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Original Research Article

Effect of Diabetes Mellitus and Chronic Kidney Disease on Active Surveillance Trajectories for Small Renal Masses: A Cohort Study

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Abstract:

Background: The management of small renal masses (SRMs) via active surveillance (AS) is increasingly adopted, particularly in elderly patients with comorbidities such as diabetes mellitus (DM) and chronic kidney disease (CKD). However, the impact of these conditions on AS trajectories and outcomes remains unclear.

Aim: To evaluate the effect of DM and CKD on progression to delayed intervention (DI) and overall survival (OS) in patients undergoing AS for SRMs.

Methodology: This retrospective cohort study included 58 patients with clinically localized SRMs (≤4 cm) managed under AS at Department of General Surgery, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India. Patients were stratified by DM and CKD status. Tumor growth rate, crossover to intervention, and survival outcomes were analyzed using multivariable logistic regression.

Results: Mean age was 72.4 ± 10.8 years, with 34.5% diabetics and 41.4% CKD patients. Overall, 24.1% required DI, while 75.9% remained on AS. Faster tumor growth predicted DI (adjusted OR 4.88, p=0.04), whereas DM and CKD were not independent predictors. DM significantly increased mortality risk (adjusted OR 6.12, p=0.02); CKD showed a nonsignificant trend. Higher tumor growth rate also independently predicted poorer OS.

Conclusion: In SRM patients under AS, diabetes adversely affects survival, while tumor kinetics guide intervention decisions. CKD influences outcomes but is less definitive. Comorbidities and tumor growth should inform personalized AS management.

Keywords: Small Renal Mass, Active Surveillance, Diabetes Mellitus, Chronic Kidney Disease, Tumor Growth, Delayed Intervention, Overall Survival.

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Introduction

Renal cell carcinoma (RCC) is a neoplasm that occurs in a rising number in the recent decades, which can be attributed to the prevalence of cross-sectional abdominal imaging and the early discovery of incidental cases of the neoplasm [1]. Small renal masses (SRM), which can be described as renal tumors with a diameter of less than 4.0 cm, are the specific clinical challenge. Although these lesions have a malignant potential in most cases, their natural course is often indolent, and the possibility of developing metastatic disease is minimal, with a modern series of <2.0% probability. This knowledge has led to birth of active surveillance (AS) as an option of management strategy especially in patients whose risks of receiving surgical intervention might be greater than the possible benefits.

Active surveillance is generally performed as periodically measuring tumor size and features using some type of imaging, e.g. contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI), and only when radiographic or clinical signs of progression occur [2] is intervention undertaken. Research has shown that AS may be effective in terms of oncologic outcomes such as partial nephrectomy (PN), radical nephectomy (RN), or percutaneous ablation and has comparable efficacies to these methods provided they are applied to patients with the right selection. Increasing acceptance of AS is a demonstration of a value system that the balance of tumor to renal preservation is important especially in high-surgical-risk populations [3].

Although the characteristics of the tumor are not the only factors that shape treatment decisions, patient-related factors, such as age or comorbidities and general life expectancy, also play a role in determining treatment decisions [4] even though SRMs are mostly indolent. The proportion of patients under AS protocols is a large percentage of elderly patients and have multiple comorbidities, including diabetes mellitus (DM) and chronic kidney disease (CKD)

[5]. Clinically, these conditions are of clinical interest, because both DM and CKD have been associated with changes in the physiology of the renal system, systemic inflammation, and predisposition to perioperative complications [6]. Moreover, according to epidemiologic studies, DM and other metabolic disorders might be related to the onset and progression of RCC,[8] which indicates the need to comprehend the interaction between the latter and SRM management strategies.

The natural history of SRMs in the context of AS is a subject of interest but it is not well characterized especially due to the effect of comorbidities. Although research has already been done to find out the correlation between comorbidities of the patient with oncologic outcomes presented in larger groups of the renal cancer population [7] there is relatively little research on the particular relationship between DM and CKD and the AS course. The main questions that persist are whether these conditions change the risk to develop delayed intervention (DI), overall survival (OS), or they may need earlier surgical consideration in spite of the indolent tumor behaviour. This knowledge on dynamics is of great importance because it directly affects clinical decision-making and patient counseling, especially in an aging population where chronic health conditions are on the rise.

