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Original Research

OUTCOME OF STAGE T1 RENAL CELL CARCINOMA TREATED WITH PARTIAL NEPHRECTOMY: INITIAL EXPERIENCES FROM A TEACHING HOSPITAL IN BANGLADESH

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ABSTRACT
Background: Renal cell carcinoma accounts for 85% of all solid tumors of the kidney. For many years, radical nephrectomy was the standard treatment for RCC. Partial nephrectomy has gradually replaced radical nephrectomy over the past decade, especially for T1 stage renal cell carcinoma. However, the benefit of partial nephrectomy on oncologic outcomes is not well known.
Objective: to investigate the clinical outcome of partial nephrectomy on T1 renal cell carcinoma.
Methods: This prospective observational study was conducted in a single unit of urology department of Dhaka Medical College Hospital, Bangladesh from the period September 2014 to September 2017. Fourteen patients underwent partial nephrectomy during this period with renal mass based on eligibility criteria. Two follow up was done at three months and six months.
Result: Mean age of the patients undergoing surgery was 52.0± 3.8 (46.0 to 57.0 years) years. For the majority of the patients, tumour size was in a range of 3-7 cm. Average operative time was 90 minutes and mean ischaemic time was 16.5 ± 4.6 minutes (14.5 to 21.0 minutes). Histopathological reports correlated with clinical diagnosis and showed adequate surgical clear margin in every case. There was no recurrence of tumour noticed during the two follow up periods. The different investigation did not reveal the impaired renal functional test during the follow-up period.
Conclusion: The clinical outcome of partial nephrectomy was found better in this study. Partial nephrectomy has the potential to replace radical nephrectomy for managing T1 tumours. However, there are some controversies regarding the post-operative oncological outcome. More studies are recommended to investigate the effect of partial nephrectomy for T1 tumours.

Keywords: Partial Nephrectomy, T1 Renal Cell Carcinoma, Bangladesh

INTRODUCTION

Renal cell carcinoma accounts for 2% to 3% of all malignant diseases in adults (Siegel, Naishadham, & Jemal, 2012) and responsible for causing 85% of all solid tumours in the kidney (Robson, 1963). In recent years, the diagnosis of early-stage RCC has increased primarily due to the broad utilization of imaging examinations including CT scan, ultrasonography, and MRI (Hollingsworth, Miller, Daignault, & Hollenbeck, 2006). For many years, radical nephrectomy was considered as the standard treatment for renal cell carcinoma. However, with increased awareness of the risk for the development of

chronic kidney disease (CKD) following radical nephrectomy, there has been growing evidence to recommend partial nephrectomy to avoid CKD (Huang et al., 2006). Partial nephrectomy has gradually replaced radical nephrectomy over the past decade, especially for the T1 stage of renal cell carcinoma. Emerging evidence suggests that it might be possible to achieve a similar result for the patients of undergoing partial nephrectomy who have tumours less than 4 cm (Joniau, Eeckt, Srirangam, & Van Poppel, 2009). Several studies also suggested that partial nephrectomy is recommended for T1 stage renal cell carcinoma (Campbell et al., 2009). This recommendation was based on hospital based retrospective studies. Due to practice of partial nephrectomy, previous studies showed that patient's quality of life was improved, psychological trauma was reduced, and renal function was not compromised in patients with RCC (Campbell et al., 2009; Ljungberg et al., 2015).

Understanding and preventing renal ischaemic damage, the development of certain radiological imaging facility before and after surgery, and improved surgical techniques have established partial nephrectomy as one of the most acceptable therapeutic options for treating small renal masses (Lam, Shvarts, & Pantuck, 2004). While there is no doubt that partial nephrectomy has a surgical advantage over radical nephrectomy for managing small renal cell carcinoma, but the benefit of partial nephrectomy on oncologic outcomes is still controversial especially for the T1b stage. Moreover, there is lack of evidence about the effectiveness of partial nephrectomy in patients with renal cell carcinoma in developing countries. In Bangladesh, the practice of partial nephrectomy has recently established to treat small renal cell carcinoma. For example, Dhaka Medical College Hospital, a tertiary hospital in Bangladesh, had started partial nephrectomy for last 3-4 years and the aim of the study to share the initial experience regarding the outcome of partial nephrectomy for T1 renal tumour. At present, many types of research are going on to explore the effectiveness and patient compliances of partial nephrectomy as treatment alternatives. Therefore, we investigated the result of partial nephrectomy for treating T1 renal mass in patients with renal cell carcinoma.

