worldwide in adult patients.[11,12,14] In our study, CCRCC was the most common variant and constituted 68.5%, followed by PRCC, which constituted 9%. The other variants were rare. Our results are generally comparable to the previously published literature.[5,12,17] On the other hand, Lopez and coworkers reported CCRCC in 51% of patients,[19] while Eggener and associates reported its incidence in up to 76%.[11] Low incidence of 21% for CCRCC had also been reported,[20] but this study included children as well. Incidence of PRCC in our study is almost similar to other studies.[11,19] On the other hand, 50% incidence of PRCC reported by Renshaw and associates[20] may be because of the fact that this study also included children. Chromophobe RCC (CRCC) was found in 2% of our patients and is almost compatible to

previous studies.[12,17] But there are studies in which CRCC has been reported in up to 10% of patients.[11,19] Sarcomatoid variant is a rare presentation, substantiated by this study as well as other studies.[17,18] Among malignant tumors, early stage disease has better survival as observed in our study and also other studies.[6-8,14,21-23]

Sanchez-Ortiz and colleagues reported that young patients had more unfavorable histology and higher incidence of lymph node metastases, but the survival is better than the older adults.[23] We also observed in the present study that the younger the patient, the better the survival, as also demonstrated by Taccoen and associates.[12] The tumor size is also a good predictor of CFS as observed in this study. Goetzl and coworkers reported similar findings; the larger the tumor size, the worse the outcome.[13] Histopathological types of renal tumors in young adults also affect the CFS, as we observed a better survival in RCC group compared to non-RCC group.

Renal pelvis TCC accounts for only 5% of renal malignancies.[24,25] It is difficult to determine the exact incidence of the renal pelvic tumors because statistics vary substantially worldwide between different geographical areas and even an incidence as high as 40% had been reported in Balkan countries.[22] Very limited data are available for transitional cell carcinomas of the renal pelvis in young adults. Incidence of 1.7% and 5.5% had been reported in different studies on young adults.[11,14] We report a somewhat higher incidence of transitional cell carcinomas, which is slightly greater than 7%. Primitive neuroectodermal tumor (PNET) is rarely localized primarily in the kidney.[26] We found primary renal PNET in approximately 4% of our young adult patients. Thyavihally and colleagues reported the mean age of patients with renal PNET as 27 years at the time of presentation[27] reflecting the fact that PNET is a disease of young adults,[23] similar to our findings.[26]

In our study, 11% of the patients had benign renal tumors. Angiomyolipoma was the most common benign renal tumor in our study and constituted up to 73% of total benign tumors, but overall incidence was 8%. Even lower incidence of angiomyolipoma was reported in previous studies.[11,14] We also found a few cases of rare benign renal tumors, such as oncocytoma and schwannoma, which were surgically removed with suspicion of renal cancer.

## CONCLUSION

In conclusion, a wide heterogeneity of renal tumors in young adults is documented in this study with somewhat late presentation as compared with western studies. Despite limitations inherent in the study design, the findings are an important contribution from a developing country to the scanty literature on the subject throughout the world.

## CONFLICT OF INTEREST

None declared.

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