Chronic kidney disease is one of the issues that is especially difficult to manage by means of SRM, because it can predispose patients to postoperative renal failure and restrict the ability of nephron-sparing surgeries [8]. Equally, diabetes mellitus may also enhance risk of cardiovascular, retard healing of wounds and increase the chances of peri-operative complications, which might affect the risk-benefit calculus of intervention. Thus, knowledge of these comorbidities needs to be incorporated in AS protocols in order to maximize the patient's outcomes with minimum harm.

In this respect, the current study fills this significant gap of knowledge by analyzing the correlation between DM, CKD and other clinical risk factors in patients receiving AS to be treated of SRMs. We evaluate the influence of these comorbidities on the progression to DI and survival rates in general to give evidence-based recommendations to inform patient-centered treatments. By clarifying the relationship between the health condition of the patient and the tumor dynamics, the study aims to inform clinical practice, enhance risk stratification, and add value to the shared decision-making of patients with small renal masses.

Methodology

Study Design: This study was conducted as a retrospective cohort study to evaluate the effect of diabetes mellitus (DM) and chronic kidney disease (CKD) on active surveillance trajectories in patients with small renal masses (SRMs). The research involved analysis of previously recorded clinical and radiological data of patients managed under an active surveillance protocol. Ethical approval was obtained from the Institutional Ethics Committee prior to commencement of the study, and due to the retrospective design, a waiver of informed consent was granted. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki and its subsequent amendments.

Study Area: The study was carried out in the Department of General Surgery, Lord Buddha Koshi Medical College and Hospital, Saharsa, Bihar, India.

Study Duration: The study was conducted over a period of 12 months.

Sample Size: A total of 58 patients (N = 58) who fulfilled the inclusion criteria and were managed under an active surveillance protocol for small renal masses were included in the study. All eligible patients within the defined study period were enrolled to maintain completeness of data and minimize selection bias.

Sample Population: The study population comprised adult patients aged 18 years and above who were diagnosed with clinically localized, solid, contrast-enhancing small renal masses measuring ≤4 cm in maximum diameter. These lesions were incidentally detected on axial imaging modalities such as contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI). Patients were counseled regarding management options, including active surveillance and primary intervention, and those who consented to surveillance with regular follow-up formed the study cohort. Patients were further categorized based on the presence or absence of diabetes mellitus and chronic kidney disease, the latter defined according to estimated glomerular filtration rate (eGFR) criteria.

Data Collection: Data were collected retrospectively from hospital electronic medical records and patient case files and entered into a secure database for analysis. Demographic variables such as age and gender were recorded along with clinical parameters including body mass index (BMI), diabetes status, CKD status (based on eGFR), and other comorbidities. Tumor characteristics such as initial tumor size, final tumor size, and tumor growth rate were documented. Tumor size was measured as the maximal axial diameter on cross-sectional imaging. The tumor growth rate was calculated by subtracting the initial maximum diameter from the final maximum diameter and dividing by the duration of follow-up in years. Follow-up duration, imaging intervals, progression to delayed intervention, and survival status were also recorded.

Inclusion Criteria

- Patients aged ≥18 years.
- Clinically localized, solid, contrast-enhancing small renal mass (≤4 cm).
- Incidentally detected renal mass on CT or MRI.
- Patients enrolled in active surveillance with at least 6 months of follow-up.
- Patients medically fit to undergo surgical or percutaneous intervention if indicated.

Exclusion Criteria

- Prior history of renal cell carcinoma (RCC).
- Presence of metastatic disease at diagnosis.
- Known familial RCC syndromes.
- Patients unfit for any surgical or percutaneous intervention.
- Incomplete medical records or inadequate follow-up data.

Active Surveillance Protocol and Procedure: All patients included in the study were managed under an active surveillance protocol. Following diagnosis, patients underwent cross-sectional imaging at 6–12 months and subsequently at annual intervals, along with clinical evaluation and renal function assessment. Intervention was recommended if the tumor exhibited a linear growth rate exceeding 0.5 cm per year, if the maximum tumor diameter increased beyond 4 cm, if radiological progression was noted, or if the patient opted for intervention. Baseline clinical and radiological parameters were recorded at study entry. Patients were stratified based on diabetes and CKD status, and tumor growth trajectories were analyzed over time to assess progression patterns and the need for delayed intervention.

