ORIGINAL ARTICLE

RENAL TUMOURS OF NON-CLEAR CELL HISTOLOGY; 10 YEARS' EXPERIENCE IN A SPECIALIZED CENTRE

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Background: Non-clear cell renal cell carcinomas are uncommon renal tumours with diverse histologically and genetically defined entities. Due to limited clinical outcomes data, no standardized management approach can be offered to these patients. This study aimed to analyse outcomes of non-clear cell renal cell carcinoma after surgical resection of localized renal tumours in our population. **Methods**: Patients with renal tumours who underwent partial or radical nephrectomy at the Department of Urology, from January 2010 to December 2019 were identified and evaluated, in terms of prevalence, presentation, recurrence, and survival outcome. **Results**: Non-clear cell tumours were found in one-fourth of the total number of nephrectomies performed during this period for renal cell carcinoma (RCC). The mean age was 50.48±14.76 years (range 18–89 years) with 57% being of the male gender. The predominant types were chromophobe RCC, papillary RCC, and sarcomatoid RCC, in all non-clear cell renal tumours. Mean Recurrence Free Survival (RFS) for all tumours was 75.26±2.7 months. The projected 5 years RFS of papillary RCC, chromophobe RCC and sarcomatoid RCC were 94.2%, 84.3% and 62.5% respectively. **Conclusion**: RCC of non-clear-cell histology depicts excellent survival in patients with localized renal tumours. Furthermore, sarcomatoid RCC has worse recurrence free survival followed by chromophobe RCC and papillary RCC, in our population subset.

Keywords: Renal Tumour; RCC; Survival; Chromophobe; Sarcomatoid

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INTRODUCTION

Renal cell carcinoma (RCC) has a worldwide prevalence of about 4%, variable in different parts of the world. This incidence is growing partly credited to the increased use of abdominal imaging for other reasons.[1] RCC is not a homogenous entity and a number of malignant histologic subtypes are documented by the Heidelberg classification system.[2]

About 75% of RCCs are of the clear cell type (ccRCC) and the rest of the proportion comprising of papillary, chromophobe, sarcomatoid, collecting-duct tumours and unclassified histology RCC, collectively referred to as non-clear cell renal cell carcinoma (nccRCC).[3] In modern years, the management of RCC has undergone great changes but surgery remains the foundation stone and probably the only curative approach in localized RCC. These developments have reduced morbidity and have advanced towards the less invasive resection approaches, which achieve comparable oncologic outcomes to the traditional open nephrectomy.[4]

The phenomena of renal cancer as not being one disease but several disease entities has led to the argument that RCC subtypes might behave in a different way in terms of metastasis, recurrence free survival and overall survival. Rapid advances and developments are taking place in the treatment of ccRCC leading to guidelines updated each year, as it remains the most common type of RCC. Even with recent developments, the optimal treatment guidelines for patients with non-clear cell renal cell carcinoma (nccRCC) remain unclear.[5] Patients with nccRCC were studied for survival outcomes after nephrectomy for localized disease in this retrospective study.

MATERIAL AND METHODS

After the formal approval from the Institutional Review Board, records of all patients, who underwent open partial or radical nephrectomy for renal tumours from January 2010 to December 2019 at the Department of Urology, were reviewed. These patients were followed as per their risk group according to the European Association of urology guidelines. All patients with age above 18 years, localized disease, solitary tumour and proven nccRCC on final histology were included in the study. Patients with an age less than 18 years, nodal or distant metastatic disease, history of previous renal tumour, clear cell histology or locally advanced disease were excluded from this study. Patient demographics, presenting concerns, preoperative and postoperative tumour characteristics and time of recurrence were analysed. Statistical analysis was carried out using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp., Armonk, NY). Continuous variables

were stated as mean±standard deviation and categorical variables were computed as frequencies and percentages. The Kaplan-Meier method was used to estimate recurrence free survival.

RESULTS

Non-clear cell tumours were found in 149 (24.3%) patients out of the cumulative number of nephrectomies (612) performed during this period. Only 13 (8.7%) patients had partial nephrectomy. Mean age was 50.48 ± 14.76 years (range 18–89 years) with 57% of the male gender, and 58.3% with age <55 years. Diabetes Mellitus and Hypertension were found in 19 (12.7%) and 31 (20.8%) patients respectively. 51.7% of patients had left-sided tumour. These tumours were identified incidentally on ultrasound in nearly half of patients (52.3%). Only 13% had a history of smoking. A family history of renal cancers was positive in three patients, which is an associated risk factor for renal tumours. The prevalent types were chromophobe RCC, papillary RCC, and sarcomatoid RCC, in all patients with non-clear cell renal tumours (Figure-1). Most of these cases presented with T1 (40.3%) or T2 (35.6%) stage clinically (Table-1). Mean tumour size was 8.2 ± 3.5cm (range 3-20cm).