METHODS

Study design and period

A hospital-based prospective observational study was performed between September 2014 and September 2017.

Data source

This study was conducted in the urology department of Dhaka Medical College Hospital (DMCH). DMCH is a tertiary level teaching hospital situated in Dhaka, Bangladesh. Fourteen patients were enrolled from the urology department of DMCH into the study based on their eligibility criteria. Inclusion criteria were renal mass ≤7 cm with no lymph node involvement and without features of metastasis. On physical examination, we have examined the patient and included those who showed general physical fitness at the time of the participation. Patients who were able to maintain his or her daily regular activities (ambulatory) and agreed to attend regular follow up visit in two-point time (3 months and six months). Patients with renal mass more than 7 cm, tumour with lymph node involvement, features of metastasis, not physically fit to maintain her/his daily regular activities were not included in the study. Participants who had suffered from recent myocardial infarction were excluded from the study.

Operative procedure and follow up

A detailed history taking and clinical examination of the renal mass were performed, appropriate serological investigations were performed, and renal cell carcinoma was suspected of radiological characteristics. Tumour node metastasis (TNM) staging was performed after applying the seventh edition of American Joint Committee on Cancer TNM staging system. The diagnosis of renal cell carcinoma was confirmed base on histopathological reports. After proper evaluation and counseling

of the patients, the patient were underwent partial nephrectomy through retroperitoneal approach under general anesthesia. During the procedure, after dissection of fascia of gerota, tumour was identified, and the renal artery was clamped after hilar dissection, and ice slushes were given surround the kidney maintaining the standard operative procedures. This study observed little post-operative complication. After the provision of usual post-operative care, patient was sent to inpatient management. Follow up of the patient at 3 months and 6 months was advised during the discharge of patient to observe the outcome of the study. Patients were followed up base on history (pain, haematuria, lump, any features of metastasis), physical examination (anaemia, jaundice, renal mass), imaging (CT scan of abdomen/ ultra-sonogram of the whole abdomen, Chest X-ray), serological (Liver function test, Serum creatinine and Complete blood count) when they came to hospital.

Data collection

Data were collected from the participants using semi-structured questionnaires. Data extraction was conducted from the patient record form, investigation record and histopathological report by a trained physician. The semi-structured pre-tested questionnaire was verified and finalized by a group of an expert nephrologist and urologist for collecting the data. Another case record form to record the follow-up information was developed and pretested. The interview questionnaire was translated into the local language (Bengali) and afterward, it was translated back to English to check the translation consistency. Four hospital nurses were assigned to identify the parti-cipants based on eligibility criteria and collected the data from the hospitals. Four medical officers supervised the overall data collection, and a data management officer was responsible for checking the quality control of the data entry process.

Data analysis

Descriptive statistics were used to present the study findings. Frequency distribution was used to display the categorical variables. Mean and standard deviation was used for continuous variables. Total 17 patients underwent partial nephrectomy, and after the initial hospital discharge, three patients did not comply with the follow-up plan. Therefore, they were excluded from the study and intention to treat approach was used to analyze the exposure and outcome of interest. SPSS was used to enter the data and Stata version 13 (College Station, Texas, USA) was used for the analysis. Data management was performed by the residential medical officer of the urology department of the hospital.

Ethical approval

Written informed consent was collected from each participant at the time of enrolment and before surgery. Every participant was explained about the aims and objectives of the study. The study protocol was approved by the research review committee of the Dhaka Medical College Hospital, Dhaka, Bangladesh. Hospital permission to collect data were used maintaining the formal procedure.