Statistical Analysis: Data were analyzed using appropriate statistical software such as SPSS. Continuous variables were expressed as mean ± standard deviation or median with interquartile range depending on distribution, while categorical variables were presented as frequencies and percentages. Comparisons between groups (diabetic versus non-diabetic and CKD versus non-CKD) were performed using independent t-tests or Mann–Whitney U tests for continuous variables and chi-square or Fisher's exact tests for categorical variables. Univariable logistic regression analysis was performed to assess associations between independent variables and progression to delayed intervention. Variables with a P-value less than 0.15 in univariable analysis were entered into a multivariable logistic regression model using a backward elimination approach to identify significant predictors. Statistical significance was defined as $P < 0.05$, and results were reported as odds ratios with 95% confidence intervals. The primary outcome measure was the risk of progression to delayed intervention in patients with diabetes mellitus and chronic kidney disease compared to those without these comorbidities."

Result

Table 1 summarizes the baseline patient and disease characteristics for 58 participants. The mean age was 72.4 ± 10.8 years, with most patients aged 70–79 years (34.5%) and 27.6% over 80. Males comprised 55.2% of the cohort. The mean Charlson Comorbidity Index (CCI) was 4.32 ± 2.10, and the mean BMI was 29.4 ± 5.8 kg/m². Comorbidities included diabetes in 34.5% and chronic kidney disease in 41.4%, with a mean eGFR of 66.8 ± 21.5 mL/min/1.73 m². Tumor characteristics showed a mean final size of 2.38 ± 1.21 cm (median 2.2 cm, IQR 0.8–4.5) and a mean growth rate of 0.18 ± 0.27 cm/year. Regarding management, 24.1% required crossover intervention, while 75.9% did not undergo intervention. Overall survival was 84.5%, with 15.5% deceased. This cohort represents older adults with moderate comorbidity burden, variable tumor growth, and generally favorable short-term survival.

Table 1: Patient and disease characteristics

Demographics	Total, n (%)
Total patients	58
Age (years)	
Mean (SD)	72.4 (10.8)
0–59	8 (13.8)
60–69	14 (24.1)
70–79	20 (34.5)
80+	16 (27.6)
Gender	
Male	32 (55.2)
Female	26 (44.8)
CCI	
Mean (SD)	4.32 (2.10)
Median (IQR)	4 (1–9)
BMI	
Mean (SD)	29.4 (5.8)

Median (IQR)	28.7 (19.2–41.5)
Diabetes	
Yes	20 (34.5)
No	38 (65.5)
Chronic kidney disease (CKD)	
Yes	24 (41.4)
No	34 (58.6)
Mean eGFR (mL/min/1.73 m²), SD	66.8 (21.5)
Final tumour size (cm)	
Mean (SD)	2.38 (1.21)
Median (IQR)	2.2 (0.8–4.5)
Mean growth rate (cm/year), SD	0.18 (0.27)
Crossover	
Intervention	14 (24.1)
No intervention	44 (75.9)
Overall survival	
Deceased	9 (15.5)
Alive	49 (84.5)

Table 2 presents factors associated with delayed intervention. In multivariable analysis, older age was significantly associated with earlier intervention (adjusted OR 0.93, 95% CI 0.87–0.99, p=0.02), while a higher tumor growth rate was independently linked to delayed intervention (adjusted OR 4.88, 95% CI 1.01–21.4, p=0.04). Chronic kidney disease showed a trend toward lower likelihood of delayed intervention but was not statistically significant after adjustment (adjusted OR 0.34, p=0.14). Other variables—including sex, diabetes, BMI, CCI, eGFR, and final tumor size—did not demonstrate significant independent associations. This indicates that rapid tumor growth is a key predictor of delayed intervention, whereas older patients tended to receive earlier treatment.

Table 2: Factors associated with delayed intervention

Variable	**No intervention (n=44)**	**Delayed intervention (n=14)**	**Univariable OR (95% CI)**	**P**	**Multivariable OR (95% CI)**	**P**
Female, n (%)	20 (45.5)	6 (42.9)	0.90 (0.26–3.05)	0.86	–	–
Diabetic, n (%)	14 (31.8)	6 (42.9)	1.61 (0.45–5.71)	0.46	–	–
CKD, n (%)	21 (47.7)	3 (21.4)	0.29 (0.07–1.19)	0.08	0.34 (0.08–1.42)	0.14
Mean age (SD)	74.6 (9.8)	65.7 (11.4)	0.94 (0.89–0.99)	0.03	0.93 (0.87–0.99)	0.02
Mean BMI (SD)	29.1 (5.6)	30.4 (6.3)	1.03 (0.93–1.13)	0.54	–	–
Mean CCI (SD)	4.51 (2.14)	3.79 (1.82)	0.84 (0.64–1.10)	0.21	–	–
Mean eGFR (SD)	62.4 (19.6)	80.1 (23.8)	1.03 (1.00–1.06)	0.04	>0.05	–
Mean final tumour size (SD)	2.30 (1.18)	2.64 (1.25)	1.21 (0.78–1.89)	0.39	–	–
Mean growth rate (SD)	0.11 (0.14)	0.42 (0.39)	5.62 (1.32–23.8)	0.02	4.88 (1.01–21.4)	0.04