Only 12 (8.1%) out of the total 149 patients had a recurrence of the disease, within 1 year in 10 patients. 11 out of 12 patients had multifocal recurrences. Only palliative treatment was offered to all these patients. Mean RFS for all tumours was 75.26±2.7 months. The projected 5 years RFS of papillary RCC, chromophobe RCC and sarcomatoid RCC were 94.2%, 84.3% and 62.5% respectively, (Figure 2-4). No recurrences were noted during follow-up period in patients with multiloculated RCC and unclassified RCC. Death was reported in only 9 cases, all because of the recurrence of the disease. Sarcomatoid RCC (n=5) was the predominant histology in these patients. In all patients, mean follow-up duration was 23.2 months (range: 1–84 months).

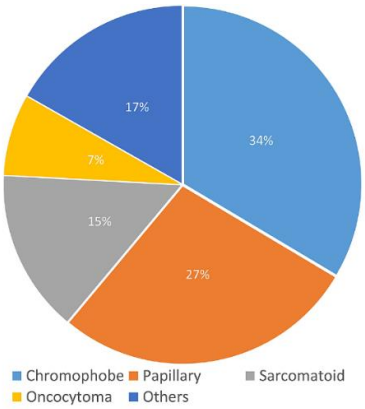

Figure-1: Incidence of non-clear cell renal tumours

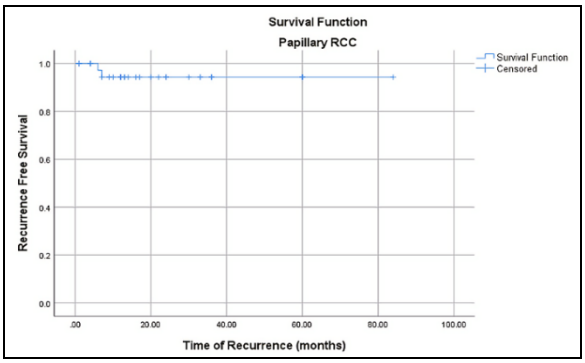

Figure-2: Recurrence Free Survival for papillary RCC

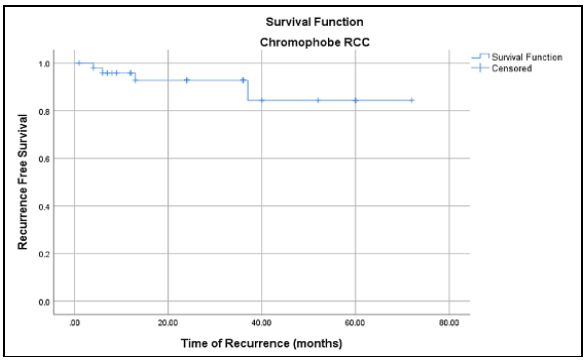

Figure-3: Recurrence Free Survival for chromophobe RCC

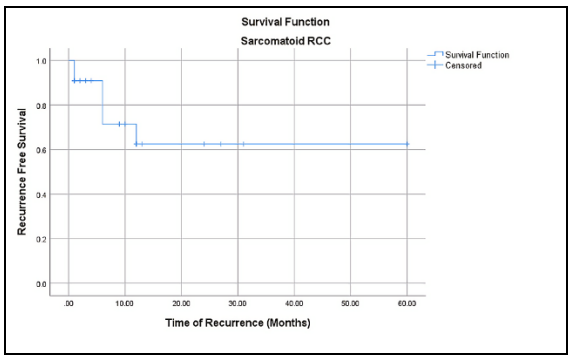

Figure-4: Recurrence Free Survival for sarcomatoid RCC

Table-1: Clinical stage on presentation: T1, tumour size <7cm. T2, tumour size >7cm. T3, tumour extension into major veins or perinephric tissues and/or renal sinus. T4: involves ipsilateral adrenal gland or invades beyond Gerota's fascia

	T1	T2	T3	T4	Total (%)
Chromophobe RCC	14	25	10	1	50 (33.5%)
Papillary RCC	22	12	7	0	41 (27.5%)
Sarcomatoid RCC	6	9	5	2	22 (14.7%)
Oncocytoma	1	6	4	0	11 (7.3%)
Unclassified RCC	2	4	2	0	8 (5.3%)
Multiloculated RCC	4	2	0	0	6 (4%)

DISCUSSION

Renal tumours of non-clear cell histology embody a highly diverse group of pathologies. Although nccRCC account for only 15–30% of renal tumours, current management strategy of nccRCC is based mainly on guidelines established for clear cell tumours, the most common subtype, however, this approach remains undefined.[6] In our study, nccRCC were found in 24.3% of the total nephrectomies performed in the duration of 10 years, from 2010 to 2019.