RESULTS

General Characteristics of the participants

Table 1 showed that mean age of the patients was 56.0 ± 3.9 years. Most of the patients (64.3%) belonged from 51-60 years of age group. Among 14 participants, only three were female patients. About 18.0% of the patients were presented with acute loin pain, and the same percentage of patients reported presence of blood in the urine (hematuria). Among the other co-morbidities, this study found the frequency of hypertension and diabetes mellitus (DM) was 25.0% and 16.7%, respec-tively.

Tumour Characteristics of the participants

Table 2 represented the characteristics of a tumour among the participants. About six patients were presented with left-sided, and eight had right-sided renal mass. Five patients presented with renal mass from 4 cm to 7 cm in size and renal mass was situated in lower pole (57.1%).

Table 1 Distribution of participants according to age and clinical presentation

Characteristics	No. of patients (n=14)	Percentage
Age group, years		
40-50 years	2	14.3%
51-60 years	9	64.3%
61-70 years	3	21.4%
Mean (SD)	56.0 (3.9)	
Sex		
Male	11	68.7%
Female	3	21.3%
Clinical presentation*		
Asymptomatic/incidental	8	50.0%
Loin pain	3	18.8%
Hematuria	3	18.8%
Loin pain and Hematuria	1	6.3%
Co-morbid disease*		
Diabetes Mellitus (DM), yes	2	16.7%
Hypertension, yes	3	25.0%
DM and Hypertension, yes	2	16.7%
Chronic Kidney Disease, yes	2	16.7%

* The summation of clinical presentation and co-morbid disease condition is not equal to 100%

Table 2 Distribution of patients according to tumour characteristics

Tumour-related information	**No. of patients (n=14)**	**Percentage**
Location		
Upper pole	4	28.6%
Middle portion	2	14.3%
Lower pole	8	57.1%
Site of tumour		
Right sided	8	57.2%
Left sided	6	42.8%
Size of tumour		
Up to 4 cm	9	64.3%
4-7 cm	5	35.7%

cm: Centimeter

Surgical approach and procedure

Table 3 showed the operation related information for the patients that went through the retroperitoneal approach. Mean warm ischaemic time and cold ischaemic time was 2.3 and 14.4 minutes respectively for the operative patients. Average operative time was 90 minutes, and hospital stay was eight days. Catheter removal was advised on the second postoperative day.

Table 3 Operation related information

Operation related information	**Findings**
The operative position of the patients	Right/left lateral
Approach	Retroperitoneal
Total operation time	Average 90 minutes (75-128 min)
Mean warm ischaemic time	2.3 ± 1.1 minutes
Mean cold ischaemic time	14.5 ± 4.3 minutes
Drain kept in situ	Average 4 days (± 2)
Catheter removal	2nd postoperative day
Hospital stay	Average eight days (± 2)

Histopathological investigation of the dissected tumour

Table 4 revealed that all renal mass was proved to be malignant of which clear cell type was most common (70%), Furhman grade I, II and II was in 10,3 and 1 cases respectively. The TNM staging was T1 N0M0, and surgical margin was evident in every situation.

Table 4 Histopathological report of renal mass

Variables	Number	Percentage
Types of tumour		
Clear cell type RCC	11	78.6%
Papillary type of RCC	2	14.3%
Chromophobe type of RCC	1	7.1%
Furhman grade		
Grade I	10	71.4%
Grade II	3	21.3%
Grade III	1	7.1%
Margin free from tumour (after partial nephrectomy)	14	100%
TNM Status (T1a N0 M0/T1b N0M0/T1 N0M0)	14	100%

Tumour node metastasis (TNM)

Follow up schedule and findings of the patients

Follow-up status of the patients was updated in three months (1st follow up) and six months (2nd follow up) to evaluate the outcome of patients according to AUA guideline. Findings were gained after conducting history taking, clinical examination, and routine investigation. This study did not report any recurrence of tumour during the follow-up period.