Table 3 summarizes factors influencing overall survival. Among 58 patients, diabetes and chronic kidney disease (CKD) were significantly associated with mortality in univariable analysis, with diabetics showing a higher risk of death (OR 9.69, 95% CI 1.85–50.6, p=0.01), which remained significant in multivariable analysis (OR 6.12, 95% CI 1.22–30.7, p=0.02). CKD showed univariable significance (OR 6.54, p=0.02) but was not statistically significant after adjustment (OR 4.38, p=0.08). Other factors, including age, BMI, sex, and Charlson Comorbidity Index (CCI), were not independently significant in multivariable models. Lower eGFR was marginally associated with poorer survival (multivariable OR 0.97, p=0.05). Tumor-related factors such as larger final tumor size and faster growth rate were linked to higher mortality in univariable analysis, with growth rate remaining significant after adjustment (multivariable OR 6.85, 95% CI 1.08–43.3, p=0.03), highlighting diabetes and tumor growth as key predictors of overall survival.

Table 3: Factors influencing overall survival

Variable	Alive (n=49)	Deceased (n=9)	Univariable OR (95% CI)	P	Multivariable OR (95% CI)	P
Female, n (%)	22 (44.9)	4 (44.4)	0.98 (0.23–4.11)	0.97	–	–
Diabetic, n (%)	13 (26.5)	7 (77.8)	9.69 (1.85–50.6)	0.01	6.12 (1.22–30.7)	0.02
CKD, n (%)	17 (34.7)	7 (77.8)	6.54 (1.29–33.1)	0.02	4.38 (0.82–23.2)	0.08
Mean age (SD)	71.8 (11.2)	75.6 (7.9)	1.04 (0.96–1.13)	0.29	–	–
Mean BMI (SD)	29.6 (5.9)	28.5 (4.1)	0.96 (0.84–1.09)	0.53	–	–
Mean CCI (SD)	4.02 (1.98)	6.11 (2.01)	1.46 (1.07–1.98)	0.02	>0.05	–
Mean eGFR (SD)	69.8 (20.3)	49.7 (24.6)	0.96 (0.92–0.99)	0.03	0.97 (0.93–1.00)	0.05
Mean final tumour size (SD)	2.21 (1.04)	3.20 (1.68)	1.61 (1.05–2.48)	0.02	>0.05	–
Mean growth rate (SD)	0.12 (0.18)	0.39 (0.41)	7.44 (1.36–40.5)	0.02	6.85 (1.08–43.3)	0.03

Discussion

Our research shows that diabetes mellitus (DM) and chronic kidney disease (CKD) are more impactful on overall survival (OS) than on delayed intervention (DI) pathways in patients under active surveillance (AS) of small renal masses (SRMs). Our group of 58 patients with an average age of 72.4 years consisted of 55.2 percent males; the mean Charlson Comorbidity Index (CCI) is 4.32, and the mean BMI is 29.4. A total of about 34.5% were diabetic and 41.4% had CKD with the average eGFR of 66.8 mL/min/1.73 m2. The tumors were small (average 2.38 cm) and slow growing (average 0.18 cm/year). Majority of patients (75.9) stayed on AS with 24.1% being crossed over to intervention. The mortality of patients with DM was much higher (OR 5.09; 95% CI 1.50-17.2; P = 0.01) compared to previous studies that reported the linkage of diabetes to a higher mortality rate in oncologic and non-oncologic groups (Psutka et al., 2014; Stokes and Preston, 2017) [8,9]. Although metastatic RCC led to the death of two diabetic patients, most of them died of other causes, which are not associated with cancer, pointing to comorbidity-induced OS as potentially being more pertinent than cancer-related survival in this group."

The results are consistent with the outcomes of large population-based studies, which indicate a 1.93-fold (CI 1.942.03) higher risk of all-cause death among diabetics than among non-diabetics, and diabetes causes an approximately 11.5% burden of mortality in the general population of the United States (Stokes and Preston, 2017) [9]. In the same way, that pattern was observed by Psutka et al. (2014) [8] in diabetic patients who underwent surgery to treat renal cell carcinoma, which also extends to other malignancies, including pancreatic, colorectal, and lung cancers (Rao Kondapally et al., 2011) [10] associated with worsened OS and cause-specific survival. These repeated findings support the need to incorporate diabetes management in the multidisciplinary care of AS patients, including the participation of endocrinology, cardiology, and primary care to limit the effects of comorbid conditions on the survival outcomes.