With recent advances and improvements in the availability and cost of diagnostic imaging modalities, more than 60% of renal tumours are now detected coincidentally. As a result, there is a decline in the stage and size of renal tumours at presentation. In a study by the Memorial Sloan-Kettering Cancer Centre, 80% of patients had their tumours diagnosed incidentally before undergoing surgery for renal cancer.[7] In our study, 52.3% of the tumours were found incidentally during examinations performed for other reasons and unrelated to the patient's presenting complaints. Furthermore, the mean tumour size was 8.2±3.5cm with mostly presented with T1 or T2 disease in this study (Table-1).

Globally, RCC is twice as common in men as women after adjusting for age. In addition, >50% of RCC is diagnosed among people aged 55–74 years.[8] Present study demonstrated 57% nccRCC cases in males and mean age was 50.48±14.76 years (range 18-89 years) with 58.3% of the cases were in the age group of <55 years. Smoking and family history of renal tumours are listed in the most important risk factors in renal cancer.[9] Merely 13% of the selected patients had a history of smoking whilst family history was found in only three patients in this study, however, data on other risk factors were not analysed in this study.

In total, about 15 nccRCC entities are listed in the World Health Organization (WHO) classification of RCC. The most frequent subtypes of nccRCC are papillary RCC, chromophobe RCC collecting (Bellini) duct carcinoma, medullary carcinomas, and MiT family translocation RCC.[10] In our study the commonest type was chromophobe RCC (33.5%) followed by papillary RCC (27.5%), sarcomatoid RCC (14.7%), and others types (17%) (Figure -1).

The 5-year recurrence rate for all nccRCC were 13% in our population, while mean RFS was 75.26±2.7 months, for all patient in our study. However, the data reported in the literature for the same time period varied as per the histology, from 4–19%.[11] The projected 5 years RFS of papillary RCC, chromophobe RCC and sarcomatoid RCC were 94.2%, 84.3% and 62.5% respectively in this series (Figure 2-4). As per the common understanding of RCC, chromophobe RCC has a better prognosis followed by papillary and clear cell RCC.[12, 13] Beck, S.D.W., *et al*. reported nearly the same 5-year survival for papillary and chromophobe RCC 81.7% and 80.1% respectively in his study of 263 patients.[14] However, papillary RCC demonstrated better survival as compared to chromophobe RCC in our series of 149 patients. Sarcomatoid RCC patients had worse survival outcome as compared to all other types, 62.5% RFS at 5 years. Merrill MM, *et al*. also described poor survival outcomes of sarcomatoid RCC in his study of 77 patients with a median recurrence time of 26.2 months.[15] Rest of the tumours in our study did not show any recurrences with mean follow up duration of 25.3±16 months.

There were a few limitations to our study, as it was a retrospective analysis with a small number of cases, lacking data on sub-classification and grade, post operative complications and lower mean follow up duration. Therefore, our study reflects a real-life phenomenon at individual institution practice. On the other hand, this study enlightens the outcomes of non-clear renal tumours after radical nephrectomy for localized tumours. It also shows a better understanding of various types of nccRCC in our region which will help in standardizing the management guidelines of these rare tumours as most of the strategies are based on studies from developed countries. To our knowledge, this is the first study from this subset of the population, especially from Pakistan, on outcomes of non-clear cell renal tumours.

CONCLUSION

Renal tumours of non-clear cell histology have excellent survival outcomes after curative resection. Renal tumours are equally common in middle age as well as the elderly. However, chromophobe RCC was the commonest histology in this study. Furthermore, sarcomatoid RCC has worse recurrence free survival followed by chromophobe RCC and papillary RCC, in our population subset.

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AUTHORS' CONTRIBUTION

YM: Interpretation, write-up, study design, proofreading. SA, SF, SH: Data collection, literature search. ZAC: Study design, proof reading. KM: Study design, write-up.

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