DISCUSSION

This study found that partial nephrectomy might be a suitable method for the patients with renal cell carcinoma stage Ta. Based on several large retrospective series, and most recent evidence from a randomized controlled trial, partial nephrectomy has been recommended as a standard therapeutic method for organ-confined T1 renal masses (Butler, Novick, Miller, Campbell, & Licht, 1995; Lee et al., 2000; Lerner et al., 1996; Van Poppel et al., 2011). Though it was established that oncological outcome after partial nephrectomy was excellent for T1a group, however, several antecedent studies showed that partial nephrectomy could be safely performed with the similar oncological outcome for T1b renal cell carcinoma. For example, studies conducted by Leibovich et al. (Leibovich et al., 2004), Mitchell et al. (Mitchell et al., 2006), Becker et al. (Becker et al., 2006), Dash et al. (Dash et al., 2006) and Patard et al. (Patard et al., 2007) have compared both the outcome of partial and radical nephrectomy in patients with T1b tumour and they did not get significant differences. Moreover, Pahernik et al. showed that oncological outcome after performing partial nephrectomy was near similar for T1a and T1b tumour (Pahernik, Roos, Röhrig, Wiesner, & Thüroff, 2008).

Furthermore, one of the advantages of partial nephrectomy is that it can preserve the maximum amount of viable renal parenchyma. It has been linked to demonstrate the benefit of patients in improving their quality life expectancy (Link et al., 2005; Zaman, 2017).

Patients undergoing a radical nephrectomy have been shown to have a higher risk of subsequent development of chronic renal insufficiency, proteinuria, and metabolic acidosis as compared to partial nephrectomy (Lau, Blute, Weaver, Torres, & Zincke, 2000). Patients who underwent radical nephrectomy needs comparatively longer follow-up follow up period, which is cumbersome for remote

patients. One previous study suggested that radical nephrectomy might adversely influence long-term survival when compared with partial nephrectomy due to its high risk of cardiovascular morbidity and progressive end-stage of renal disease (Link et al., 2005). Study showed that partial nephrectomy is associated with higher health-related quality of life due to the benefit of preserved minimal renal function (Link et al., 2005).

In addition to the oncological efficacy of partial nephrectomy in treating T1bN0M0 masses, favorable outcomes of renal preservation have shown to promote health-related quality of life (HRQL) measures. Improved HRQL substantiate the premise that partial nephrectomy might be a preferred option for T1 tumours considering both patient and clinician perspective.

In this present study, the mean age of the patient was 56.0 ± 3.8 years with male patients predominant. Survey conducted by Margulis et al. found that mean age among their study participants was 59.9± 11 years, and Fernando et al. (Fernando et al., 2016) revealed mean age of 64.0 years in their study. However, a study conducted in Nepal reveals the mean age was 45.0 years where the study was comprised of eight participants (Gupta et al., 2014).

Warm ischaemic time and cold ischaemic time are considered as an essential factor for preservation of renal function. This study found that warm ischaemic time (WIT) was 2.3±1.3 minutes and cold ischaemic time (CIT) was 14.4± 4.6 minutes. It is advised that WIT and CIT should be less than 20 minutes according to a new set of recommendations. Fernando et al. (Fernando et al., 2016) found a WIT of <20 min was recorded in 81% (176/218) and of 21-30 min in 18% (40/218) cases. The Nepal study showed that the mean warm ischaemic time was recorded in their series as 16.4± 7.8 minutes (Gupta et al., 2014). In our study, the average operation time was 90 minutes while the maximum time was 150 minutes for few cases. No blood transfusion was indicated in this study, and average hospital stay was 7 days. Fernando et al. in their research showed that their mean operative time was 2-3 hours and median hospital stay was 5 days (Fernando et al., 2016). The research done in Nepal had reported 5 days of hospital stay for the study participants (Gupta et al., 2014). Another study which was conducted by Margulis et al. (Margulis, Tamboli, Jacobsohn, Swanson, & Wood, 2007) showed surgical time for partial nephrectomy was 186.8 min.