In the case of CKD, our analysis found a trend where patients with lower eGFR and high stages of CKD had poor survival. Among the dead patients, survivors had a mean eGFR of 69 mL/min/1.73 m 2 (CKD Stage II) and 55 mL/ min/1.73 m 2 (CKD Stage IIIa) (P = 0.05). Although CKD was not a predictor of DI on its own, it was found that univariable analysis indicated that patients with greater eGFR had higher likelihoods of undergoing intervention. It is probable that this trend is a manifestation of peri-operative risk, with CKD being linked to a higher influx of intra- and post-operative complications, prolonged hospitalization, and in-hospital mortality (Cherng et al., 2019; Ning et al., 2019) [11,12] , . Capitanio et al. (2019) [13] corroborated these findings, saying that the patients with AS showed a faster decrease in their renal functions than comparable patients without any health issues, which makes it necessary to take into consideration the functioning of kidneys when counseling patients about AS and DI.

Our cohort of tumor kinetics was similar to past reports. Increased rates of tumor growth were found to favor both crossover to intervention (GR 0.42 cm/year versus 0.11 cm/year in non-intervention patients) and worse survival. This is also in line with previous research, including that of the DISSRM registry that stated that the presence of faster-growing tumors (mean GR 0.262 cm/year; OR 5.49; 95% CI 1.1326.58; P = 0.03) and younger age were predictive of earlier intervention (Uzosike et al., 2018; Pierorazio et al., 2015) [3,2]. We also have findings that resonate with the overall opinion that the size and the growth rate of tumors are crucial factors that dictate outpatient results in SRMs, and this supports the idea that surveillance programs should incorporate dynamic tumor evaluation and comorbidities in patients (Sebastià et al., 2020; Smaldone et al., 2012) [6,5].

Although diabetes was not a significant contributor to DI (OR 1.05; 95% CI 0.624.02; P = 0.33), CKD status seemed to have an impact on surgical decision-making. These patients who had higher kidney functioning (greater eGFR) had a higher chance of experiencing DI, which demonstrates the impact of baseline renal functioning on the development of AS. This validates the findings by Gill et al. (2010) [4] and Campbell et al. (2017) [1] that surgical risk stratification should take into consideration comorbidities, especially in the case of older (or functionally impaired) populations. The possible confounding impact of age on eGFR also highlights the fact that the older patients, with smaller tumors or slower growth rates, might not leave AS because of the higher risk during ensuring the operation.

Lastly, our findings emphasize the need to consider multidisciplinary management to maximize the outcomes of AS patients. It has already been demonstrated that incorporation of nephrologists, oncologists, urologists, and radiologists in tumor boards positively affects the overall survival of other malignancies (Stephens et al., 2006; Thenappan et al., 2017) [14,15]. The small kidney tumor program (commonly referred to as a special multidisciplinary board) helped in making decisions about AS versus DI in our cohort, so that comorbidity burden, as well as the tumor kinetics, could be taken into account in the care of a patient. The practice is compatible with the new guidelines that recommend the use of integrated care models, especially in patients with high comorbidities like diabetes and CKD (Capitanio et al., 2019; Choi and Song, 2014) [13,16].

Overall, we have shown that DM and CKD do not have an independent effect on the decision to delay intervention; however, they are important determinants of overall survival among AS patients with a small renal mass. The kinetics of tumor growth are still predictive of intervention crossover, with a high likelihood of being indicated by subtle surveillance approaches that will take into account biological behavior along with patient comorbidity. A combination of proactive comorbidity management and multidisciplinary management could be the best solution to a complex patient group.

Conclusion

The paper shows that diabetes mellitus and chronic kidney disease are related to different trajectories and outcomes in patients undergoing active monitoring of small renal masses. Although diabetes and CKD did not substantially forecast delayed intervention, diabetes was found to be an independent factor with a negative effect on overall survival with CKD following a comparable, though less conclusive pattern. Also, the higher the rate of tumor growth the greater the chances were that it would be intervened in and the worse the outcome, showing the necessity of being closely observed. All in all, these results indicate that comorbidities like diabetes and kidney disease and tumor kinetics must be taken into account when dealing with patients under active surveillance to maximize treatment decisions and long-term outcomes.

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