In this study, partial nephrectomy was done with 1 cm margin, and the histopathology reports revealed that the surgical margin was free from tumour. After evaluating the Furhman grading system, we found that the number of patients with grade I, grade II, and grade III was 10, 3, and 1 respectively. A large portion (20-25%) of all renal masses finally was proved as benign, which was consistent with other study findings (Robson, 1963; Zaman, Hossain, Rahman, & Islam, 2017). However, in the current study, the histo-pathology report revealed malignancy in all cases, and clear cell type of was the highest variety (78.57%). According to different research findings, clear cell type renal cell carcinoma accounts for most of the tumor ranging from 80-90% (Belldegrun, Tsui, deKernion, & Smith, 1999; Gill et al., 2003). Recent reports suggested that patients with renal mass treated with radical nephrectomy can develop renal insufficiency than patients treated with partial nephrectomy. Defining chronic renal insufficiency as a measurement of serum creatinine level >2 mg/dL (Margulis et al., 2007), investigators from the Mayo Clinic showed a higher cumulative incidence of renal failure in patients treated with radical nephrectomy as compared to the matched patients managed with partial nephrectomy (22.4% versus 11.6% in 10 years) (Lau et al., 2000). Similarly, at a median follow up 25 months, investigators from the Memorial Sloan-Kettering Cancer Center detected signi-ficant differences in mean postoperative serum creatinine among well-matched patients treated with radical and partial nephrectomy for treating renal cell carcinoma (1.5 versus 1.0 mg/Dl) (McKiernan, Simmons, Katz, & Russo, 2002). In our series, two patients had deve-

loped chronic renal insufficiency follow by partial nephrectomy at time of hospital stay. However, serum creatinine was static for these patients during the first and second follow up period. Renal function status was regular after partial nephrectomy for rest of the patients irrespective of their metabolic condition.

This study reported that one patient developed superficial surgical site infection, which was managed conservatively with regular dressing and strict glycemia control. One patient had persistent hematuria for five days, and it was conservatively treated. In this study, follow up protocol for the patients was strictly maintained at three months and six months. In our series, this study showed zero reportable occurrences during nearly half-year follow up after going through the extensive investigation. Therefore, application of higher imaging technologies at the follow-up period is highly recommended for proper evaluation (Zaman, Hossain, Ahammed, & Ahmed, 2017). However, cost-effective surgery like partial nephrectomy in treating renal problems is recommended for the poor people living in countries where patient need to pay out of pocket expenditure (Zaman & Hossain, 2017).

This study has certain limitations. The participants were only the stage 1 (T1) group, and it was a single-hospital study. The follow-up period was short which did not allow the researcher to collect information after six months to follow up the RN outcome. Though it is recommended to follow up patients up to five years, this study took six months to follow up data as the patients were not convinced to revisit the hospital due to financial issues and non-re-appearance of their problem. As our patients were exposed to various medications and lifestyle after the initial hospital discharge, it was not possible to obtain medicine, food, and behavior related information from the participants. However, the data were derived from a large tertiary level hospital with good operative and investigation facility, which is a strength. The number of participants was quite large in comparison to previous studies. Adequate quality control of the data was one of the major advantages.

CONCLUSION

Partial nephrectomy can be considered as an effective treatment module for treating small renal cell carcinoma. The clinical and functional outcome of partial nephrectomy was excellent considering a short follow up period. Therefore, partial nephrectomy has the potential to replace radical nephrectomy for managing T1 tumours in the near future. However, there are some controversies regarding the oncological outcome for T1b neoplasms. More longitudinal studies are recommended to investigate the effect of partial nephrectomy for treating patients with T1b tumours.

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Author's Contribution

Conception and design: MSM, HAA, MSA, ANMLH, MTB, AKMSH, SBZ
Acquisition of data and analysis: MSM, HAA, MSA, ANMLH, MTB, AKMSH, SBZ
Interpretation of data: MSM, HAA, MSA, ANMLH, MTB, AKMSH, SBZ

Conflict of Interests

The authors firmly declare that there is no conflict of interests regarding the publication of this paper.

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